Optimize antibody-RNA conjugate for treating adult-onset myotonic dystrophy type 1

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Abstract:

Myotonic dystrophy type 1 (DM1) is a progressive disease that affects skeletal, smooth and cardiac muscles and is characterized as muscle weakness, myotonia and shorter life span. With no approved disease-modifying therapy, DM1 is affecting ~1:20,000 people worldwide and causes substantial disease burden.

DM1 is a monogenic disease, inherited in an autosomal dominant manner, and caused by CTG expansion in the noncoding region of DMPK gene. Muscle targeted silencing of aberrantly transcribed CUG bearing DMPK mRNA by antibody-RNA conjugate (ARC) is one of the therapeutic approaches under development and shows promise of alleviating myotonic symptoms in early stage clinical trials for DM1.

We carefully review the target product profile of existing ARC therapeutics and optimize the drug design. In brief, our proprietary ARC, CGB1001 demonstrates 1) up to 5x improvement in DMPK silencing efficiency in human muscular cells, 2) 7-10x more of siRNA delivery into skeletal muscles, 3) 10x lowering in transferrin competition by a distal antibody binding epitope, and 4) higher yield and purity of ARC through a proprietary manufacturing process vs. existing ARC therapeutics.

The features enable us to develop CGB1001 with better efficacy, less anemia risk, better purity and improved affordability. CGB1001 has recently completed a 12 weeks toxicology studies in non-human primates and shows good tolerability and safety profile. CGB1001 is on schedule to a first-in-human trial by the end of 2024.