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(54) Title: RNAI AGENTS FOR INHIBITING EXPRESSION OF COMPLEMENT FACTOR B (CFB) PHARMACEUTICAL COMPOSITIONS THEREOF, AND METHODS OF USE

(57) Abstract: The present disclosure relates to RNAi agents able to inhibit Complement Factor B (CFB) gene expression. Also disclosed are pharmaceutical compositions that include CFB RNAi agents and methods of use thereof. The CFB RNAi agents disclosed herein may be conjugated to targeting ligands, including ligands that comprise N-acetyl-galactosamine, to facilitate the *in vivo* delivery to hepatocyte cells. The RNAi agents can be used in methods of treatment of diseases, disorders, or symptoms mediated in part by CFB gene expression, including IgA nephropathy (IgAN), C3 glomerulopathy (C3G), immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN), lupus nephritis (LN), Anti-Glomerular Basement Membrane disease (anti-GBM), ischemia reperfusion injury and T-cell mediated rejection (TCMR) in kidney transplantation, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, age-related macular degeneration (AMD), including early and/or intermediate AMD, geographic atrophy (GA), glaucoma, Doyne honeycomb retinal dystrophy, paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), pre-eclampsia, rheumatoid arthritis (RA), and/or other complement-mediated diseases.



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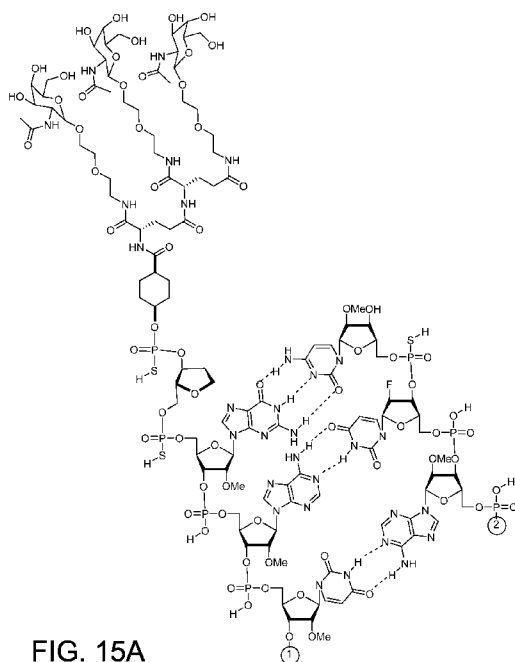


FIG. 15A

(57) Abstract: The present disclosure relates to RNAi agents able to inhibit Complement Factor B (CFB) gene expression. Also disclosed are pharmaceutical compositions that include CFB RNAi agents and methods of use thereof. The CFB RNAi agents disclosed herein may be conjugated to targeting ligands, including ligands that comprise N-acetyl-galactosamine, to facilitate the *in vivo* delivery to hepatocyte cells. The RNAi agents can be used in methods of treatment of diseases, disorders, or symptoms mediated in part by CFB gene expression, including IgA nephropathy (IgAN), C3 glomerulopathy (C3G), immune complex-mediated membranoproliferative glomerulonephritis (IC-MPGN), lupus nephritis (LN), Anti-Glomerular Basement Membrane disease (anti-GBM), ischemia reperfusion injury and T-cell mediated rejection (TCMR) in kidney transplantation, anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, age-related macular degeneration (AMD), including early and/or intermediate AMD, geographic atrophy (GA), glaucoma, Doyme honeycomb retinal dystrophy, paroxysmal nocturnal hemoglobinuria (PNH), atypical hemolytic uremic syndrome (aHUS), pre-eclampsia, rheumatoid arthritis (RA), and/or other complement-mediated diseases.



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