Press Release:
The Rett Syndrome Research Trust Announces Roadmap to Cure Devastating Neurological Disorder that Afflicts 350,000 Girls and Women

HUMAN CLINICAL TRIALS OF GENE THERAPY ON THE HORIZON

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TRUMBULL, CT — The Rett Syndrome Research Trust (RSRT) announced today a historic plan to cure Rett Syndrome, a devastating neurological disorder that afflicts 350,000 individuals worldwide. Rett Syndrome is caused by alterations in a single gene, *MECP2*, located on the X chromosome, and almost exclusively strikes females. Following a normal infancy, Rett Syndrome takes effect in toddlerhood depriving children of speech, hand use, and normal movement often including the ability to walk. Other common symptoms include extreme anxiety, tremors, seizures, breathing difficulties, and digestive problems. Cognitive abilities remain largely intact trapping able-minded children in disabled bodies. Although most children survive to adulthood, they require total round-the-clock care.

RSRT has developed a three-year, $33 million transformational research plan called the *Roadmap to a Cure*. At the core of the *Roadmap* are four curative approaches, all attacking the root cause of the disorder, *MECP2*. Gene therapy, the delivery of healthy copies of the *MECP2* gene to compensate for the mutated copy, is the most advanced and will be RSRT's lead program. Contingent on sufficient funding and requisite FDA approvals, the *Roadmap* is anticipated to enable the first clinical trial of gene therapy for people with Rett Syndrome.

RSRT's founder and executive director, Monica Coenraads, adds, "Our goal at RSRT has always been a cure, not merely symptom improvement. With that goal in mind RSRT assembled a team of elite scientists and in 2014 launched the *MECP2 Gene Therapy Consortium*. The results have exceeded expectations. In just three years, our consortium has developed a therapy that is safe and effective in animal models. The next step is to test safety and efficacy in individuals with Rett Syndrome, providing an opportunity our children so richly deserve. RSRT will do everything in its power to expedite the process."

Randall Carpenter, MD, RSRT's Chief Scientific Officer with decades of translational medicine experience says, "The magnitude of efficacy in the mouse models of Rett Syndrome is much greater than that of any drug in development and suggests that significant benefit may be achieved in people. Importantly, gene therapy is applicable to any and all *MECP2* mutations and deletions." Beyond gene therapy RSRT will pursue other curative approaches including protein replacement, RNA editing and MECP2 Reactivation.

In addition to the curative approaches the *Roadmap* will lay the groundwork for the development of objective, sensitive and FDA- and EMA-approvable outcome measures. This will enhance clinical trial effectiveness and help attract industry investments in Rett Syndrome.

RSRT's research is also yielding key insights relevant for treating related neurological diseases such as autism and neurodevelopmental disorders like CDKL5, Fragile X and Angelman Syndrome. Although the genetic causes vary, some individuals with these disorders have alterations in the same brain pathways and should therefore respond to the same treatments. The gene therapy trials will inform development for all single-gene disorders that, like Rett, require broad distribution of the gene therapy product to the brain. The potential to impact millions of lives is significant.

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Adrian Bird, PhD, RSRT trustee and the scientist responsible for the discovery of MeCP2 and for the remarkable experiments that showed the world that Rett Syndrome is dramatically reversible in animal models says, "These are exciting times in biomedical research and the RSRT Roadmap fully exploits a new optimism. Gene therapy, so long an unfulfilled possibility, has at last become a serious therapeutic option. Even gene editing may soon be on the agenda. Meanwhile, as we learn more about how diseases of this kind disrupt the brain's essential pathways, novel therapeutic opportunities are popping up. This is a time for renewed hope and RSRT, which has done so much to develop our knowledge of these disorders, is ready for the new era."

RSRT's funding comes in large part from the networks of families with an affected child. The $33 million *Roadmap to a Cure* budget will require support from the global Rett Syndrome community and extended networks to meet the ambitious three-year goal. Nearly $6 million has already been pledged from generous families and their networks towards the total $33 million needed. If this fundraising momentum continues and all goes according to plan, Rett Syndrome stands to be the first cured brain disorder.

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. In search of a cure and effective treatment options, RSRT operates at the nexus of global scientific activity. We enable advances in knowledge and drive innovative research through constant engagement with academic scientists, clinicians, industry, investors and affected families. These relationships catalyze the development and execution of a research agenda that neither academia nor industry could achieve alone. 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. Since 2008, RSRT has awarded $41 million to research projects. To learn more about the Trust, please visit ***www.ReverseRett.org***.