Approved October 1, 2015

RE: Research Study entitled *"Placebo-controlled trial of Dextromethorphan in Rett Syndrome"*
JHM IRB Study # NA_00064949

Dear Parent,

We would like to invite your child who has Rett syndrome (RTT) to take part in our research study. Females and males with RTT, one year of age – 9.99 years of age, who have a mutation in the *MECP2* gene, may join this study.

This research is being done to study the effects of a drug known as dextromethorphan (DM) to see if it helps RTT patients. In RTT, there is an increase in the number of brain receptors for a substance known as glutamate. This substance and its increased receptors cause damage to the brain's nerve cells (called neurons). We will try to block this harmful over-stimulation of the neurons by use of DM to find out if the 5mg/kg/day of DM will improve cognition, behavior, or seizures, when compared to a solution not containing the DM medication (placebo).

If you agree to have your child join this study, s/he will be admitted to the Johns Hopkins Pediatric Clinical Research Unit (PCRU) in the Johns Hopkins Institute for Clinical and Translational Research (ICTR) for an initial one-day/one-night inpatient admission, during which s/he will be given a test dose of DM to see how it is cleared from his/her body. If the DM is cleared rapidly, s/he would be able to take part in the 3-month trial where s/he would be randomized to the drug or placebo. There will be two required interim evaluations to be done at 2 weeks and at 1 month after starting the DM study, and an extended day outpatient end-of-study visit to the PCRU after 3 months of being on the DM. Our research nurse or research associate will contact you at least weekly during the first month of the study, and then at least monthly through the end of the 3-month study. The total length of time in the study is 3 months.

This research study is funded by the Food and Drug Administration and the Johns Hopkins Institute for Clinical and Translational Research (ICTR)/NBRU. Therefore, all test procedures as part of the study protocol will be performed free-of-charge, at no cost to you or your child. The DM or placebo will be provided to your child free-of-charge during this 3-month drug study.

The study will reimburse up to $2,000 for the cost of your RTT child and one parent's travel (a total of up to $1,000 for each of the two visits) to and from Johns Hopkins..

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If you are interested in having your child participate in this research study, please contact us at phone # (443) 923-2778, or 1-800-873-3377 ext 2778, or by emailing Barbara Ann Bradford, Research Coordinator, bradford@kennedykrieger.org.for further details, including a read-only version of the *"Research Participant Informed Consent and Privacy Authorization Form"* which explains all details of the study's Procedures, Risks, and Benefits.
If you have continued interest after reading the study documents, please feel free to contact us at any time to answer any further questions you may have regarding details of the study, after which a mutually-convenient date can be scheduled for the initial admission to our research unit.

If you ***do not*** wish to participate in this study, please send us the attached "Not Interested" form, or you can email Barbara Ann at bradford@kennedykrieger.org expressing your disinterest in this study, so that we do not contact you again.

If your child does not participate in this study, his or her care at Johns Hopkins or Kennedy Krieger will not be affected.

Sincerely,

SakkuBai Naidu, MD
Principal Investigator

SN/bab

Enclosure: Not interested response

JOHNS HOPKINS
MEDICINE

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IF NOT INTERESTED, PLEASE COMPLETE THIS FORM AND MAIL IN A SEALED ENVELOPE TO:

The Kennedy Krieger Institute
707 North Broadway
5th Floor Tower
Baltimore, MD 21205
Attn: Dr. Sakkubai Naidu

( ) I am *not* interested in participating in this clinical trial/research study (PCTDMRTT)

Name of Participant: _____

Name of Parent: _____