

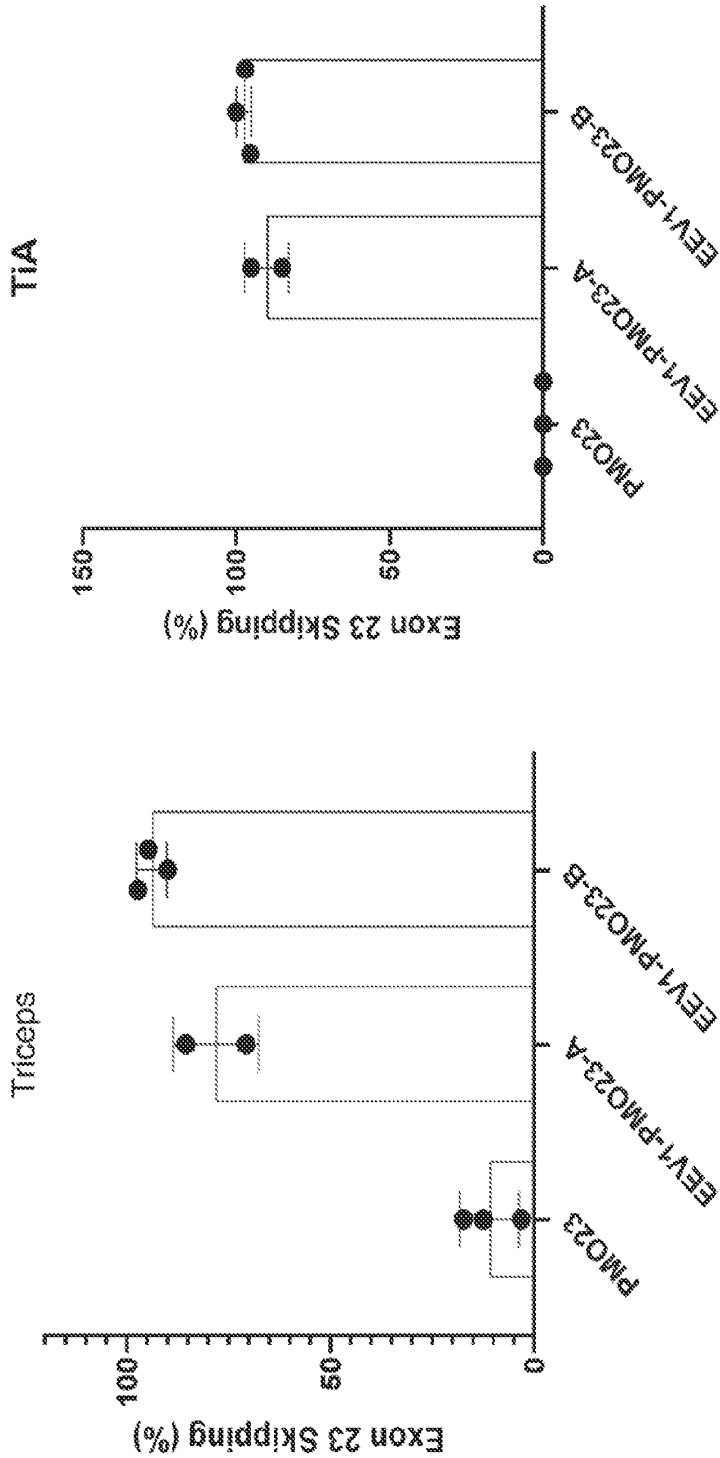
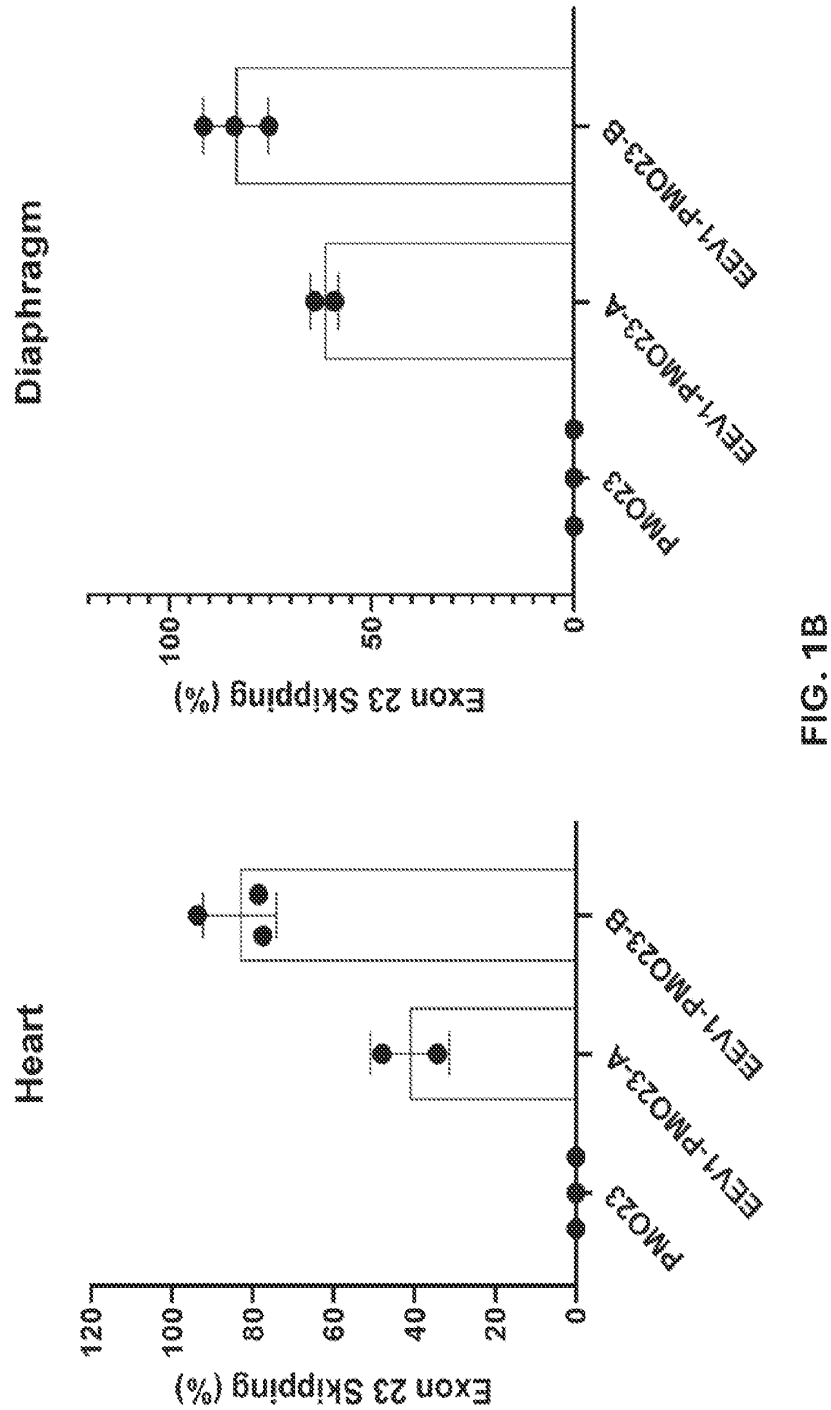
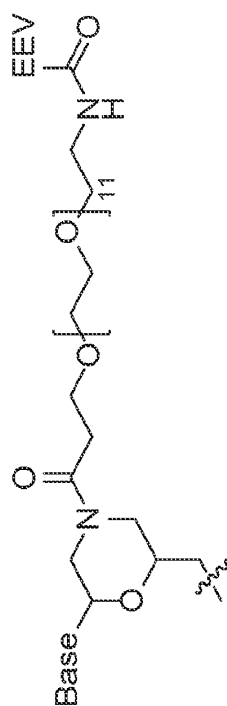


FIG. 1A

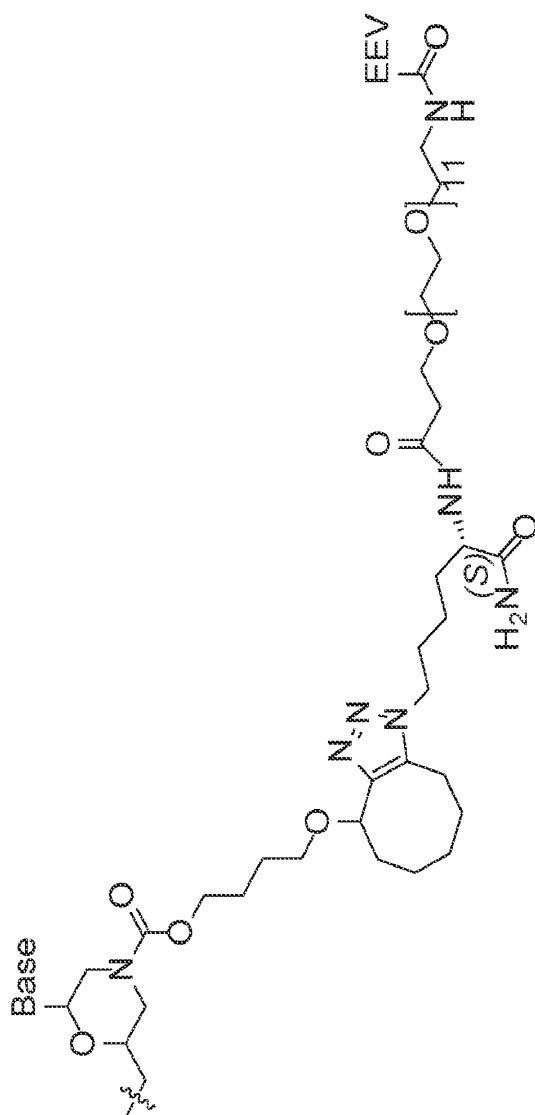




Linker for EEV1-PMO23-A
Installed using amide conjugation

PMO-23: GGCCAAACTCGGCTTACCTGAAAT

FIG. 1C

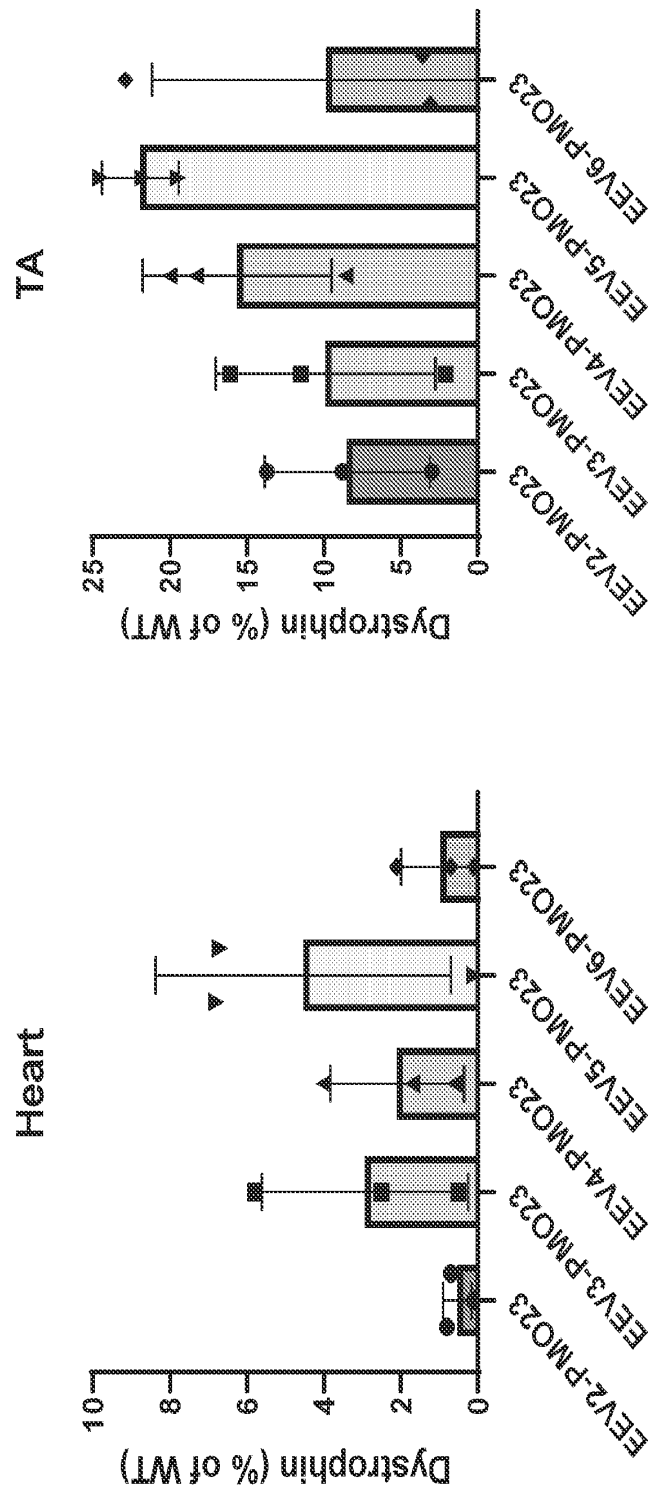


**Linker for EEV1-PMO23-B
Installed using strain-promoted
alkyne azide cycloaddition (SPAAC)**

EEV1: Ac-PPKKRKV-PEG₂-K(*cyclo*[Ff-Nal-Cit-r-Q])-Linker-PMO







2022 MDX-003 (AG): 7 d PI, 30 mpk (~40 mpk whole drug)

FIG. 2A

Peptide ID	Sequence
EEV2	Ac-PKKKKRKV-PEG ₂ -K-(cyclo[(GfGGrGrQ)]-PEG ₁₂ -OH
EEV3	Ac-PKKKKRKV-PEG ₂ -tetrazine-(cyclo[FGFGRGRQ]]-PEG ₁₂ -OH
EEV4	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ]]-PEG ₁₂ -K(2-Nal)-OH
EEV5	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ]]-PEG ₁₂ -(2-Nal)-OH
EEV6	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ]]-PEG ₁₂ -C6-OH

FIG. 2B

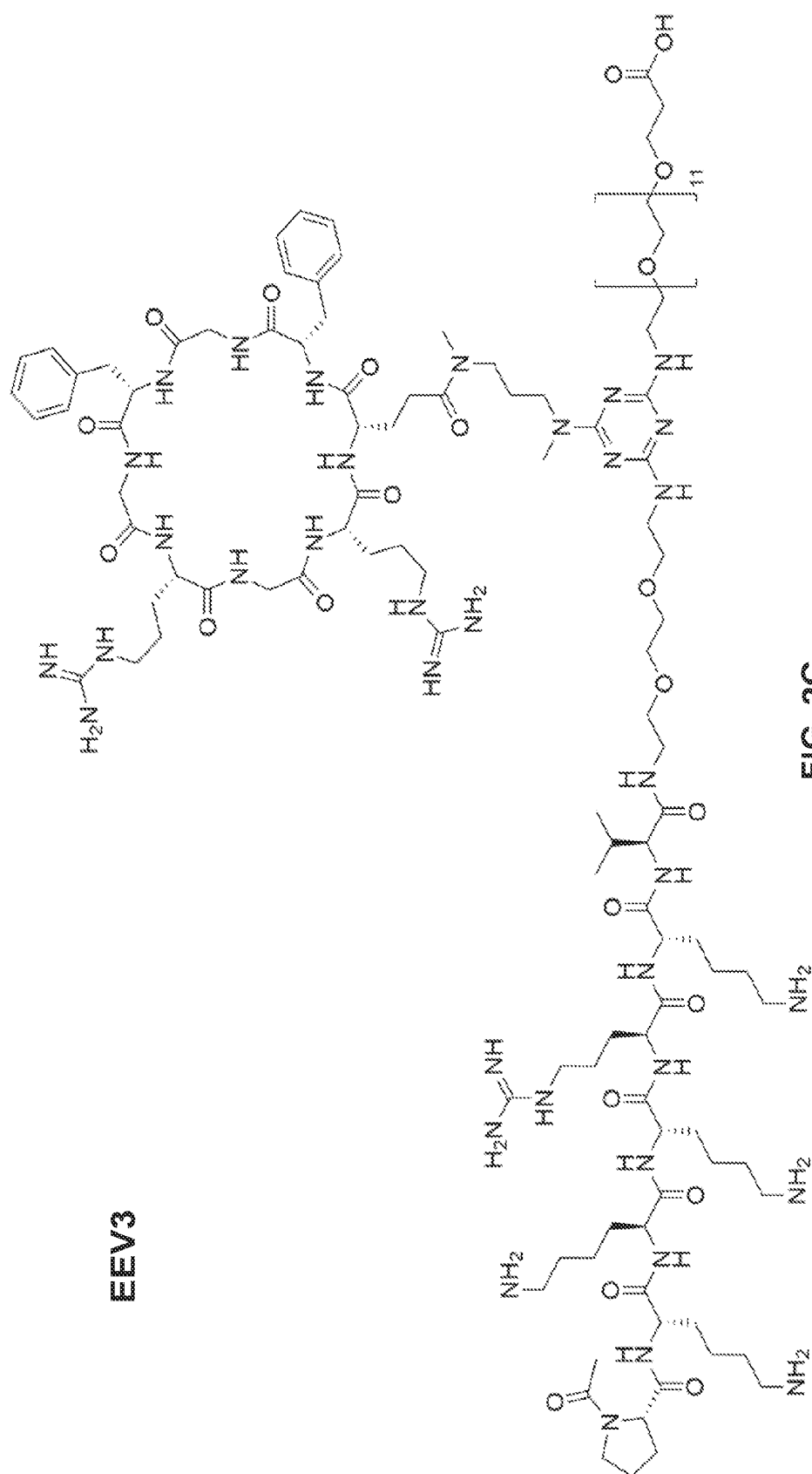


FIG. 2C

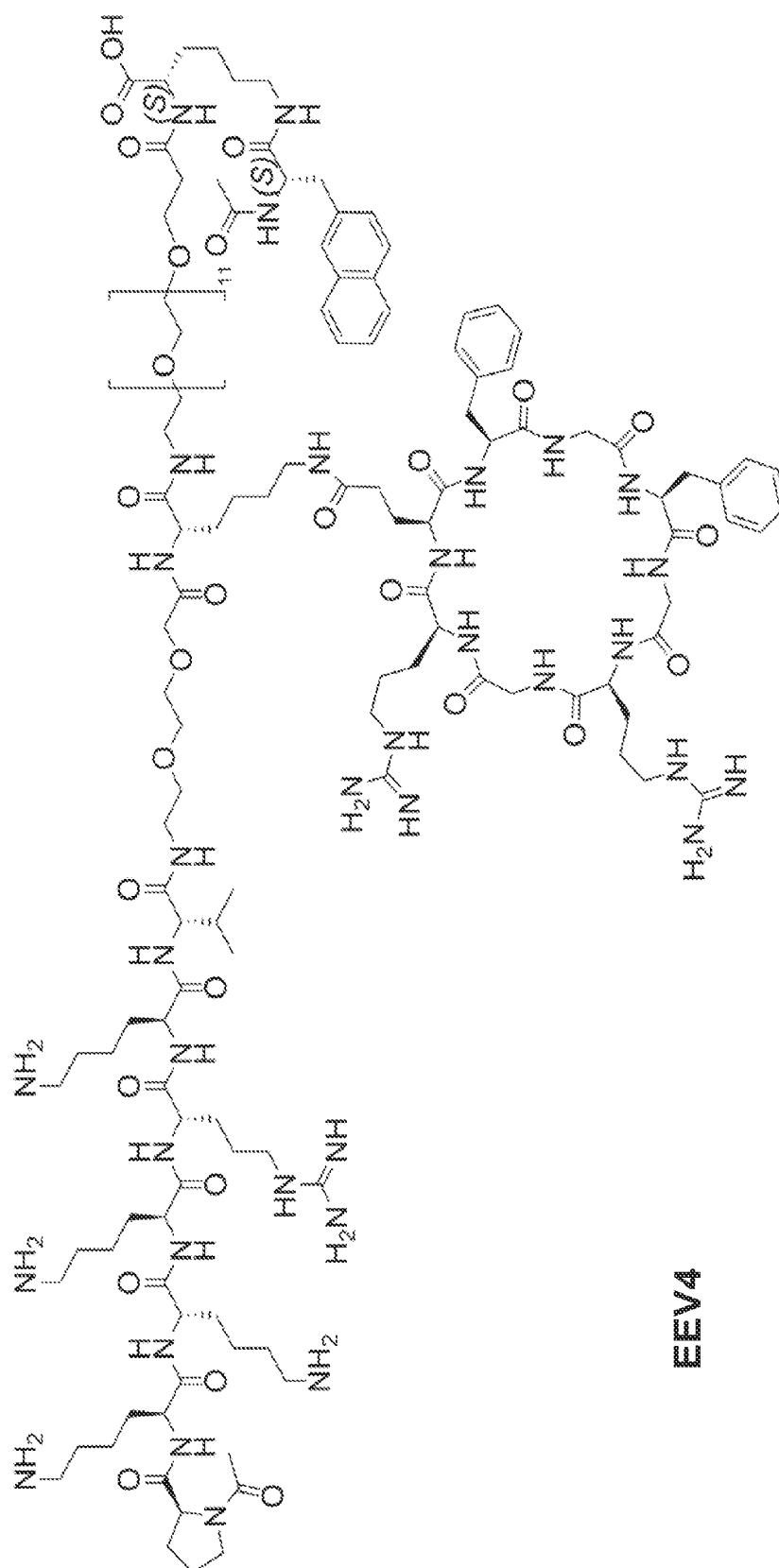


FIG. 2D

EEV4

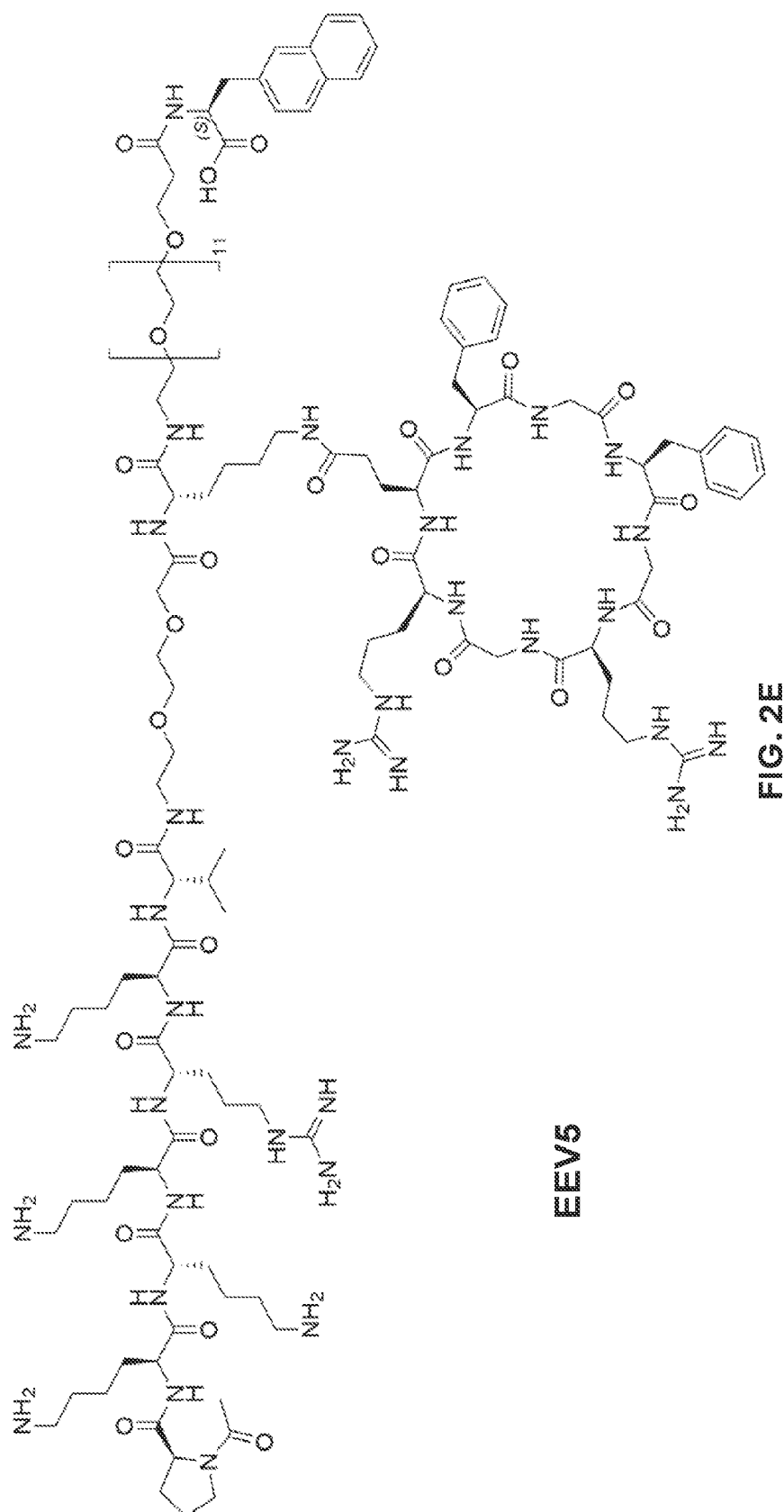


FIG. 2E

EEV5

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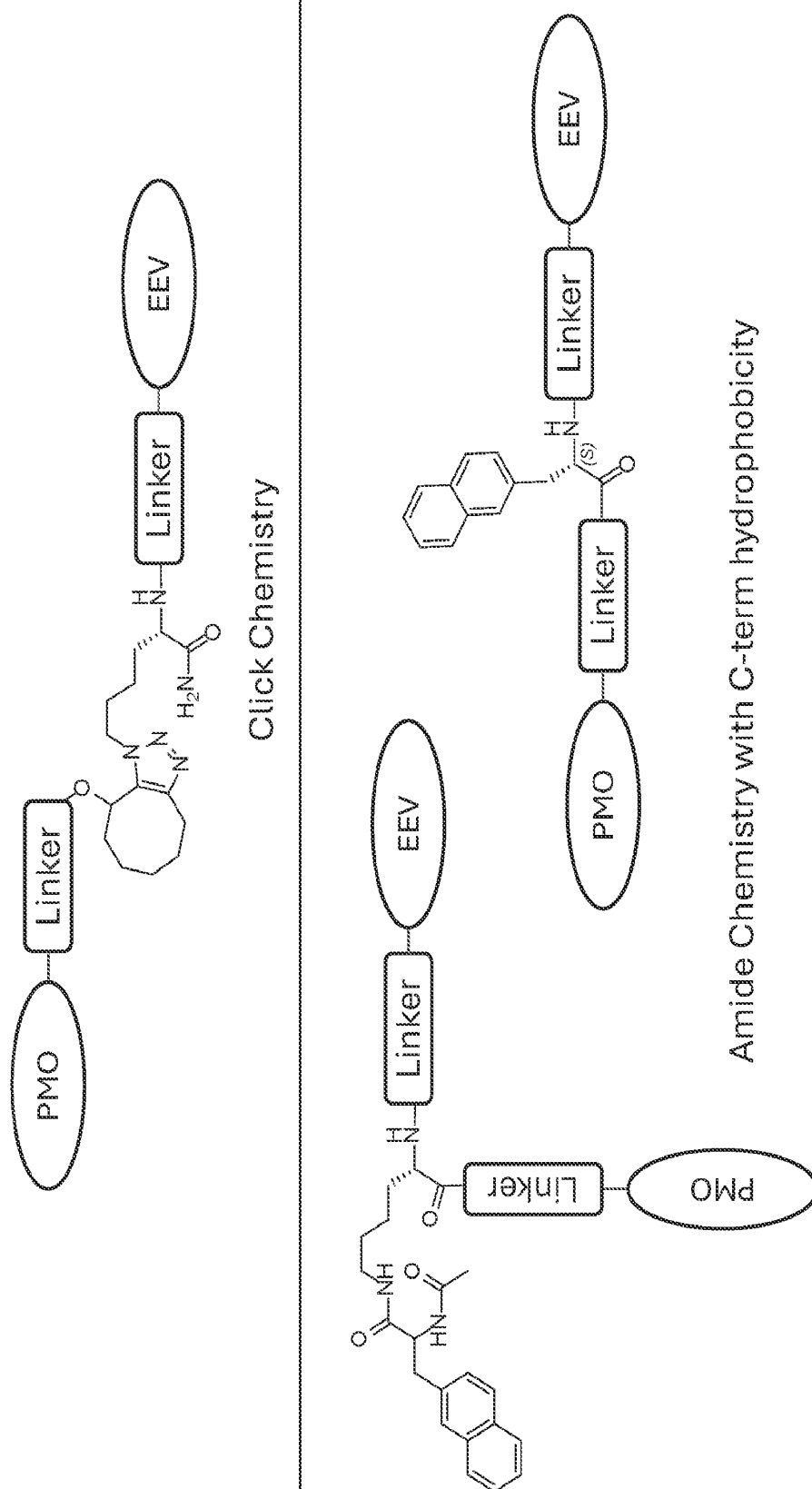
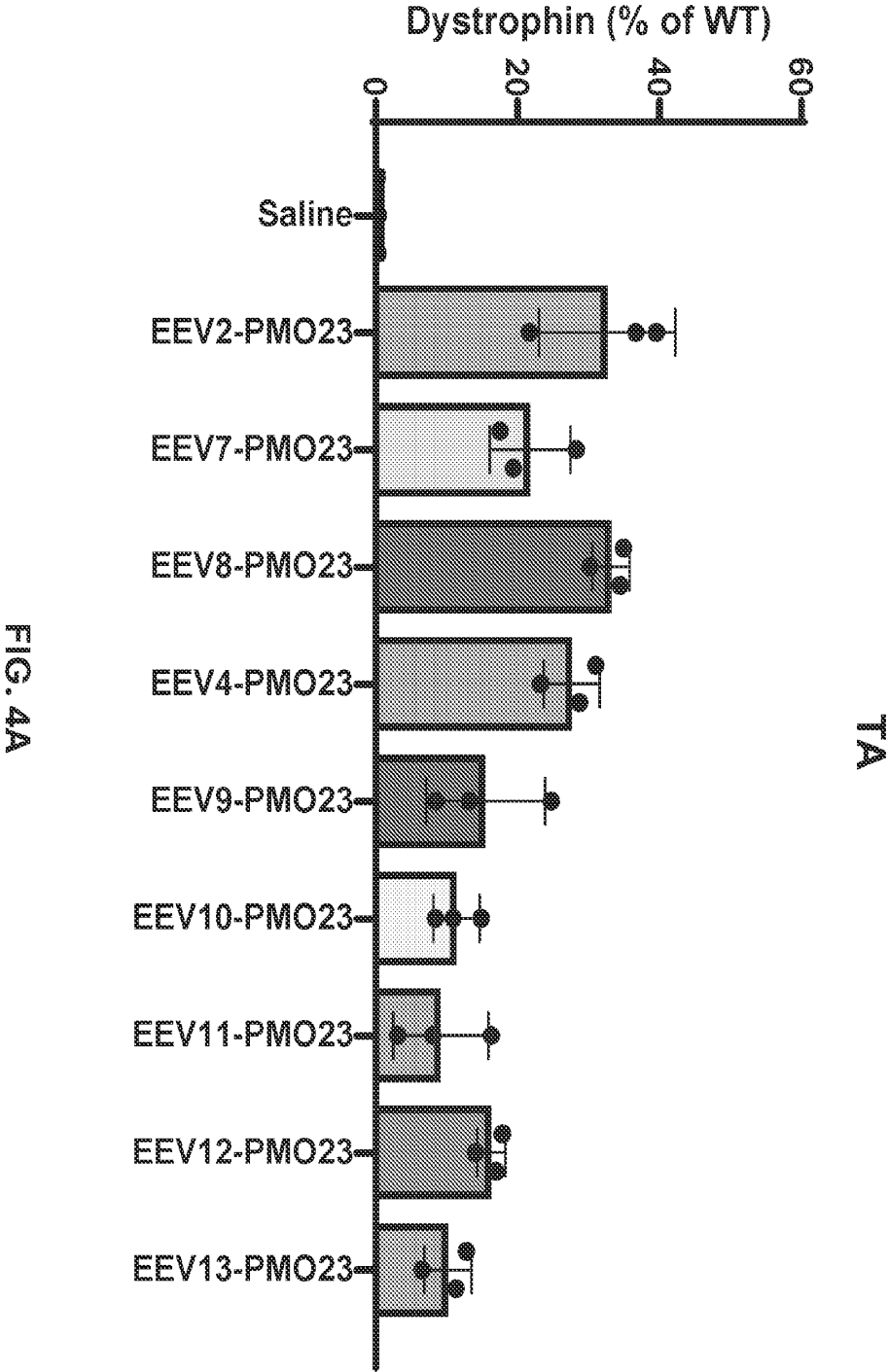
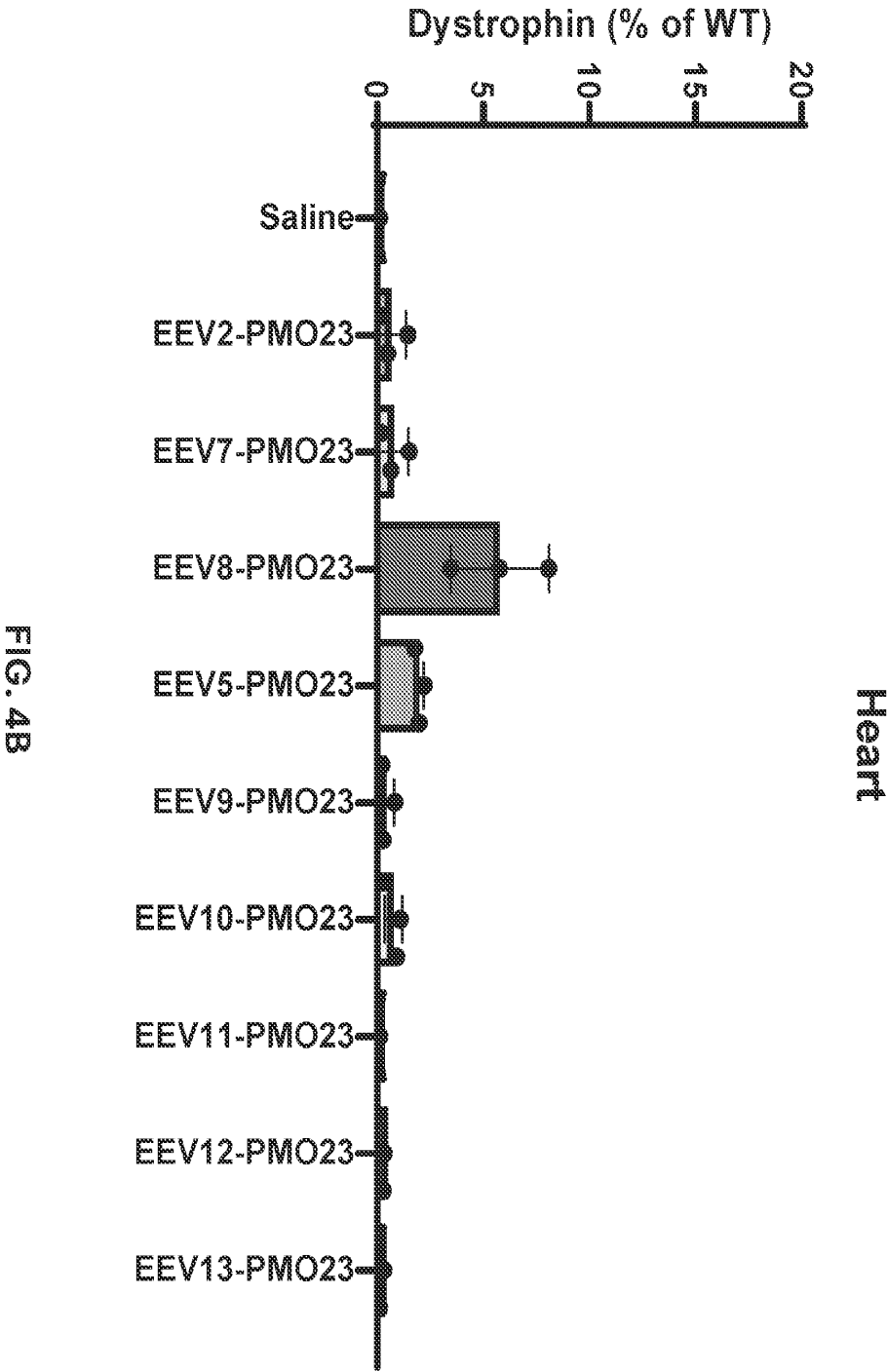


FIG. 3

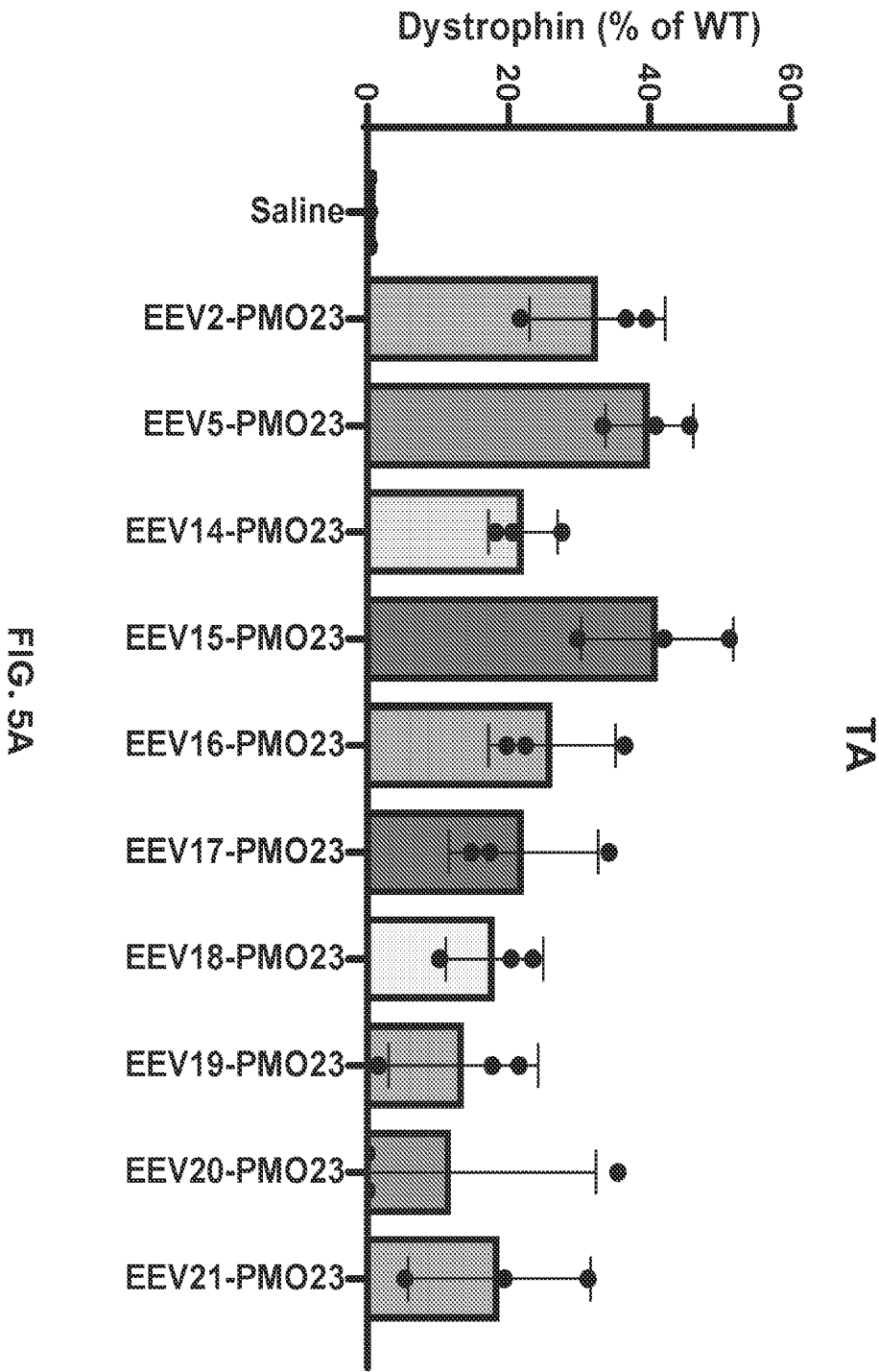


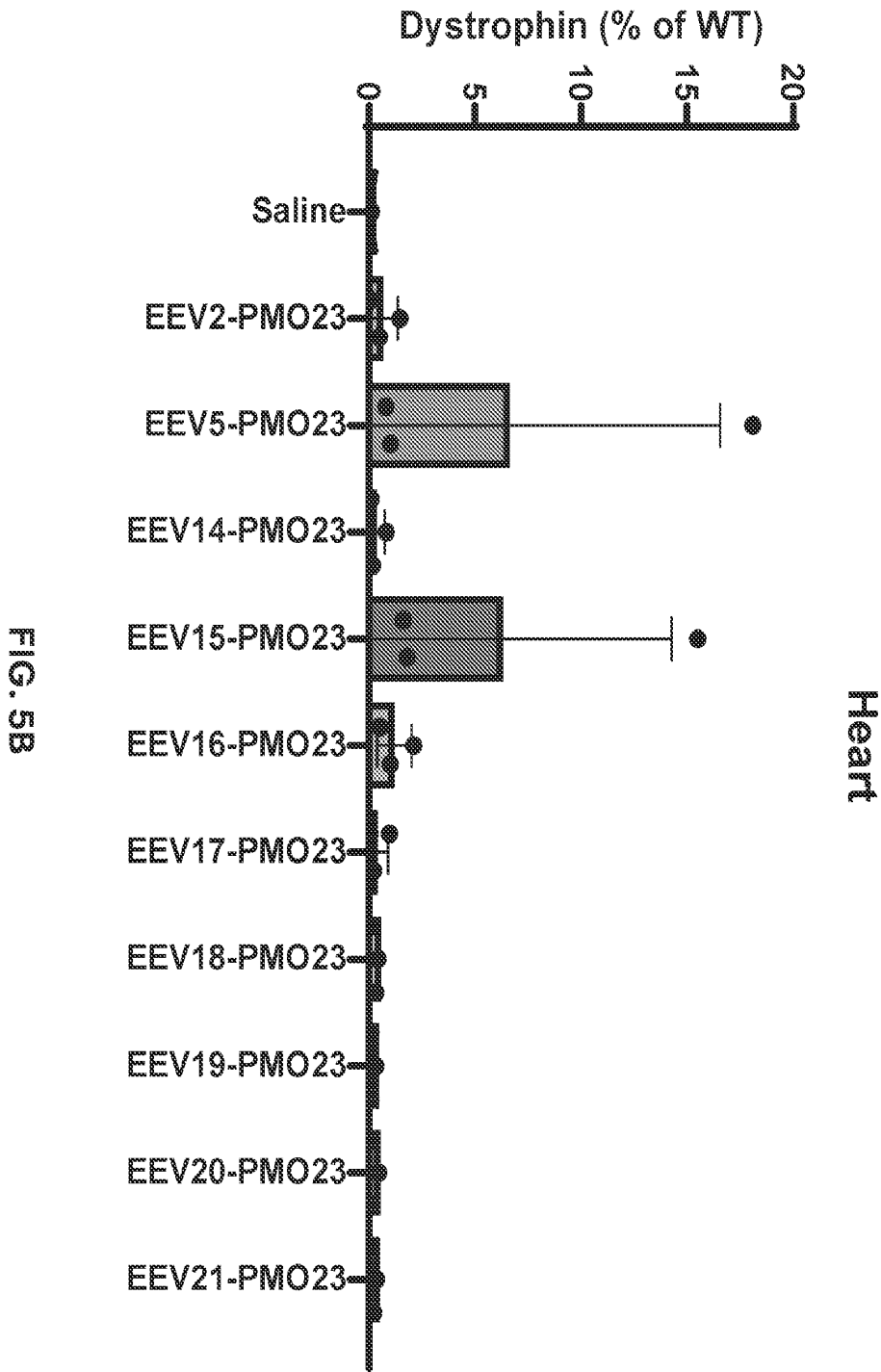


Name	Sequence
EEV2	Ac-PKKKKRKV-PEG ₂ -K-(cyclo[GfGfGrGrQ])-PEG ₁₂ -OH
EEV7	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(F)-OH
EEV8	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(Bip)-OH
EEV4	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(Nal)-OH
EEV9	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(W)-OH
EEV10	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(Y)-OH
EEV11	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(I)-OH
EEV12	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(L)-OH
EEV13	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG ₁₂ -K(H)-OH

Bip = 4-biphenyl-L-alanine
All ε-functionalized Lys residues (e.g. N^ε-(N^ω-acetyl-L-leucyl)-L-lysine); see structure **EEV4** in FIG. 2D.

FIG. 4C

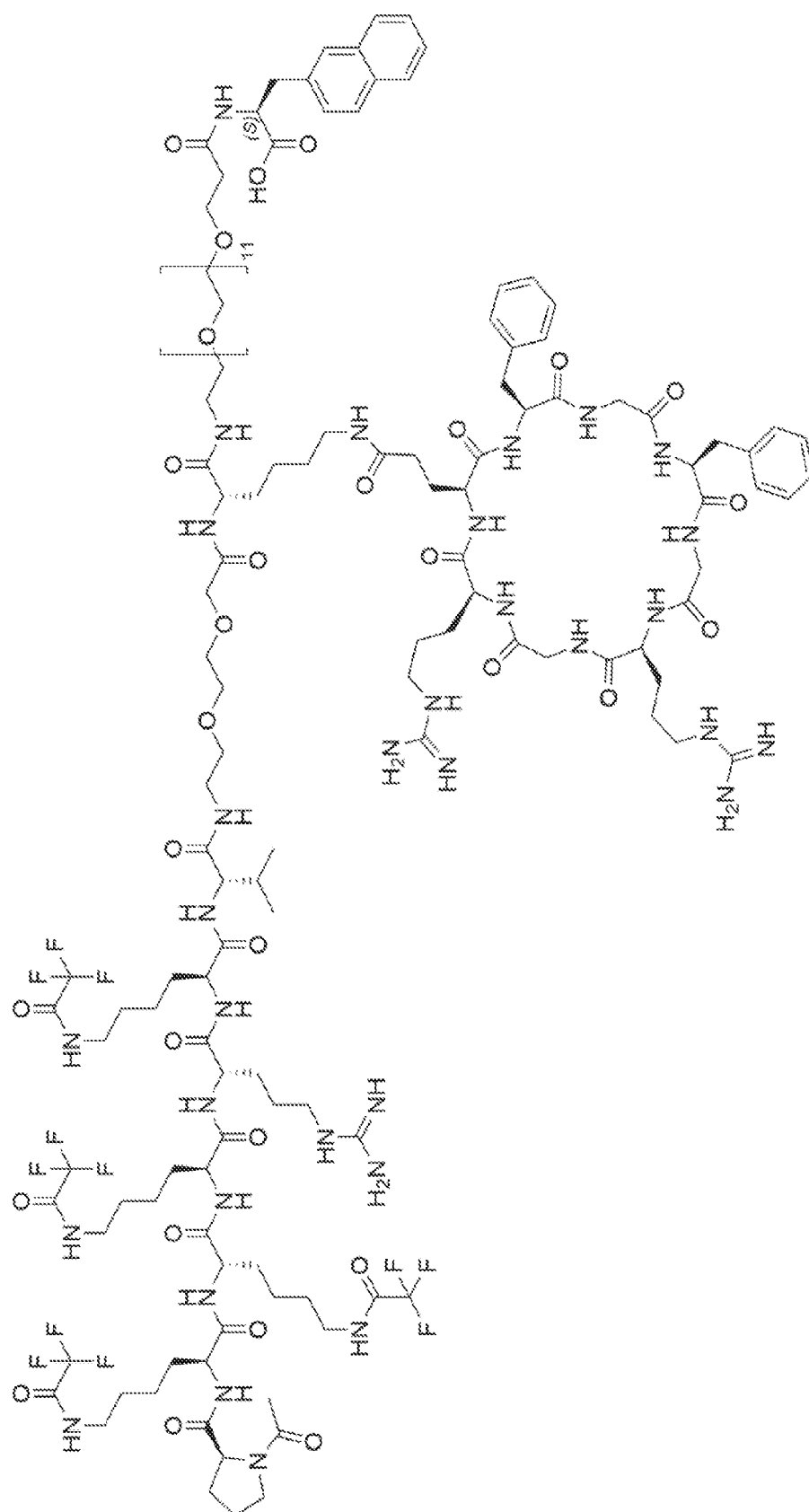




Name	Sequence
EEV2	Ac-PKKKKRKV-PEG ₂ -K-(cyclo[(GfGrGrQ)]-PEG12-OH
EEV5	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-Nal-OH
EEV14	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-F-OH
EEV15	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-Bip-OH
EEV16	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-W-OH
EEV17	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-Y-OH
EEV18	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-V-OH
EEV19	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-I-OH
EEV20	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-L-OH
EEV21	Ac-PKKKKRKV-PEG ₂ -K(cyclo[FGFGRGRQ])-PEG12-H-OH

Bip = 4-biphenyl-L-alanine
See structure **EEV5** on FIG. 2E as an example

FIG. 5C



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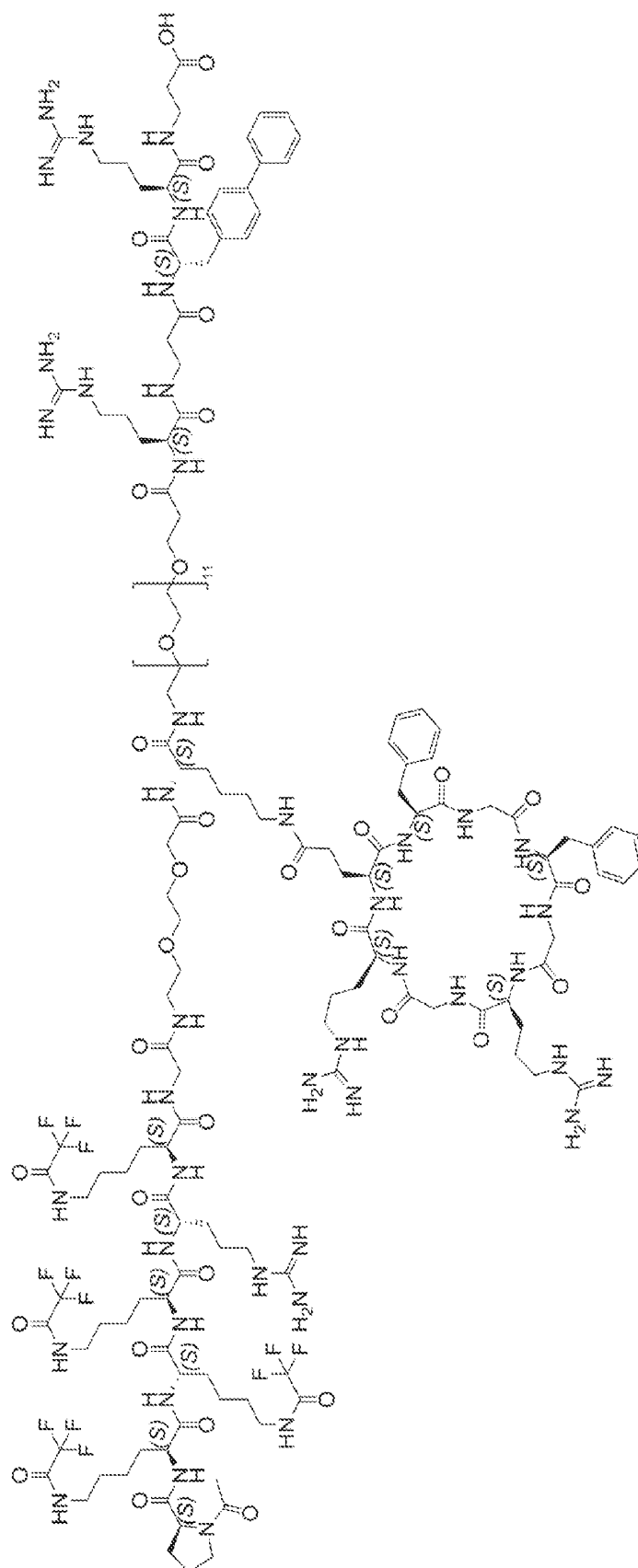


FIG. 7

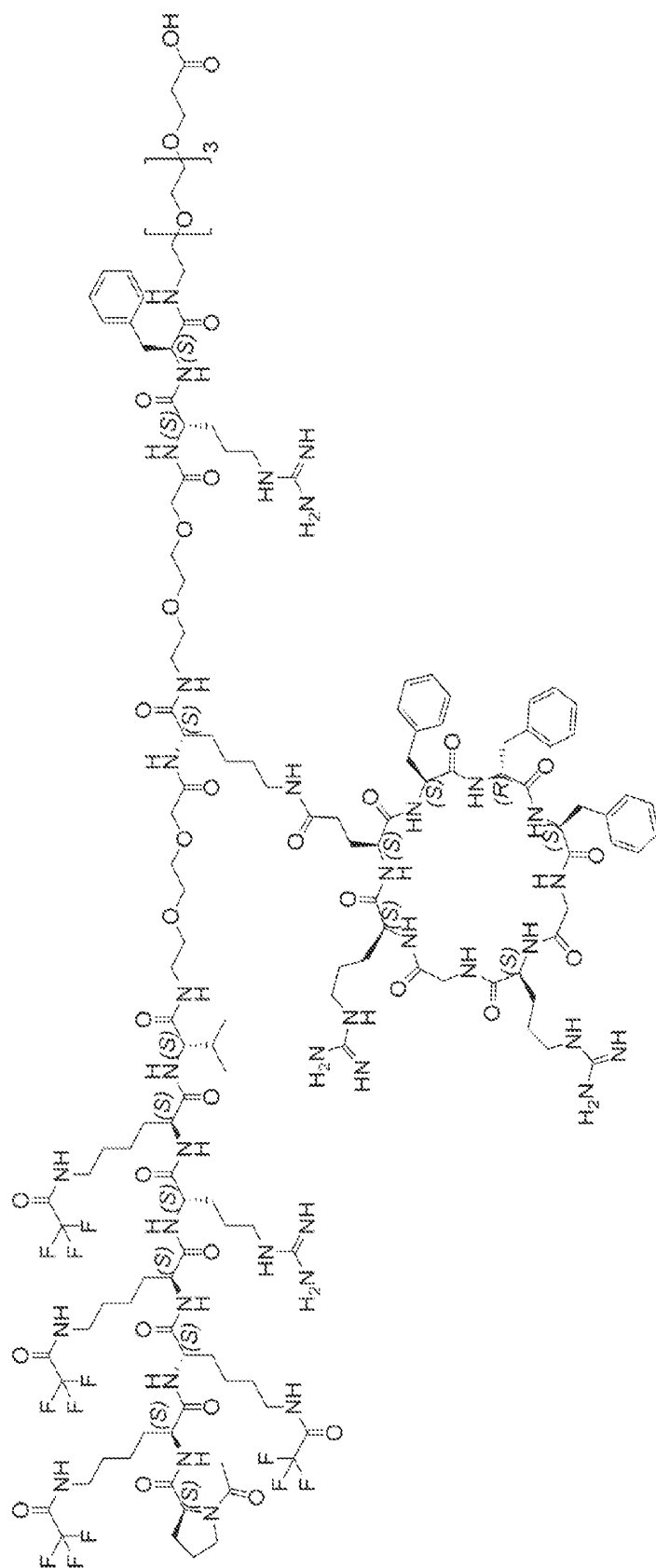
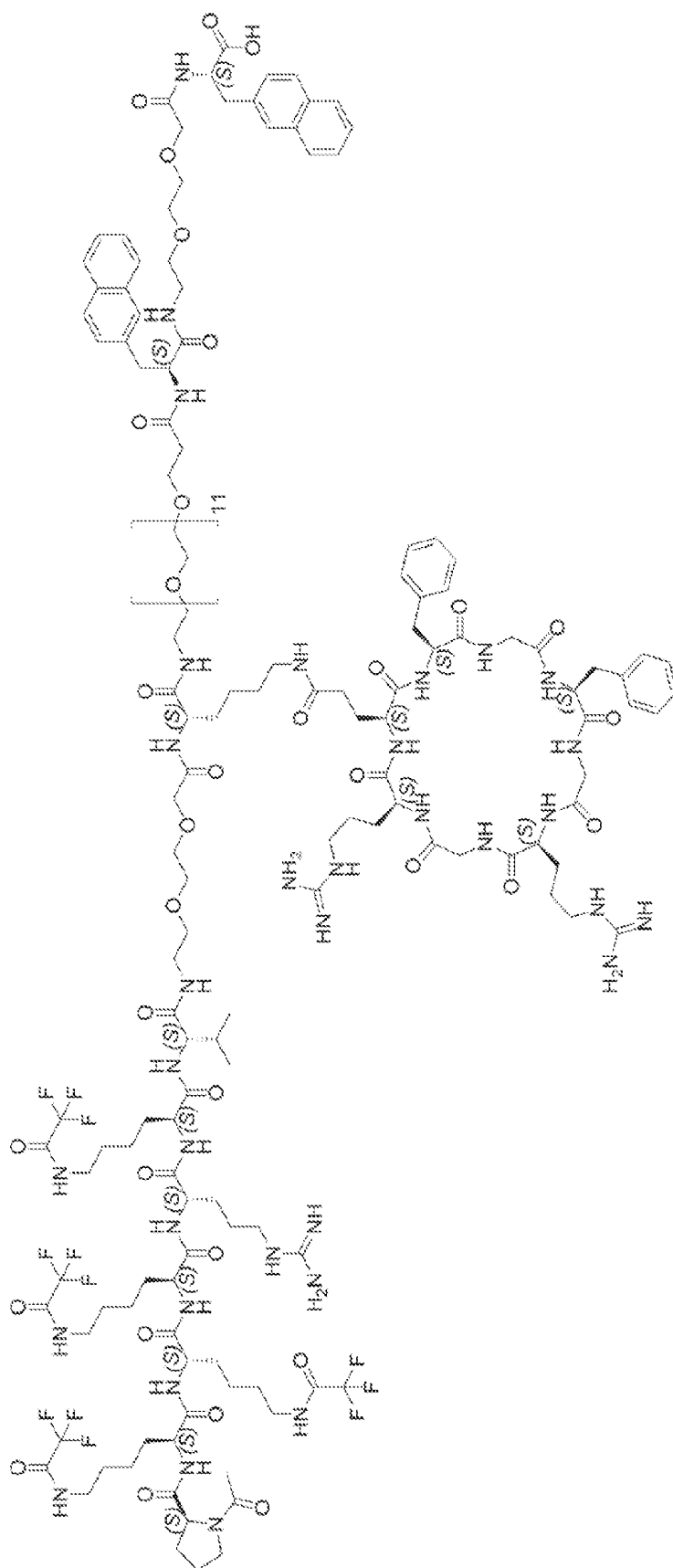


FIG. 9



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FIG. 10

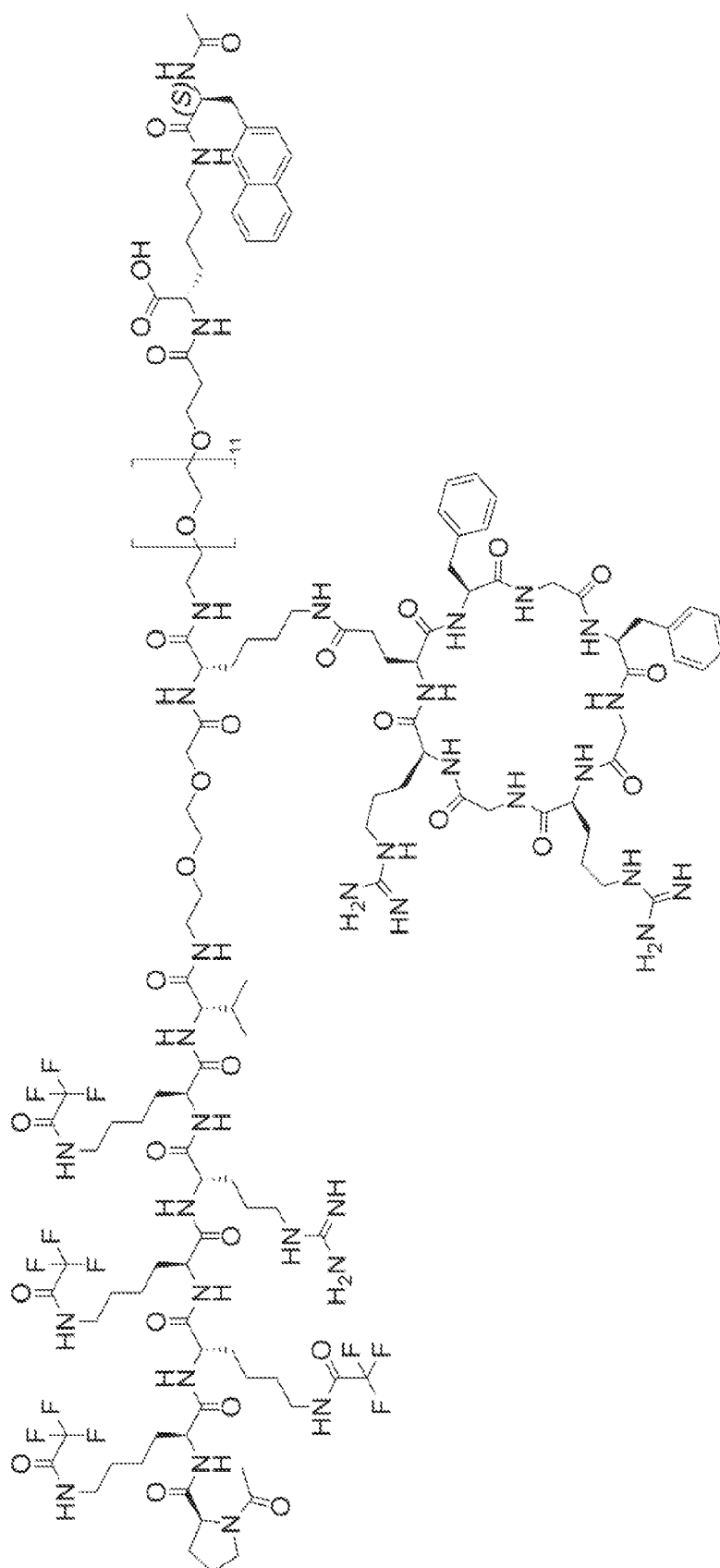


FIG. 11

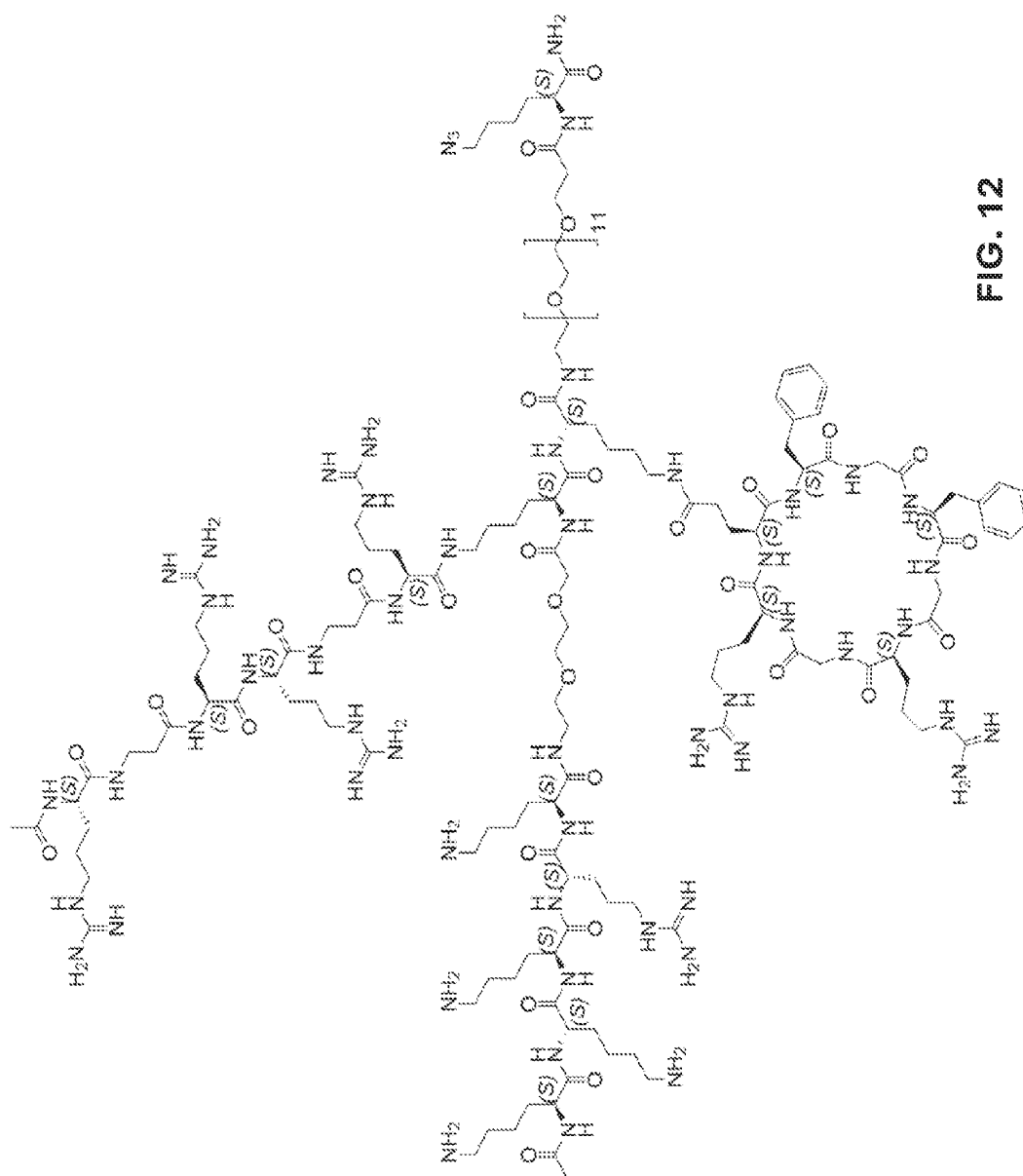


FIG. 12