Press Release:
Momentum Builds in Rett Research as RSRT Awards a Record $7.2 Million in 2013

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Continuing to expand the depth and breadth of high-impact research, the Rett Syndrome Research Trust (RSRT) awarded a record **$7.2 million** to new scientific explorations in 2013. Since RSRT's inception five years ago, the organization has committed almost **$20 million** to novel research and basic science to decode and defeat Rett Syndrome.

This investment is made possible through the enterprise of highly motivated families and supporters of children and adults with Rett Syndrome in the United States, and through our growing global alliances listed below. We are especially grateful for our partnership with **Reverse Rett** (UK), **Rett Syndrome Research & Treatment Foundation** (Israel) and the **MECP2 Duplication Syndrome community**.

Rett Syndrome is caused by mutations in a gene called MECP2 that causes numerous devastating symptoms that worsen over time. These begin to manifest in early childhood and leave Rett sufferers completely dependent on 24-hour-a-day care for the rest of their lives. While the function of MECP2 remains elusive we know that it acts globally and impacts numerous systems in the body.

RSRT stimulates, organizes and funds research to defeat this disorder via three essential approaches:

- **Treatment** – Targeting downstream effects of MECP2 mutations via drugs and/or procedures. This is largely a symptom-by-symptom approach to relieving some of Rett Syndrome's many manifestations and improving quality of life.
- **Basic science** – Investing in rigorous science to develop an accurate, detailed knowledge base of the neurobiology of Rett as a direct conduit to the creation of new strategies to overcome it.
- **Reversal** – Approaches that target the underlying cause of Rett, aberrations in MECP2, in efforts to actualize the 2007 pre-clinical reversal for human clinical application. Included are gene therapy; activation of the silent MECP2 gene on the inactive X; identification and deployment of modifier genes.

This past summer saw a flurry of high-profile papers published by RSRT-funded scientists. Among these was a study from Gail Mandel showing, for the first time, the reversal of multiple symptoms in adult female mice using gene therapy. Advancing to human clinical trials will require optimizing vectors, delivery routes and definitively ruling out the potential for toxicity due to overexpression of the MeCP2 protein.

To achieve those goals, RSRT launched the MECP2 Gene Therapy Consortium bringing together the labs of Gail Mandel and Stuart Cobb and their expertise in Rett /MeCP2 with those of Steven Gray and Brian Kaspar, with substantive vector design/development and gene therapy clinical trial experience.

RSRT's original consortium, the MECP2 Consortium, organized in 2011 to address the function of MECP2, has had a highly successful first phase. Building on this momentum, RSRT has renewed funding for this unique international collaboration between the laboratories of Adrian Bird, Michael Greenberg, and Gail Mandel. RSRT is extremely grateful to its Board Chairman, Tony Schoener and his wife Kathy, for the initial million-dollar lead gift that launched this collaboration and their recent second million-dollar pledge to continue the work.

"Just as Rett research is gaining momentum, federal research dollars are declining, making the role of RSRT more essential than ever. If, like Kathy and I, you love a child with Rett and want nothing more than to see her restored to health, then I invite you to join us in our critical work," says Tony Schoener.

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"One of my prime responsibilities is to identify barriers to the development of therapeutics, troubleshoot and problem solve. Making progress by leaps rather than small incremental steps requires forging bold and innovative ways of conducting research that will maximize resources, save time and deliver results. We thank our donors for their trust and support. We look forward to reporting on our progress, " says Monica Coenraads, Executive Director of RSRT.

A complete list of 2013 awards follows categorized by approach:

Treatment

- $600,000 to support two clinical trials testing Copaxone in people
  Aleksandra Djukic – Tri-State Rett Syndrome Center at Montefiore
  Bruria Ben Zeev – Sheba Medical Center
- $150,000 to David Katz at Case Western Reserve University
  Preclinical evaluation of therapeutics that modulate the NMDA pathway that controls synaptic plasticity and memory.
- $130,000 to Michela Fagiolini at Boston Children's Hospital
  A joint collaboration between RSRT, Mnemosyne Pharmaceutical and Boston Children's Hospital to perform preclinical testing of selective novel NMDA receptor modulators.
- $72,000 to Aleksandra Djukic at Tri-State Rett Syndrome Center at Montefiore
  Support for continuing work at the Rett Syndrome Center.
- 50,000 to Mark Bear of MIT
  To explore potential benefits of pharmacological manipulations of mGluR signaling.

Basic Science

- $3.4 million to the MECP2 Consortium
  Adrian Bird – University of Edinburgh
  Michael Greenberg – Harvard University
  Gail Mandel – Oregon Health and Sciences University
  Please see accompanying blog post for details.

Reversal

- **$1.6 Million** to launch the MECP2 Gene Therapy Consortium
  Gail Mandel – Oregon Health and Sciences University
  Stuart Cobb – University of Glasgow
  Steve Gray – University of North Carolina Chapel Hill
  Brian Kaspar – Nationwide Children's Hospital
  Please see accompanying blog post for details.
- **$750,000** to Michael Green at University of Massachusetts
  Testing drugs that modulate X chromosome inactivation to reactivate the silent MECP2.
- **$367,000** to Huda Zoghbi of Baylor College of Medicine
  To conduct a screen to discover compounds that can reduce levels of MeCP2 for the duplication/triplication syndrome.
  These funds were awarded via the MECP2 Duplication Syndrome Fund at RSRT.

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- **$100,000** to Jeannie Lee at Harvard University
  To explore a novel approach to awaken the MECP2 gene by disrupting the binding that occurs between the lncRNA and the Polycomb complexes.
- **$39,000** to Kevin Foust at Ohio State University
  To explore using gene therapy to deliver RNA interference to lower the amount of MeCP2 protein. These funds were awarded via the MECP2 Duplication Syndrome Fund at RSRT.

About Rett Syndrome

Rett Syndrome is a genetic neurological disorder that almost exclusively affects girls. 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 girls of speech, hand use, normal movement often including the ability to walk. As the girls enter childhood the disorder brings anxiety, seizures, tremors, breathing difficulties, severe GI 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.

About the Rett Syndrome Research Trust

RSRT is a non-profit organization with a highly focused and urgent mission: eradicate Rett Syndrome and related MECP2 disorders. In search of a cure and effective treatment options, RSRT operates at the center of global scientific activity, funding bold projects that are unlikely to be supported by the NIH or other more traditional funding agencies. RSRT refutes the conventional practice of labs working in isolation, instead seeking out, promoting and funding collaborations and consortia in which scientists work across multiple disciplines. These relationships enable the development and execution of a research agenda that neither academia nor industry could achieve alone. Since 2008, RSRT has provided $25 million of financial support to: 4 clinical trials testing 3 compounds, 33 scientists in 27 academic institutions and 3 biotech firms. To learn more about the Trust, please visit **www.ReverseRett.org**.

About the MECP2 Consortium

The MECP2 Consortium, launched by the Rett Syndrome Research Trust in 2011, fosters novel alliances among leading scientists to interrogate the molecules at the root of Rett Syndrome and apply these discoveries to treatments. Consortium members include Adrian Bird of the University of Edinburgh, Michael Greenberg of Harvard University and Gail Mandel of Oregon Health and Sciences University.

Our partners in supporting this work are parents' organizations worldwide including **Reverse Rett (UK)**, **Rett Syndrome Research & Treatment Foundation (Israel)**, **Skye Wellesley Foundation (UK)**, **Rett Syndrome & CDKL5 Ireland**, **Rett Syndrom Deutschland**, **Stichting Rett Syndrome (Holland)**.

Our U.S. partners that helped make this research possible include **Girl Power 2 Cure**, **Eva Fini Fund at RSRT**, **Kate Foundation for Rett Syndrome Research**, **Rocky Mountain Rett Association**, **Anastasi Fund**, **Claire's Crusade**, **New Jersey Rett Syndrome Association**, **Rett Syndrome Association of Massachusetts**, and the **MECP2 Duplication Syndrome Fund** at RSRT.