Roadmap to Cures 2.0

RETT SYNDROME RESEARCH TRUST

Accelerating the timeline to advance genetic medicines for Rett

We have launched a bold new **$40 million initiative**, *Roadmap to Cures*, that seeks to select and develop three genetic medicines that attack the root-cause of Rett syndrome, and advance them into clinical trials by 2028. *Roadmap to Cures* brings together the latest genome-editing technology with RSRT's in-house expertise.

Our original plan, *Roadmap to a Cure* and *the Gene Therapy Consortium* that came before it, laid the foundation for the current gene therapy clinical trials. However, developing cures for Rett syndrome is an iterative process. Next-generation medicines have the potential to provide additional benefit. Time is of the essence and the greatest likelihood of achieving cures in Rett is to advance, in parallel, as many shots on goal as possible.

Our internal team of staff and advisors bring decades of biotech industry and clinical trial experience. Enhancing our team is a large network of outside experts in genomic medicine, clinical trial design, and regulation to tap as needed.

Genetic Medicines = Cargo + Delivery. We'll select three of these Cargo + Delivery combinations to advance.

CARGO

Gene Editing: Introduces healthy genes to compensate for mutated genes. The most advanced is already in clinical trials.

Base Editing: Enables precise changes to the DNA sequence at specific locations to correct mutations.

Prime Editing: Extends beyond base editing and addresses a wide array of mutations including insertions and deletions. It can correct multiple mutations that are near each other on the gene.

MECP2 Reactivation: All females have two X chromosomes, one active and one inactive. The goal of this approach is to awaken the healthy, silenced gene on the inactive X chromosome.

RNA Editing: Converts one nucleotide to another within the RNA.

RNA Trans-splicing: MECP2 consists of 4 exons. This approach replaces mutated exons with healthy exons and is relevant for all MECP2 mutations

DELIVERY

Viral: Viruses are very efficient at delivering their own genetic material into cells during infection. This function can be harnessed to allow viruses to serve as delivery vehicles for genetic cargos.

Non-VIral: Delivery vehicles extend beyond viruses to include approaches such as lipid nanoparticles and exosomes. Non-viral delivery offers a number of important advantages.

Small RNA: Small RNA are able to self deliver and do not need viral or non viral delivery. They have been used clinically for many years with much success and can therefore advance rapidly into the clinic.

To execute on Roadmap to Cures, we need to raise a minimum of **$10 million a year for the next four years**. Our success depends on the Rett community coming together and inspiring their networks to give through **fundraising events** and **crowdfunding campaigns**.

Contact **Tim Freeman** to brainstorm how you can get involved and help: tim@rsrt.org or **609.815.5102**