Why “models” matter - one step in the journey to Clinical Trial Readiness

Rodney Samaco, PhD
Rare Collective Strategies LLC

A bit about how I got here (past-to-now)

Leveraging rodent models as tools to optimize the translational framework → **Strategy & Business Development** → **Principal Rare Collective Strategies LLC**

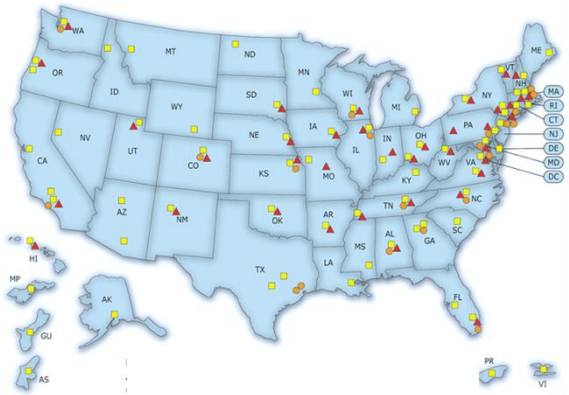
- Focus on Neuro Rare Genetic Conditions
- Optimized experimental and therapeutic proof of concept for rare genetic conditions (neurodevelopmental, behavioral epilepsy)

AUCD

Association of University Centers on Disabilities

143 Network Member Organizations

- University Centers for Excellence in Developmental Disabilities (UCEDD)
- Leadership Education in Neurodevelopmental and Related Disabilities (LEND)
- Intellectual and Developmental Disabilities Research Centers (IDDRC)



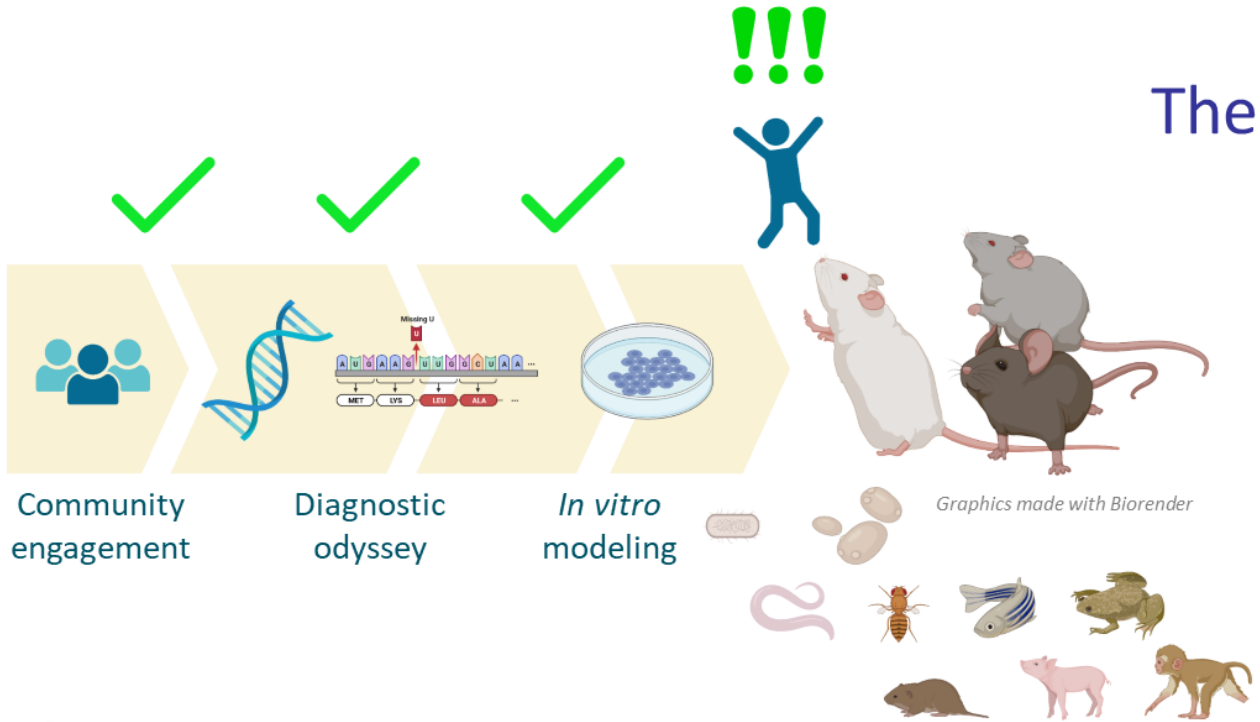
MOTIVATION

1. Can we identify reproducible, reliable preclinical surrogate endpoints in rodent models?
   - Outcome Measures and Biomarkers
   - Proof of concept studies needed in model organisms before testing in people

2. Do they track with experimental therapeutic manipulation(s) paired with features of disorder (e.g. onset, progression, severity)

3. Overcoming challenges to team science – conceptual, technical, operational, logistical [human capital & relationships]

Focus on *your* 'north star' with model studies



Unpack the 'what, why & how'

The goal ⟷ The motivation

Discovery vs. Hypothesis

- Developmental delay
- Seizures/EEG
- Speech
- Cognitive, Motor
- Regression
- Autonomic dysfunction

Leveraging *in vivo* models

Genetic deficiency in brain cells and during different periods of life → instructive but again - what is the intent

Tile image scan, *Gad2*-CRE inhibitory CKO

- Developmental
- Seizures/EEG
- Speech
- Behavior, Cognitive
- Motor
- GI
- Sleep

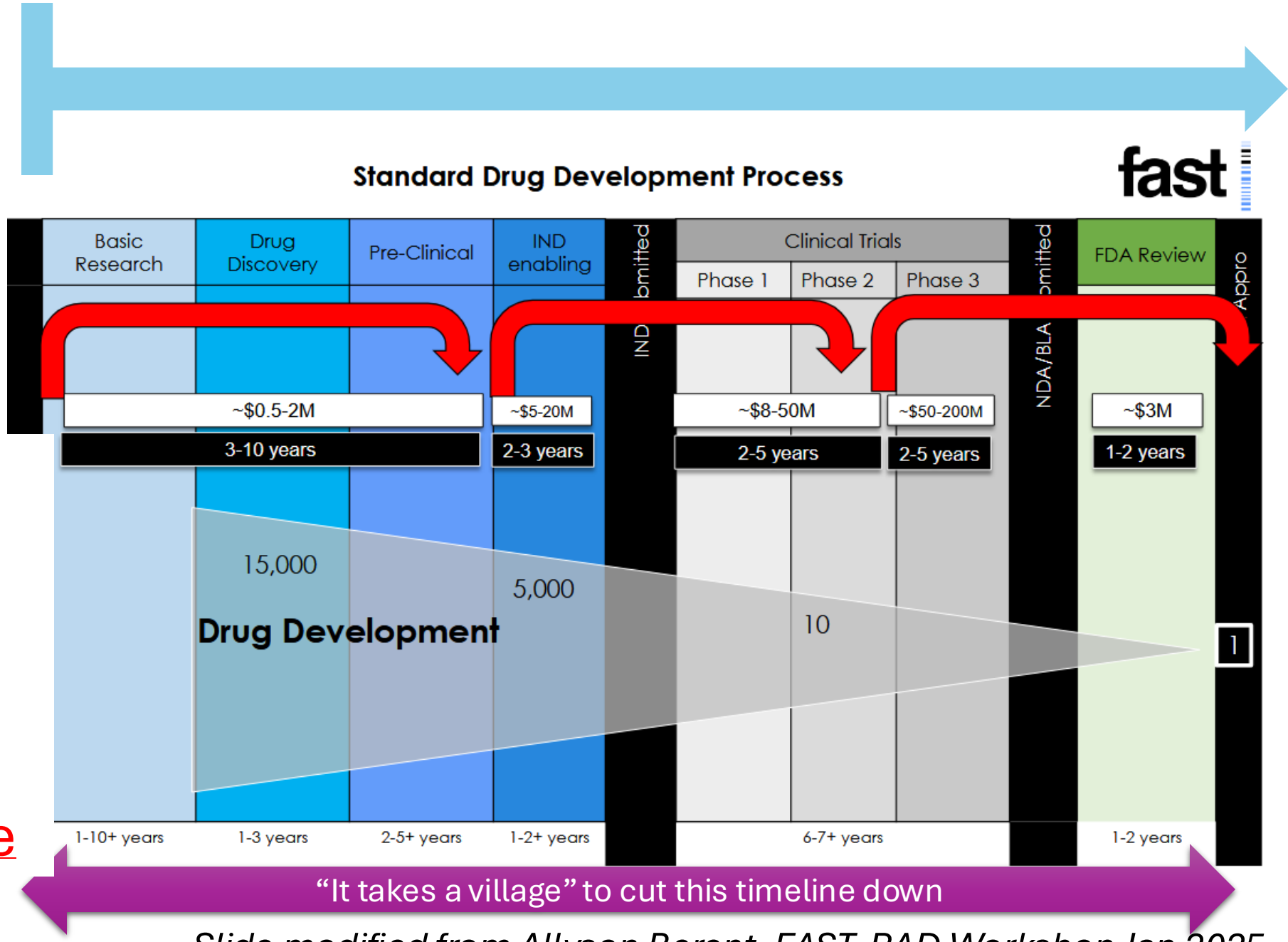
- What can we learn? Tools for the "why" [gene X] deficiency results in issues
- How can we leverage them? Identify actionable therapeutic targets, even independent of the "why"

So how does ‘model’ work fit in the journey to being clinical trial ‘ready’ - what does this mean, all together?

- Who should care, why should you care?
- What do we do next?
- How, when and where do you get involved?

You are here today, now!

Through proactive, committed & sustained community effort, others reduced this timeline – so can we



Slide modified from Allyson Berent, FAST, RAD Workshop Jan 2025

HOPE in ACTION

Ongoing Key Assets

1. Breadth & Depth of CTNNB1 & MED13L Clinical Features
   - Disease Concept Model
   - Natural History Study
2. Meaningful Readouts
   - Biomarkers
   - Outcome Measures
3. Preclinical Models
   - Preclinical Genetic Models
   - Patient-derived Cellular Models
4. Partnerships & Collaborations
   - Established Relationships
   - Ongoing Academic-Industry Partnerships
5. Proactive & Engaged Global Community
   - Involved with Broader Patient Group Efforts
   - Needs Assessment & Evaluation Data

Closing the clinical knowledge gap

Preclinical models ensure comprehensive tool box

Active Patient-Family Communities will drive the end-goal

Community, Domain Expertise, & Resources are necessary components to find answers - quickly and often

Community Expertise Resources

Tell me more - how can I get involved now?

SCIENCE AND RESEARCH

FUNDRAISING

COMMUNICATIONS

COMMUNITY ENGAGEMENT

ADMIN/FINANCE COMMITTEE

Connect with your org leadership members, volunteer and get involved

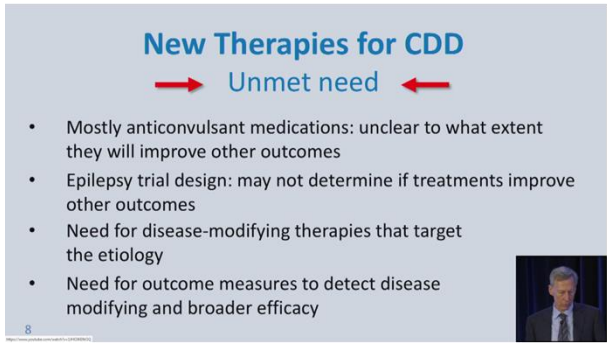
- Fundraising
- Social Media/Marketing
- Writing (grants, articles, blogs, your story, etc.)
- Community and Patient Engagement
- Event Planning
- Graphic Design
- Website Development
- Organizational and Strategic Planning
- Finance and Budgeting
- Scientific Research
- Other? You tell us!

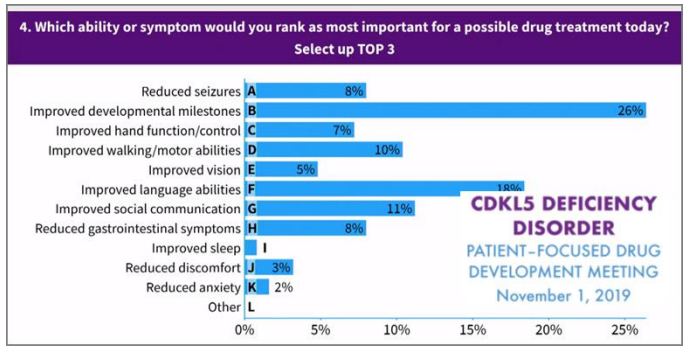
ONGOING CTNNB1 and MED13L community needs & engagement –

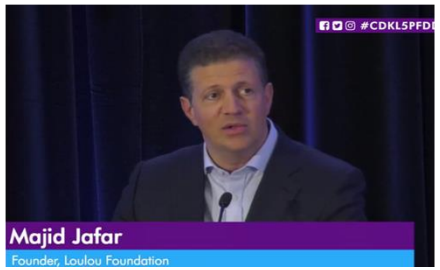
just one example of how your involvement will lead to ongoing attention

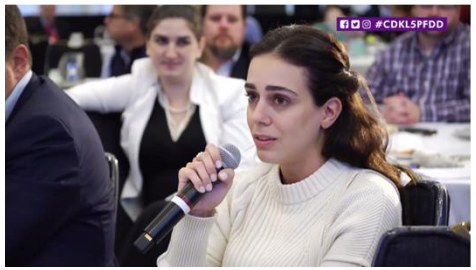
Meeting with FDA

- Aligning needs
- Patient-focused drug development meeting (2019) for another rare group









Be part of the solution.

Shape the End-Game for CTNNB1 & MED13L

CHAMP1 RESEARCH FOUNDATION

SETBP1 SOCIETY

Schinzel-Giedion Syndrome Foundation

SLC6A1 Connect
SLC6A1 Research & Support

FOXG1 RESEARCH
foxg1research.org

JJ,
Mia, Katis & Jeff

Cole,
Hugh, Haley & Eric

Ophelia,
Nuala & Rafe

Maxwell,
Riley, Mark & Amber

Amara
& Nasha

Samantha & Karen

IFCR
International Foundation for CDKL5 Research

2018 International CDKL5 Family Education & Awareness Conference

loulou FOUNDATION

2019 CDKL5 Forum

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CTNNB1
CONNECT AND CURE

THE MED13L FOUNDATION

CCC
COALITION TO CURE CHD2

2025 CHD2 Science and Family Conference

INADCURE FOUNDATION
FIGHTING INFANTILE NEUROAXONAL DYSTROPHY

Ariya
Alina, Leena & Anil Panwala