U.S. FOOD & DRUG ADMINISTRATION

Warrior Families: Advancing Regenerative Medicine Through Science

Thursday, October 5, 2023, 11:00 a.m. – 12:15 p.m. ET

Office of Therapeutic Products (OTP)
Center for Biologics Evaluation and Research (CBER)
U.S. Food and Drug Administration (FDA)

Hosted by:
Anne Rowzee, PhD
Senior Policy Advisor, PSPS, OTP, CBER, FDA

Webinar Agenda

11:00 a.m. Welcoming Remarks — Dr. Nicole Verdun, OTP Director

11:05 a.m. Presentation — Advancing Regenerative Medicine for Angelman Syndrome Through Science (Allyson Berent, DVM)

11:30 a.m. Panel Discussion

11:55 a.m. Q&A

12:10 p.m. Closing Remarks

Introduction: Dr. Verdun

Nicole Verdun, MD

Director, Office of Therapeutic Products

Center for Biologics Evaluation and Research

U.S. Food and Drug Administration

RegenMedEd Series

- OTP's event series about regenerative medicine
- Goals of the RegenMedEd Series:

Discuss foundational information about regenerative medicine therapies, including gene therapy and cell therapy

Explore opportunities to engage with FDA and advance regenerative medicine research and drug development

Hear from FDA, patients, advocates, researchers, and other important stakeholders about their experiences

Virtual Meeting Considerations

- The webinar will be recorded and available online after the event.
- Closed captioning is available in Zoom.
- Use the Q&A box to submit questions throughout the event.
- Use the chat box to share general comments and report technical difficulties.

Introduction: Dr. Allyson Berent

Allyson Berent, DVM, DACVIM

Chief Science Officer

Foundation for Angelman Syndrome Therapeutics (FAST)

Warrior Families:
Advancing Regenerative Medicine For Angelman Syndrome Through Science

How parents and patients are taking the lead

Allyson Berent, DVM, DACVIM

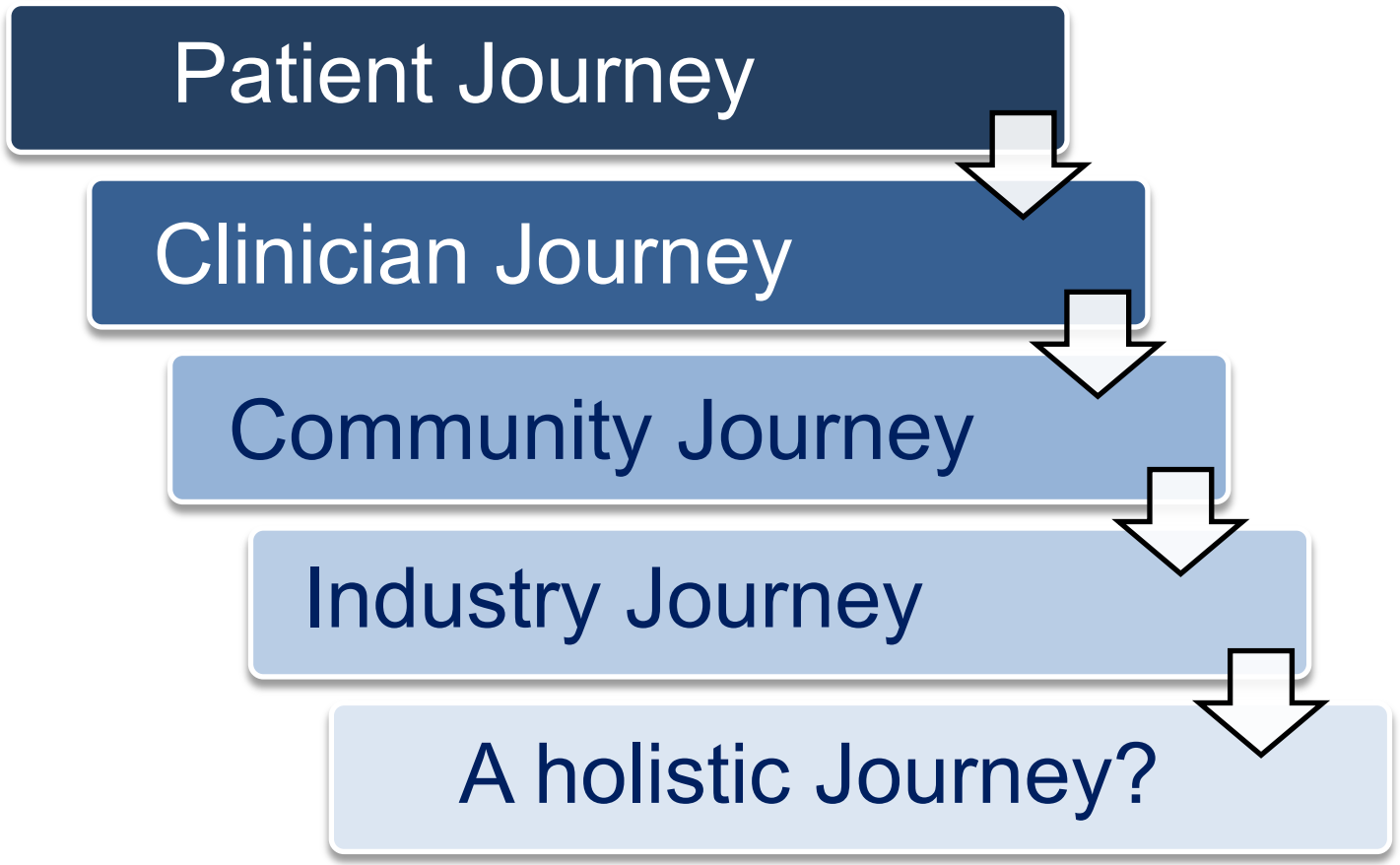
Allyson Berent, DVM, DACVIM

- Chief Science Officer for the **Foundation for Angelman Syndrome Therapeutics**
- Co-Director at **Angelman Syndrome Biomarker** and **Outcome Measure Consortium**
- Co-Director at **INSYNC-AS: International Angelman Syndrome Research Council**
- Chief Development Officer at **Mahzi Therapeutics**
- Veterinary Internal Medicine Clinician Director at Interventional Endoscopy
- **Mother of Quincy**

Disclosures

- Co-founder, former COO, and equity shareholder of GeneTx Biotherapeutics recently acquired by Ultragenyx Pharmaceutical
- Consultant for Ultragenyx Pharmaceutical
- Consult and advise drug development initiatives for numerous AS programs and other rare disease organizations
- Member of N=1 Collaborative

A Journey


Patient Journey
Clinician Journey
Community Journey
Industry Journey
A holistic Journey?

A day in the life of a child with Angelman Syndrome. To view this video, and the entire online presentation, visit **https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/warrior-families-advancing-regenerative-medicine-through-science-10052023**, timestamp 00:09:57.

Patient Journey

- How do you spell “Angelman syndrome?”
- ALL THE NOT’s!!!!
- What WILL she be able to do?
- What is the prognosis for survival?
- How do I give her the best life and advocate for all she is capable of?
- How do I ensure she is accepted and lives the most independent and fulfilled life?
- **I MUST ADVOCATE FOR QUINCY**
- **I MUST LEARN and EXECUTE IF I CAN CHANGE HER TRAJECTORY**

Patient Journey (cont.)

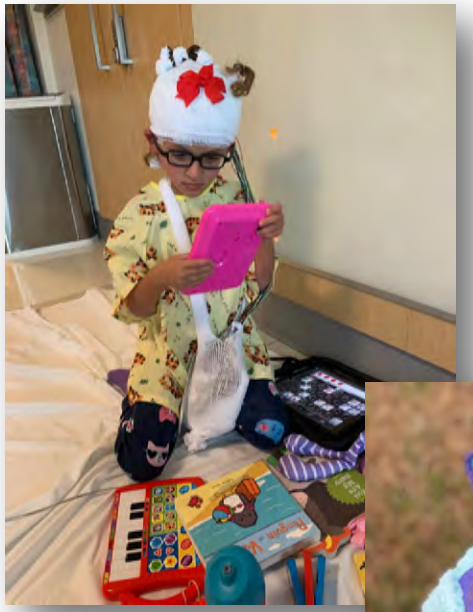
- I can't do this…and I don't want to!
- What kind of mother am I?
- How do we handle this as a family?
- How do we navigate the world of disability?
- How do I manage a life of therapy and a full-time job?
- There must be a solution to this problem!
- **"KNOWLEDGE IS POWER"**
- **"THINGS ARE EITHER POSSIBLE OR IMPOSSIBLE AND THERE IS NO INBETWEEN"**

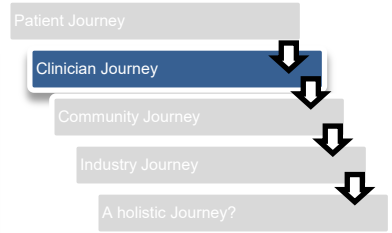
I MUST BE <u>BRAVE</u>

I MUST BE <u>SMART</u>

Clinician Journey

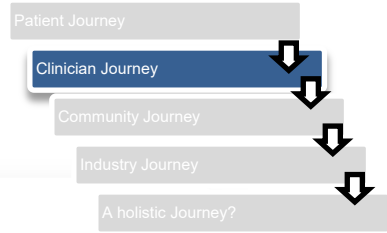
- Called every senior author on every publication
- Attended every scientific conference I could
- Something was very clear!
- **This is a great decade to be a mouse with Angelman syndrome!**
- Translational science was outside of the wheelhouse of many scientists in the space
- **We MUST NOT WAIT FOR A TREATMENT →We must help shepherd one**
- **I MUST BE A CLINICIAN**



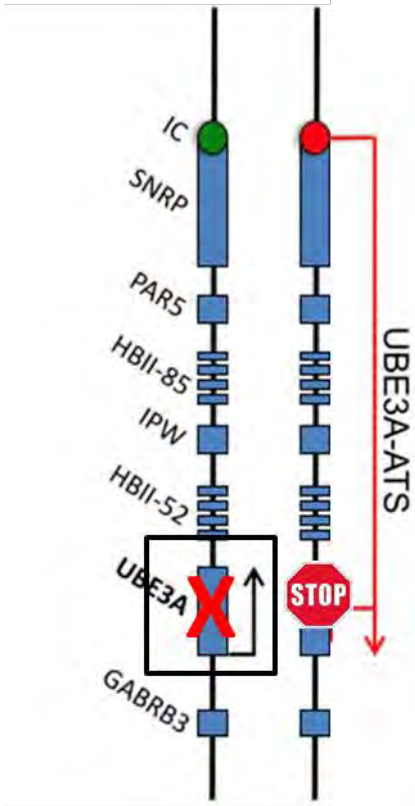


Angelman Syndrome:

Monogenetic, Non-degenerative, Random, Neurologic Disorder



Maternal allele (M)	Paternal allele (P)
	

Maternal allele (M)	Paternal allele (P)
	

N. Khatri et al. *Front. Mol. Neurosci.* 2019

Imprinted Gene=Paternal silenced

Clinical Manifestations of AS are Severe, with Lifelong Impact on the Patient and Their Caregivers

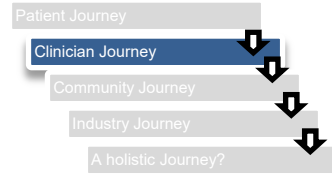
Symptoms of AS

- Universal lack of speech
- Life-threatening/debilitating seizures
- Severe developmental delays
- Ataxia/incoordination
- Apraxia/Dyspraxia
- Sleep disturbances/severe insomnia
- Feeding issues/GI issues
- Aggressive/disruptive behavior
- Unable to live independently
- **Significant clinical unmet need**

Impact on Family

- Inability to maintain employment
- Anxiety
- Depression
- Stress
- Loss of sleep
- Social isolation
- Impact on family relationships
- Difficulty caring for other children/home
- Fatigue

Strong Hypothesis to Support Human Translation



- **1-5%** UBE3A → few-no seizures, ambulatory, some ataxia, some speech
- **~20%** UBE3A → no seizures, ambulatory, minimal to no ataxia and speak in sentences
- **>40%** not reported to be symptomatic

Human Molecular Genetics, 2004, Vol. 13, No. 21
doi:10.1093/hmg/ddh296
Advance Access published on September 22, 2004

Somatic mosaicism in patients with Angelman syndrome and an imprinting defect

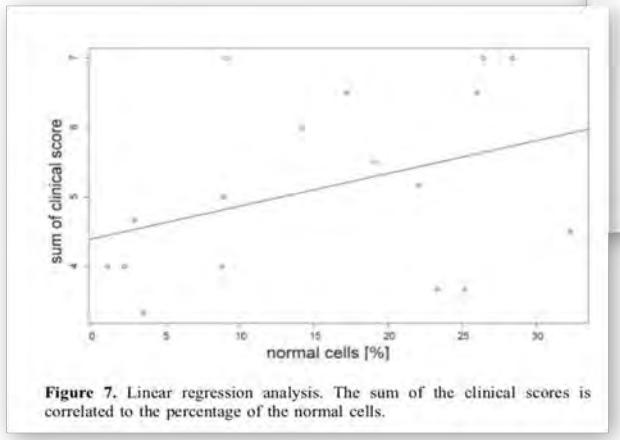
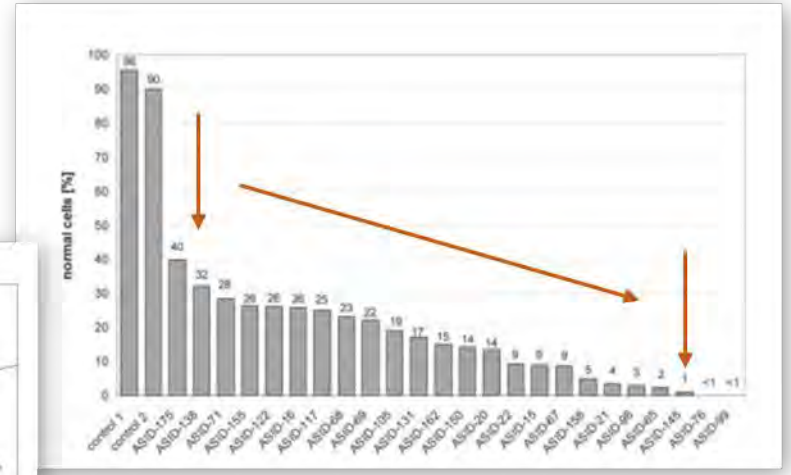
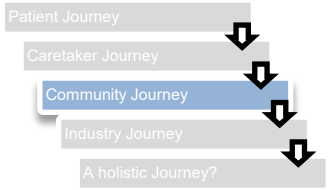


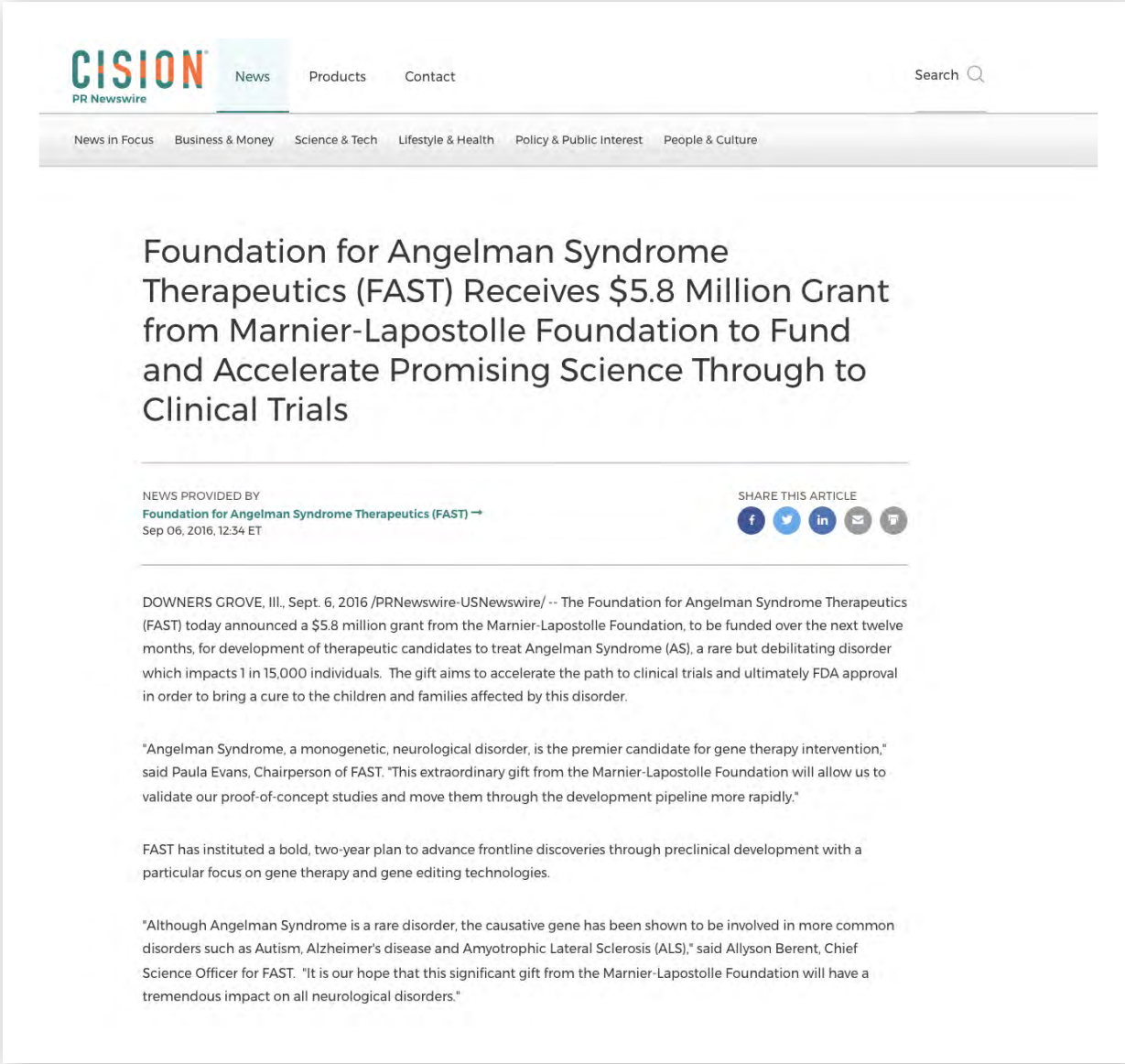
Figure 7. Linear regression analysis. The sum of the clinical scores is correlated to the percentage of the normal cells.



Community Journey



- October 2015 joined the BoD as CSO → **FAST**
- Consortium of scientists with therapeutic focus since 2008
- Consider ALL therapeutic strategies
- Scientifically de-risk each approach
- Different approaches may benefit different populations
- Create a **Roadmap to a Cure → YOU NEED AN ASK!**
- The largest influx of funds to translate 6 platforms from bench to human candidate for GO/NO GO Decisions → **$5.8 million**
- **WE *MUST* DO THIS IN 24 MONTHS**



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Foundation for Angelman Syndrome Therapeutics (FAST) Receives $5.8 Million Grant from Marnier-Lapostolle Foundation to Fund and Accelerate Promising Science Through to Clinical Trials

NEWS PROVIDED BY
Foundation for Angelman Syndrome Therapeutics (FAST)
Sep 06, 2016, 12:34 ET

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DOWNERS GROVE, Ill., Sept. 6, 2016 /PRNewswire-USNewswire/ -- The Foundation for Angelman Syndrome Therapeutics (FAST) today announced a $5.8 million grant from the Marnier-Lapostolle Foundation, to be funded over the next twelve months, for development of therapeutic candidates to treat Angelman Syndrome (AS), a rare but debilitating disorder which impacts 1 in 15,000 individuals. The gift aims to accelerate the path to clinical trials and ultimately FDA approval in order to bring a cure to the children and families affected by this disorder.

"Angelman Syndrome, a monogenetic, neurological disorder, is the premier candidate for gene therapy intervention," said Paula Evans, Chairperson of FAST. "This extraordinary gift from the Marnier-Lapostolle Foundation will allow us to validate our proof-of-concept studies and move them through the development pipeline more rapidly."

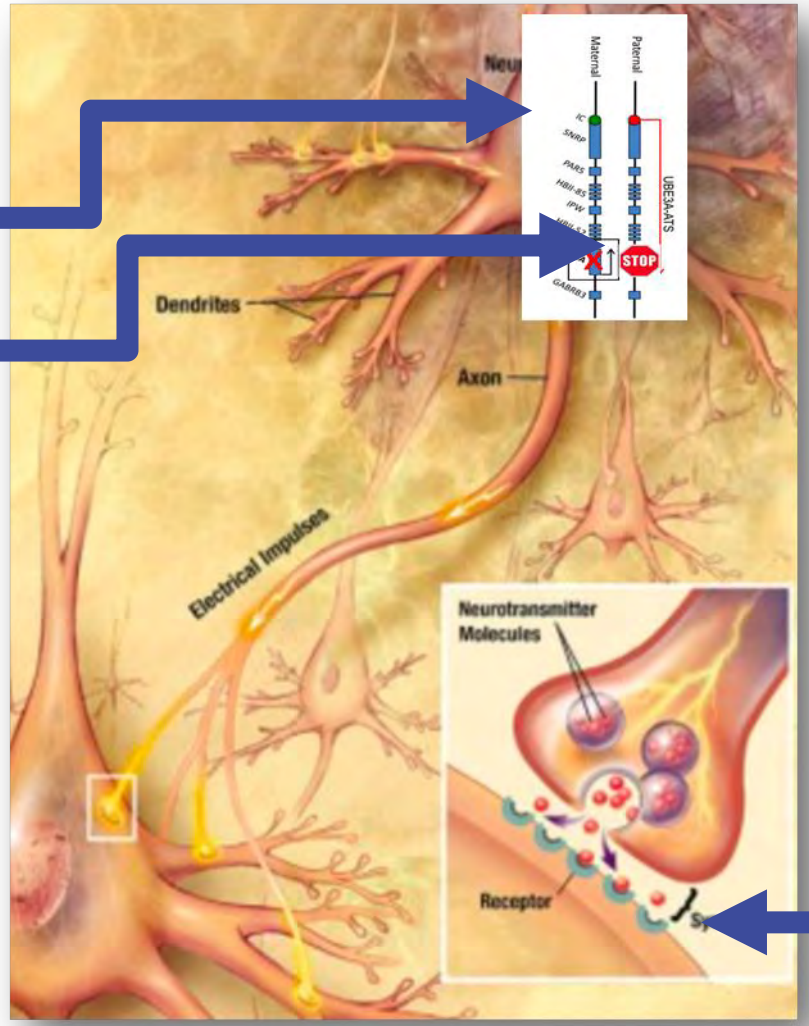
FAST has instituted a bold, two-year plan to advance frontline discoveries through preclinical development with a particular focus on gene therapy and gene editing technologies.

"Although Angelman Syndrome is a rare disorder, the causative gene has been shown to be involved in more common disorders such as Autism, Alzheimer's disease and Amyotrophic Lateral Sclerosis (ALS)," said Allyson Berent, Chief Science Officer for FAST. "It is our hope that this significant gift from the Marnier-Lapostolle Foundation will have a tremendous impact on all neurological disorders."

FAST's Roadmap for Success: 4 Pillars

Investigate therapeutic strategies

1. Gene/Protein Replacement Therapy
2. Paternal Gene Activation



3 Identify Symptomatic Treatments

- Down stream therapeutics
- Symptomatic relief

4 PREPARE!

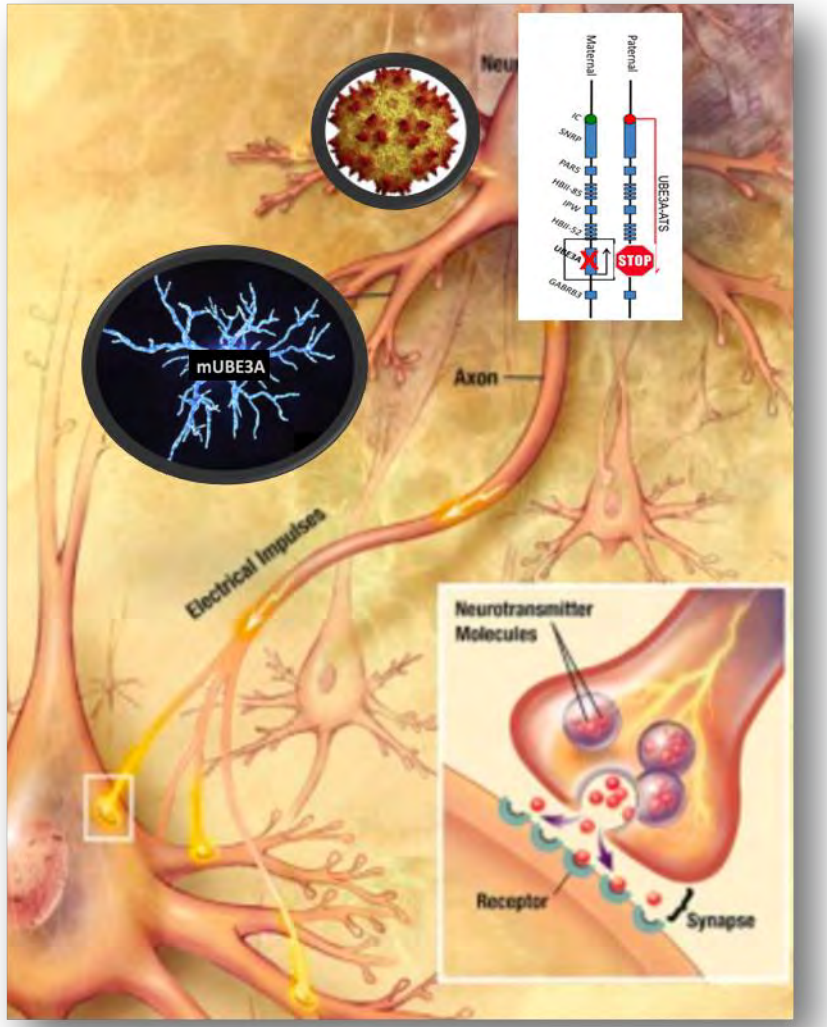
- Create/Characterize animal models
- Biomarkers and outcome measures (ABOM)
- Clinical Trial Design/ Execution
- Genotype specific testing

Gene/Enzyme Replacement Therapy

1

- **AAV** in AS model: published in a mouse model in 2011 (Daley et al. 2011)
- **HSC-LV-GT (autologous ex-vivo GT)**: AS mouse model 2021 (Adhikari et al. 2021)
- **ERT (enzyme replacement therapy)**
- 4+ additional programs being actively pursued toward clinical trials for Angelman syndrome

Penn · TRANSFORMATX · stridebio · UNC · UNIVERSITY OF SOUTH FLORIDA

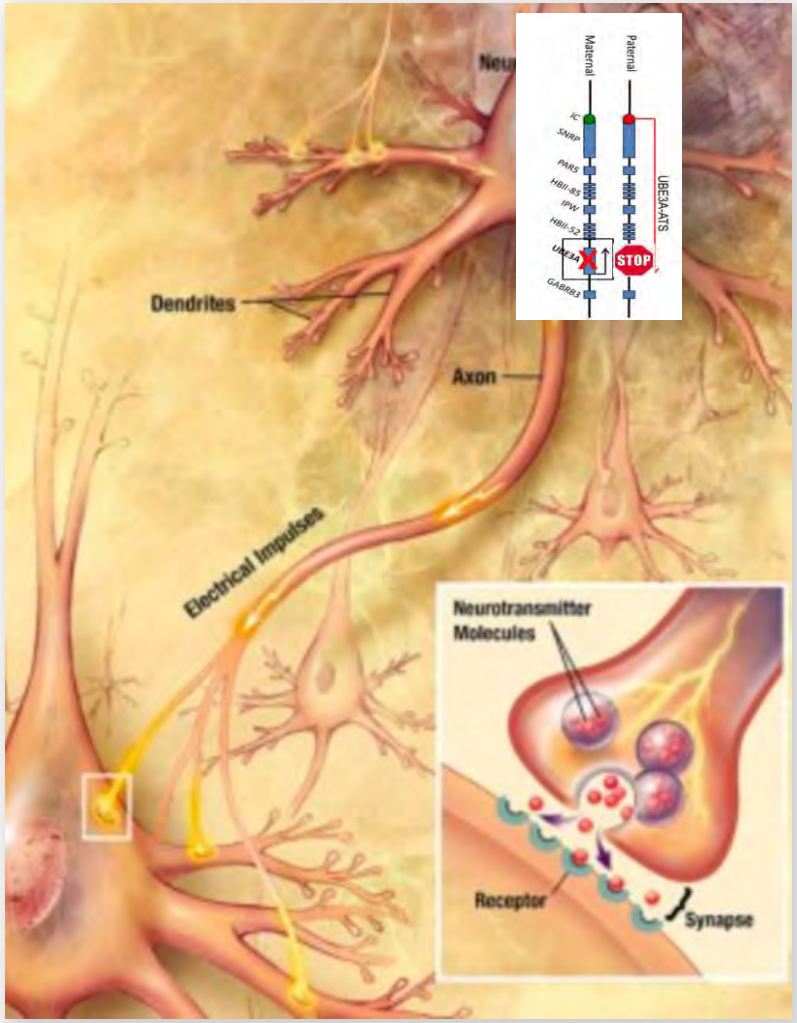


Paternal Activation Via Antisense Knockdown

2

- **Topoisomerase inhibitors**
  B. Philpot et al. Topotecan. Nature; 2011
- **ASOs (antisense oligonucleotides)**
  A. Beaudet et al. Nature; 2015
  S. Dindot et al. 2021
- **Artificial Transcription Factors (Zinc Fingers)**
  D. Segal et al. Molec Therapy; 2016
- **shRNA/miRNA**
- **CRISPR**
  M. Zylka et al. UNC 2019
  J. Wilson et al. UPenn 2020

UC DAVIS
UNC
YALE
ultragenyx
scribe THERAPEUTICS
IONIS
Encoded THERAPEUTICS
Ovid THERAPEUTICS



Rotarod (8 to 9 weeks of age)

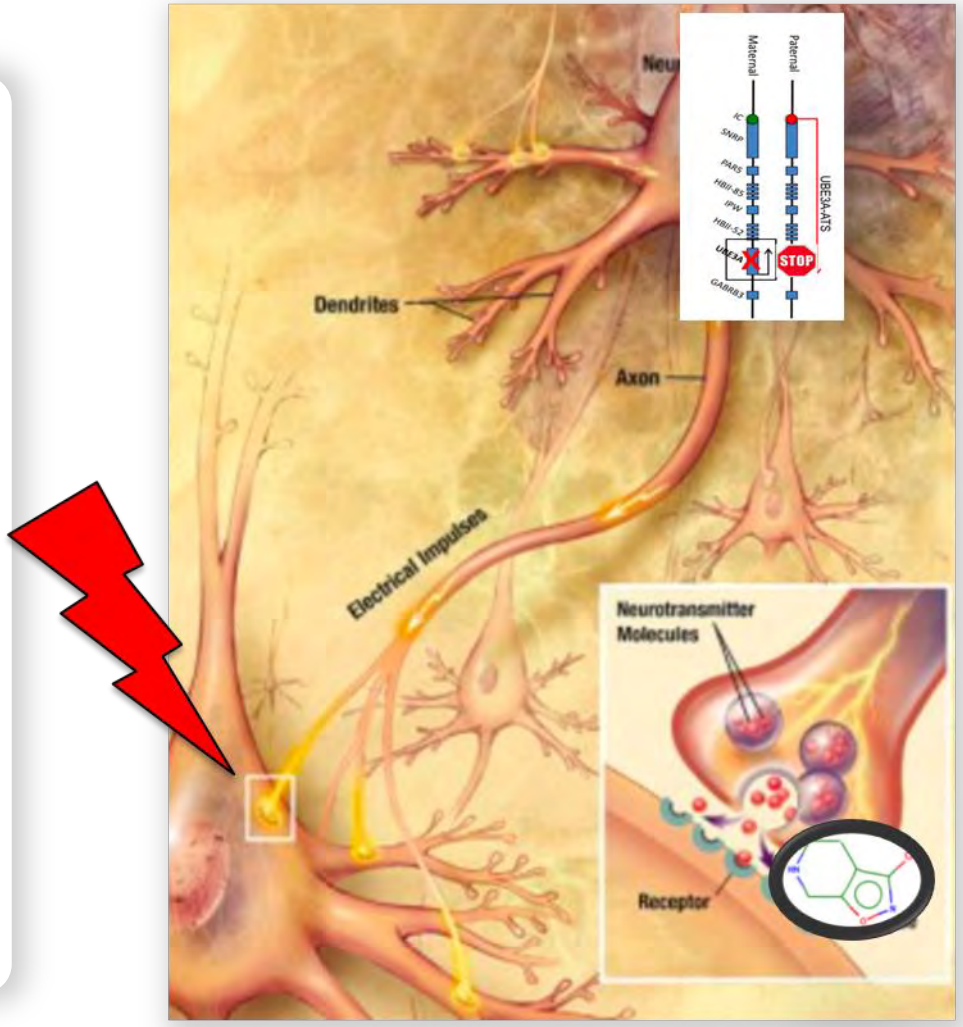
In a Rotarod test, an adult AS mouse treated with CRISPR paternal activation outperformed an untreated AS mouse and performed as well as or better than a wild mouse. To view this video, and the entire online presentation, visit https://www.fda.gov/news-events/fda-meetings-conferences-and-workshops/warrior-families-advancing-regenerative-medicine-through-science-10052023. The Rotarod test video is at timestamp 00:26:43.

Downstream Therapeutics

3

- **Ketone Supplements**
  Ciarlone, Weeber et al. Neurobio Dz; 2016; Carson et al. 2021
- **IGF-1, 2 Ligands**
  Cruz E et al. Autism Research; 2020
- **BDNF Analog**
  Cao C et al. PLOS Biol; 2014
- **GABAA-α5 positive allosteric modulator**
  Restore deficient GABAergic signaling
  Improves tonic inhibition

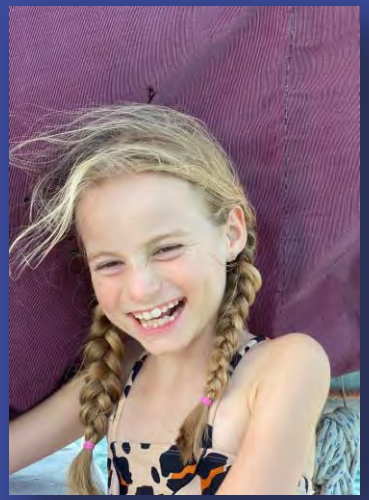
Roche BROWN neuren pharmaceuticals DISRUPTIVE enterprises

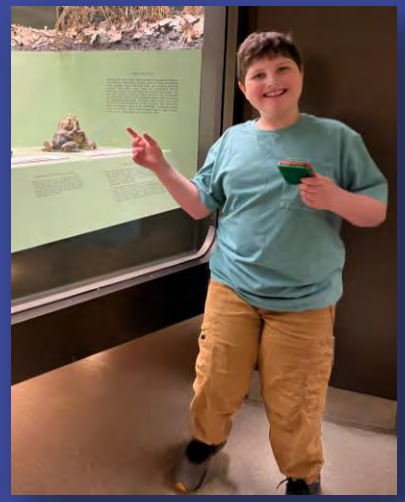
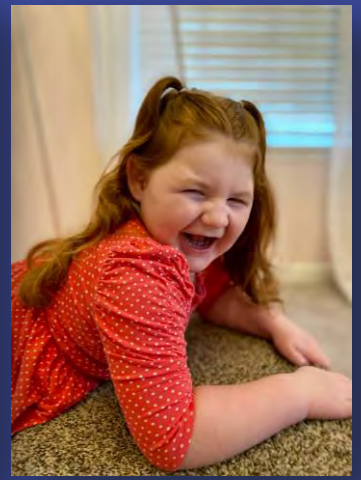




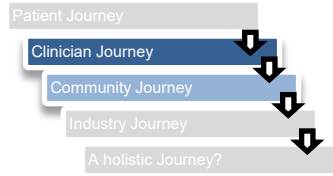


4 Preparing for Clinical Trials and Patient Access



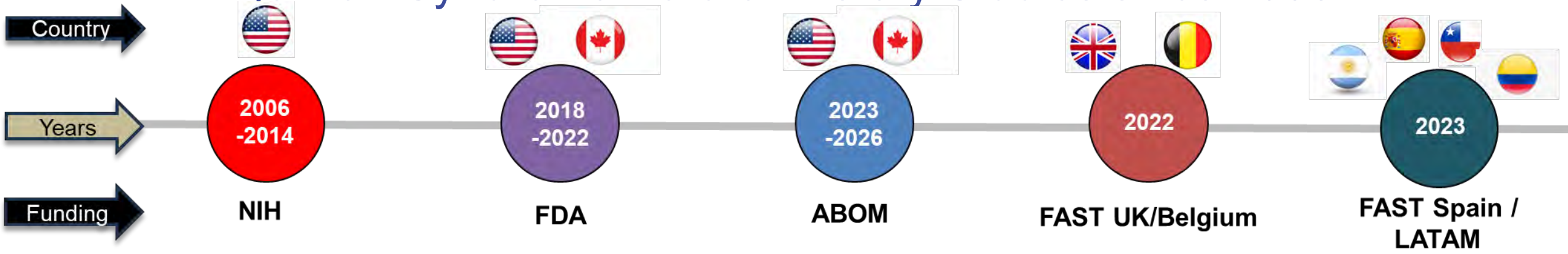

Efforts to Support Clinical Readiness for Innovative Therapies



4

- **Developing models for all genotypes of AS**
  Rat/Pig/large deletion mouse +/- Ube3a/iPSC/organoids/Landing pads
- **INSYNC-AS: International Angelman SYNdrome Research Council**
- **NIH-funded NH study (2006-2014); FDA-funded NHS (2019-2022); ABOM funded 2022-2025 over 600 patients enrolled**
  - FAST UK, LatAm, Italy, Spain
- **Global Angelman Syndrome Registry (GASR)**
  >2300 patients enrolled
- **Linking AS and Dup15q Data for Expanded Research (LADDER)**
  ~332 AS patients enrolled (ASF/Dup15q Alliance)
- **FAST Global-Search and Rescue Initiative**
  >2000 patients enrolled
- **Newborn Screening Efforts**
  Global patient identification initiative with centralized data access
- **Global COEs for Clinical Trials, Training, and Innovative Therapies for AS**
  F.A.S.T Rush Center for Translational Research
- **Angelman syndrome Biomarker and Outcome Measure Consortium (ABOM)**
  Developing AS-specific endpoints (e.g ORCA, Actimyo, CGI-AS)
  Disease concept model (Roche/ABOM): Willgoss et al. 2020

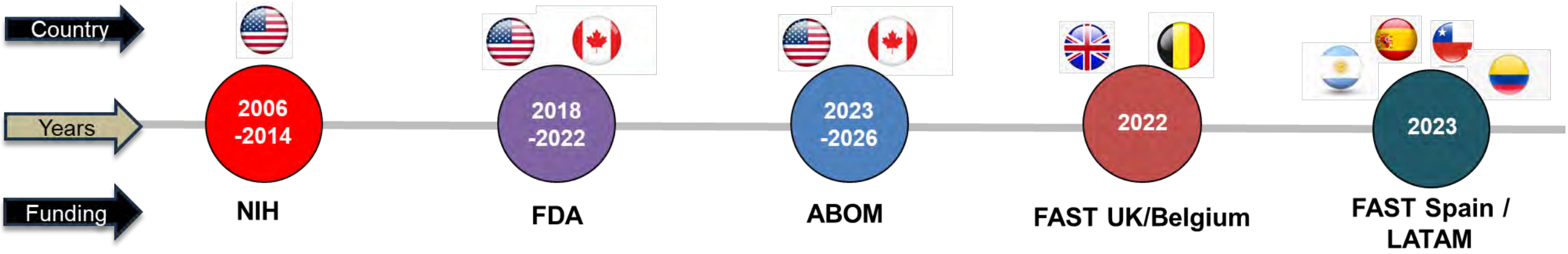
Angelman Syndrome Natural History Studies since 2006

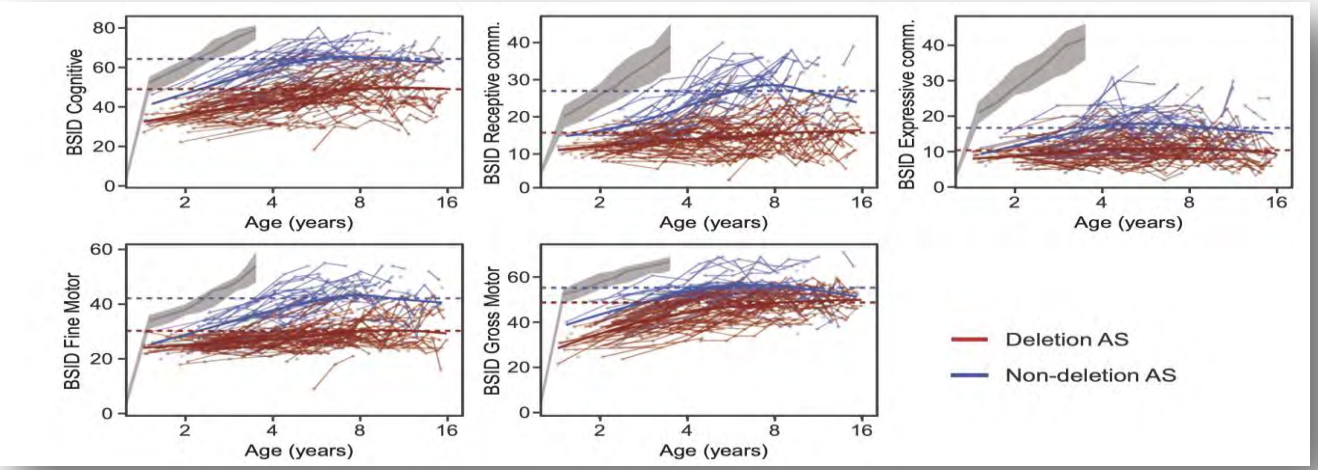


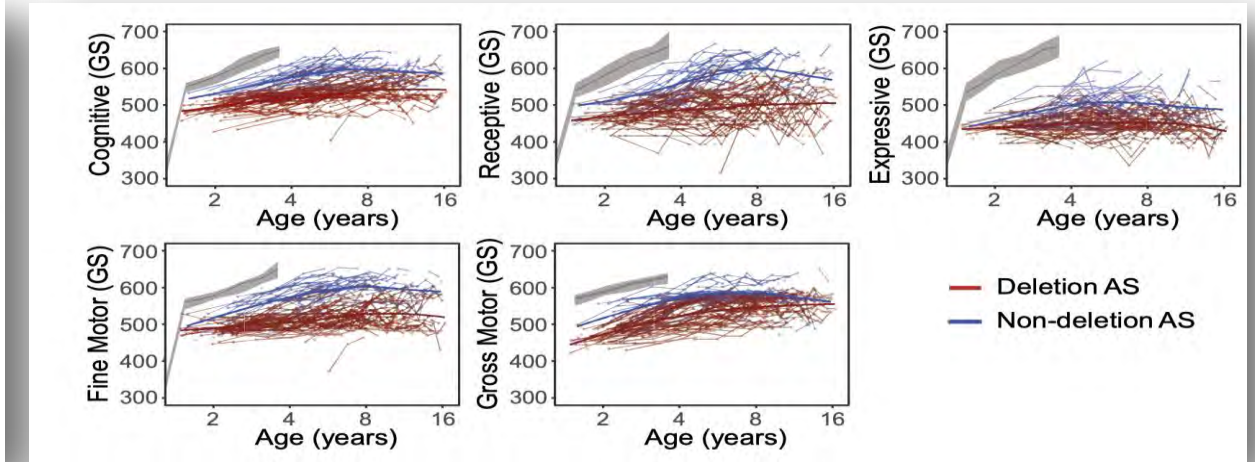
Assessment	All Patients	Pediatric Patients	Pediatric Patients	Adult Patients	Adult Patients
	At enrollment	Every 6 mos.[a]	Every 12 mos	Every 6 mos. [a]	Every 12 mos.
EEG	X	-	X	-	-
ORCA	X	X	X	X	X
Bayley-4	X	-	X	-	X
VABS-3	X	-	X	-	X
Sleep diary	X	X	X	X	X
Seizure diary	X	X	X	-	X
ABC	X	-	X	-	X
CGI-S-AS	X	X	X	X	X
QOL	X	X	X	X	X

30+ publications; 5 manuscripts submitted/in preparation

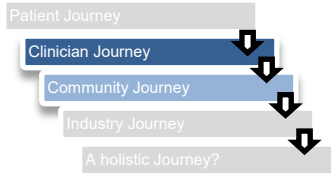
Angelman Syndrome Natural History Studies since 2006 (continued)







*special support by Drs. Wen-Hann Tan, Lynne Bird, Anjali Sadhawani, Anne Wheeler, Laurent Servais, et al.



ABOM: History and Vision

Est. 2016

A pre-competitive and collaborative spirit

- 2 advocacy groups
- 5 academics
- 3 pharma companies

Focus on priorities for industry/gap analysis on endpoints and biomarkers

Vision

1) **Parent/caregiver survey** to understand priorities by a larger number of global families through social media (2018)
   - 332 individual responses in 1 month
   - Demographics matched Global AS Registry

2) **Disease concept model** to understand the burden of disease, what is most meaningful and impactful to patients and their families (2018; 2020)

3) **Patient Focused Listening Session with FDA** (2018)
   - Invited to present the disease to the agency and discuss what the impact of this disease was on patients and caregivers

4) **Bring all partners to the table** to have pre-competitive understanding of correspondence with agency, needs of the families and meaningfulness of most sensitive and appropriate endpoints

5) **Gap analysis on Natural History Data** collected out of 6 US Institutions over 10 years
   - Different databases not integrated
   - Supporting data publication

Collecting Patient Experience Data

Important Outcomes to Caregivers of Patients with AS

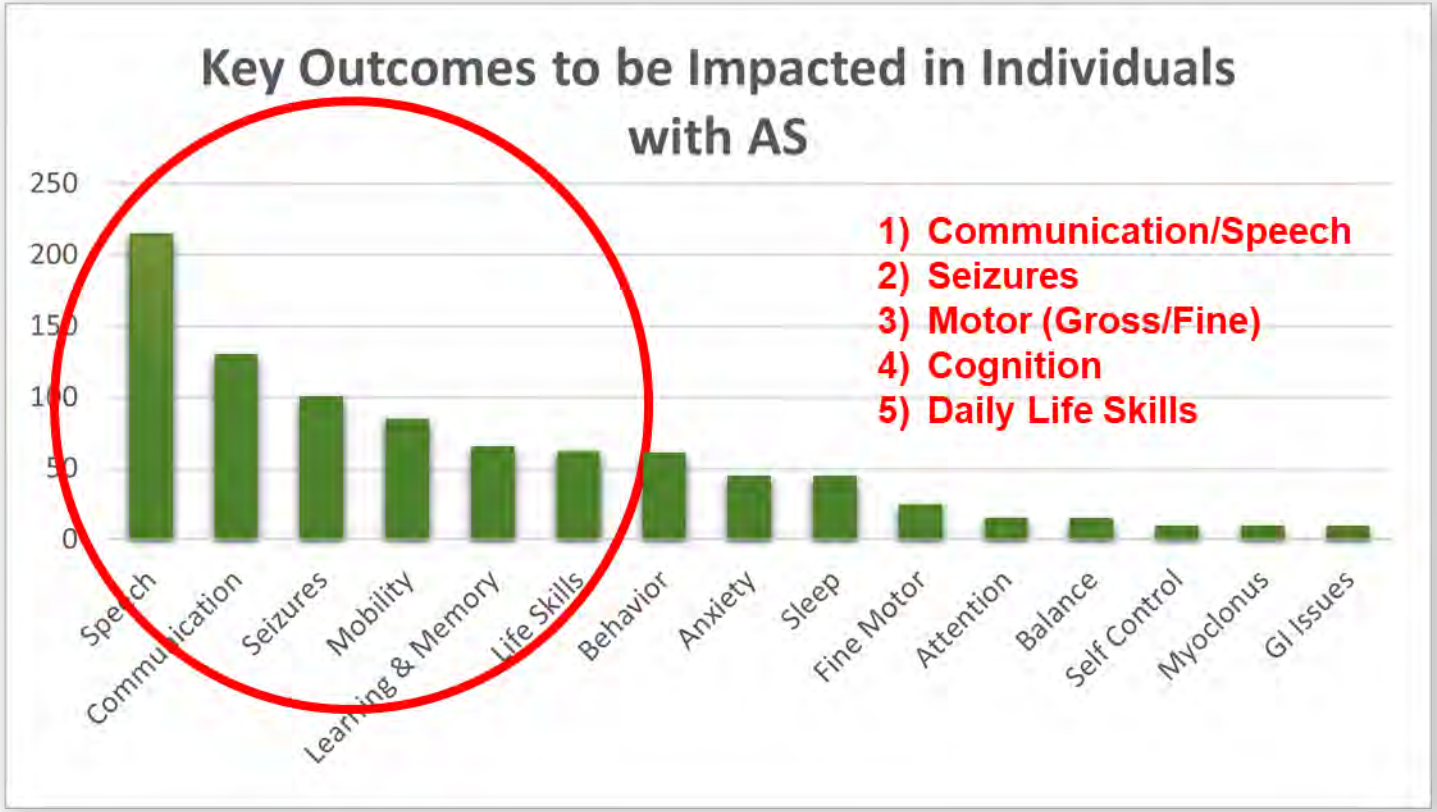
Table 4 Caregiver-rated most challenging AS symptoms, by age group

Most challenging symptoms	Number of caregivers reporting this AS symptom was challenging, per AS age group		
	≤5 years	6–12 years	15–17 years
Communication impairment or decreased speech	**3**	**5**	**4**
Seizures	**5**	2	1
Disruptive behavior	1	**3**	1
Learning challenges	1	1	1
Walking difficulties	**3**	2	1
Sleep issues	**4**	2	1
Ability to use the toilet	1	**3**	1

Bold, underlined numbers show where three or more caregivers reported this AS symptom as being challenging

AS Angelman syndrome

Willgoss, et al., 2020, *Child Psychiatry Hum Dev*

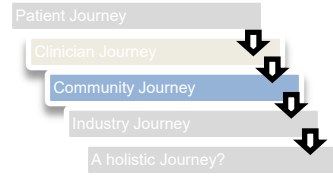


FAST SM Survey 2018: N=332 parent/caregiver responders

Collation courtesy of T. Bichell

Preparing Stakeholders for Trials

Patient Focused Listening Session 2018



- FDA-requested patient-led initiative to share perspectives with the FDA
- June 2018: Meeting of FAST, CDER/CBER, Orphan Products, Rare Disease Staff, etc.
- Introduced FDA to patients and caregivers
- Education on AS, outcomes most important to caregivers, existing measures and limitations
- Clear message from parents that such changes would be clinically meaningful and dramatically impact their child's activities of daily living
- Encouragement to develop a novel communication PRO
  - Reeve et al. ORCA development for Angelman syndrome

A-BOM
ANGELMAN SYNDROME
BIOMARKER & OUTCOME MEASURE CONSORTIUM

ABOM: 2022

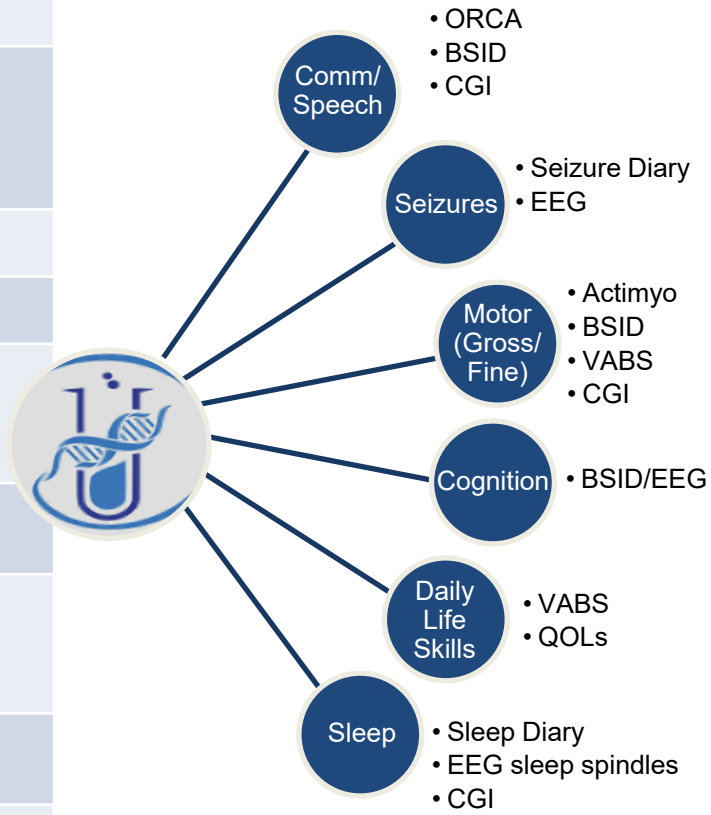
Patient Journey
Clinician Journey
Community Journey
Industry Journey
A holistic Journey?

- Currently 42 Steering Committee Members including 4 PAGs, Academic KOLs and Industry partners
- Pre-competitive → NO CDA/NDA
  - Progress tremendously accelerated
- FAST committed $1M per year to accelerate priority endpoints for all stakeholders to remain pre-competitive and ensure robust progress
- 3 (2016) → 5 (2018) → 13 (2022) Pharma on steering committee
  - (of 15+ invested in the space + 10+ academic programs)
- Quarterly meetings
  - Voices heard/seat at the table
- One scientific meeting a year for all ABOM consortia members (n=325)
  - Pilot studies
  - Clinical Research Abstracts
  - Progress based on priorities
  - **FDA engagement**
- Pre-competitive support to engage regulators and a community of industry, foundation, academics and clinicians

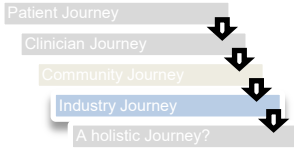
angelman SYNDROME FOUNDATION
fast cureangelman.org
IONIS
ultragenyx pharmaceutical
Biogen
Roche
Ovid THERAPEUTICS
Boston Children's Hospital
TRANSFORMATX
PTC THERAPEUTICS
THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL
healx
Encoded THERAPEUTICS
neuren pharmaceuticals

A-BOM
ANGELMAN SYNDROME
BIOMARKER & OUTCOME MEASURE CONSORTIUM

Focus Domain	Measures to consider	Measures specifically assessed for AS
Communication	• ORCA • BSID-3, BSID-4 • VABS-2, VABS-3 • Communication Matrix • ASVA • CGI-AS	• ORCA • BSID-3, BSID-4 • VABS-2, VABS-3 • Communication Matrix • CGI-AS
Fine Motor	• BSID-3, BSID-4 • VABS-2, VABS-3 • ASVA • CGI-AS	• BSID-3, BSID-4 • VABS-2, VABS-3 • CGI-AS
Gross Motor	• BSID-3, BSID-4 • VABS-2, VABS-3 • Actimyo • GMFM • ASVA • CGI-AS	• BSID-3, BSID-4 • VABS-2, VABS-3 • Actimyo • CGI-AS
Global	• CGI-S-AS, CGI-I-AS • Caregiver CGI-AS	• CGI-S-AS, CGI-I-AS
ADL	• VABS-2, VABS-3 • ASVA	• VABS-2, VABS-3
QOL	• QOL Inventory • Caregiver Burden Inventory • Parent Adjustment Questionnaire • EQ-SD-Y • Quality of Life Disability Measure	
Cognition	• BSID-3, BSID-4 • VABS-2, VABS-3 • EEG	• BSID-3, BSID-4 • VABS-2, VABS-3 • EEG
Sleep	• Sleep Diary • EEG • Wearables • CGI-AS • Sleep Mats	• EEG • Sleep Diary • CGI-AS
Seizure	• Seizure Diary • EEG • CGI-AS	• Seizure Diary • EEG • CGI-AS
Behavior	• VABS-2, VABS-3 • ABC-C • BIAPAS	• ABC-C
Biomarkers	• EEG • AERP • APP (plasma) • CSF: UBE3A others	• EEG



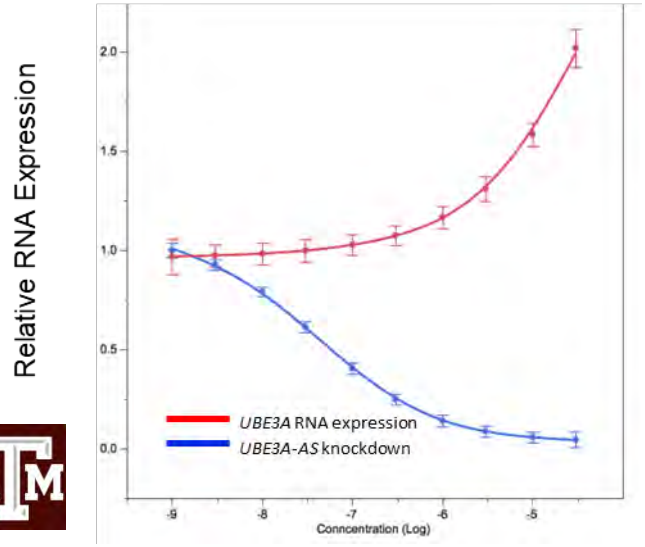
2017: Everything Changed



Human Neuronal Stem Cells

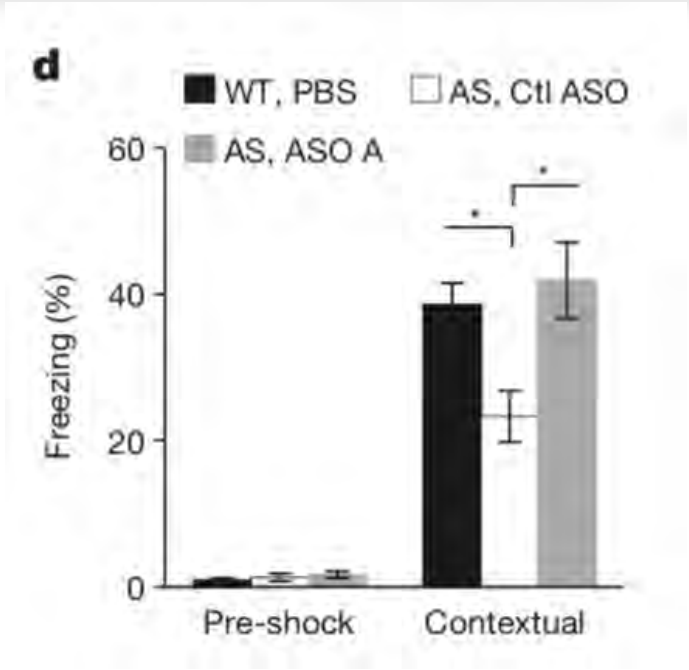
- *UBE3A-AS* knockdown by nearly 100% in human AS neurons after treatment with GTX-102 in vitro.
- Direct correlation with *UBE3A* RNA supporting robust re-activation of the paternal *UBE3A* gene.

Relative Expression of RNA after ASO exposure in cultured AS neurons



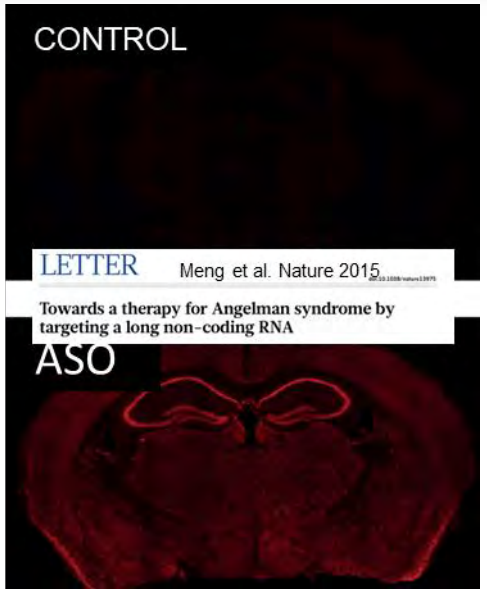
Rodent Testing

- In an adult mouse model of AS, mouse specific ASO showed successful rescue of various phenotypes (Meng et al. 2015).
- GTX-102 target region in rodent neurons showed knockdown of the Ube3a-AS approaching 100%.



Rodent Proof-of-Concept

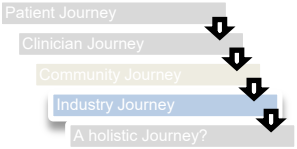
- Paternal expression of Ube3a in ADULT mice
- Ube3a-AS knockdown 60-70%
- Cognitive deficits rescued
- Knockdown >16 weeks
- ICV injection at 700ug/mouse (~210mg/NHP equivalent)
  - **GTX-10**2 effective in NHPs via lumbar puncture at doses dramatically less



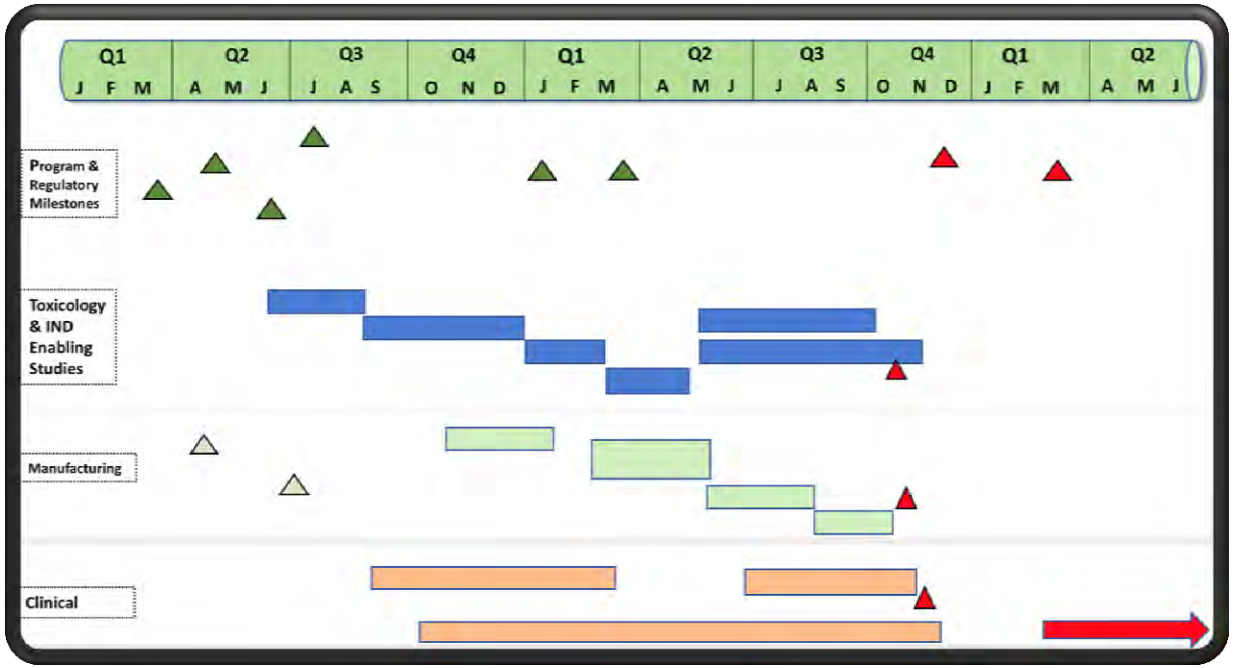
(ge•net•ics)
success is our target

an antisense oligonucleotide
treatment for
Angelman syndrome

Industry Journey

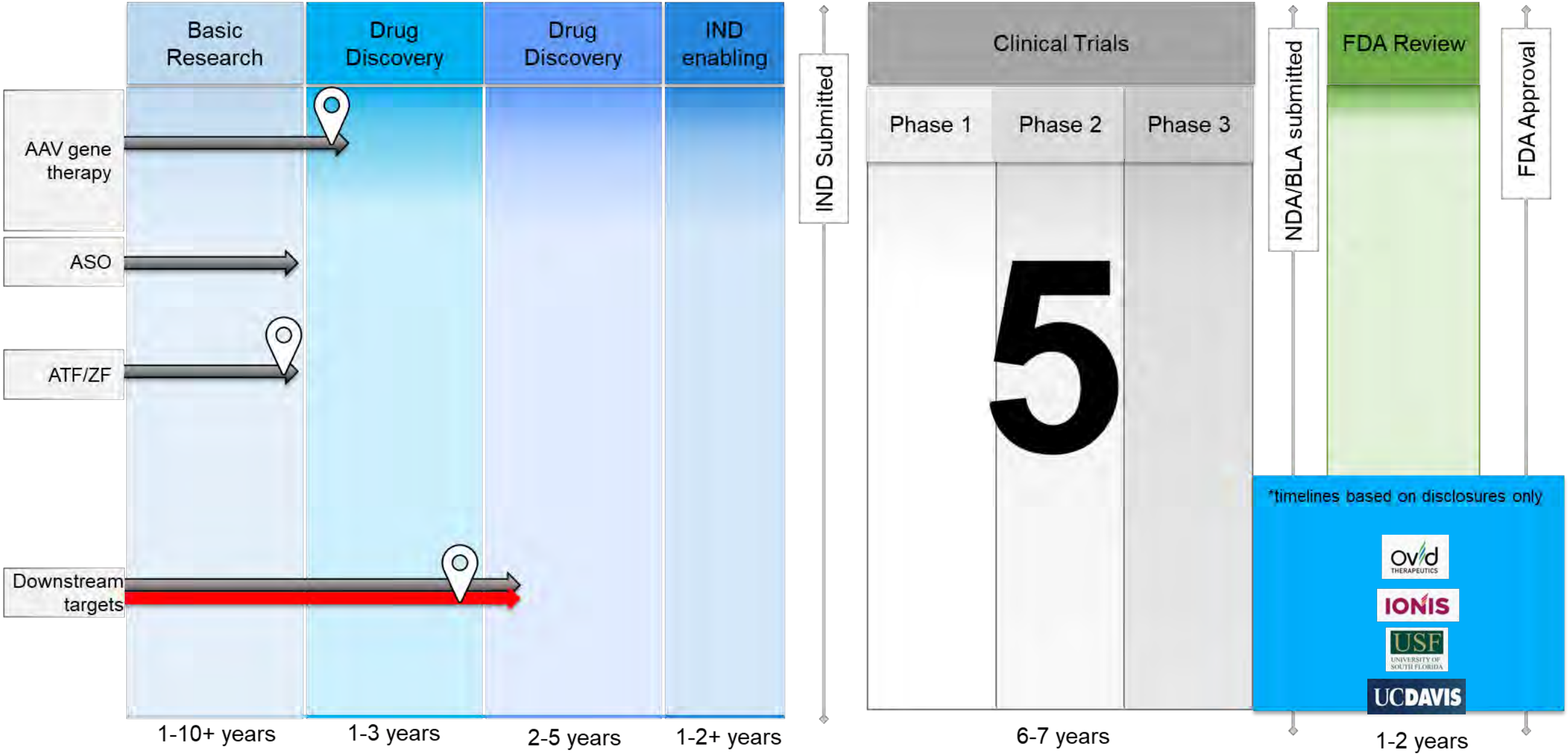


- FAST launched **GeneTx** Dec. 2017
- FAST + TAMU + Angel investors → for-profit biotech from non-profit work
- Singular focus → develop ASO for the potential treatment of AS
- Unique genetic conservation with NHP
- One species for PD/PK/Toxicology
- World renowned team of consultants
  - Non-clinical
  - Manufacturing
  - Chemistry
  - Regulatory
  - Clinical
- Obtained ODD/RPD/FTD
- 2019 Collaboration with Ultragenyx Pharmaceutical to launch Phase 1/2 trial (US, UK, Canada)



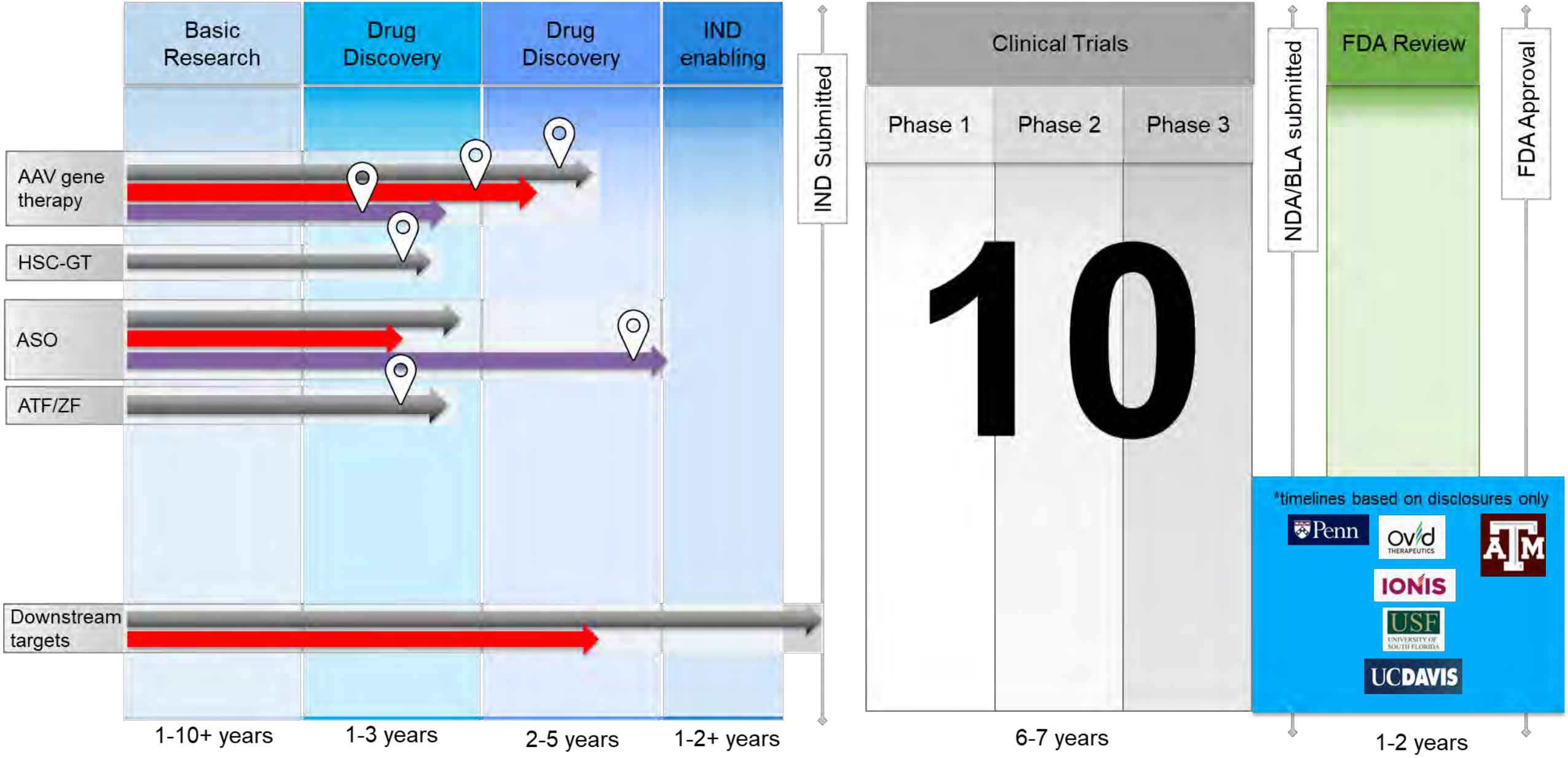
3 FAST-FUNDED PROGRAMS

Angelman Syndrome Therapeutic Pipeline: 8 years ago



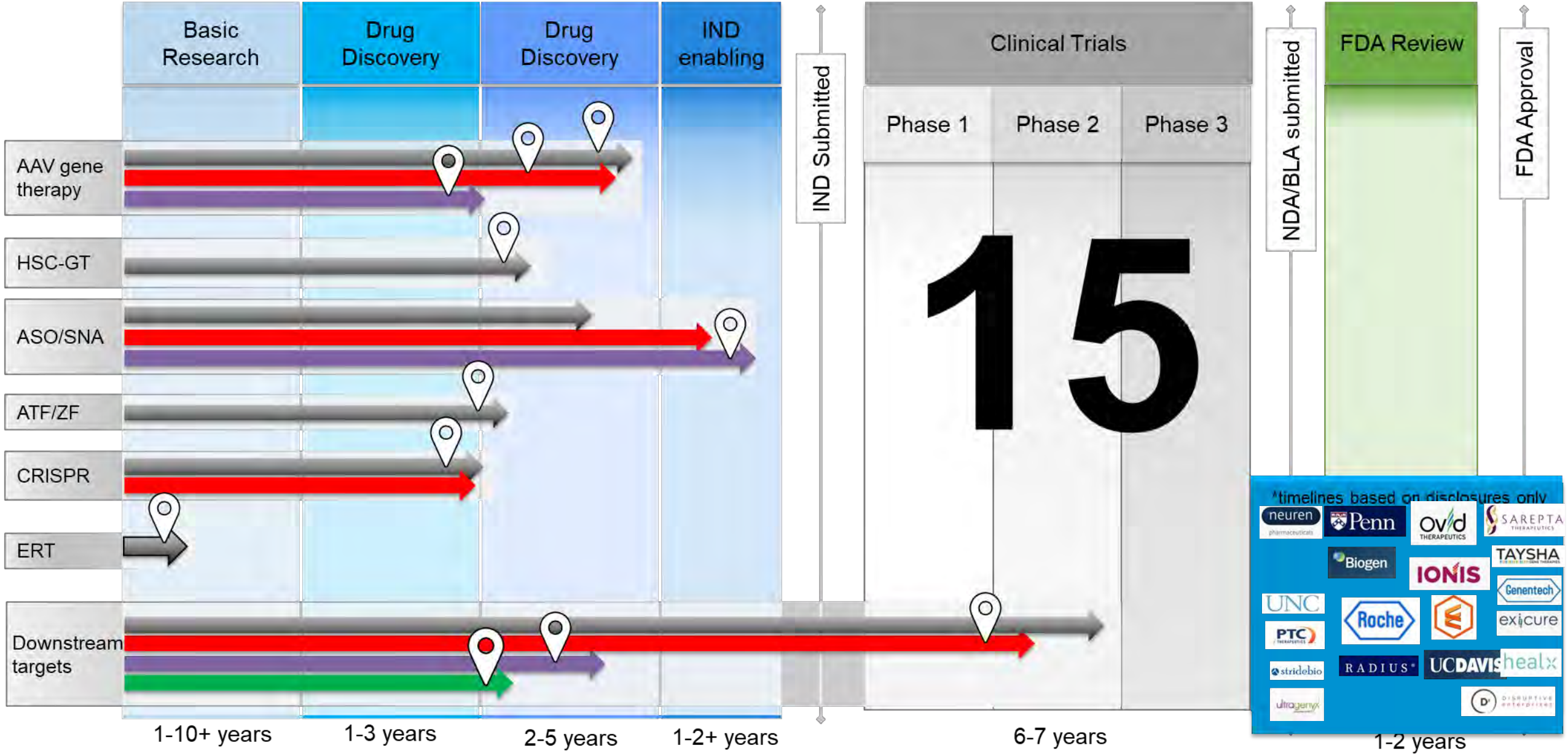
Angelman Syndrome Therapeutic Pipeline: 7 years ago

6 FAST-FUNDED PROGRAMS



10 FAST-FUNDED PROGRAMS

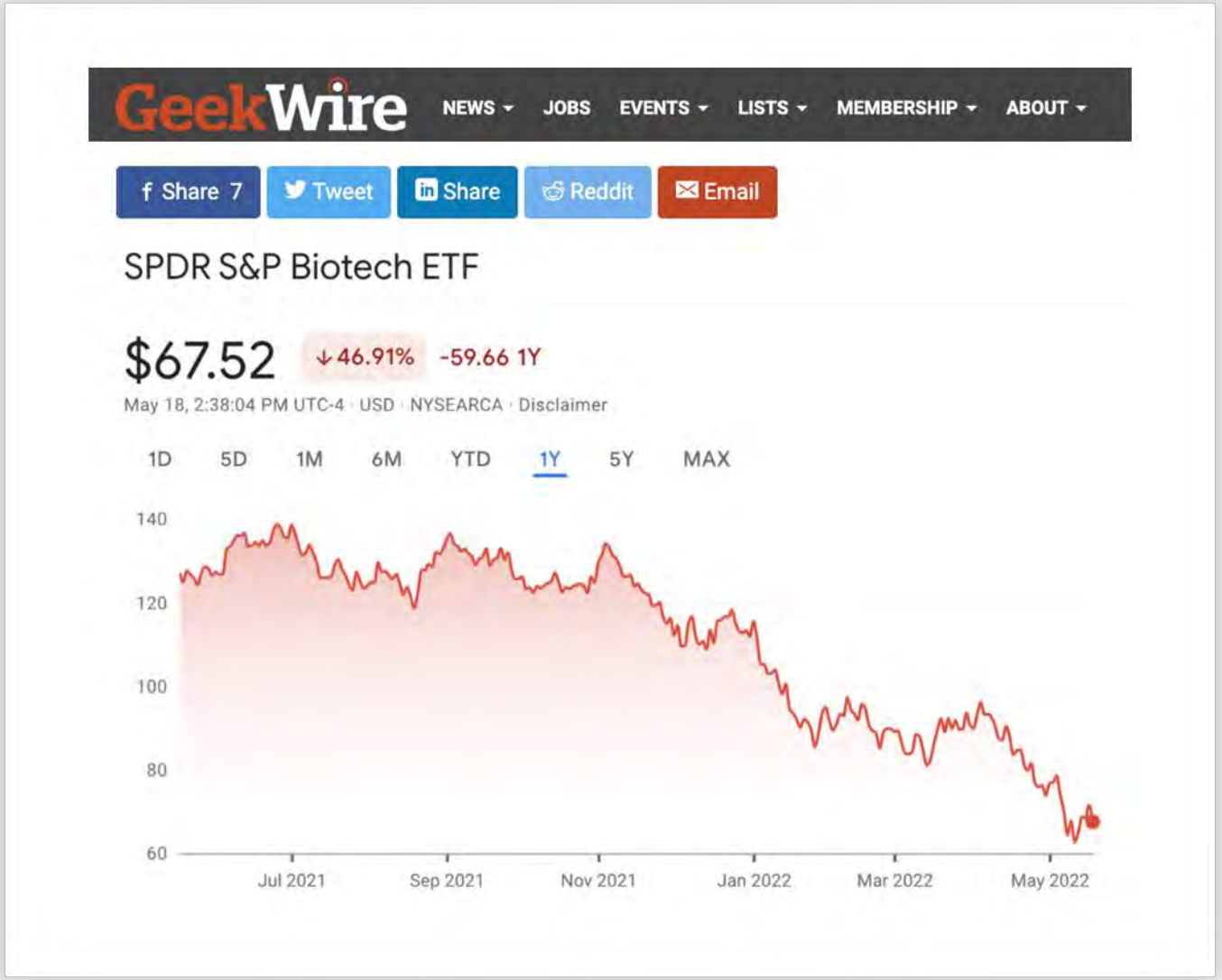
Angelman Syndrome Therapeutic Pipeline: 6 years ago



12 FAST-FUNDED PROGRAMS

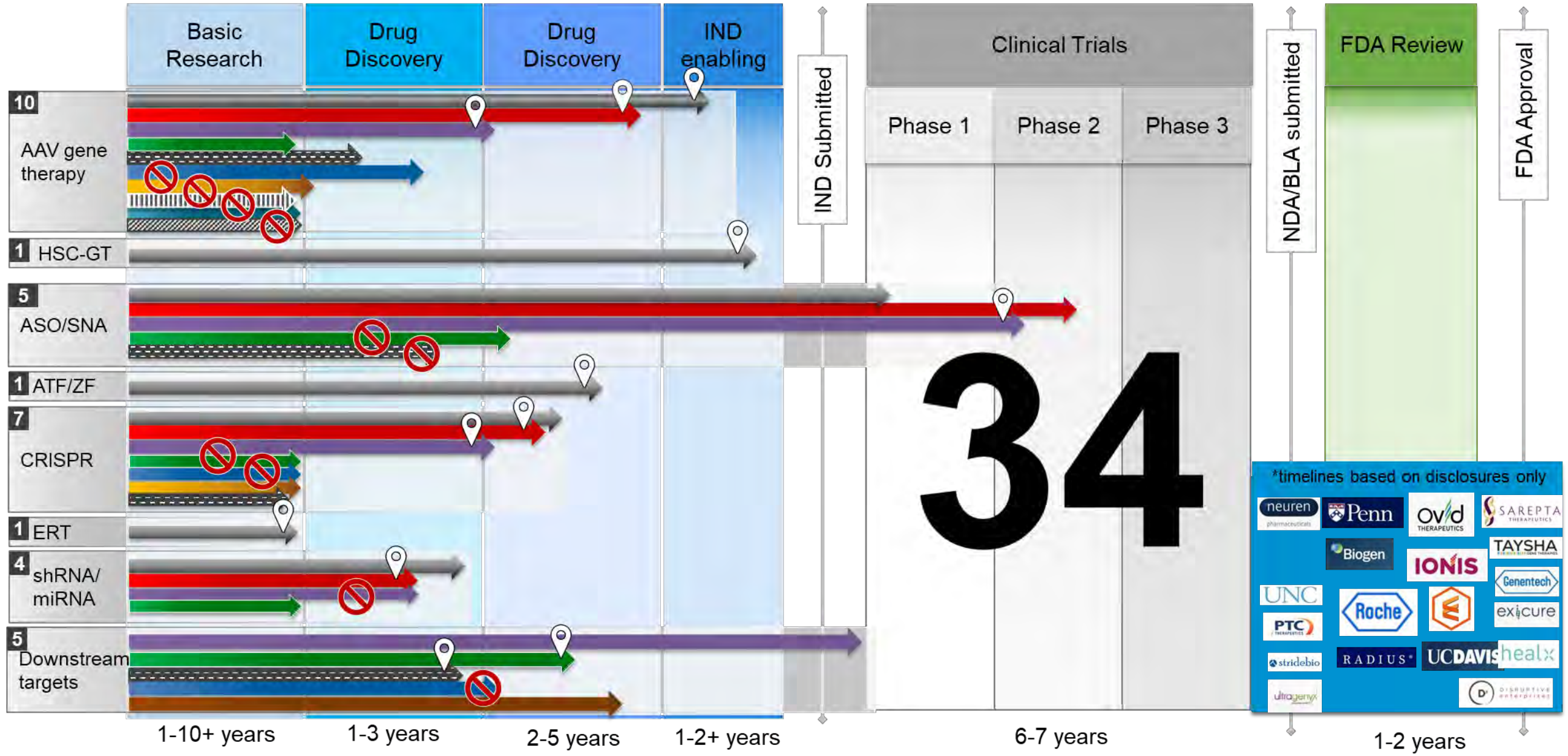
Angelman Syndrome Therapeutic Pipeline: ~2 years ago

Biotech Stocks are getting crushed



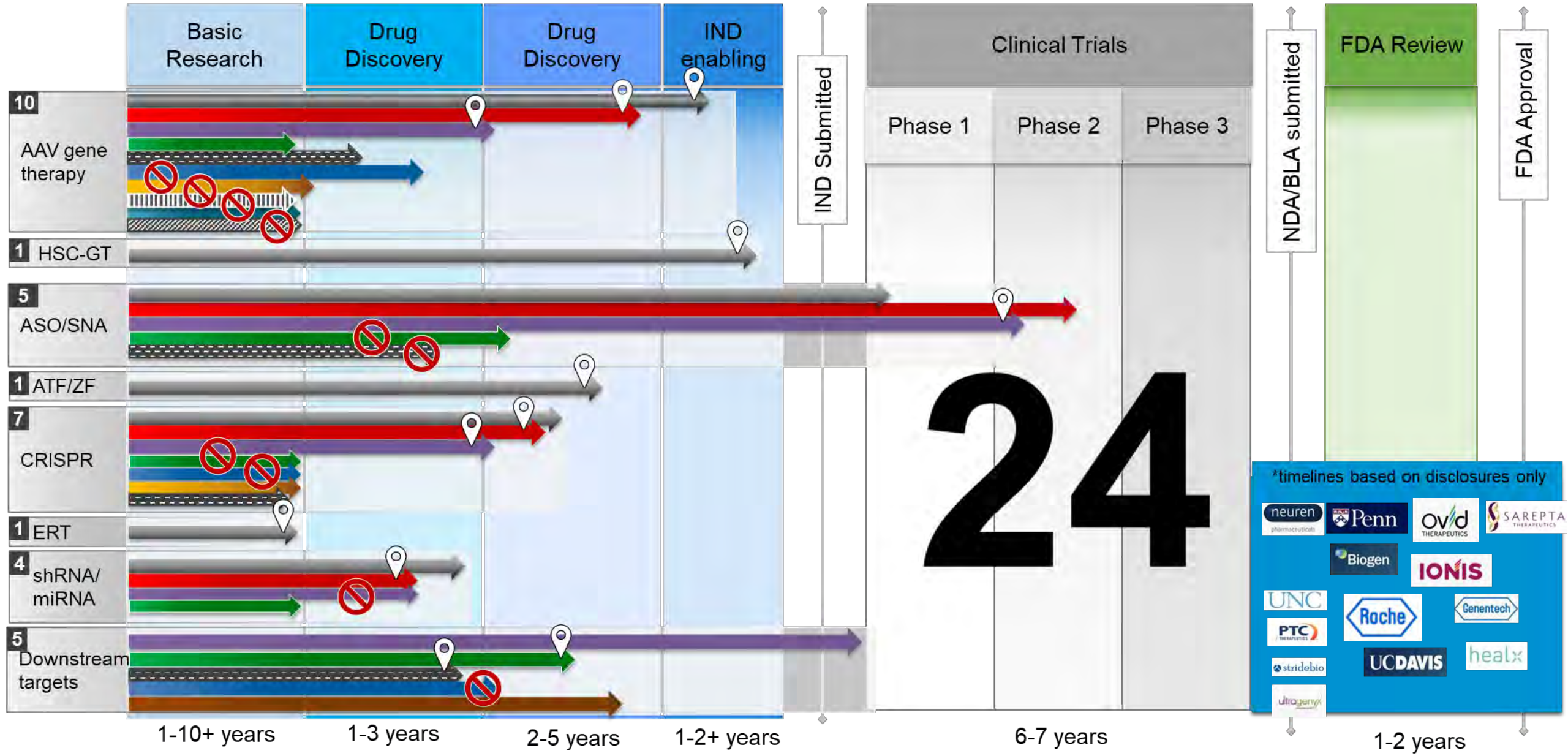
12 FAST-FUNDED PROGRAMS

Angelman Syndrome Therapeutic Pipeline: ~2 years ago



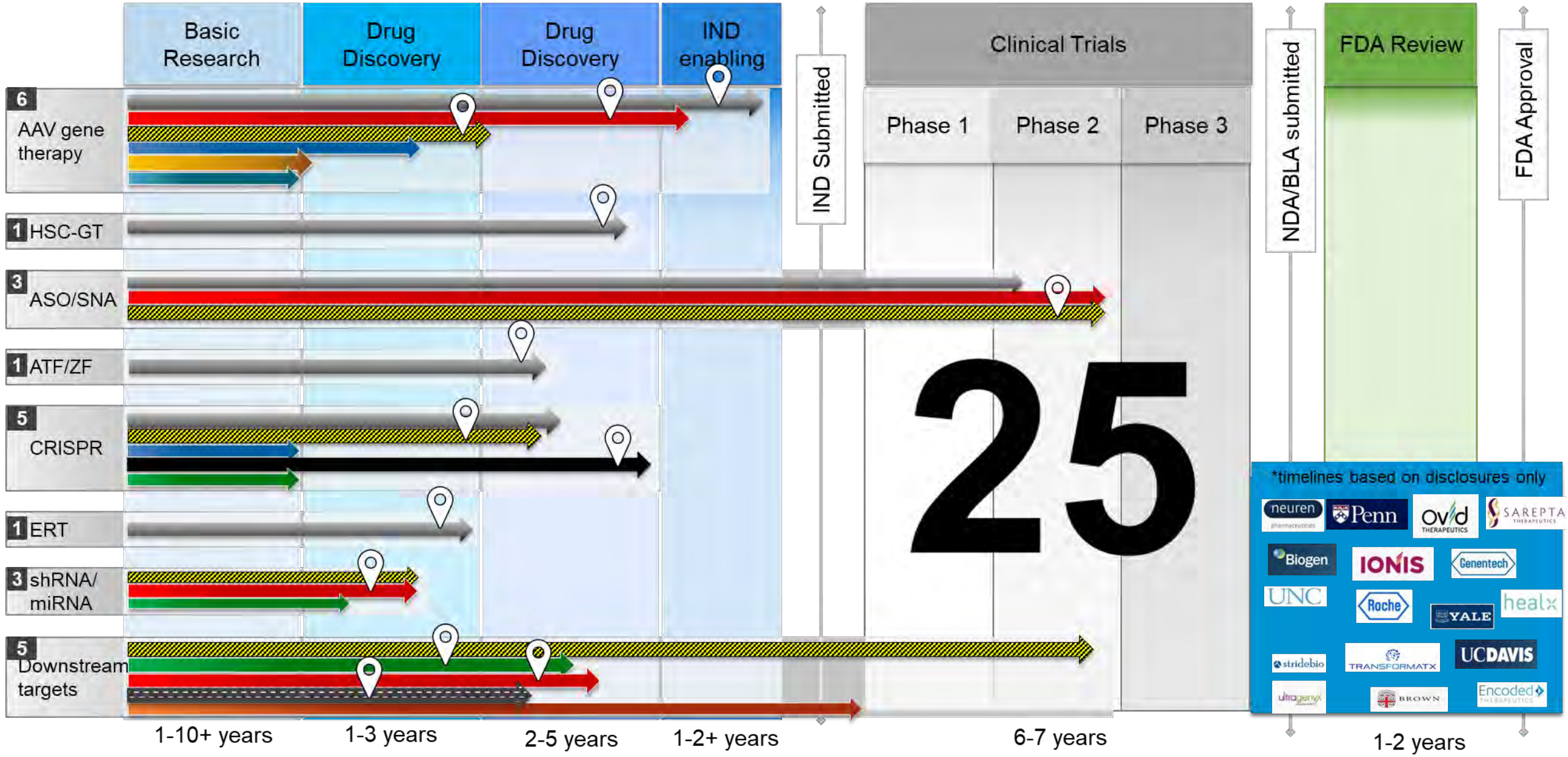
12 FAST-FUNDED PROGRAMS

Angelman Syndrome Therapeutic Pipeline: 1 year ago



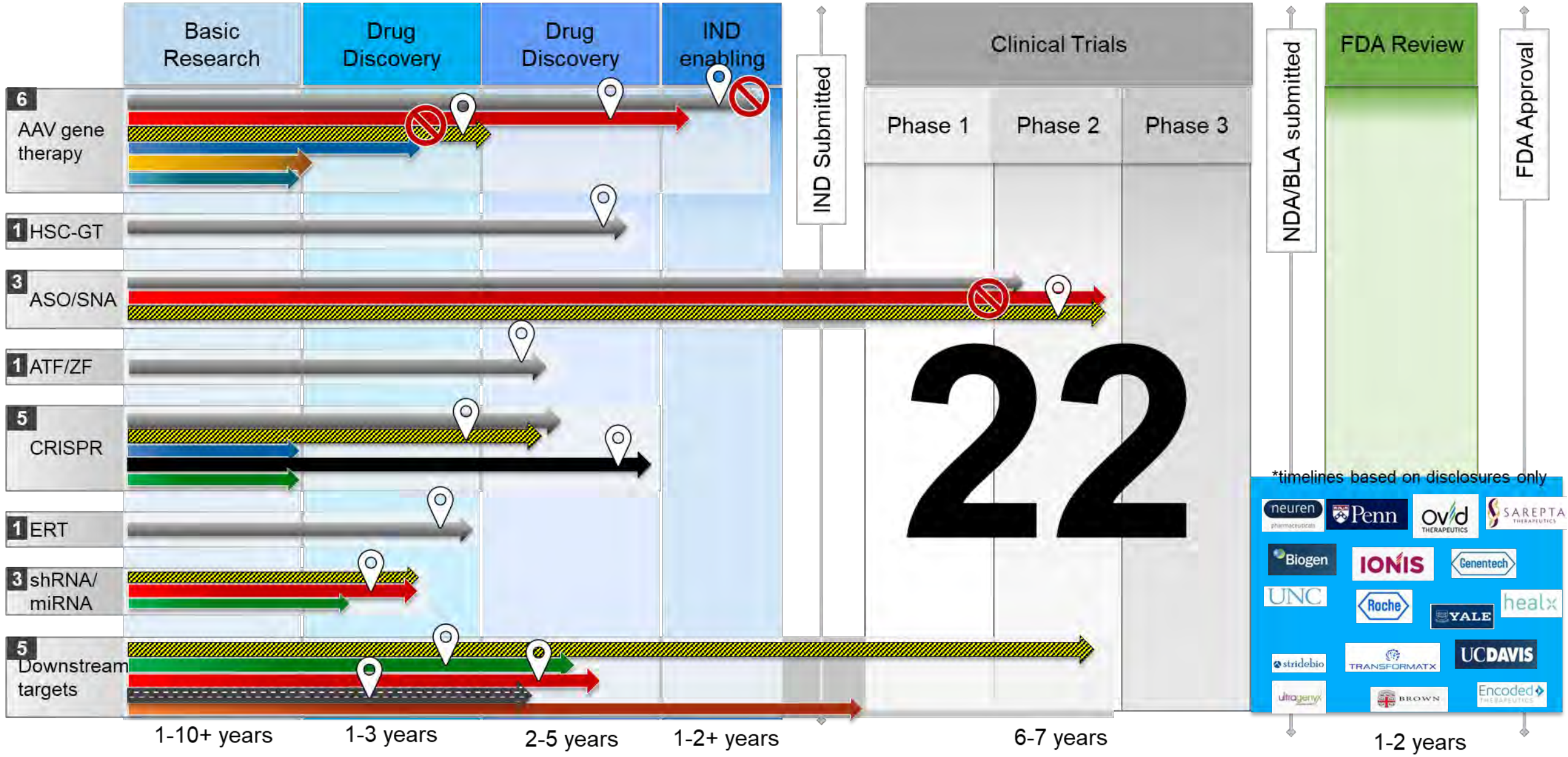
13 FAST-FUNDED PROGRAMS

Angelman Syndrome Therapeutic Pipeline: 6 months ago



13 FAST-FUNDED PROGRAMS

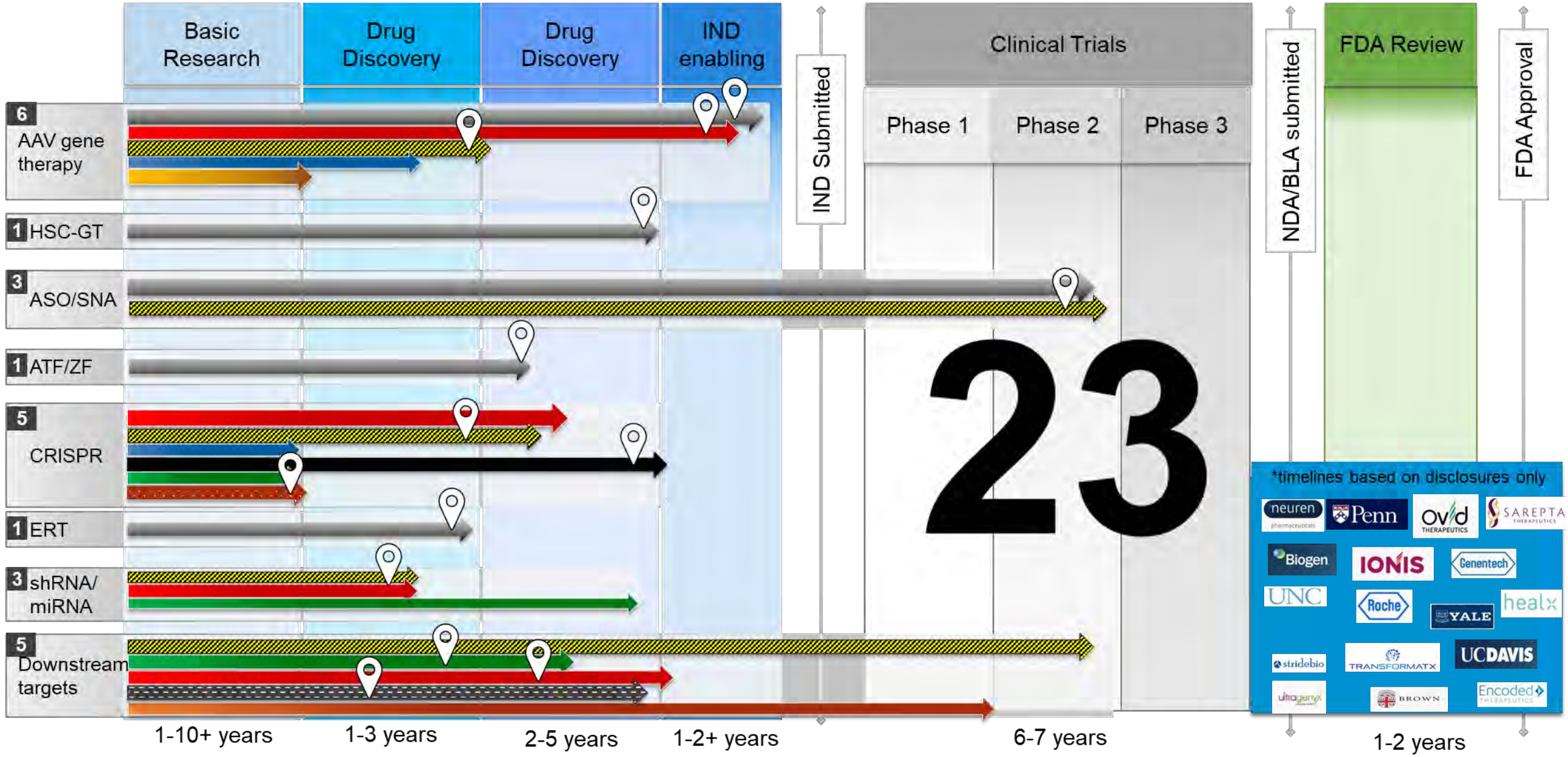
Angelman Syndrome Therapeutic Pipeline: 6 months ago



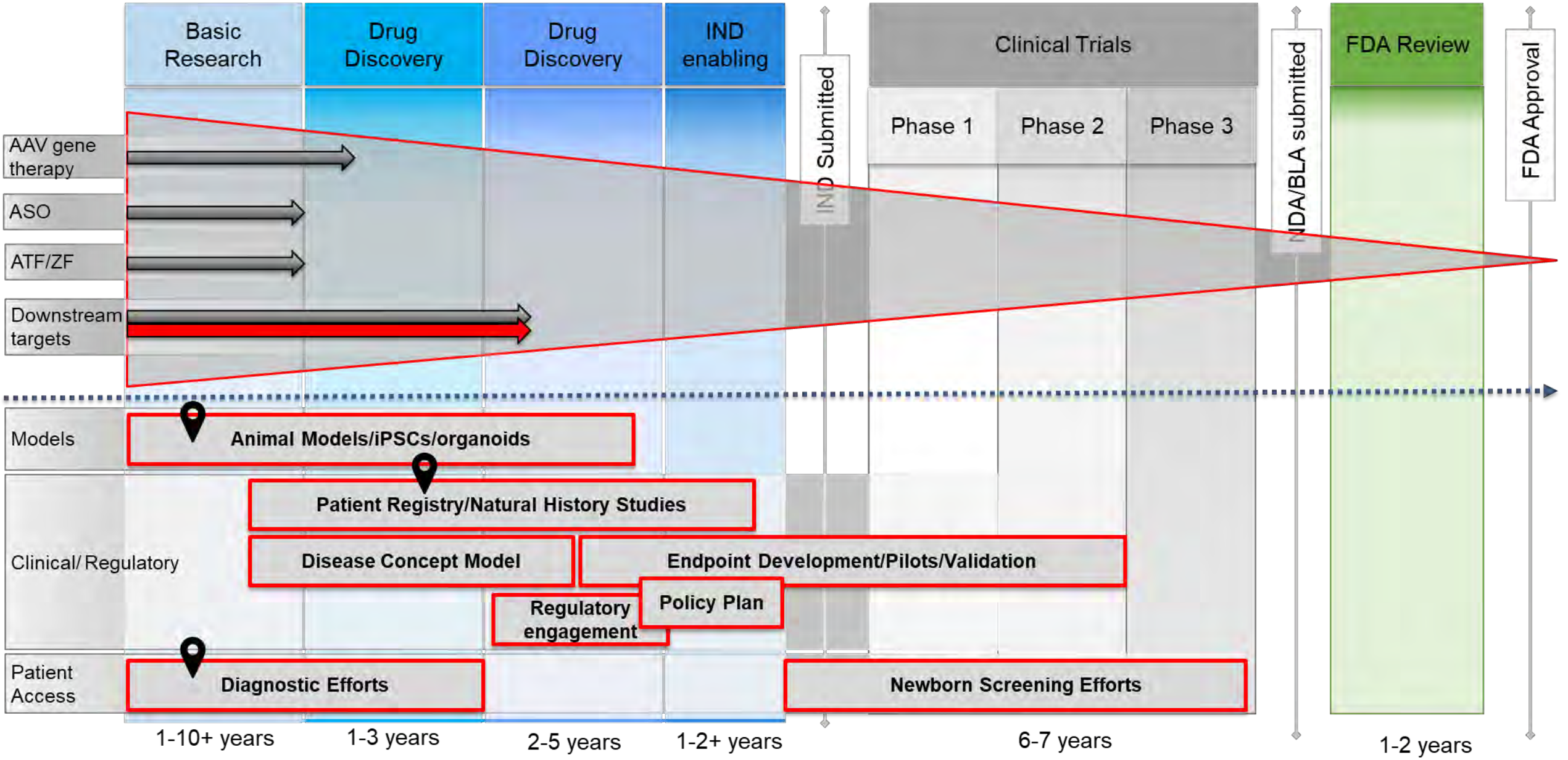
Chutes and Ladders

13 FAST-FUNDED PROGRAMS

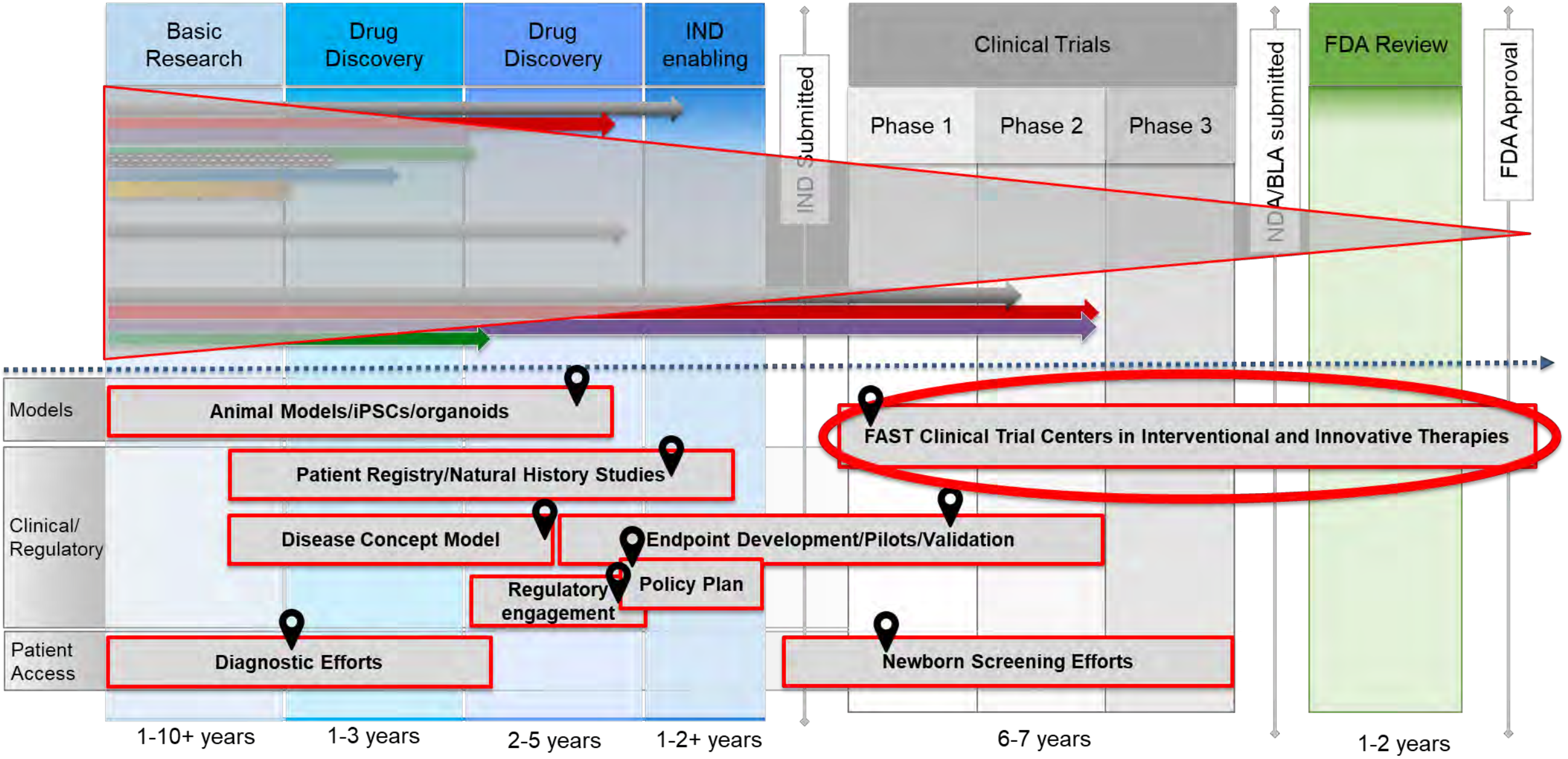
Angelman Syndrome Therapeutic Pipeline: Today



FAST's Research & Development Process: 8 years ago



FAST's Research & Development Process: **Today**



FOUNDATION FOR ANGELMAN SYNDROME THERAPEUTICS (FAST) ANNOUNCES $5 MILLION GIFT TO ADVANCE CLINICAL TRIALS IN RARE NEURODEVELOPMENTAL DISORDERS

NEWS PROVIDED BY
Foundation for Angelman Syndrome Therapeutics →
Dec 02, 2022, 11:14 ET

The Center at Rush University Will Be Directed By Dr. Elizabeth Berry-Kravis

MIAMI, Dec. 2, 2022 /PRNewswire/ -- The Foundation for Angelman Syndrome Therapeutics (FAST) announced today a $5 million gift to establish the new clinical trial and translational research effort for rare neurodevelopmental disorders, a first-of-its-kind flagship center to be directed by Dr. Elizabeth Berry-Kravis. Named the Rush F.A.S.T. Center for Translational Research, it will be the global headquarters for training individuals in how to run neurogenetic clinical trials and deliver innovative interventional therapies that require novel delivery methods and specialized care.

RUSH

Pediatric Neurosciences

F.A.S.T. CENTER FOR TRANSLATIONAL RESEARCH

Foundation for Angelman Syndrome Therapeutics

Urgent mission to **BRING** transformative treatments for our **Global** community:

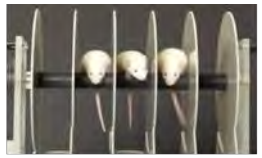
fast
cureangelman.org

Discovery

Penn, Yale, UCDAVIS, BROWN, TEXAS A&M UNIVERSITY

Academic collaborators

Preclinical



UCDAVIS, NC STATE UNIVERSITY

Testing infrastructure

Endpoints

A-BOM ANGELMAN BIOMARKER AND OUTCOME MEASURE CONSORTIUM

ORCA Observer-Reported Communication Ability Measure

Pre-competitive Consortium

Community

GLOBAL ANGELMAN SYNDROME REGISTRY

fast Search & Rescue

Connect with patients

Clinical trials

RUSH

Pediatric Neurosciences

F.A.S.T. CENTER FOR TRANSLATIONAL RESEARCH

FAST Clinical Trial Centers

NIH Announces Large Grant for Gene Editing Platform to Yale University, Foundation for Angelman Syndrome Therapeutics and RUSH University Medical Center

October 3, 2023

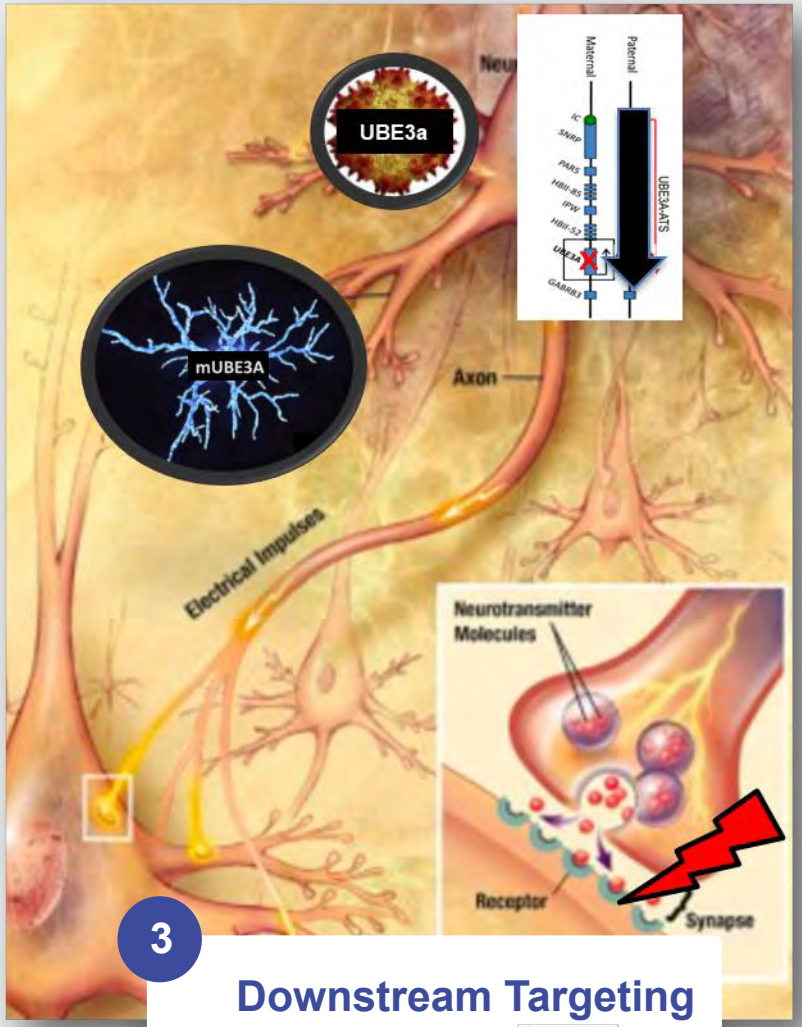
Disease Modification Strategies

1 Gene/Protein Replacement Therapy

- **AAV**
  - Gene replacement
  - Secretory Protein replacement
- **Lentivirus** with **HSC**
- Enzyme replacement therapy **(ERT)**

Penn · TRANSFORMATX · UNIVERSITY OF SOUTH FLORIDA · UNC · stridebio

*other programs are currently under development that may not be represented/disclosed



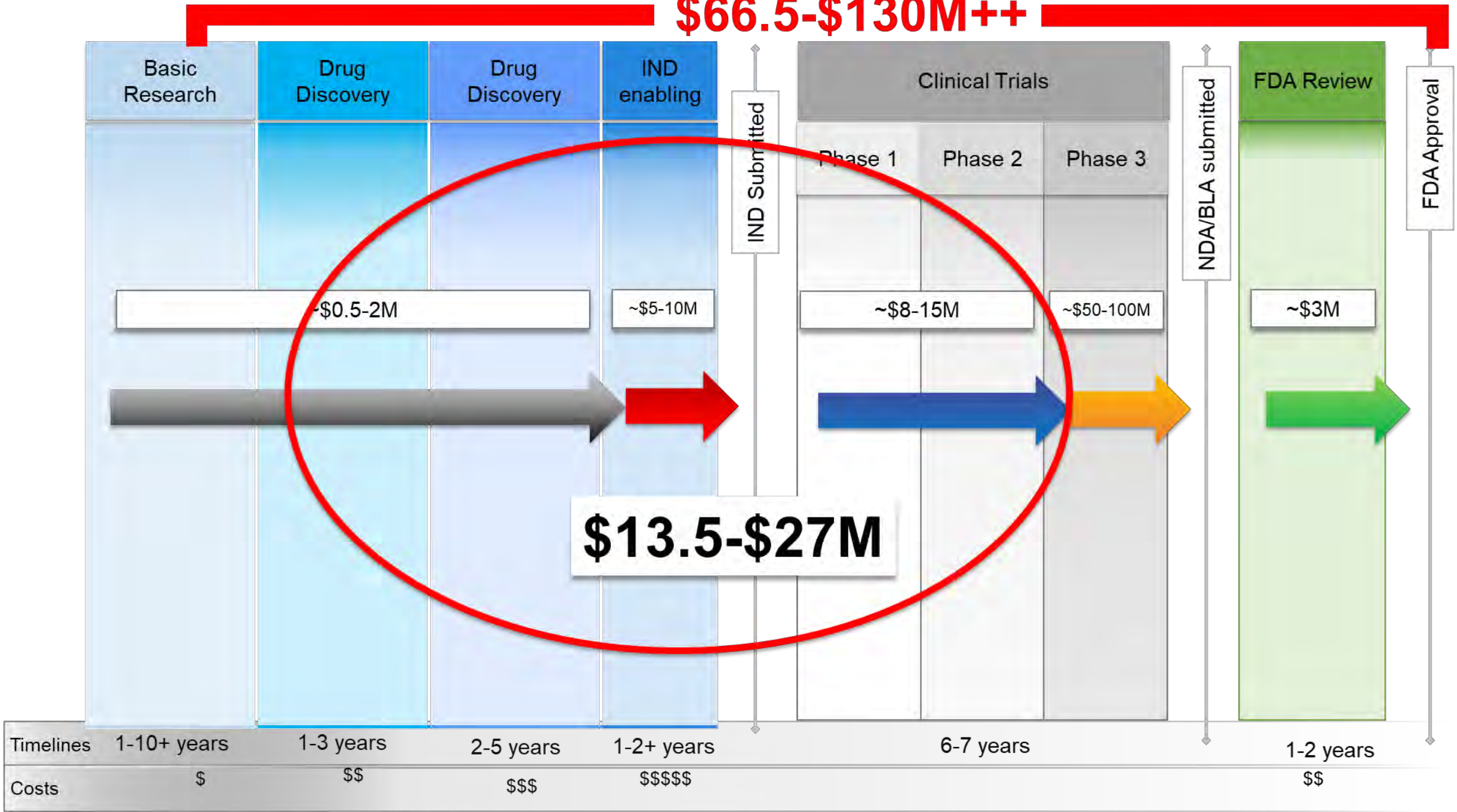
3 Downstream Targeting

Small Molecules/ Ligands

neuren · healx · BROWN

2 Paternal Gene Activation = "STOP THE STOP"

ASOs	IONIS · ultragenyx
ATFs	UCDAVIS
CRISPR	UNC · Penn · UCDAVIS · YALE
shRNA/ miRNA	ovid · Encoded THERAPEUTICS


$66.5-$130M++
Basic Research
Drug Discovery
Drug Discovery
IND enabling
IND Submitted
Clinical Trials
Phase 1
Phase 2
Phase 3
NDA/BLA submitted
FDA Review
FDA Approval
~$0.5-2M
~$5-10M
~$8-15M
~$50-100M
~$3M
$13.5-$27M
Timelines
1-10+ years
1-3 years
2-5 years
1-2+ years
6-7 years
1-2 years
Costs
$
$$
$$$
$$$$$
$$

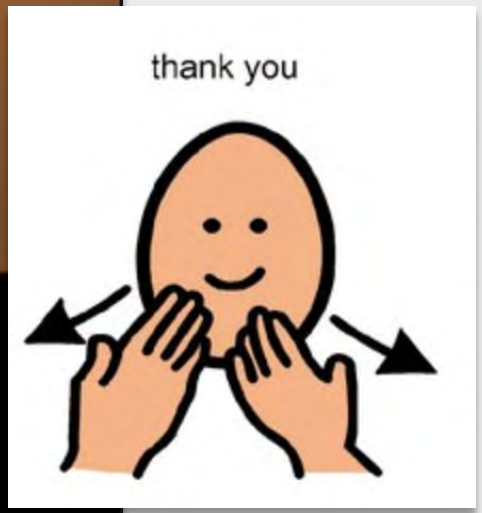
Drug development is hard…

- Living with rare disease is far harder!
- FAST works to **accelerate** and de-risk **FOR ALL LIVING WITH AS**
- Hard to rely on other parties to make your disorder a priority when times are tough, and **priorities change** sometimes overnight
- FAST will continue to accelerate excellent science for **ALL SHOTS ON GOAL**
- The priorities for FAST and the AS community will only change when every individual globally has access to transformative therapeutics
- BUT…we are not doing this alone

Quincy is #myreason:

TO FIGHT EVERY DAY…FOR A BETTER LIFE

Thank you



allyson.berent@cureangelman.org

Panel Discussion

Moderator:

Anne Rowzee, PhD

Meet Our Panelists

Erin Ward, MEd
President & Co-Founder
MTM-CNM Family Connection

Suzette James
Board of Directors, BDSRA Foundation
CLN2 Batten disease parent and advocate

Allyson Berent, DVM
Chief Science Officer, FAST

Questions?

Please submit your questions in the Zoom Q&A box.

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Thank you!

Webinar materials will be available in the coming weeks on FDA.gov.

#RegenMedEd