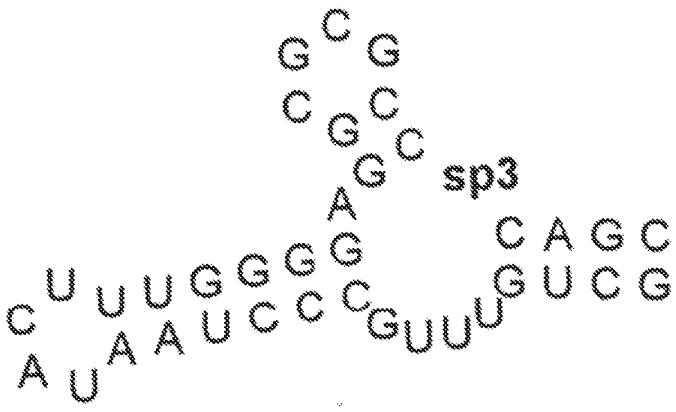


FIG. 1A

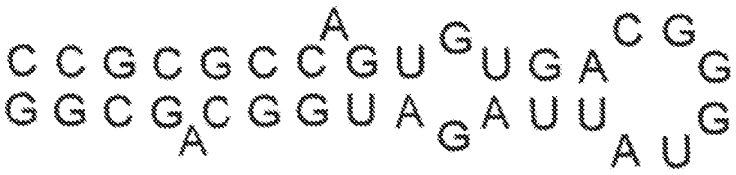


FIG. 1B

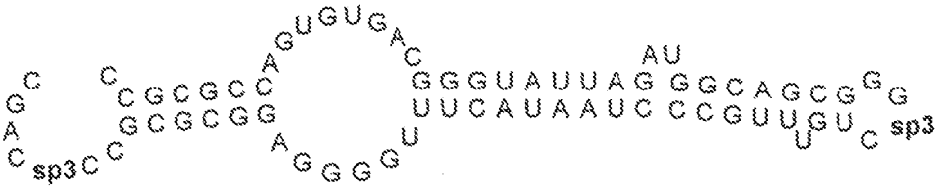


FIG. 1C

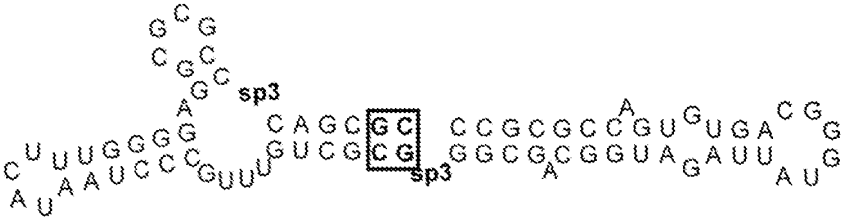


FIG. 1D

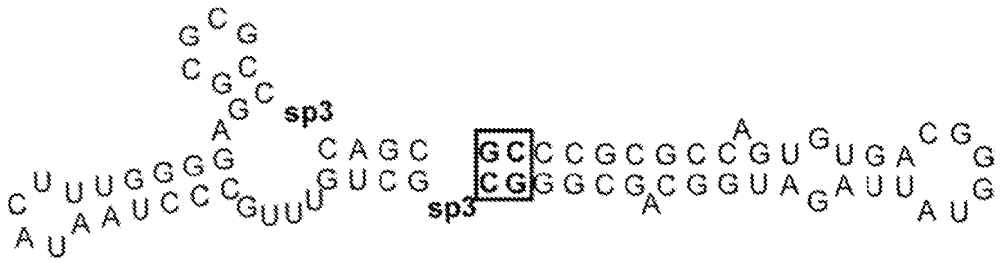

sp3
sp3

FIG. 1E

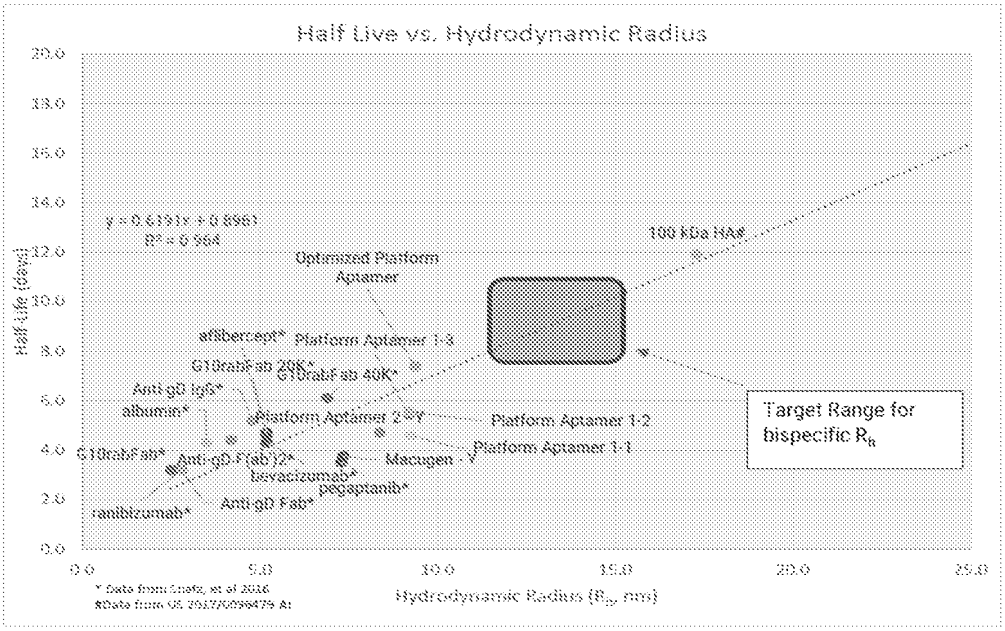

Half Live vs. Hydrodynamic Radius
Half Life (days)
Hydrodynamic Radius (R_H, nm)
y = 0.6191x + 0.8961
R² = 0.564
Optimized Platform Aptamer
100 kDa HAS
aflibercept*
Platform Aptamer 1-3
G1DrabFab 20K*
G1DrabFab 40K*
Anti gD IgG*
albumin*
Platform Aptamer 2-1
Platform Aptamer 1-2
Platform Aptamer 1-1
G1DrabFab*
Anti gD F(ab')2*
Macugen
bevacizumab*
pegaptanib*
ranibizumab*
Anti gD Fab*
Target Range for bispecific R_h
* Data from Duata, et al 2016
&Data from US 20170058479 A1

FIG. 2

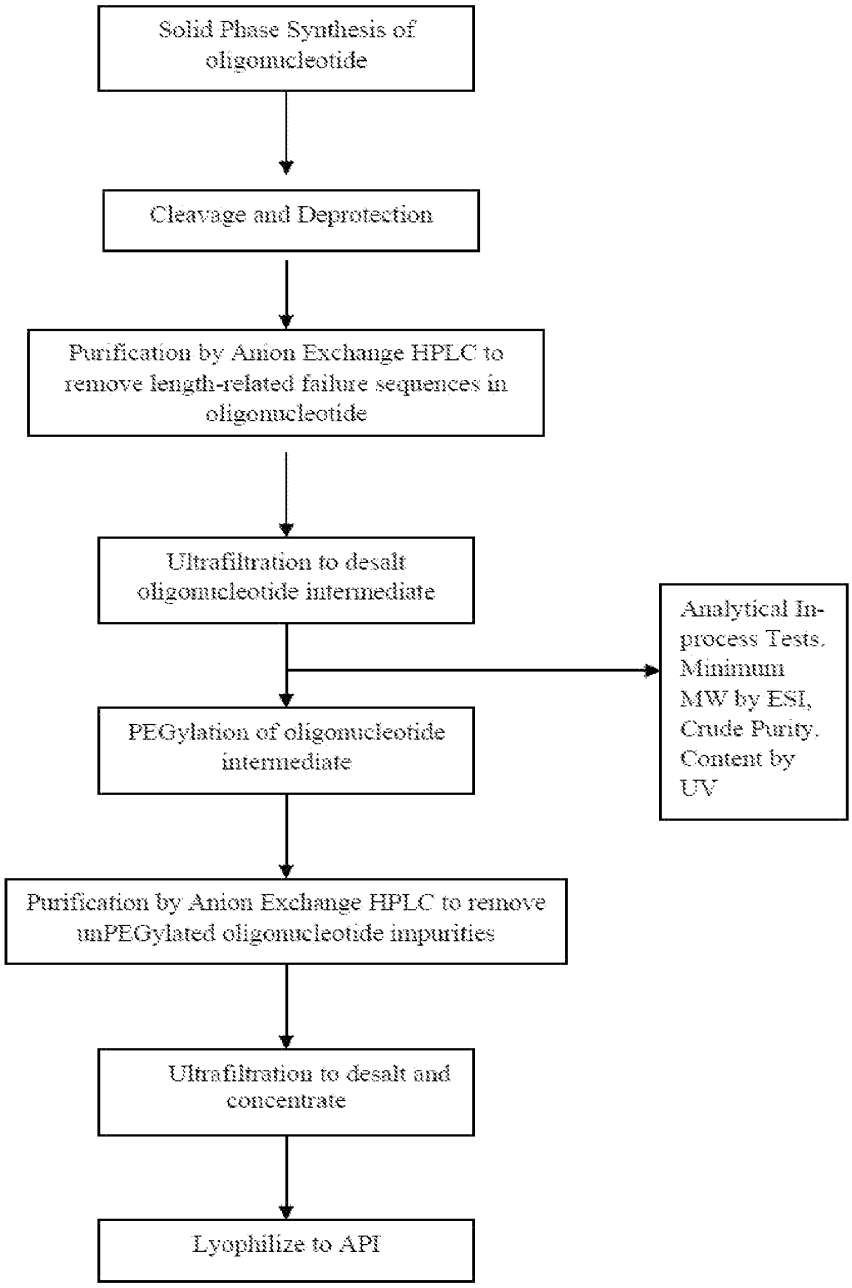

Solid Phase Synthesis of oligonucleotide
Cleavage and Deprotection
Purification by Anion Exchange HPLC to remove length-related failure sequences in oligonucleotide
Ultrafiltration to desalt oligonucleotide intermediate
Analytical In-process Tests, Minimum MW by ESI, Crude Purity, Content by UV
PEGylation of oligonucleotide intermediate
Purification by Anion Exchange HPLC to remove unPEGylated oligonucleotide impurities
Ultrafiltration to desalt and concentrate
Lyophilize to API

FIG. 3

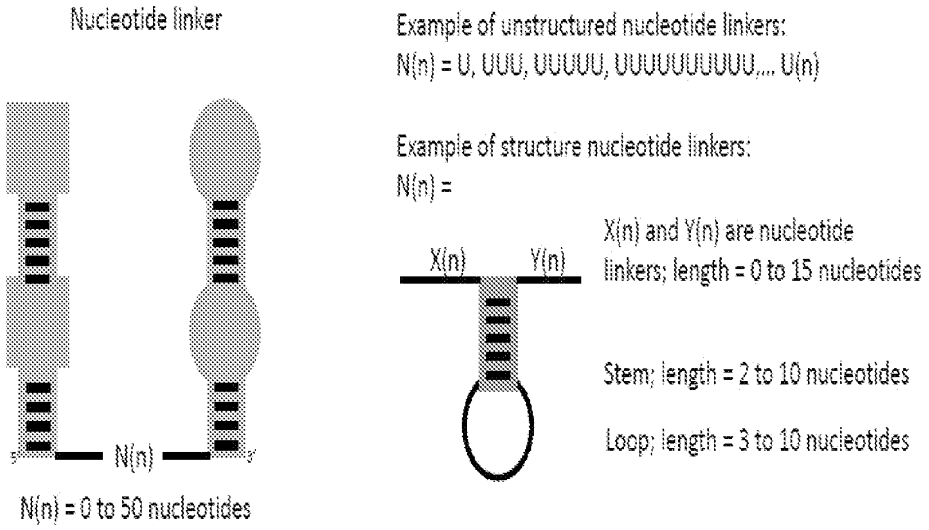

Nucleotide linker
N(n)
N(n) = 0 to 50 nucleotides
Example of unstructured nucleotide linkers:
N(n) = U, UUU, UUUUU, UUUUUUUUUU,... U(n)
Example of structure nucleotide linkers:
N(n) =
X(n)
Y(n)
X(n) and Y(n) are nucleotide linkers; length = 0 to 15 nucleotides
Stem; length = 2 to 10 nucleotides
Loop; length = 3 to 10 nucleotides

FIG. 4

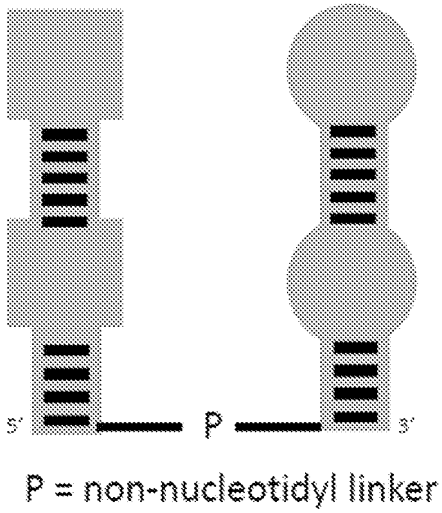


FIG. 5A

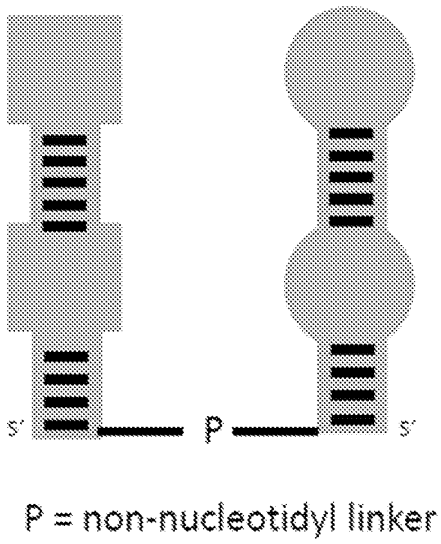


FIG. 5B

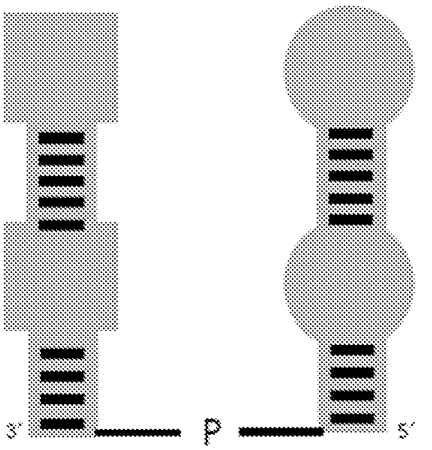


FIG. 5C

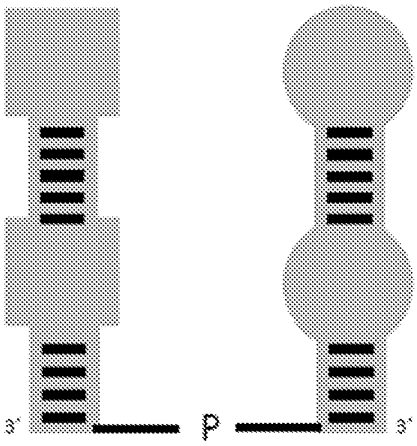


FIG. 5D

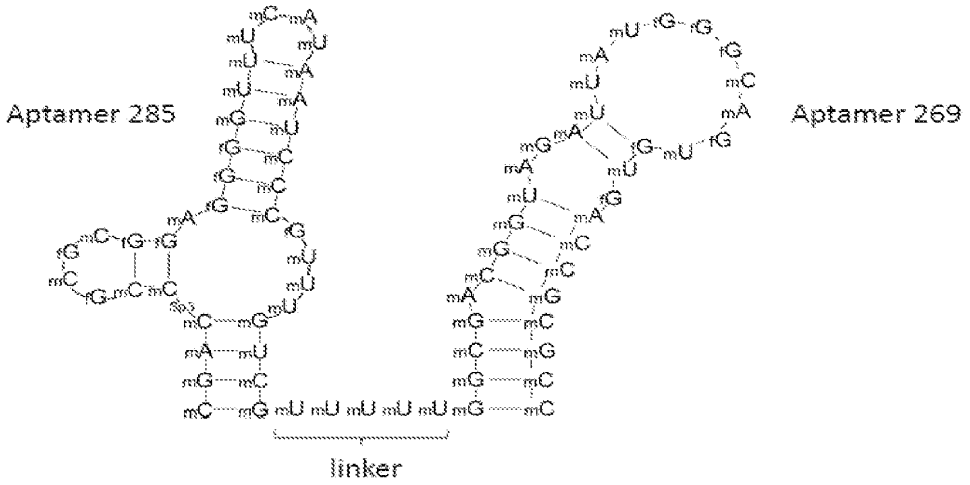

Aptamer 285
Aptamer 269
linker

FIG. 6

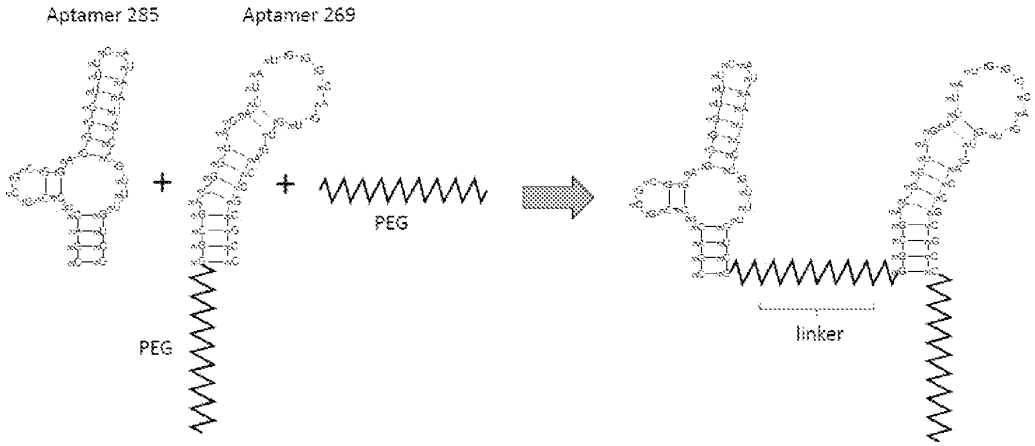
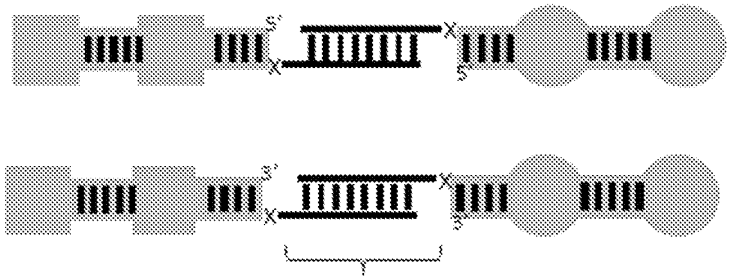

Aptamer 285
Aptamer 269
PEG
PEG
linker

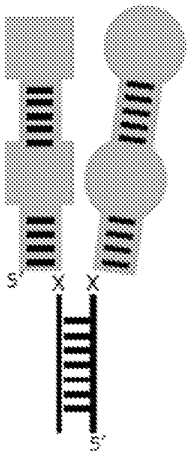
FIG. 7



DL = duplex length = 3 to 25 nucleotides

X = any nucleotidyl linker, 0 to 25 nucleotides long
any non-nucleotidyl linker (e.g. PEG)

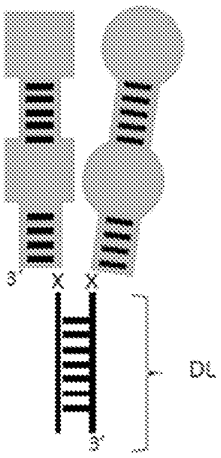
FIG. 8A



DL = duplex length = 3 to 25 nucleotides

X = any nucleotidyl linker, 0 to 25 nucleotides long
any non-nucleotidyl linker (e.g. PEG)

FIG. 8B



DL = duplex length = 3 to 25 nucleotides

X = any nucleotidyl linker, 0 to 25 nucleotides long
any non-nucleotidyl linker (e.g. PEG)

FIG. 8C

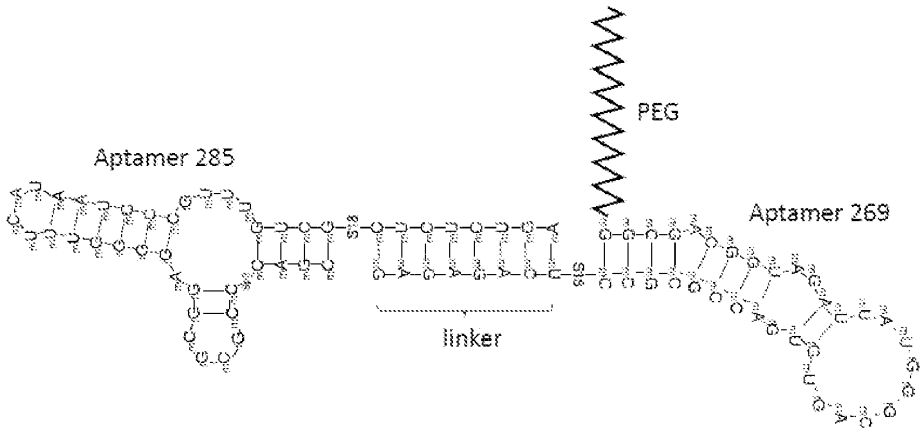


FIG. 9