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(54) Title: THERAPEUTIC ADENO-ASSOCIATED VIRUS USING CODON OPTIMIZED NUCLEIC ACID ENCODING ALPHA-GLUCOSIDASE (GAA) FOR TREATING POMPE DISEASE, WITH SIGNAL PEPTIDE MODIFICATIONS

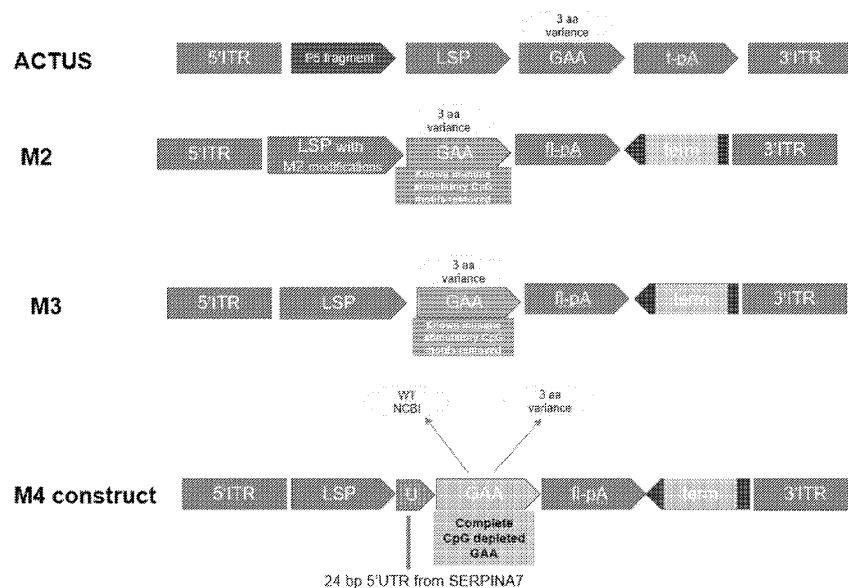


Fig. 15

(57) Abstract: Disclosed herein is a method for the treatment of Pompe Disease comprising administering a recombinant AAV (rAAV) vector comprising a rAAV genome comprising a heterologous nucleic acid encoding a GAA signal peptide or portion thereof, a heterologous signal peptide, and an acid alpha-glucosidase (GAA) polypeptide, or N-terminal truncation thereof, where the heterologous nucleic acid is operatively linked to a liver-specific promoter, where the nucleic acid encoding GAA polypeptide can be wild type nucleic acid sequence, or modified nucleic acid sequence, or a codon optimized nucleic acid sequence, and can optionally be modified to reduce or completely eliminate CG and CpG dinucleotides and, optionally eliminated alternative reading frames (ARF) content.

[Continued on next page]

**(81) Designated States** (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

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**Declarations under Rule 4.17:**

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- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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