

**PRESS RELEASE:**

# Rett Syndrome Research Trust Awards \$6.2 Million in 2017 to Speed a Cure for Rett Syndrome

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## Rett Syndrome Research Trust Awards \$6.2 Million in 2017 to Speed a Cure for Rett Syndrome



**TRUMBULL, CT** – The Rett Syndrome Research Trust (RSRT) announced today research awards of **\$6.2 million** made in 2017. RSRT’s sole and urgent goal is to abolish Rett Syndrome and related disorders. To that end, RSRT has awarded **\$47 million** to research, both basic and clinical, since its launch in 2008.

Rett Syndrome is caused by mutations in a gene called *MECP2* that result in a cascade of devastating symptoms that worsen over time. These symptoms begin to manifest in early childhood and leave Rett sufferers dependent on 24-hour-a-day care for the rest of their lives.

Last year RSRT implemented a three-year, \$33 million, strategic research plan, *Roadmap to a Cure* that includes four key components: *Cure, Treat, Enable, Learn*. The 2017 awards strengthen and enhance the *Cure* and *Enable* components of the *Roadmap*. The *Cure* component features four bold approaches that attack Rett at its core: gene therapy, reactivation of the *MECP2* on the inactive X chromosome, RNA modification and protein replacement. The *Enable* component ensures that potential therapeutics can be successfully measured both in the lab and the clinic; through the generation of cell lines and other valuable resources necessary to test new therapies at the bench, and through the outcome measures and biomarkers development initiative to identify key parameters that predict or correlate with efficacy in patients.

“RSRT’s mission is to develop new therapies and a cure for Rett syndrome. The remarkable progress in the past year has elicited a palpable sense of optimism that a cure for Rett Syndrome is possible. Since it is not possible to predict where therapeutic breakthroughs will first occur, RSRT seeks to increase the odds of success by pursuing the most promising therapeutics in parallel. Thus, our key metric for measuring success is the breadth and strength of our therapeutic development pipeline,” stated Randall Carpenter, MD, Chief Scientific Officer of RSRT.

### **Highlights of RSRT's 2017 awards:**

- **An award of almost \$1.6 million** was made to James Wilson, MD, PhD who joins our *Gene Therapy Consortium* with a primary focus of improving delivery of genes to the brain. Dr. Wilson has been a pioneer and a leader in the gene therapy field for three decades making a number of seminal discoveries. He runs the largest academic based gene therapy program in the world. Dr. Wilson’s involvement in our *Consortium* will leverage deep expertise and resources as well as ongoing gene therapy collaborations with several major pharmaceutical and biotech partners.

### Highlights of RSRT's 2017 awards (cont):

- Stuart Cobb, PhD is also part of our *Gene Therapy Consortium*. Beyond traditional gene therapy the Cobb lab is also pursuing a therapy called Spliceosome-Mediated RNA Trans-splicing (SMaRT). This technology would enable the correction of the vast majority of *MECP2* mutations by splicing out exons 3 and 4 and replacing with mutation free exons. **The recent award of \$290,000** provides funding to accelerate this exciting technology. The SMaRT reagents will need to be delivered to the brain via vector so our gene therapy efforts will also be very relevant for this approach.
- **An award of \$600,000** was made to Rudolf Jaenisch, PhD that leverages a novel technology, CRISPR, that has taken the scientific world by storm. CRISPR will be used to deliver epigenetic molecules to the inactive *MECP2* with the goal of activating it by synergistically removing methyl tags and adding acetyl tags. It's important to note that the CRISPR guides and epigenetic molecules will need to be delivered to patients via vectors in much the same way as gene therapy. Any valuable insights learned from our gene therapy work will be applicable to this strategy as well.
- **Funding of \$142,000** will fund a pilot study in the lab of Ben Philpot, PhD to explore reactivation of the silent *MECP2* with a novel approach using genetic tools, called zinc finger proteins, that directly interact with the chromosome region responsible for switching the *MECP2* gene on and off, called the promoter. In diseased Rett neurons the promoter of the normal *MECP2* gene copy is kept in the "off" state by certain modifications that prevent binding of proteins, called transcription factors. Zinc finger proteins are designed to specifically target the *MECP2* promoter and locally deliver transcription factors to override the silenced state and jump-start gene activation. Ultimately, promising zinc finger/transcription factor complexes will need to be delivered to the brain. Vectors being developed by our *Gene Therapy Consortium* can be easily adapted to enable delivery.
- **An award of \$500,000** was made to the biotechnology company, Q-State Biosciences, and \$54,000 to collaborator Michael Greenberg, PhD to advance our goal of precision medicine for individuals with Rett Syndrome. The company has developed methods that use cells from individuals with mutations in *MECP2*, to study disease, explore possible treatments, and, hopefully predict an individual's response to specific therapeutics. In the present study, the processes for generating the "brain in a dish" will be optimized and the changes that result from Rett mutations will be fully characterized. Drugs and biological therapeutics will then be tested in these cells. This platform has implications for all of our programs – from our curative programs such as gene therapy, RNA editing, *MECP2* reactivation and RNA trans-splicing to downstream targeted drugs such as ketamine.

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## Highlights of RSRT's 2017 awards (cont):

- An award of almost \$2.4 million has made possible the launch of the *Rett Syndrome Clinical Trial Consortium* with the primary objective of providing expert Rett physicians with the personnel and resources necessary to execute high-quality clinical trials in a timely and efficient manner. This *Consortium* will initially fund the following Rett Syndrome Clinics: *Boston Children's Hospital; Drs. David Lieberman & Mustafa Sahin | Children's Hospital of Philadelphia; Dr. Eric Marsh | Vanderbilt University Medical Center; Dr. Jeff Neul | Children's of Alabama; Dr. Alan Percy | Center for Rare Neurological Diseases (Atlanta); Dr. Daniel Tarquinio*

"I have an 8-year-old daughter with Rett Syndrome. What I care about is research that can profoundly change her life and the lives of all children and adults who fight this disorder so bravely every day. RSRT's 2017 research awards aim to do just that, and I'm honored and proud to be associated with them. Every single family that fundraises for us and every one of our donors make this research possible, and for that they have my deepest thanks. These awards are also a testament to how Monica Coenraads and Randy Carpenter have recruited a team of world-class scientists to attack Rett head on," states Tim Freeman, RSRT's Chief Development Officer.

## List of 2017 Awards by Roadmap to a Cure category:

### CURE

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*Gene Therapy Consortium*

**James Wilson (University of Pennsylvania)**

**\$1,585,886**

*Optimizing Gene Therapy for Rett Syndrome*

**Kathrin Meyer (Nationwide Children's Hospital)**

**\$221,004**

*Additional Support for RNA-trans splicing Efforts in Rett Syndrome*

**Stuart Cobb (University of Edinburgh)**

**\$290,000**

*Reactivation of MECP2 with Epigenome Editing Tools to Rescue Rett Syndrome*

**Rudolf Jaenisch (Whitehead Institute for Biomedical Research)**

**\$599,850**

*Pilot Study for Reactivation of Silenced Mecp2 by Artificial Transcription Factors*

**Ben Philpot (University of North Carolina - Chapel Hill)**

**\$141,912**

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### List of 2017 Awards by Roadmap to a Cure category (cont):

#### ENABLE

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*Development of an In-Vitro Cell System For Discovering and Evaluating the Effects of Therapeutic Candidates on Neurons Produced Using Rett Patient Ips Cells*

**Q State BioSciences and Michael Greenberg (Harvard University)**

**\$553,967**

*Tri-State Rett Syndrome at Montefiore*

**Aleksandra Djukic**

**\$103,000**

*Clinical Trial Consortium*

**David Lieberman & Mustafa Sahin, Eric Marsh, Jeff**

**Neul, Alan Percy, Daniel Tarquinio**

**\$2,375,000**

#### MECP2 Duplication Syndrome

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*Investigating the Potential of Antisense Oligonucleotide Therapy for MECP2 Duplication Syndrome*

**Huda Zoghbi (Baylor College of Medicine)**

**\$299,898**

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## **Our Partners**

RSRT's partners in supporting this work include every affected family that fundraises for us and every individual and organizational donor who shares with us a sense of urgency to change the lives of all who suffer with Rett and related disorders. Some of the parents' organizations around the world that play a key role in making this research possible include Reverse Rett (UK), Rett Syndrome Research & Treatment Foundation (Israel), Rett Syndrome Ireland, and Rett Syndrom Deutschland. Major parent-led organizations in the U.S. that support our work include Girl Power 2 Cure, Eva Fini Fund at RSRT, Kate Foundation for Rett Syndrome Research, New Jersey Rett Syndrome Association, and Rett Syndrome Association of Massachusetts.

## **About the Rett Syndrome Research Trust**

The Rett Syndrome Research Trust (RSRT) is a nonprofit organization with a highly personal and urgent mission: a cure for Rett Syndrome and related *MECP2* disorders. RSRT operates at the nexus of global scientific activity enabling advances in knowledge and driving innovative research. In March of 2017 RSRT announced *Roadmap to a Cure*, a three-year, \$33 million strategic research plan. The plan prioritizes four curative approaches with gene therapy as our lead program. In June of 2017 the biotechnology company, AveXis, announced its intent to advance RSRT's gene therapy program to clinical trials. Since 2008, RSRT has awarded \$47 million to research. To learn more, please visit [www.reverserett.org](http://www.reverserett.org)

## **About Rett Syndrome**

Rett Syndrome is a genetic neurological disorder that affects predominately girls but can rarely also affect boys. It strikes randomly, typically at the age of 12 to 18 months, and is caused by random mutations of the *MECP2* gene on the X chromosome. Rett Syndrome is devastating as it deprives young children of speech, hand use, and normal movement often including the ability to walk. Symptoms can also include anxiety, seizures, tremors, breathing difficulties, and severe gastrointestinal issues. While their bodies suffer, it is believed that their cognitive abilities remain largely intact. Although most children survive to adulthood, they require total round-the-clock care.