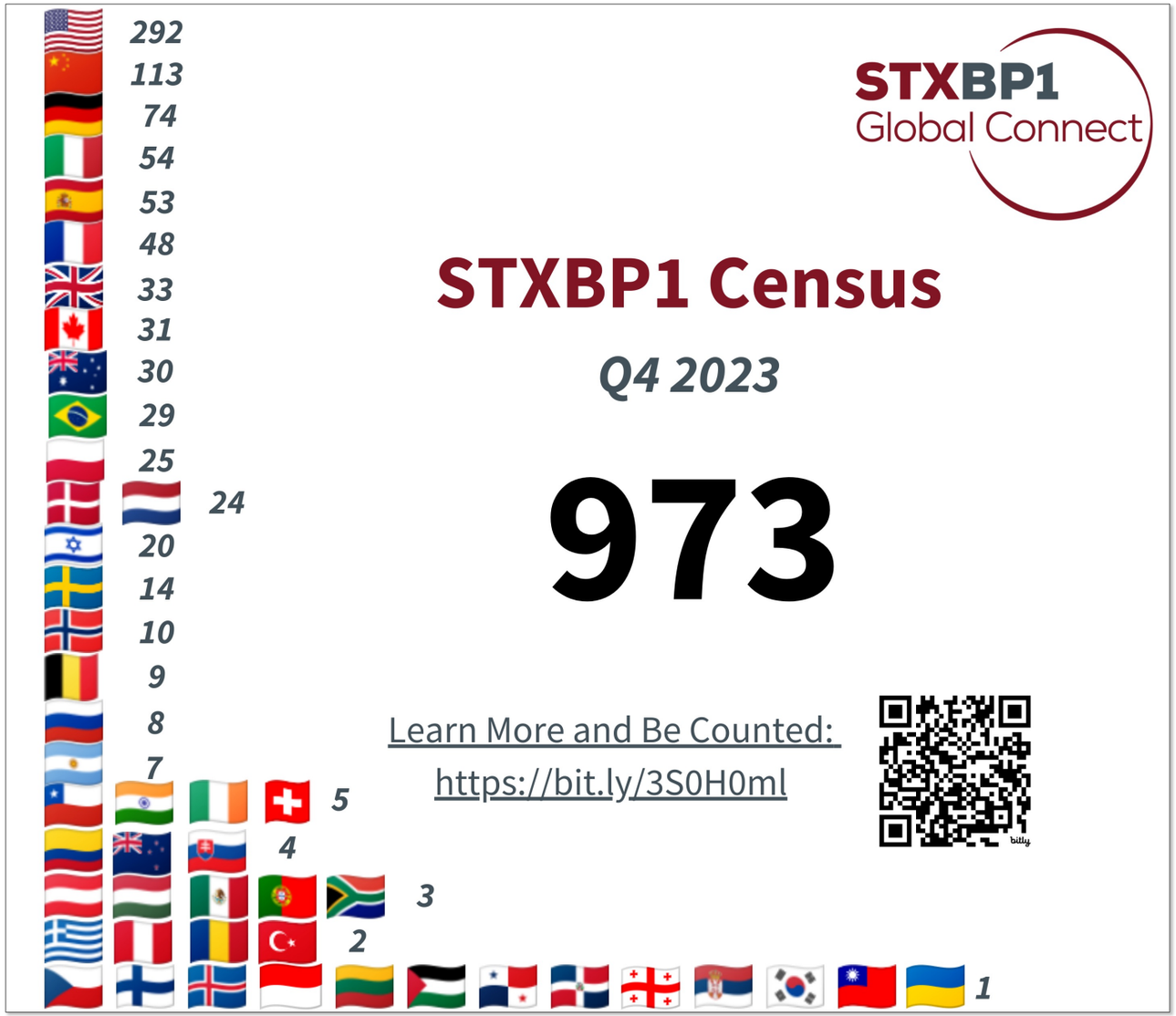
STXBP1 disorders

Q1 Global Connect Call

21 January 2024

Agenda

- ESCO update - 20 min
- STXBP1 therapy pipeline update - 20 min
- Regional updates and calendar - *including any updates you want to share!* - 20 min



STXBP1 Global Connect

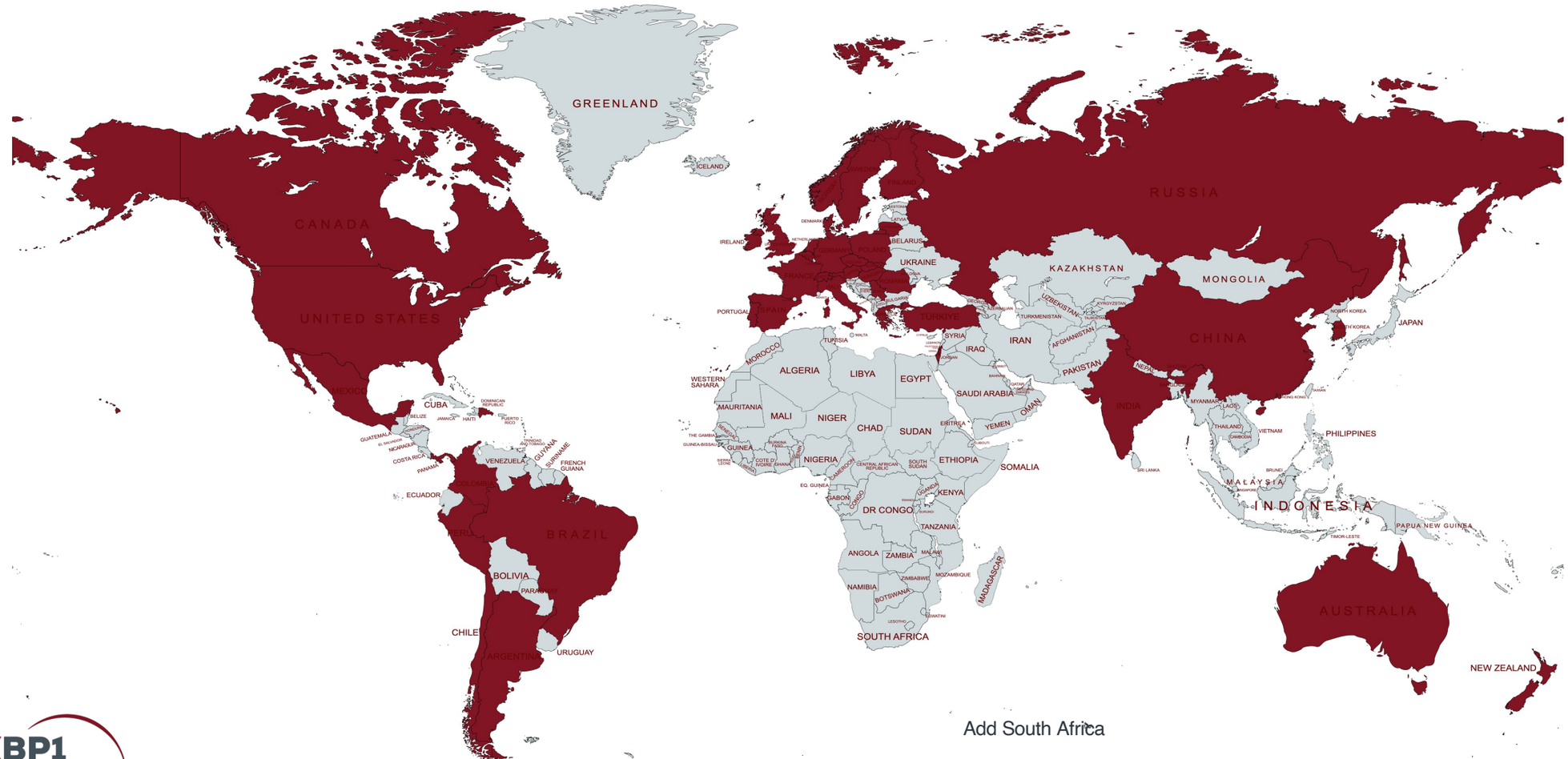
STXBP1 Census

Q4 2023

973

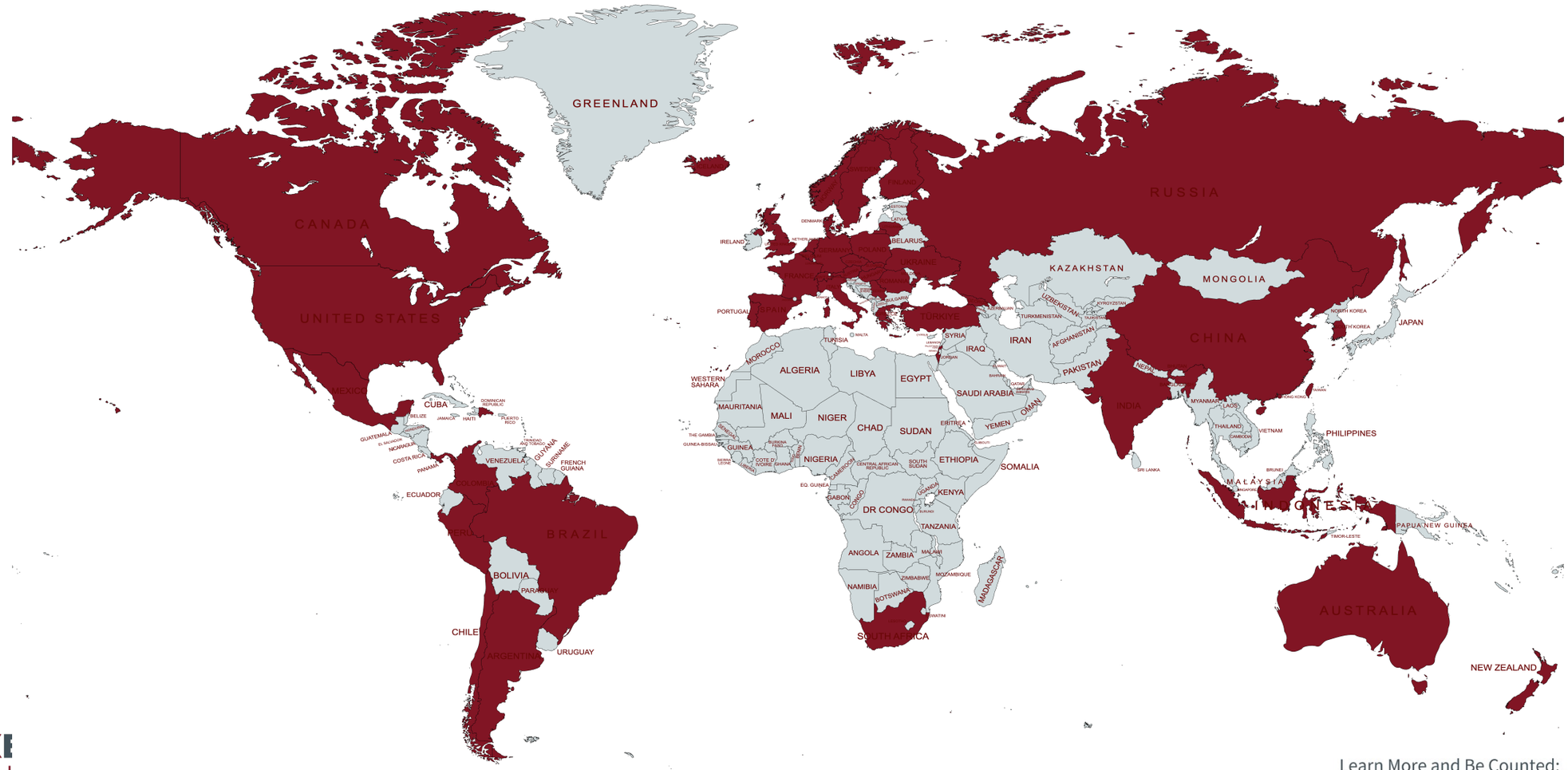
Learn More and Be Counted:
https://bit.ly/3S0H0ml

STXBP1 March Census Included 903 Patients in 45 Countries



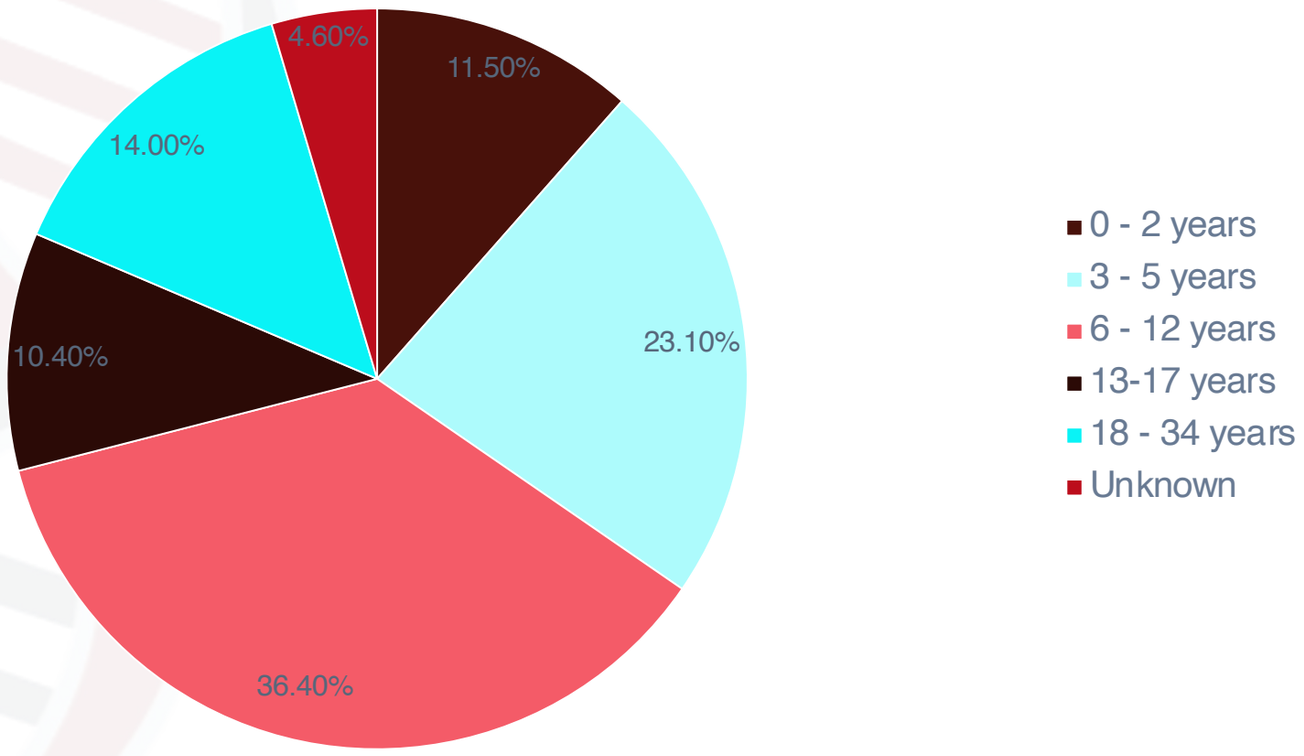
STXBP1
Global Connect

STXBP1 Dec Census Included 973 Patients in 48 Countries



Learn More and Be Counted:
https://bit.ly/3S0H0ml

Q4 2023 Census Age Groups



A Big Thank You to all Global Connect!

Next Census Opens 1 March 2024

Data Collection Closes 27 March 2024

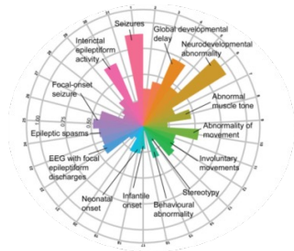
Q1 2024 Census Published 31 March 2024

The current landscape of STXBP1 research: a giant leap

2008 ⟶ *today*

4 individuals
(Saitsu et al, 2008)

>1000 individuals
9 associations
23 countries in STXBP1 Global Connect



Ohtahara syndrome

1 animal model

>20 animal and human-iPSCs models

0 drug programs

>10 drug programs
in academia and industry

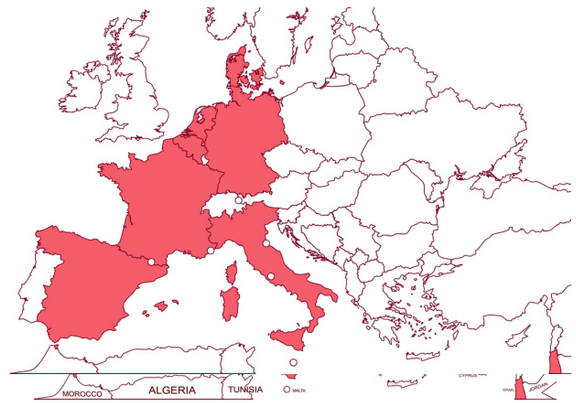
STXBP1foundation
Science + L♥ve = Cure

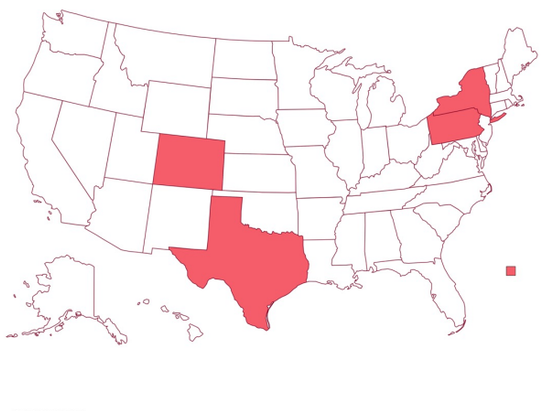
Adapted from Dr. Ganna Balagura

Natural History Studies – US and Europe

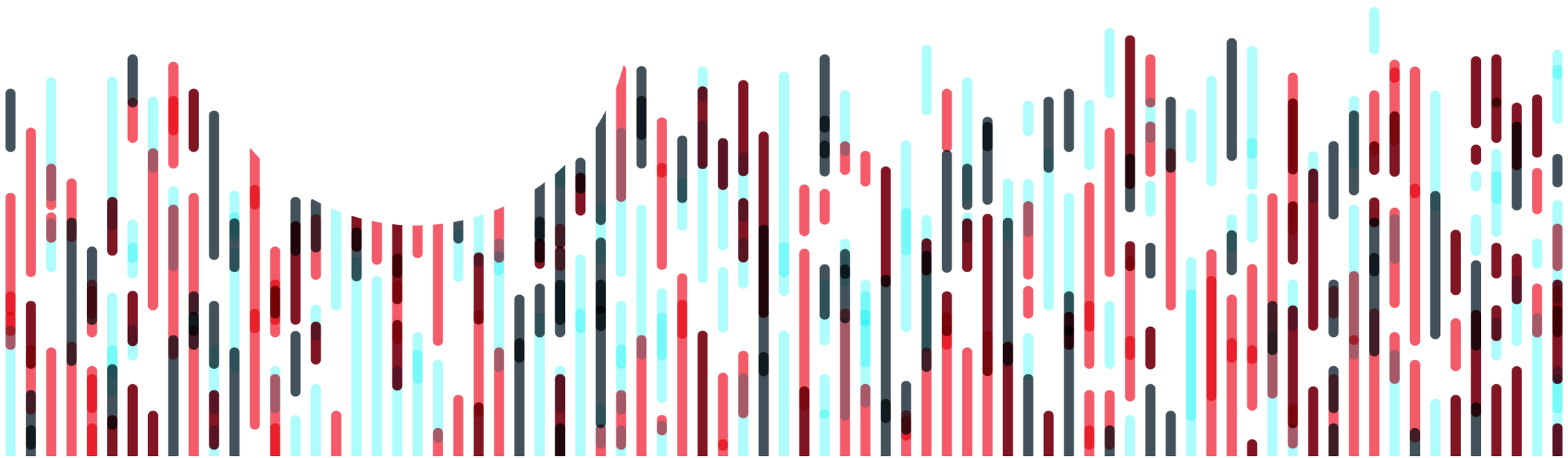
Overview

- Parallel longitudinal studies being launched in US and Europe
  - 9 European countries/sites
  - 4 US sites
- Aligning protocols
  - Core measures across all domains
  - Age cohorts

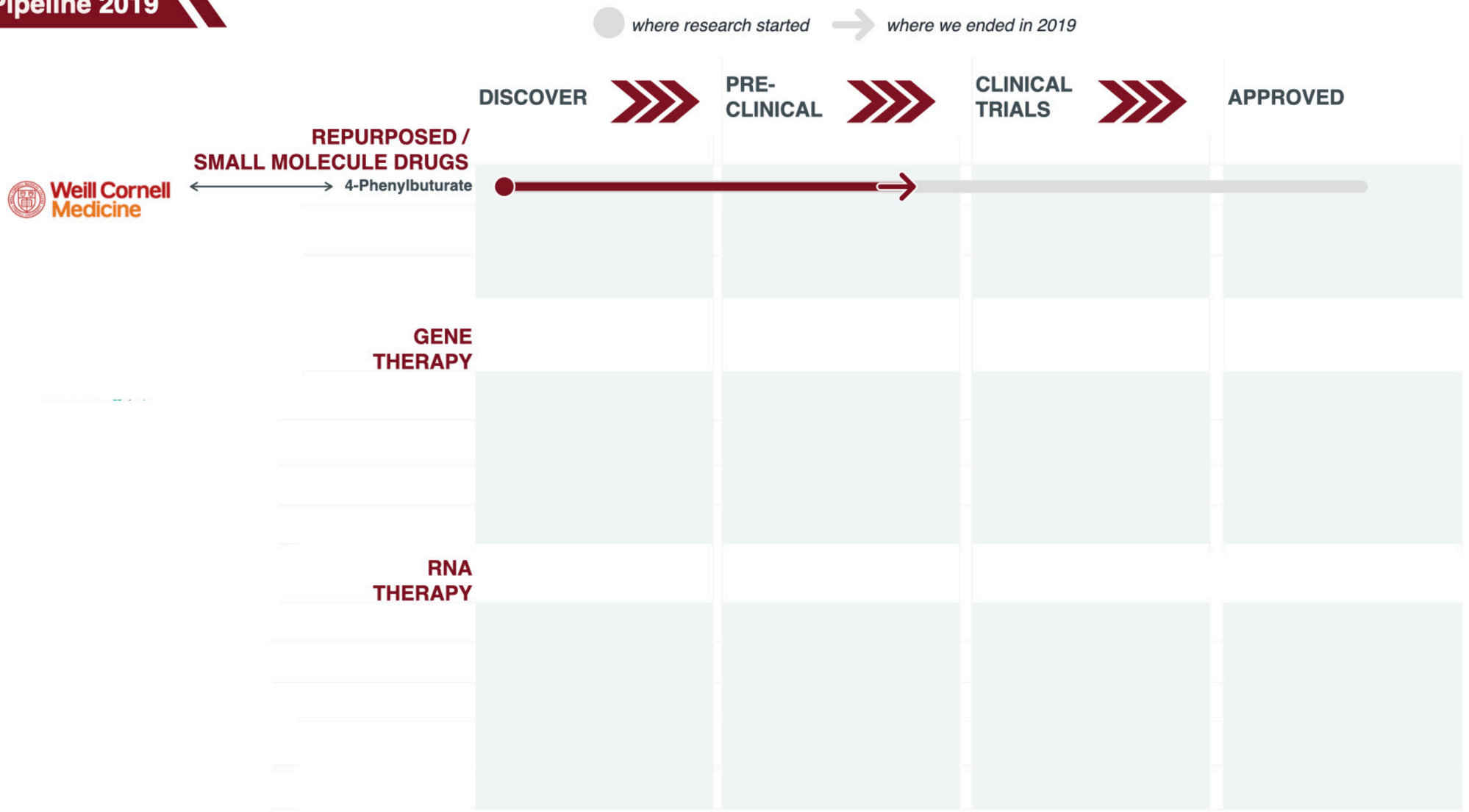




STXBP1 Therapy Pipeline Update

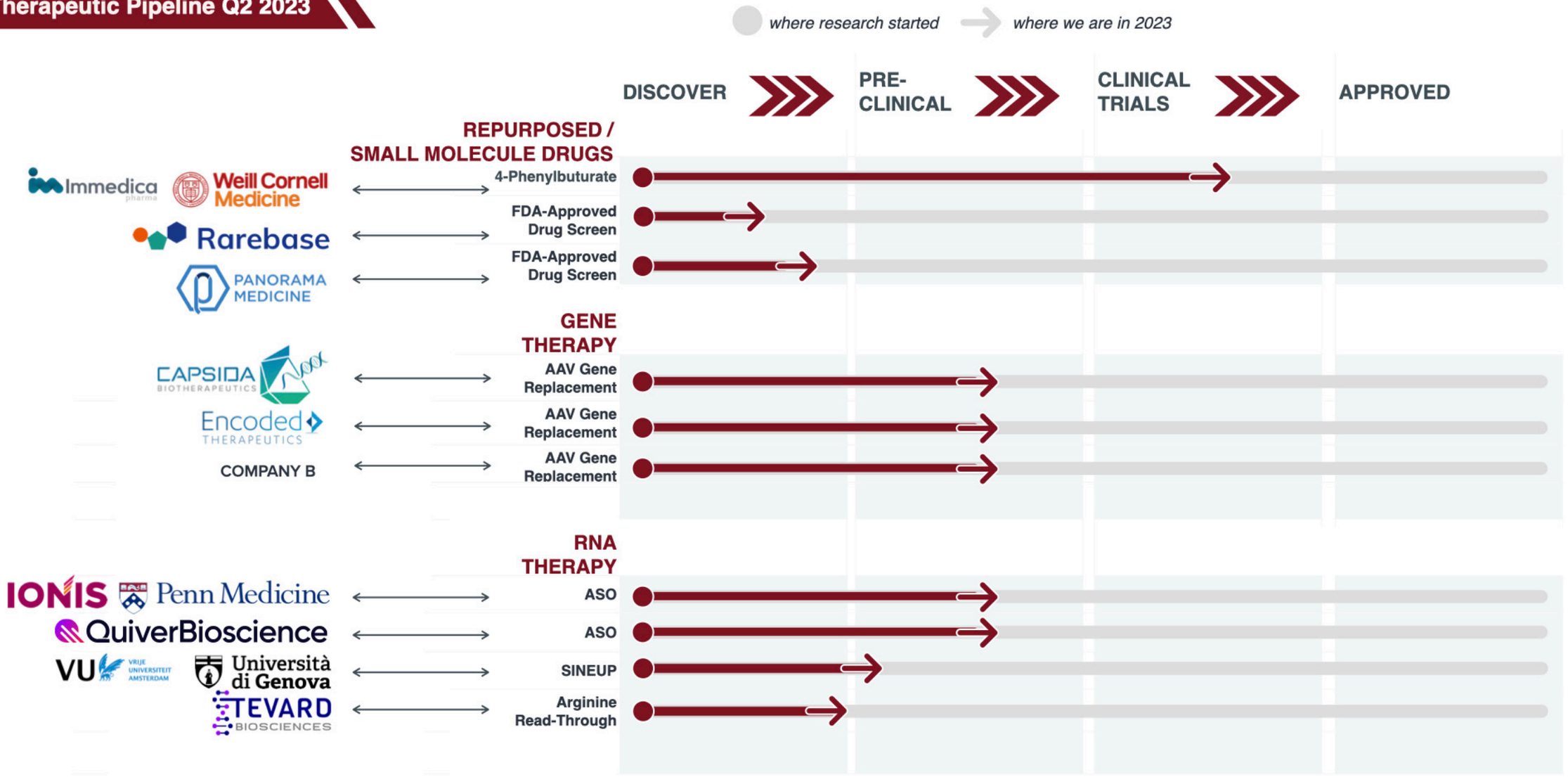


Therapeutic Pipeline 2019

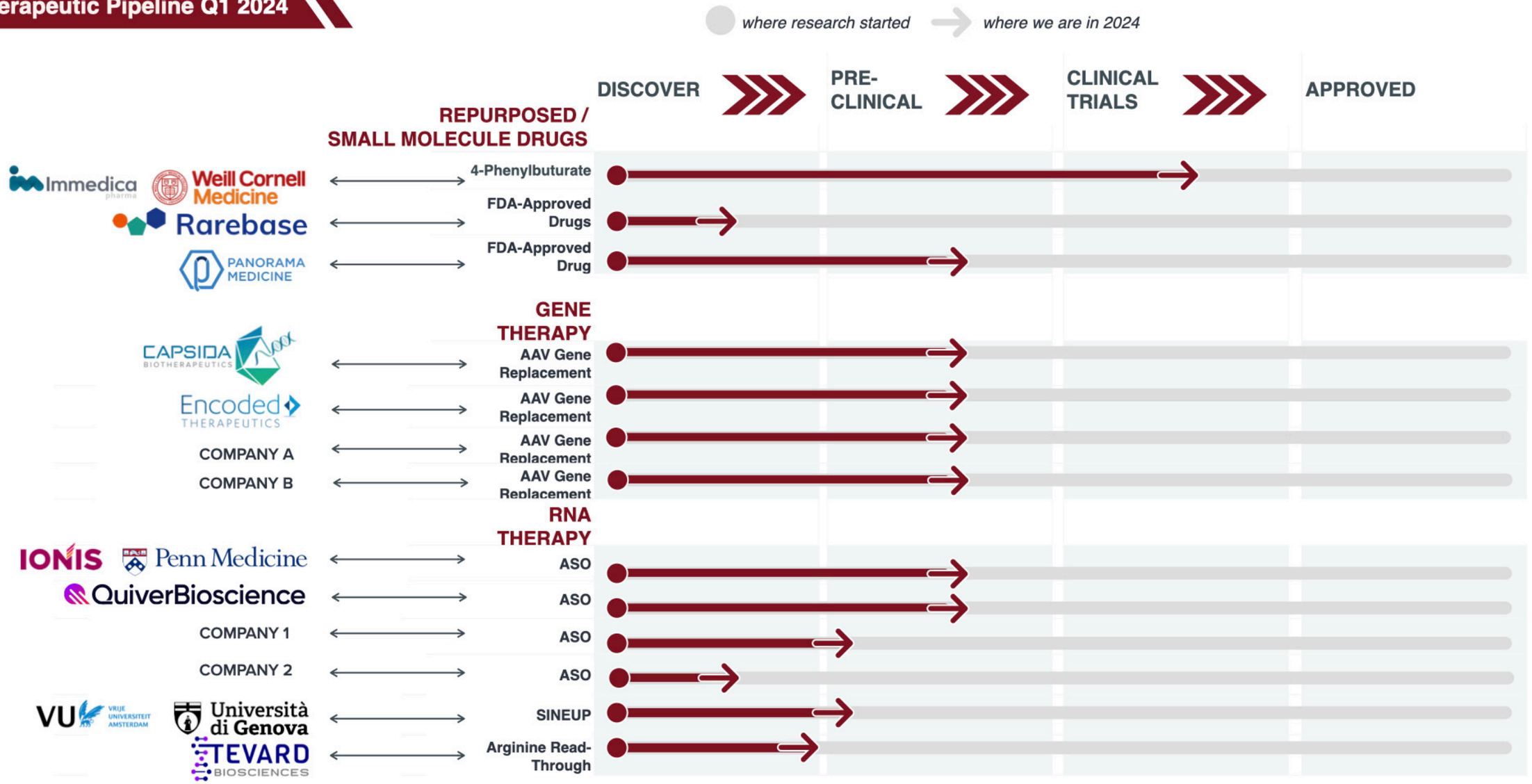


Weill Cornell Medicine

Therapeutic Pipeline Q2 2023



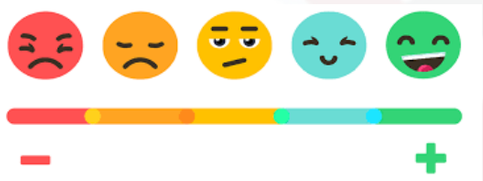
Therapeutic Pipeline Q1 2024

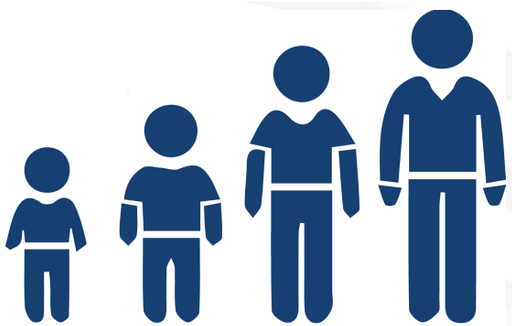


Key Takeaways

- Clinical trials are possible in 2025 for genetic therapies
- Repurposed drugs continue to show promise, may be faster
- Getting more data on efficacy for ravicti / phenylbutyrate important, Access is big issue and very uneven even within countries
- Clinical trial readiness work is critical now
  - Families participate in ESCO & STARR
  - Biomarker development
  - Regulatory engagement with EMA, FDA, MHRA and others

Clinical Trial Readiness Initiatives





Disease Concept Model - *published*

Scale and Endpoint Development

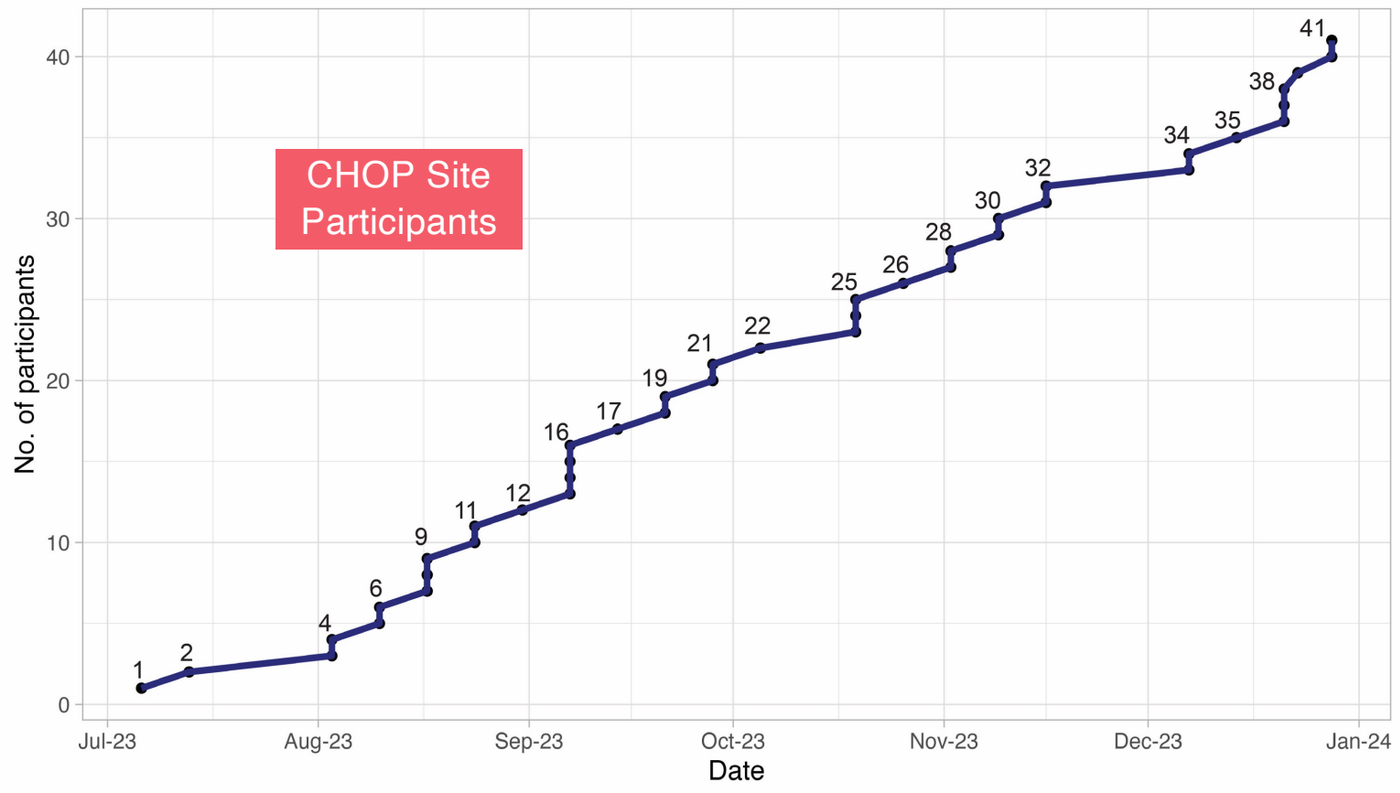
Natural History Studies – *ESCO & STARR*

Development of Clinical Centers

FDA & EMA Engagement

Finding Patients including ICD-10 & ICD-11

Our knowledge of *STXBP1* is growing => 71 STX'ers seen in STARR Study



Other STARR sites:
27 more individuals evaluated so far

STARR

STXBP1 NATURAL HISTORY STUDY PROTOCOL, STARR STUDY

Week prior to appointment
Caregiver Surveys

Domains Evaluated

- Daily functioning
- Communication
- Sensory processing
- Quality of life
- Adaptive behavior
- Behavior
- Sleep
- Seizures
- Autism features

1. Computerized Pediatric Evaluation of Disability Inventory (PEDI-CAT)
2. Sensory profile 2
3. Quality of Life Inventory-Disability, QI-Disability
4. Vineland
5. Observer-Reported Communication Ability (ORCA)
6. Modified Checklist for Autism in Toddlers (MCHAT)
7. *STXBP1*-Clinical Severity Assessment (S-CSA)
8. Child Behavior Checklist (CBCL)
9. Children's Sleep Habit Questionnaire (CSHQ)
10. Rome IV (GI scale)
11. Seizure diary

Day of appointment
Clinician Evaluations

Domains Evaluated

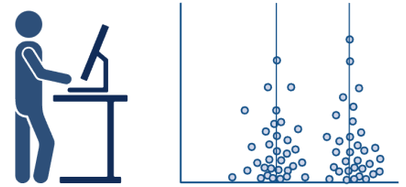
- Gross motor
- Fine motor
- Behavior
- Cognitive and social development
- Language and communication
- Visual impairments
- Autism features

1. Childhood Autism Rating Scale (CARS)
2. Gross Motor Function Measure (GMFM-88)
3. Alberta Infant Motor Scale (AIMS)
4. BAYLEY-4
5. MACS or mini-MACS
6. CFCS
7. GMFCS
8. Peabody

Example schedule

Time	Individual 1
8:00-9:00	Research Consent
9:00-10:00	Dev peds evaluation
10:00-11:00	OT evaluation
11:00-12:00	Break qEEG
1:00-2:00	PT evaluation
2:00-3:00	Neuro evaluation
3:00-4:00	Developmental testing
4:00-5:00	

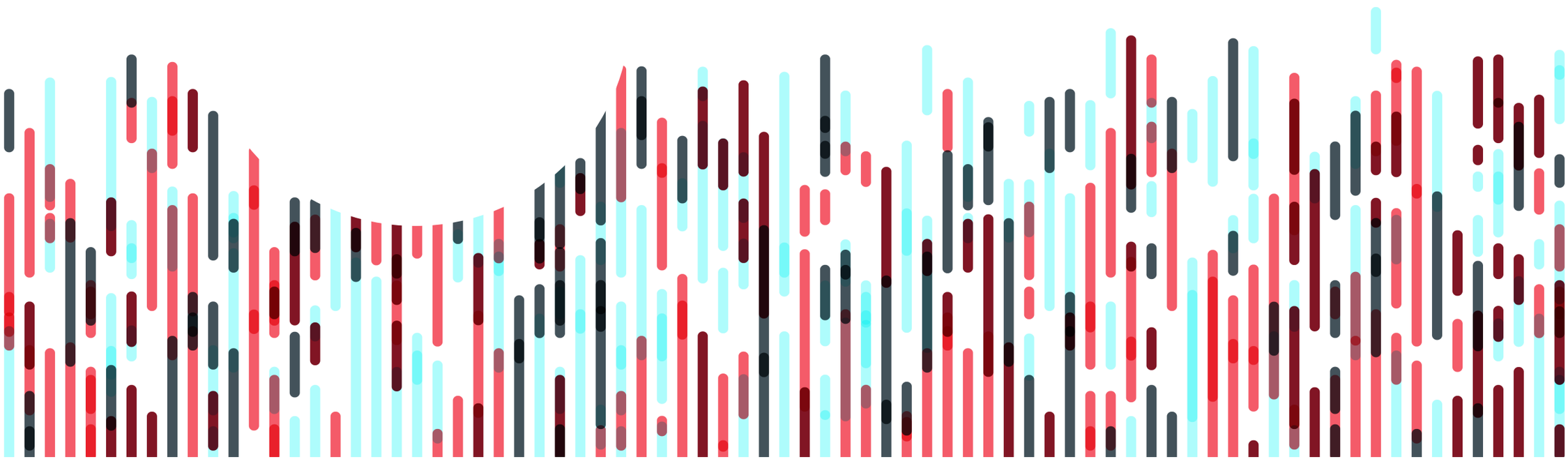
Weeks after appointment
Data Analysis



Analyses performed

- qEEG analysis
- Seizure reconstruction
- Developmental outcomes
- Genotype phenotype correlations
- Outcome prediction

Regional Updates



2024 Confirmed Events

ILAE

International Epilepsy Day
12 Feb

SEIZURE ACTION PLAN AWARENESS WEEK

F12 – 16 Feb
seizureactionplans.org

RARE DISEASE DAY®

29 Feb
Share your patient story*
NIH conference
Eurodis Photo Award

ENCUENTRO FAMILIAR & CIENTIFICO STXBP1

Asociación Síndrome STXBP1

9 March
Research & Family Meeting in Madrid

MILLION DOLLAR BIKE RIDE

LULU'S CREW

Million Dollar Bike Ride

8 June

STXBP1 SUMMIT+

17 – 21 July
Research & Family Meeting in Philadelphia

STXBP1 Awareness Month

All of September!

Move to Cure STXBP1 Disorders

Move to Cure
End of Sept

#GIVING TUESDAY™

3 Dec

2024 Events!

*https://www.eurordis.org/black-pearl-awards/photo-award/
https://rarediseases.org/rare-disease-day/rare-disease-day-share-your-story/

Asociación Síndrome STXBP1

9 MARZO 2024 MADRID

ENCUENTRO FAMILIAR & CIENTÍFICO STXBP1

Organiza
ASOCIACIÓN SÍNDROME STXBP1

Asamblea General de Socios
Ponencias Científicas
Jornadas Familiares
Actividades Infantiles

Mas info
www.stxbp1.es


STXBP1disorders
STXBP1 SUMMIT+
Presented by the STXBP1 Foundation
2024
FEATURING
RESEARCHER & FAMILY MEETINGS
18-21 JULY
RESEARCHER MEETING JULY 18-19
RESEARCHER & FAMILY DINNER JULY 19
FAMILY MEETING JULY 20-21
MORE INFORMATION :
STXBP1DISORDERS.ORG/2024-SUMMIT
LOCATION
The Drexelbrook Event Center
4700 Drexelbrook Drive
Drexel Hill, PA 19026

Top 10 Impact Report 2023

1 Fast Forward

Launched new STXBP1 **Fast Forward 3-Year Strategic Plan**.

2 Disease Concept Model

Published the first peer-reviewed STXBP1 Disease Concept Model documenting our patients' **most significant symptoms** and their impact.

3 European Research Roundtable

Held first Research Roundtable in Europe bringing together **over 100 researchers** and clinicians in Milan.

4 STARR Natural History Study

Launched first longitudinal Natural History Study for STXBP1-related disorders **enrolling at least 100 patients at 4 sites** across the USA.

5 FDA Listening Session

Orchestrated first externally-led Patient-Focused Drug Development meeting with the FDA for STXBP1, as **288 attendees** joined in to discuss patient experiences and the **urgent need for treatments.**

FDA

6 Global Connect

Exceeded 20 countries in the STXBP1 Global Connect, our coalition of STXBP1 foundations and country liaisons.

STXBP1 Global Connect

20+ Countries

7 Patient Census

Initiated an STXBP1 patient census, which has counted **over 973 patients in 48 countries** around the world.

973 patients

48 countries

8 Grants & Research Funding

Awarded over **$1.5M** to date for Patient Studies and Translational & Pre-Clinical Research projects around the world.

9 Patient Assistance Grants

Awarded over **$20K** to date for support of STXBP1 patients and their families.

$20K

10 STXBP1 Summit + Annual Conference

Held our **first Family Meeting in Colorado** with over 300 attendees.

STXBP1 Summit+

Grants 2023 – 2024YTD

INSTITUTION	RECIPIENT	YEAR	PROJECT TITLE/DESCRIPTION	AWARD AMOUNT
Funded Directly by STXBP1 Foundation				**$740,265**
Patient Studies				
Danish Epilepsy Centre	Elena Gardella, MD, PhD	2023	Early Mortality in STXBP1 Encephalopathy	$20,000
European STXBP1 Consortium (ESCO)	ESCO	2023	Research consortium for European Natural History Study and Registry	$200,000
Weill Cornell Medicine / New York-Presbyterian	Zachary Grinspan, MS, MD	2023	STXBP1 STARR Natural History Study	$165,001
Children's Hospital Colorado	Andrea Miele, PhD	2023	STXBP1 STARR Natural History Study	$155,264
Baylor College of Medicine / Texas Children's Hospital	Hsiao-Tuan Chao, MD PhD	2023	STXBP1 STARR Natural History Study	$200,000
Translational and Pre-Clinical Research				
Weill Cornell Medicine	Noah Guiberson, PhD	2024	Young Investigators Draft class for rare disease research cofunded with Uplifting Athletes	$20,000
University of Pennsylvania	Alex Felix, PhD	2023	Young Investigators Draft class for rare disease research cofunded with Uplifting Athletes	$20,000
Funded Through Orphan Disease Center MDBR, with Lulu's Crew				**$325,170**
Translational and Pre-Clinical Research				
University of Sydney	Wendy Gold, PhD	2024	Integrative omics: A novel approach to unravelling the complexity of STXBP1 encephalopathies	$75,460
Columbia University	Xuebing Wu, PhD	2024	Systematic dissection of STXBP1 3' UTR regulation to facilitate therapeutic development	$75,460
University of Genoa	Pasquale Striano, MD, PhD	2023	Fingerprinting a Multiommic Biomarker Profile in Patients with STXBP1-RD	$87,125
University of Antwerp	Sarah Weckhuysen, MD, PhD	2023	Assessing and Quantifying Gait Problems with STXBP1-Related Disorders Using Three-Dimensional Gait Analysis	$87,125

2024 Goals

- Invest in STXBP1 Fast Forward (*3 year strategic plan*)
- Support and expand preclinical research and clinical trial readiness
- Raise $5M by 2023 - 2025 to fund our research priorities
- Build Community
- Create Ongoing Awareness to Support Research Engagement and Community Development
- Maintain operational transparency

Move to Cure STXBP1 Disorders

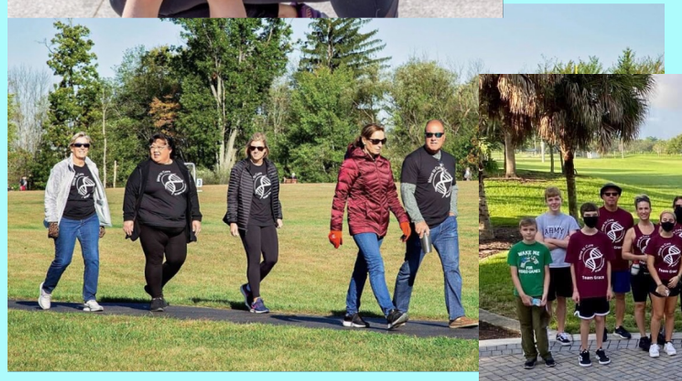
Raise funds for your association!

STXBP1 Foundation will share shirt designs

Annual Community Event

- Global
- 28-29 September 2024
- >300 participants worldwide
- Raise awareness of STXBP1 and bring the community together for an important cause and some fun!
- https://www.stxbp1disorders.org/annual-stxbp1-5k

Start a Team! Contact: melissa.hioco@stxbp1disorders.org



#move2cureSTXBP1

STXBP1 Global Connect – Looking Forward

Strengthen and formalize with in person Global Connect meeting in 2025?

Patient-driven collaborative research network

Worldwide community support and activation

STXBP1 Fast Forward: 3 Year Plan

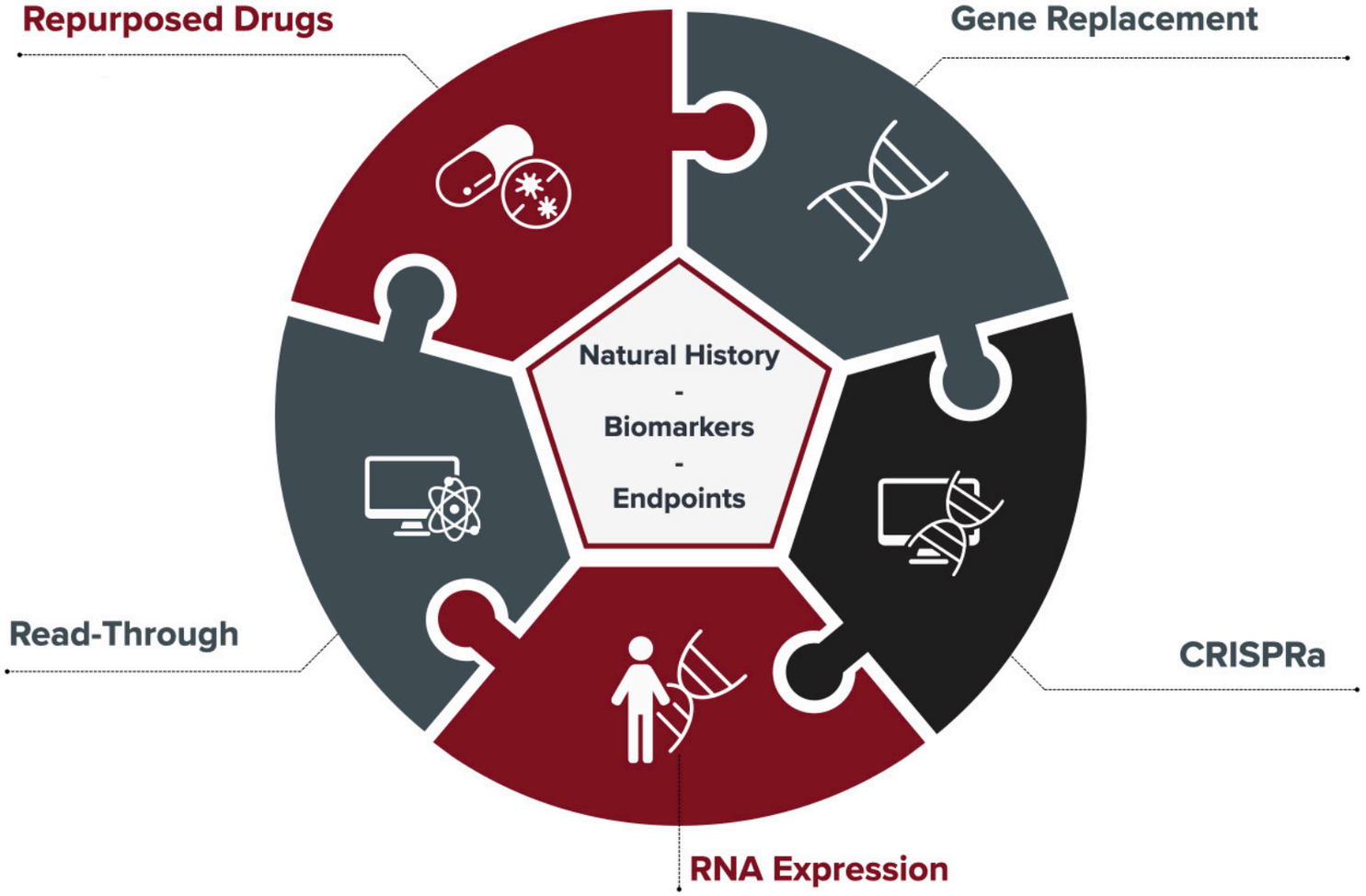
Propel Precision Therapies for STXBP1

Prepare for Clinical Trials

Build Biopharma Company Interest

Support Patients Today

STXBP1 Fast Forward



STXBP1 Foundation

Science + Love = CURE

Our Mission

Create awareness for STXBP1-related disorders * Fund and drive research to accelerate discovery of a cure

Provide families with tools to help them understand the disease & how to get involved * Advocate to improve early detection

Foster activism to help change policies in favor of orphaned diseases * Improve the lives of our STXBP1 Family