The present disclosure describes short antisense compounds, including such compounds comprising chemically-modified high-affinity monomers 8-16 monomers in length. Certain such short antisense compound are useful for the reduction of target nucleic acids and/or proteins in cells, tissues, and animals with increased potency and improved therapeutic index. Thus, provided herein are short antisense compounds comprising high-affinity nucleotide modifications useful for reducing a target RNA in vivo. Such short antisense compounds are effective at lower doses than previously described antisense compounds, allowing for a reduction in toxicity and cost of treatment. In addition, the described short antisense compounds have greater potential for oral dosing.