GALAXY Registry:
Generating Advancements through Longitudinal Analysis in X and Y Syndromes

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INTRODUCTION

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OUTLINE: RESEARCH FOR THE FUTURE

- What is research and why is it important?
- Example of a Registry in Fragile X Syndrome
- How can GALAXY benefit the X&Y Community?
- Why (and how) should I participate?

WHAT ARE OUR GOALS?

- To engage the X&Y Community in all stages of research
- To study questions that are important to individuals and families
- To support collaboration and sharing of data across centers
- To develop a sustainable infrastructure that will support future fundable research

WHAT IS RESEARCH?

"Systematic investigation in order to describe, explain, predict and control an observed phenomenon with the intent to contribute to generalized knowledge"

Systematic = scientific methods, ethical conduct

Investigation = to answer a question through study

Contribute to generalized knowledge = needs to apply to more than just one person or situation

WHY IS RESEARCH IMPORTANT?

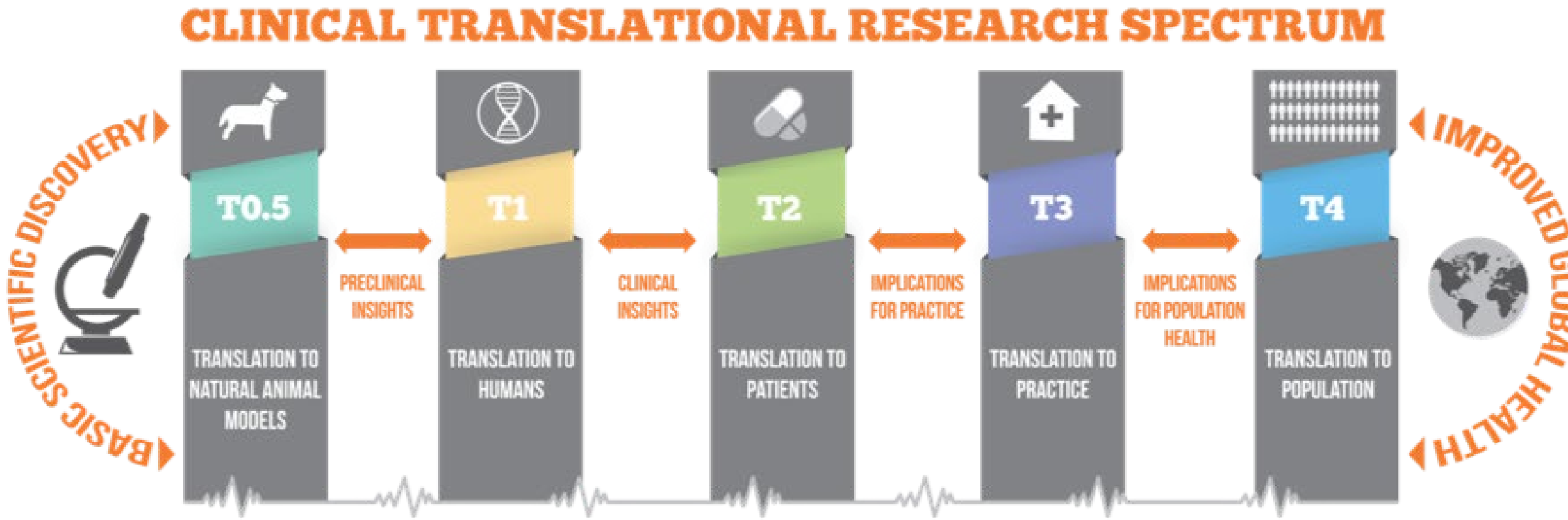
"scientific research is essential for improving the quality of human lives"

- Natural history of outcomes
- Causes of diseases
- Who is at risk
- Biological plausibility

- What works?
- What doesn't work?
- Risks and benefits

- Prevent or cure disease
- Treat conditions
- Improve quality of life

CLINICAL TRANSLATIONAL RESEARCH



RESEARCH IMPORTANCE EXAMPLE IN X&Y

Birth cohort studies of X&Y variations told us a lot about growth, development, and risks that led to changes in care and additional research areas

WHAT IS A RESEARCH REGISTRY?

- Collection of uniform information about individuals with a specific condition
- Usually longitudinal (on-going)
- Single or multicenter (or organization)
- Researcher or patient-powered (or both)
- Often connect patients and researchers
- Sometimes collect and store tissue samples (biobank)
- Power in numbers!

Why Registries Matter

Participation in a **registry** is likely to increase what we know about a specific condition, help health care professionals improve treatment, and allow researchers to design better studies on a particular condition, including development and testing of new treatments (“**clinical trial readiness**”)

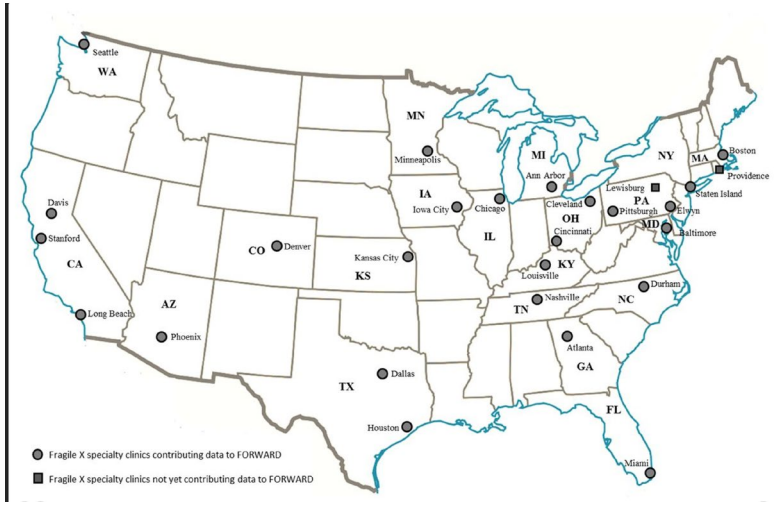
Fragile X Example

- Fragile X syndrome
  - Most common cause of inherited intellectual disability
  - Rare disease (1/4000 males; 1/8000 females)
  - Avg age of diagnosis 36 months
- Unanswered questions
  - Natural history
    - Prevalence of various problems (medical, developmental, psychological)
    - Limited information re: Aging in Fragile X
  - Medication trials
  - Newborn screening?
- Fragile X Clinic and Research Consortium
  - 2021 = 34 Clinics Nationwide

FORWARD
FRAGILE X ONLINE REGISTRY WITH ACCESSIBLE RESEARCH DATABASE

Fragile X FORWARD Registry

- **F**ragile X **O**nline **R**egistry **W**ith **A**ccessible **R**esearch **D**atabase
  - Started in September 2009
  - Funded by the Centers of Disease Control (CDC)
  - Enrolls all family members in a Fragile X family (inherited)
  - Database:
    - in-depth information about individuals with FXS
    - Data collected from each individual are longitudinal (over many years, collected annually)
    - Seek to better understand the medical, social, and behavioral changes individuals with FXS from infancy to late adult life
    - Collects: structured forms from parents and clinicians
    - De-identified data = information submitted does not contain identifying information about the participant
- Fragile X Clinic and Research Consortium



Sherman et al 2017

FORWARD Registry Success!

- >2500 patients in the database (11 years)
- Decades of longitudinal data = outcomes data
- 17 research publications resulting from FORWARD data (more pending)
- Help inform new treatments and therapies for individuals with FXS
- Help develop resources to help families
- Demonstrates the need and direction of future research
- Supports clinical trial development
- Launch of the Fragile X premutation registry 2020


GALAXY Registry
Generating Advancements through Longitudinal Analysis in X & Y Syndromes

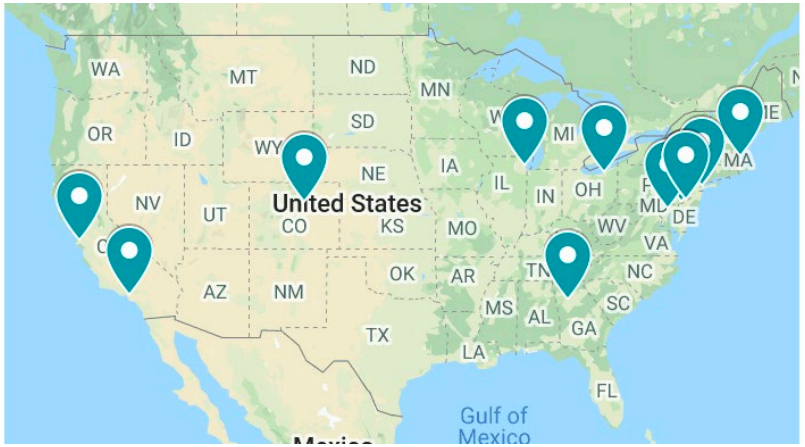
GALAXY REGISTRY

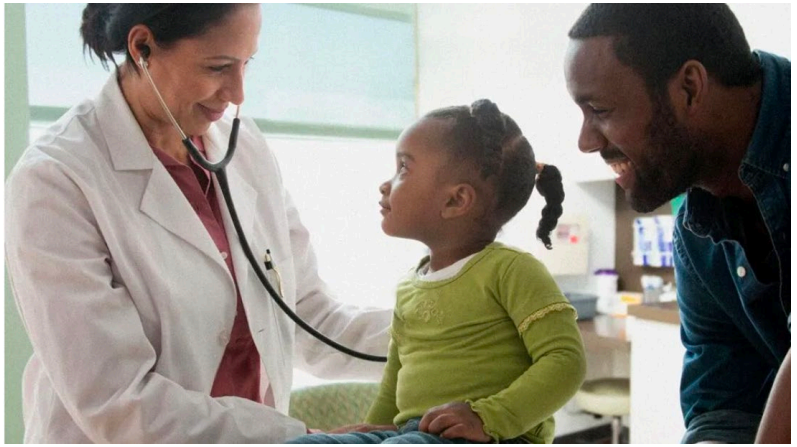
Multicenter clinical data registry and biorepository for individuals with X&Y variations to…

- quantify baseline clinical outcomes
- determine best clinical practices
- support future research and quality improvement efforts

…that will ultimately improve outcomes for individuals with X&Y variations

GALAXY REGISTRY





Steering Committee

- Sets agenda
- Integrates perspectives
- Policies & procedures
- Reports to AXYS

ACRC Clinics

- Provide patient care
- Input data into registry
- Use de-identified data for research

Patients

- Seen at a participating clinic
- Decide if their information can be used for research (consent)
- Decide if they want to participate in other ways

What is being asked of me?

- **Basic enrollment**: Giving permission for your clinical information (medical records) to be used for research
  - Nothing extra for you to do
  - Data like diagnoses, medications, test results, etc. are entered into REDCap (secure research platform) and updated each year
  - De-identified data can then be used by researchers approved by the Steering Committee
- **Additional options:**
  - Agreement to be contacted for new study opportunities
  - Participate in a couple surveys (~once per year)
  - Give a blood sample to be stored in the biobank

How is GALAXY Different?

GALAXY Registry (2021)	Previous AXYON (PEER) Registry (2015)
Clinical data entered (clinician / EMR)	Participant entered data
Minimal time from patients/families required	**Burden on participants** / families
Ongoing clinical data collection	Limited longitudinal capability (requires recontact)
Standardized and **validated data** collection	Unstandardized, **unvalidated**, free text
Full control over database platform	Difficult to make changes
GUID to track patients over time/space	No universal ID
Steering Committee structure (stakeholders) to determine policies and procedures	AXYS Board
AXYS funded start-up with Dr. Davis as PI using REDcap platform – academic center waives fees	PCORI funded through Genetic Alliance platform-**annual accumulating fees** after grant
Recruitment & consent through national ACRC clinics	Data retained and can participate in GALAXY
Goal >300 participants within 3 years	250 respondents after 2 years (but only 177 gave karyotype data)
All clinic patients eligible*	Requires internet access, time, knowledge of patient

HOW TO SUPPORT GALAXY

- Design the logo contest!
- Financial donations earmarked for GALAXY registry
  - AXYS or CHCO eXtraordinarY Kids Program
- Serve as a patient or family rep on the Steering Committee
- Help us engage the community and stakeholders
- Enroll when your center opens!

galaxy@ucdenver.edu


QUESTIONS?
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PARTICIPATING IN RESEARCH

WHY DO PEOPLE PARTICIPATE IN RESEARCH?

Possibility of Improving Own Health

MONITORING

"Just knowing more about the condition and what to expect"

"I have learned a lot about the condition"

LEARNING

"Having a child followed by a team of knowledgeable professionals is so valuable and provides so much support to parents."

"I think inaction is worse than action. Klinefelter Syndrome treatment is not well defined in infancy and neither are the benefits. I'd rather do all I can for my son in hope that he gets some benefit than do nothing and have to question if I could have done more for him."

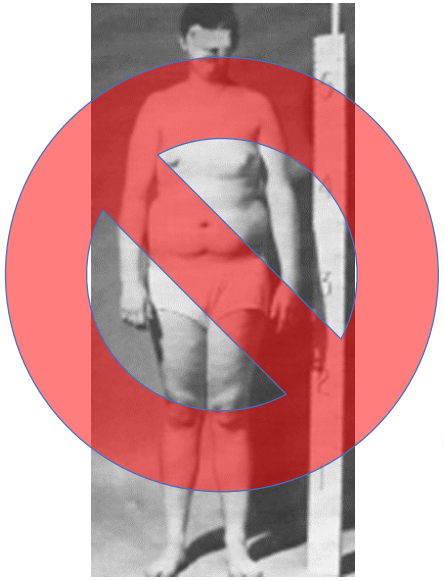
ACCESS ASSESSMENTS & INTERVENTIONS

"To provide more research on these children to help in the care and treatment of my son and all boys, current and future, who have xxy."

"Knowledge is power!"

WHY DO PEOPLE PARTICIPATE IN RESEARCH?

Altruism and Advancing Medical Knowledge



"I think there is so much misinformation about XYY in all of the research and other sources available to those newly diagnosed."

"Because the care I have received is down to people in the past taking part in studies"

"All research and information will help current and future generations"

"All patients should welcome the opportunity to help others by volunteering for research studies"

"So few providers have any experience with these chromosomal differences- the more information we can learn and pass along has the potential to help many more children."

"Knowledge is power!"

WHEN CONSIDERING PARTICIPATING

- Contact research team to learn more about the study
- Review any study website / flyers / other info
- Review consent form
- Ask questions!

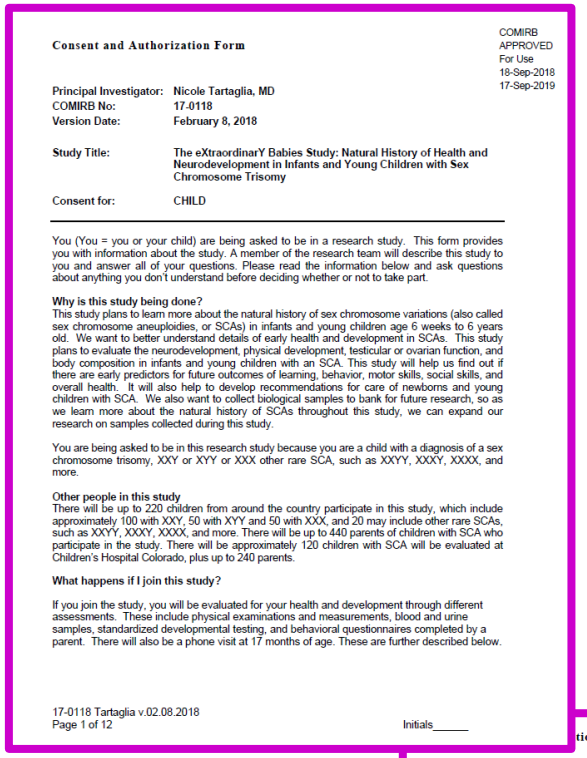
QUESTIONS TO CONSIDER ASKING

- What is the purpose of the study?
- Do I feel that this is important to be a part of?
- Who is going to be in the study? Do I qualify for the study?
- What kinds of tests and experimental treatments are involved?
- Why do researchers believe the experimental treatment being tested may be effective? Has it been tested before?
- How do the possible risks, side effects, and benefits in the study compare with my current treatment?
- Who sees my research information and how is it protected?
- How might this trial affect my daily life?
- How long will the trial last?
- Who is paying for the study?
- Will I be reimbursed for expenses? Will it cost me money?
- What type of long-term follow up care is part of this study?
- Will results of the study be provided to me? When?
- Who will be in charge of my care?

INFORMED CONSENT

Informed consent is the process of learning the key facts about a clinical trial before deciding whether or not to participate.

- Continuing process throughout the study to provide information for participants
- The researcher explains the details of the study to help someone decide whether or not to participate
- The research team provides an informed consent document that includes details about the study, such as its purpose, duration, required procedures, risks & benefits, and key contacts
- The participant then decides whether or not to participate in the study and sign the document
- Informed consent is not a contract, and the participant may withdraw from the trial at any time
- The participant gets a copy of the consent form



Consent and Authorization Form

COMIRB APPROVED For Use 18-Sep-2018 17-Sep-2019

Principal Investigator: Nicole Tartaglia, MD
COMIRB No: 17-0118
Version Date: February 8, 2018

Study Title: The eXtraordinarY Babies Study: Natural History of Health and Neurodevelopment in Infants and Young Children with Sex Chromosome Trisomy

Consent for: CHILD

You (You = you or your child) are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?
This study plans to learn more about the natural history of sex chromosome variations (also called sex chromosome aneuploidies, or SCAs) in infants and young children age 6 weeks to 6 years old. We want to better understand details of early health and development in SCAs. This study plans to evaluate the neurodevelopment, physical development, testicular or ovarian function, and body composition in infants and young children with an SCA. This study will help us find out if there are early predictors for future outcomes of learning, behavior, motor skills, social skills, and overall health. It will also help to develop recommendations for care of newborns and young children with SCA. We also want to collect biological samples to bank for future research, so as we learn more about the natural history of SCAs throughout this study, we can expand our research on samples collected during this study.

You are being asked to be in this research study because you are a child with a diagnosis of a sex chromosome trisomy, XXY or XYY or XXX other rare SCA, such as XXYY, XXXY, XXXX, and more.

Other people in this study
There will be up to 220 children from around the country participate in this study, which include approximately 100 with XXY, 50 with XYY and 50 with XXX, and 20 may include other rare SCAs, such as XXYY, XXXY, XXXX, and more. There will be up to 440 parents of children with SCA who participate in the study. There will be approximately 120 children with SCA will be evaluated at Children's Hospital Colorado, plus up to 240 parents.

What happens if I join this study?

If you join the study, you will be evaluated for your health and development through different assessments. These include physical examinations and measurements, blood and urine samples, standardized developmental testing, and behavioral questionnaires completed by a parent. There will also be a phone visit at 17 months of age. These are further described below.

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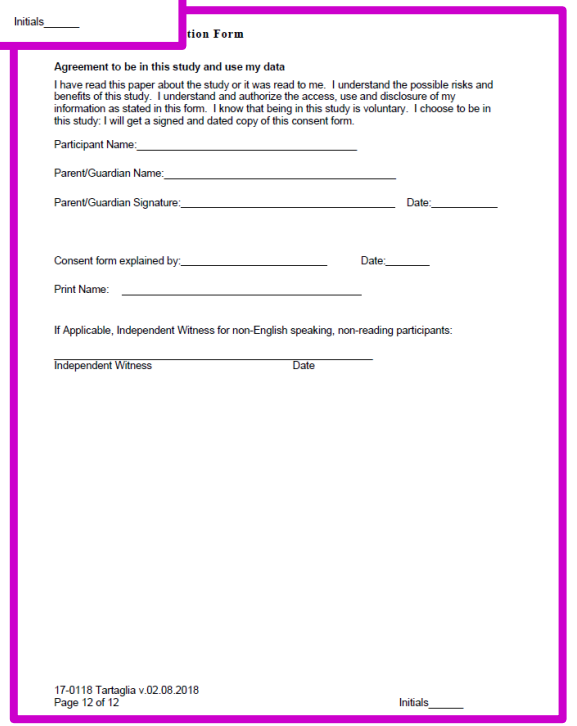
Initials_____



tion Form

Agreement to be in this study and use my data

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Participant Name:_____

Parent/Guardian Name:_____

Parent/Guardian Signature:_____ Date:_____

Consent form explained by:_____ Date:_____

Print Name: _____

If Applicable, Independent Witness for non-English speaking, non-reading participants:

_____ _____
Independent Witness Date

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Initials_____

KNOW YOUR RIGHTS!

- To have **enough time to decide** whether or not to be in the research study, and to make that decision **without any pressure** from the people who are conducting the research.
- **To refuse** to be in the study at all, or to stop participating at any time after you begin the study.
- To be told what the study is trying to find out, what will happen to you, what drug/device will be used in the study, and what you will be asked to do if you are in the study.
- To be told about the possible **risks** of being in the study.
- To be told about the possible **benefits** of being in the study.
- To be told whether there are any costs to be in the study and whether you will be compensated
- To be told who will have access to your information and how **your confidentiality** will be protected.
- To be told **whom to contact** with questions about the research, about research-related injury, and about your rights as a research subject.
- If the study involves treatment or therapy:
  - To be told about the other non-research treatment **choices** you have.
  - To be told where treatment is available should you have a research-related injury
- To **receive a copy** of the consent form that you will sign.
- To **ask any questions** you may have

THANK YOU!

EXTRAORDINARYKIDSCLINIC@CHILDRENSCOLORADO.ORG

WWW.EXTRAORDINARYKIDSCLINIC.ORG