PRESS RELEASE

RSRT Awards $10 Million to Preeminent Researchers in Pursuit of Curing Devastating Neurological Disorder

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TRUMBULL, CT - Thanks to a $10 million investment in Rett Syndrome research in 2018 — the largest annual award since the organization was founded in 2008 — the Rett Syndrome Research Trust (RSRT) is fueling exciting new collaborations and advances from an international group of world-class scientists that offer new hope for families coping with this devastating disease. Total research awards to date by RSRT have reached $57 million.

Rett Syndrome is caused by mutations in a gene known as MECP2 resulting in a constellation of serious, progressive and disabling neurological symptoms that emerge during early childhood and eventually rob sufferers of the ability to speak, move normally or use their hands, among other devastating deficits.

Yet there is reason for optimism, now more than ever. Early in 2018, RSRT made a decision to increase investment in several key areas and to recruit elite scientists to execute in these areas. These areas include 1) gene therapy, where healthy copies of the MECP2 gene are introduced to compensate for mutated ones 2) DNA editing, where a specific mutation in the genome is targeted and permanently corrected and 3) RNA editing, which focuses on correcting mutations in RNA. Given that DNA and RNA editing can be achieved in a number of different ways, RSRT is simultaneously pursuing all possible modalities to be sure to cover every therapeutic avenue.

The new awards are being made as part of RSRT’s four-pronged strategic research plan—the Roadmap to a Cure—including the components Cure, Treat, Enable, and Learn.

“At RSRT we have one bold, challenging goal – to cure Rett and related MECP2 disorders. To that end, RSRT has developed the first and only comprehensive and aggressive plan to cure Rett Syndrome. The strategies are identified, the scientists recruited and our internal research team poised to not only monitor and evaluate progress but to also be vigilant for new technologies on the horizon,” said Monica Coenraads, RSRT’s Executive Director. “Our important work is made possible by the passion and urgency felt by families affected by Rett who fundraise for us. As a parent of a young woman with Rett I am beyond grateful for these efforts. Our success will require the continued support of these families and beyond.”
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The following are highlights of the projects that earned an RSRT award in 2018, all of which focus on the vital first component of the Roadmap—a cure:

- **Almost $700,000 in additional funding for the Gene Therapy Consortium 2.0.** In 2014 RSRT conceived of and launched the Gene Therapy Consortium 1.0. Data generated by this Consortium led to the company AveXis’ decision to pursue gene therapy trials in Rett Syndrome individuals, set to begin this year. In the meantime, RSRT has recruited James Wilson, MD, PhD, to Consortium 2.0, leader of the world’s largest academic gene therapy program at the University of Pennsylvania. He joins Adrian Bird, PhD and Stuart Cobb, PhD both from the University of Edinburgh. The goal of Consortium 2.0 is to get a next generation gene therapy product ready for clinical testing by 2021.

- **Nearly $2 million to Beam Therapeutics for a DNA editing program to correct MECP2 mutations.** Founded by Keith Joung, PhD, designated as one of the most cited researchers worldwide; David Liu, PhD, named by Nature as one of 2017’s top 10 researchers in the world; and Feng Zhang, PhD, one of the pioneers of the CRISPR gene editing field, Beam is applying the cutting-edge gene editing tool known as CRISPR to target specific point mutations in DNA and permanently fix them. This exciting project harnesses the expertise, resources, and industrial approach of Beam to discover a novel class of therapeutics for Rett Syndrome.

- **More than $2.3 million to correct MECP2 mutations in RNA.** Led by investigators Guoping Feng, PhD, Feng Zhang, PhD, and Robert Desimone, PhD of MIT, the Broad Institute and Harvard University, this project will develop therapeutics using Zhang’s CRISPR Cas13 technology to target RNA rather than DNA.

- **More than $2.4 million for RNA and DNA editing to treat Rett Syndrome.** Jonathan Watts, PhD and his colleagues will put their deep knowledge of RNA chemistry to work developing RNA editing therapeutics. Their institution, University of Massachusetts Medical School, is renowned for their work on RNA with faculty receiving both a Nobel and a Breakthrough Prize. For DNA editing the aim will be to replace the two exons where 97% of MECP2 mutations reside.

- **Almost $1 million to two RNA editing projects being undertaken in the lab of long-time Rett researcher Gail Mandel, PhD and her colleague, John Sinnamon, PhD of Oregon Health and Sciences University and newcomer to Rett, Peter Beal, PhD of University of California Davis.** These two West Coast labs are editing RNA by leveraging the naturally-occurring editing enzyme in neurons known as ADAR.
**List of 2018 Awards**

**Adrian Bird/Stuart Cobb**  
University of Edinburgh  
*Gene Therapy Consortium 2.0*  
$653,856

**BEAM Therapeutics**  
*Developing a pre-clinical DNA base editing program to precisely correct the genetic cause of Rett Syndrome in the central nervous system*  
$1,870,660

**Jonathan Watts/Scot Wolfe/Eric Sontheimer/Anastasia Khvorova**  
University of Massachusetts  
*RNA and Genome editing for treatment of Rett Syndrome*  
$2,403,735

**Guoping Feng/Feng Zhang/Robert Desimone**  
Massachusetts Institute of Technology /Broad Institute/  
Harvard University  
*RNA-editing as a gene therapy approach for Rett Syndrome*  
$2,332,000

**John Sinnamon**  
Oregon Health and Sciences University  
*New editing enzymes for RNA*  
$345,000

**Peter Beal**  
University of California Davis  
*New molecular tools for directed editing of MECP2 mutations associated with Rett Syndrome*  
$563,870

**Allan Jacobson/Jonathan Watts**  
University of Massachusetts Medical School  
*Read-through of premature termination codons for treatment of Rett Syndrome*  
$323,000

**Andrea Cerase**  
Queen Mary University of London  
*Reactivation of MECP2 and CDKL5 genes by functional deactivation of Xist RNA*  
$351,022

**Additional Funding/Bridge Funding**

**David Lieberman**  
Boston Children’s Hospital  
*Clinical Trial Consortium*  
$74,792

**Antonio Bedalov**  
Fred Hutchinson Cancer Research Institute  
*Reactivating MECP2*  
$38,000

**Victor Faundez**  
Emory University  
*Outcome Measures and Biomarkers Development*  
$40,480

**Autism Science Foundation**  
$17,500

**MECP2 Duplication Syndrome**

**Huda Zoghbi**  
Baylor College of Medicine  
*A forward genetic screen to identify druggable modulators of MECP2 levels*  
$752,660
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, for which $24 million has been pledged or contributed by generous donors, 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 $57 million to research. To learn more, please visit www.reverserett.org

About Rett Syndrome
Rett Syndrome is a genetic childhood neurological disorder caused by random mutations of the MECP2 gene on the X chromosome that affects predominately girls but can rarely also affect boys. Its symptoms typically become apparent between the ages of 12 to 18 months. Rett Syndrome is devastating as it deprives young children of speech, hand use, and normal movement often including the ability to walk. As the children enter childhood the disorder brings 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.