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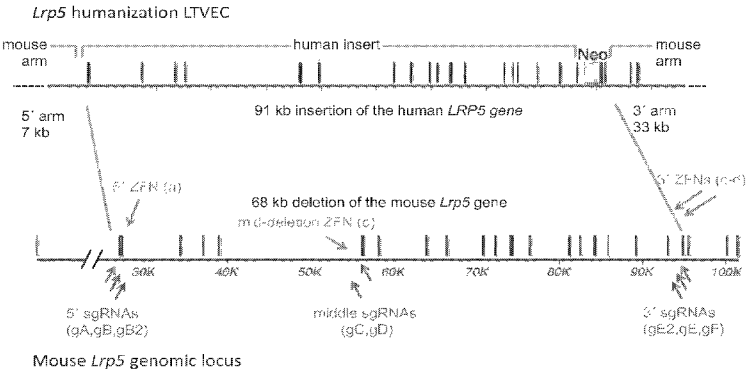
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[Continued on next page]

(54) Title: METHODS AND COMPOSITIONS FOR THE TARGETED MODIFICATION OF A GENOME

FIG. 34



(57) Abstract: Compositions and methods are provided for modifying a genomic locus of interest in a eukaryotic cell, a mammalian cell, a human cell or a non-human mammalian cell using a large targeting vector (LTVEC) comprising various endogenous or exogenous nucleic acid sequences as described herein. Further methods combine the use of the LTVEC with a CRISPR/Cas system. Compositions and methods for generating a genetically modified non-human animal comprising one or more targeted genetic modifications in their germline are also provided.

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