

IRSF awards \$2.0M for Research

IRSF awards \$2.0M for Translational Research for Rett Syndrome in the first half of 2012

The International Rett Syndrome Foundation (IRSF) announced today that the Board of Directors have approved funding in the amount of \$1.3M to support new grants for translational research ranging from clinical studies and developing outcome measures to preclinical studies of new compounds in mouse models of Rett syndrome (RTT). These new awards bring the 2012 research spending thus far to \$2.0M for Translational research.

The mission of IRSF is to advance research towards new treatments for Rett syndrome by investing in both basic and translational research grants. Applications undergo a rigorous process of review, and grants that are deemed of high scientific merit by a peer-review panel composed of members of IRSF's Scientific Review Board (SRB) are recommended for funding by Chief Science Officer Steve Kaminsky, PhD to IRSF's Board of Directors who makes the final funding decision.

The Translational Research Program of the IRSF's Grants & Research department funds early and late stage translational research to treat and reverse Rett syndrome (RTT) using two grant mechanisms, Help Accelerate Rett Therapeutics (HeART) and the Advanced Neurotherapeutic Grant of Excellence (ANGEL), respectively.

Two ANGEL grants were awarded in this first cycle of the Translational Grant Program this spring. The first ANGEL award will fund Phase I and Phase IIa of the NNZ-2566 clinical study in adult patients with Rett syndrome. This study will be spearheaded by Dan Glaze, MD and Jeffrey Neul, MD, PhD in conjunction with Neuren Pharmaceuticals. IRSF previously sent out an IRSF flash announcing Neuren's pursuit of an Investigational New Drug (IND) application for NNZ-2566. With IRSF funding, Baylor College of Medicine and Neuren are well-positioned to move forward with this clinical study upon FDA approval of the IND.

The second ANGEL award will fund a pre-clinical study of two compounds that may suppress MECP2 mutations that result in short forms of the MeCP2 protein. These types of mutations are found in 30-35% of all those with MECP2 mutations. Therefore, these compounds have the potential to help a great number in the RTT population. IRSF is excited that one of the tested compounds is already FDA approved, which will help move it faster to clinical trial in humans should it have positive results in the mouse model.

Three HeART grants were also awarded in this first cycle of the Translational Grant Program. These grants are to provide starter funds for early Translational work. In this portfolio, there are awards for a pilot pre-clinical study, a pilot eye-tracking communication study, and a pilot collaboration with a contract research organization (CRO) to help develop and test new therapeutics faster and move them through the pre-clinical stage towards clinical studies more efficiently through standardized testing.

Collectively, these awards will contribute to IRSF's program for bringing "Research to a Reality", where the awards feed into different entry points of the drug development pipeline for Rett syndrome. IRSF hopes to fill this pipeline with new treatments and compounds to meet potential therapeutic strategies at the following three levels:

- Symptomatic Therapy - targeting the symptoms associated with Rett syndrome discussed above, such as seizures or anxiety

- Disease Modifying Therapy - developing treatments that change the severity and timing of the disease course;

- Disease Reversing Therapy - reversing the disease and restoring function after disease onset.

Steve Kaminsky, PhD, Chief Science Officer of IRSF, commented, "This is an exciting time for translational research for Rett syndrome. As we look toward the horizon I am hopefully optimistic."

2012 New Translational Research Awards

Angel Awards

- Daniel G. Glaze, MD, Baylor College of Medicine and Jeffrey Neul, MD PhD, Baylor College of Medicine and the Jan and Dan Duncan Neurological Research Institute

A randomized, double-blind placebo controlled trial of NNZ-2566 (IGF-1{1-3}, glycyl-L-2-methylprolyl-L-glutamine acid) with open label extension in adults with Rett syndrome

- N. Carolyn Schanen, MD PhD, Nemours Biomedical Research and Jeffrey Neul, MD PhD, Baylor College of Medicine and the Jan and Dan Duncan Neurological Research Institute

Nonsense suppression as a therapeutic approach to Rett syndrome

- Walter Kaufmann, MD, Children's Hospital Boston

A Phase 2b placebo-controlled cross-over study of rh-IGF1 (mecasermin [DNA] injection) for treatment of Rett syndrome and development of a novel biomarker of cortical function

HeART Awards

- Aleksandra Djukic, MD PhD, Tri-State Rett Syndrome Center, Montefiore Medical Center, Albert Einstein College of Medicine

Language comprehension and processing in Rett syndrome: A pilot study of eye tracking

- Lee-Way Jin, MD PhD, Regents Of The University Of California - Davis

Preclinical studies of allopregnanolone, a positive GABAA receptor modulator

- Daniela Brunner, PhD, PsychoGenics Inc.

PPAR-sparing insulin sensitizers for Rett Syndrome

2012 New Contracts

- Jeffrey Neul, MD PhD, Baylor College of Medicine and the Jan and Dan Duncan Neurological Research Institute
Creation of a DNA repository for Rett syndrome

- Alan Percy, MD, The University of Alabama at Birmingham
Placebo-controlled trial of Lexapro (escitalopram) for anxiety in Rett Syndrome

- N. Carolyn Schanen, MD PhD, Nemours Biomedical Research
Development of a Humanized Mouse Line by Knock-in

2012 Renewed Contracts

- Walter Kaufmann, MD, Children's Hospital Boston
RettSearch Consortium's Clinical Coordinating Center

- Helen Leonard, MD, Telethon Institute for Child Health Research

InterRett - Phenotype Database

For further information on the IRSF Scientific Grant program contact Janice Ascano at jascano@rettsyndrome.org or 917-267-4504.