Efforts Toward the Synthesis of Two Small Molecule Alternative Splicing Activators

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It has been estimated that 40-60% of human genes are alternatively spliced, allowing many protein isoforms to be made from a single gene. Defects in alternative splicing are responsible for several diseases including spinal muscular atrophy (SMA) and breast cancer. Splicing factors called SR proteins bind to exonic splice-site enhancers (ESEs) through their RNA-binding domains and recruit the spliceosome via protein-protein interactions mediated by their RS domains. SMA patients lack survival motor neuron 1 gene (*SMN1*), and the identical copy of this gene, *SMN2,* contains a C→T mutation in the ESE of exon 7. This single-nucleotide mutation results in exon skipping. Herein, we report our efforts toward the synthesis of two synthetic RS domains and the experimental design to determine their possible effects on the inclusion of exon 7 in *SMN2*.