rett syndrome research trust

PRESS RELEASE

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

Media Contacts:
Monica Coenraads
Executive Director, RSRT
203.445.0041
monica@rsrt.org

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January 22, 2019

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.

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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 deactivaton of Xist RNA
$351,022

Additional Funding/Bridge Funding

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

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

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

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

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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.