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(54) Title: 5-HALOURACIL-MODIFIED DOUBLE-STRANDED NUCLEIC ACIDS AND THEIR USE IN THETREATMENT OF
CANCER

(57) Abstract: The present disclosure provides double-stranded nucleic acid compositions that incorporate uracil, gemcitabine, and methotrexate (MTX). More specifically, the present disclosure reveals that the modifications of double-stranded micro-RNA nucleotide sequences with 5-fluorouracil, gemcitabine and methotrexate (MTX) enhance the therapeutic efficacy of tumor suppression and tumor specificity. As such, the present disclosure provides various nucleic acid (e.g., microRNA) compositions having 5-fluorouracil, gemcitabine and methotrexate (MTX) incorporated in their nucleic acid sequences and methods for using the same. The present disclosure further provides pharmaceutical compositions (e.g., formulations) comprising the modified nucleic acid compositions, and methods for treating cancers, such as pancreatic cancer. This is a platform technology that can be applied to other tumor suppressor miRNAs as well as siRNAs.