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61/234,098 14 August 2009 (14.08.2009) US(71) Applicant (for all designated States except US): **ALNYLAM PHARMACEUTICALS, INC.** [US/US]; 300 Third Street, Cambridge, MA 02142 (US).

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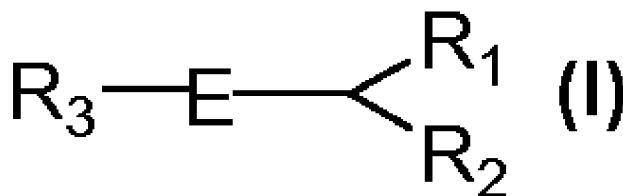
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(54) Title: NOVEL LIPIDS AND COMPOSITIONS FOR THE DELIVERY OF THERAPEUTICS



(57) Abstract: The present invention provides lipids that are advantageously used in lipid particles for the in vivo delivery of therapeutic agents to cells. In particular, the invention formula (I) provides lipids having the following structure XXXIII wherein: R_1 and R_2 are each independently for each occurrence optionally substituted C_{10} - C_{30} alkyl, optionally substituted C_{10} - C_{30} alkenyl, optionally substituted C_{10} - C_{30} alkynyl, optionally substituted C_{10} - C_{30} acyl, or -linker-ligand; R_3 is H, optionally substituted C_1 - C_{10} alkyl, optionally substituted C_2 - C_{10} alkenyl, optionally substituted C_2 - C_{10} alkynyl, alkyl hetero cycle, alkylphosphate, alkylphosphorothioate, alkylphosphorodithioate, alkylphosphonates, alkylamines, hydroxyalkyls, ω -aminoalkyls, ω - (substituted)aminoalkyls, ω -phosphoalkyls, ω -thiophosphoalkyls, optionally substituted polyethylene glycol (PEG, mw 100-40K), optionally substituted mPEG (mw 120-40K), heteroaryl, heterocycle, or linker-ligand; and E is C(O)O or OC(O).

