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(54) **Title**: NUCLEASE-MEDIATED TARGETING WITH LARGE TARGETING VECTORS

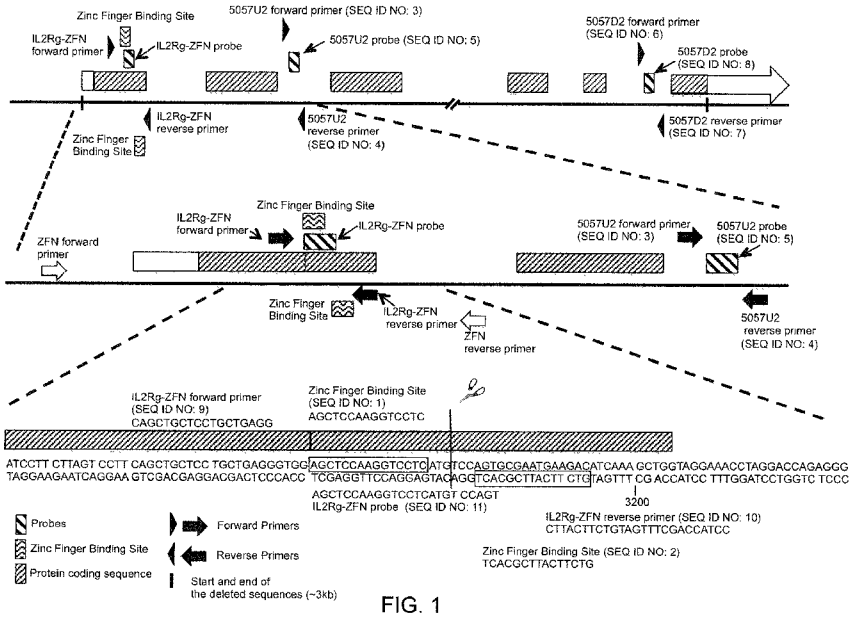


FIG. 1

(57) **Abstract**: Compositions and methods are provided for making one or more targeted genetic modifications at a target genomic locus by employing homologous recombination facilitated by single or double-strand break at or near the target genomic locus. Compositions and methods for promoting efficiency of homologous recombination between an LTVEC and a target genomic locus in prokaryotic or eukaryotic cells using engineered nucleases are also provided.

WO 2013/163394 A1