



Progress Update for Drug Discovery Research Program to Identify Potential Treatments for Spinal Muscular Atrophy (SMA)

PTC Therapeutics, Inc. (PTC) and Fight Spinal Muscular Atrophy are collaborating to discover new potential treatments for spinal muscular atrophy (SMA).

All SMA patients have at least one copy of the SMN2 gene which mainly produces the SMN2 mRNA containing an aberrant stop codon. The SMN2 mRNA is translated into an abnormal unstable protein, SMN Δ Ex7. Dr. Christian Lorson from the University of Missouri observed that certain antibiotics known to cause readthrough of premature stop codons could improve the stability of the abnormal SMN Δ Ex7 protein. These antibiotics, however, have serious toxicities, making long-term treatment with these compounds unattractive.

We previously identified compounds that selectively promote ribosomal readthrough of mRNAs containing premature stop codons. PTC's readthrough compounds are orally bioavailable and do not have antibiotic properties. PTC is exploring the application of one of its nonsense suppression compounds for SMA treatment. This compound reads through the aberrant stop codon present in the SMN Δ Ex7 mRNA and restores stability and function to the SMN protein. The goal of this collaboration is to determine the preliminary safety profile and define a process chemistry method suitable for large scale GMP chemical synthesis of the PTC compound. This will allow us to determine the feasibility of potential IND-enabling pre-clinical toxicological and toxicokinetic studies for the compound as a potential therapeutic candidate for treatment of SMA.

PTC's scientists are pleased to report that non-GLP toxicology studies for PTC's compound have been successfully completed. Based on clinical chemistry, histopathology, and hematology findings, an NOAEL (No Adverse Effect Level) has been determined. These data allow us to advance to the next steps to complete the determination of blood brain barrier permeability and detailed pharmacokinetics following administration the compound.

For more information on PTC please visit www.ptcbio.com.

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