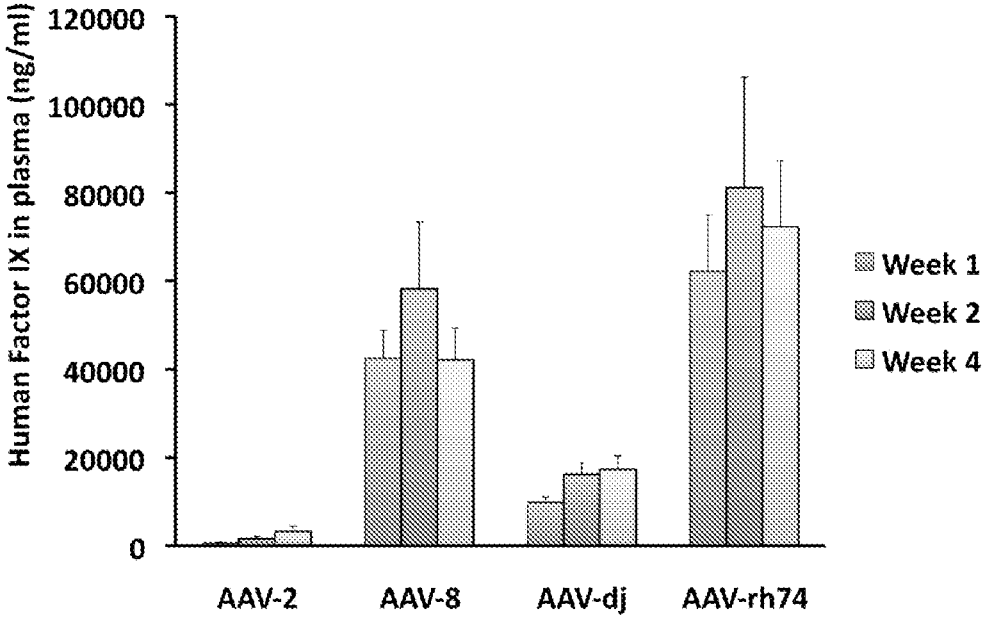
Figure 1



[0203]

Figure 2

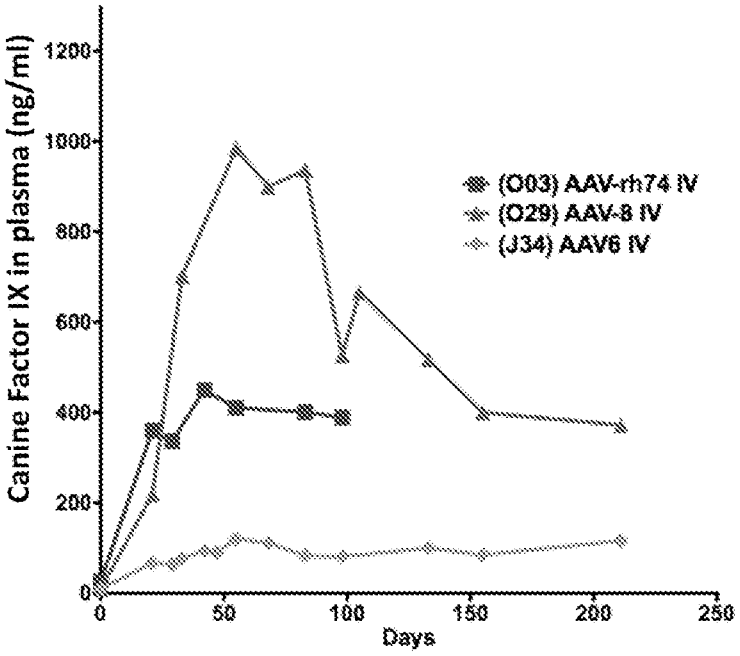

Canine Factor IX in plasma (ng/ml)
1200
1000
800
600
400
200
0
0
50
100
150
200
250
Days
(O03) AAV-rh74 IV
(O29) AAV-8 IV
(J34) AAV6 IV

Figure 3 (SEQ ID NOs:1-5)

Rh74 VP1 Amino Acid (SEQ ID NO:1):
MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDNGRGLVLPGYKYLGPFNGLDKG
EPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQAKKRV
LEPLGLVESPVKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDSESVPDPQPIGE
PPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDRVITTSTRTWALPTYN
NHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDWQRLINNNWGFRPKRLNFK
LFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGSAHQGCLPPFPADVFMIPQYGYLTL
NNGSQAVGRSSFYCLEYFPSQMLRTGNNFEFSYNFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLS
RTQSTGGTAGTQQLLFSQAGPNNMSAQAKNWLPGPCYRQQRVSTTLSQNNNSNFAWTGATKYH
LNGRDSLVNPGVAMATHKDDEERFFPSSGVLMFGKQGAGKDNVDYSSVMLTSEEEIKTTNPVAT
EQYGVVADNLQQQNAAPIVGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGG
FGLKHPPPQILIKNTPVPADPPTTFNQAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTS
NYYKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL.

Rh74 VP1 DNA (SEQ ID NO:2):
ATGGCTGCCGATGGTTATCTTCCAGATTGGCTCGAGGACAACCTCTCTGAGGGCATTCGCGAGTG
GTGGGACCTGAAACCTGGAGCCCCGAAACCCAAAGCCAACCAGCAAAAGCAGGACAACGGCCGG
GGTCTGGTGCTTCCTGGCTACAAGTACCTCGGACCCTTCAACGGACTCGACAAGGGGGAGCCCGT
CAACGCGGCGGACGCAGCGGCCCTCGAGCACGACAAGGCCTACGACCAGCAGCTCCAAGCGGGTG
ACAATCCGTACCTGCGGTATAATCACGCCGACGCCGAGTTTCAGGAGCGTCTGCAAGAAGATAC
GTCTTTTGGGGGCAACCTCGGGCGCGCAGTCTTCCAGGCCAAAAAGCGGGTTCTCGAACCTCTGG
GCCTGGTTGAATCGCCGGTTAAGACGGCTCCTGGAAAGAAGAGACCGGTAGAGCCATCACCCCA
GCGCTCTCCAGACTCCTCTACGGGCATCGGCAAGAAAGGCCAGCAGCCCGCAAAAAAGAGACTCA
ATTTTGGGCAGACTGGCGACTCAGAGTCAGTCCCCGACCCTCAACCAATCGGAGAACCACCAGCA
GGCCCCTCTGGTCTGGGATCTGGTACAATGGCTGCAGGCGGTGGCGCTCCAATGGCAGACAATAA
CGAAGGCGCCGACGGAGTGGGTAGTTCCTCAGGAAATTGGCATTGCGATTCCACATGGCTGGGC
GACAGAGTCATCACCACCAGCACCCGCACCTGGGCCCTGCCCACCTACAACAACCACCTCTACAA
GCAAATCTCCAACGGGACCTCGGGAGGAAGCACCAACGACAACACCTACTTCGGCTACAGCACCC
CCTGGGGGTATTTTGACTTCAACAGATTCCACTGCCACTTTTCACCACGTGACTGGCAGCGACTC
ATCAACAACAACTGGGGATTCCGGCCCAAGAGGCTCAACTTCAAGCTCTTCAACATCCAAGTCAA
GGAGGTCACGCAGAATGAAGGCACCAAGACCATCGCCAATAACCTTACCAGCACGATTCAGGTC
TTTACGGACTCGGAATACCAGCTCCCGTACGTGCTCGGCTCGGCGCACCAGGGCTGCCTGCCTCC
GTTCCCGGCGGACGTCTTCATGATTCCTCAGTACGGGTACCTGACTCTGAACAATGGCAGTCAGG
CTGTGGGCCGGTCGTCCTTCTACTGCCTGGAGTACTTTCCTTCTCAAATGCTGAGAACGGGCAAC
AACTTTGAATTCAGCTACAACTTCGAGGACGTGCCCTTCCACAGCAGCTACGCGCACAGCCAGAG
CCTGGACCGGCTGATGAACCCTCTCATCGACCAGTACTTGTACTACCTGTCCCGGACTCAAAGCA
CGGGCGGTACTGCAGGAACTCAGCAGTTGCTATTTTCTCAGGCCGGGCCTAACAACATGTCGGCT
CAGGCCAAGAACTGGCTACCCGGTCCCTGCTACCGGCAGCAACGCGTCTCCACGACACTGTCGCA
GAACAACAACAGCAACTTTGCCTGGACGGGTGCCACCAAGTATCATCTGAATGGCAGAGACTCT
CTGGTGAATCCTGGCGTTGCCATGGCTACCCACAAGGACGACGAAGAGCGATTTTTTCCATCCAG
CGGAGTCTTAATGTTTGGGAAACAGGGAGCTGGAAAAGACAACGTGGACTATAGCAGCGTGATG
CTAACCAGCGAGGAAGAAATAAAGACCACCAACCCAGTGGCCACAGAACAGTACGGCGTGGTGG
CCGATAACCTGCAACAGCAAAACGCCGCTCCTATTGTAGGGGCCGTCAATAGTCAAGGAGCCTTA
CCTGGCATGGTGTGGCAGAACCGGGACGTGTACCTGCAGGGTCCCATCTGGGCCAAGATTCCTCA
TACGGACGGCAACTTTCATCCCTCGCCGCTGATGGGAGGCTTTGGACTGAAGCATCCGCCTCCTC
AGATCCTGATTAAAAACACACCTGTTCCCGCGGATCCTCCGACCACCTTCAATCAGGCCAAGCTG
GCTTCTTTCATCACGCAGTACAGTACCGGCCAGGTCAGCGTGGAGATCGAGTGGGAGCTGCAGA
AGGAGAACAGCAAACGCTGGAACCCAGAGATTCAGTACACTTCCAACTACTACAAATCTACAAA

TGTGGACTTTGCTGTCAATACTGAGGGTACTTATTCCGAGCCTCGCCCCATTGGCACCCGTTACC
TCACCCGTAATCTGTAA

Rh74 VP2 Amino Acid (SEQ ID NO:3):

TAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDSESVPDPQPIGEPPAGPSGLGSGTMAAGGGAPMAD
NNEGADGVGSSSGNWHCDSTWLGDRVITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFH
CHFSPRDWQRLINNNWGFRPKRLNFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGSAHQGCLPPF
PADVFMIPQYGYLTLNNGSQAVGRSSFYCLEYFPSQMLRTGNNFEFSYNFEDVPFHSSYAHSQSLDRLMNPLIDQYL
YYLSRTQSTGGTAGTQQLLFSQAGPNNMSAQAKNWLPGPCYRQQRVSTTLSQNNNSNFAWTGATKYHLNGRDSLVNP
GVAMATHKDDEERFFPSSGVLMFGKQGAGKDNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQQQNAAPIVGAVN
SQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKHPPPQILIKNTPVPADPPTTFNQAKLASFITQY
STGQVSVEIEWELQKENSKRWNPEIQYTSNYYKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL

Rh74 VP3 Amino Acid (SEQ ID NO:4):

MAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDRVITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYST
PWGYFDFNRFHCHFSPRDWQRLINNNWGFRPKRLNFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVL
GSAHQGCLPPFPADVFMIPQYGYLTLNNGSQAVGRSSFYCLEYFPSQMLRTGNNFEFSYNFEDVPFHSSYAHSQSLD
RLMNPLIDQYLYYLSRTQSTGGTAGTQQLLFSQAGPNNMSAQAKNWLPGPCYRQQRVSTTLSQNNNSNFAWTGATKY
HLNGRDSLVNPGVAMATHKDDEERFFPSSGVLMFGKQGAGKDNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQQ
QNAAPIVGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKHPPPQILIKNTPVPADPPTTFN
QAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNYYKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL

RHM4-1 VP1 Amino Acid (SEQ ID NO:5)

1 maadgylpdwlednlsegirewwdlkpgapkpkanqqkqdngrglvlpgykylgpfngld
61 kgepvnaadaaalehdkaydqqlqagdnpylrynhadaefqerlqedtsfggnlgravfq
121 akkrvleplglvespvktapgkkrpvepspqrspdsstgigkkgqqpakkrlnfgqtgds
181 esvpdpqpigeppa**a**psg**v**g**pn**tmaagggapmadnnegadgvgsssgnwhcdstwlgdrv
241 ittstrtwalptynnhlykqisngtsggstndntyfgystpwgyfdfnrfhchfsprdwq
301 rlinnnwgfrpkrlnfklfniqvkevtqnegtktiannltstiqvftdseyqlpyvlgsa
361 hqgclppfpadvfmipqygyltlnngsqav grssfycleyfpsqmlrtgnnfefsynfed
421 vpfhssyahsqsldrlmnplidqylyylsrtqstggtagtqqllfsqagpnnmsaqaknw
481 lpgpcyrqqrvsttlsqnnnsnfawtgatkyhlngrdslvnpgvamathkddeerffpss
541 gvlmfgkqgagkdnvdyssvmltseeeikttnpvateqygvvadnlqqqnaapivgavns
601 qgalpgmvwqnrdvylqgpiwakiphtdgnfhpsplmggfglkhpppqilikntpvpadp
661 pttfnqaklasfitqystgqvsveiewelqkenskrwnpeiqytsnyykstnvdfavnte
721 gtyseprpigtryltrnl

Figure 4

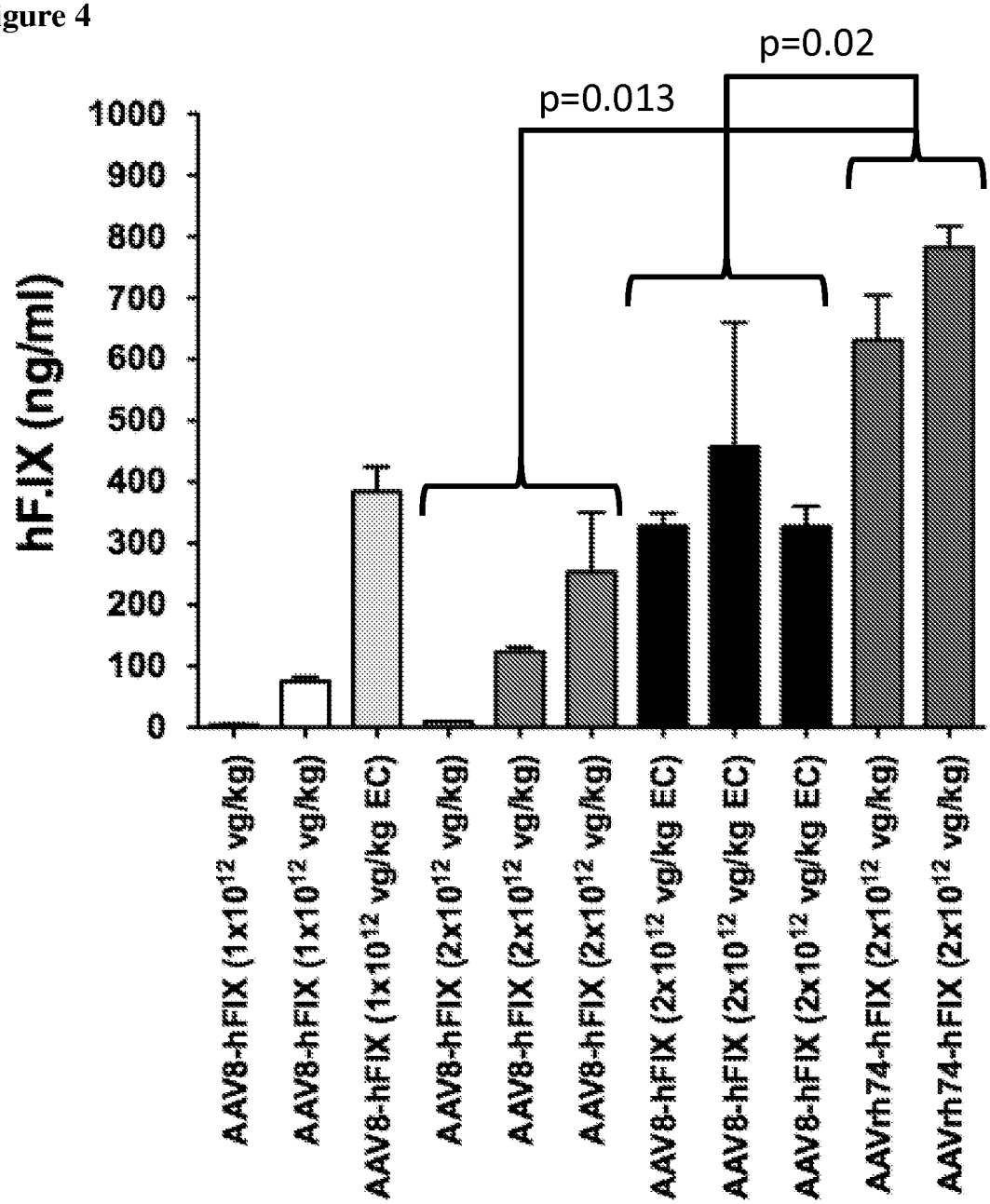
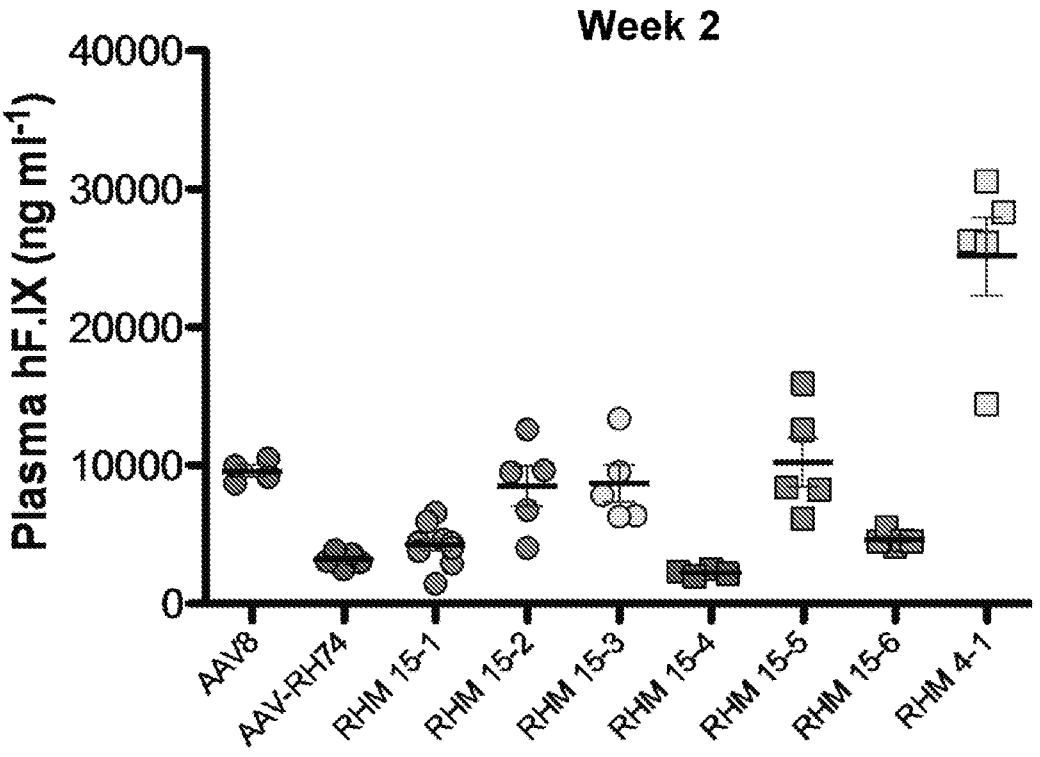
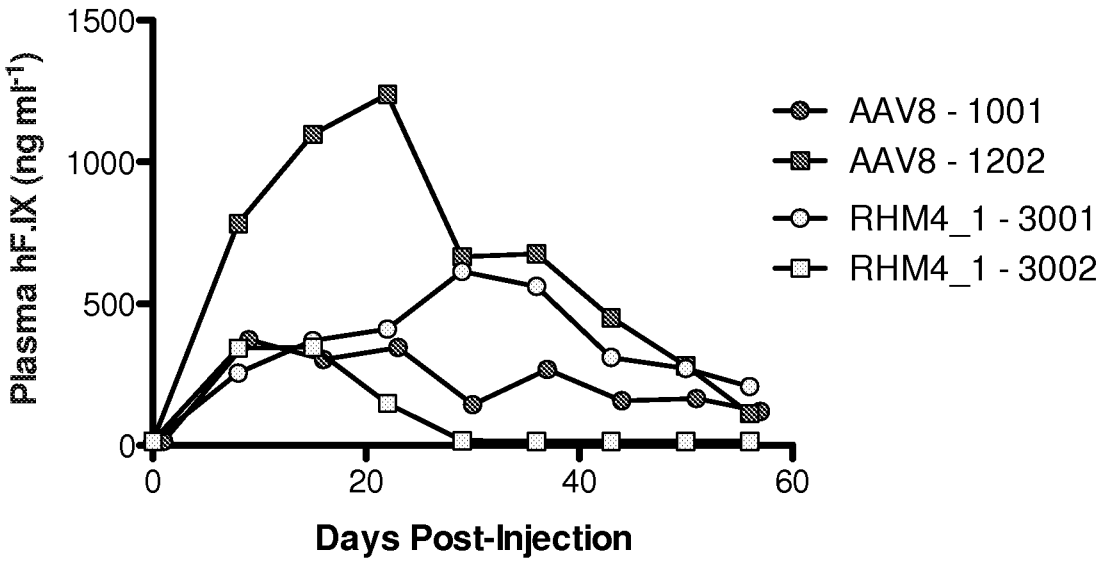

p=0.02
p=0.013
hF.IX (ng/ml)
1000
900
800
700
600
500
400
300
200
100
0
AAV8-hFIX (1x10^12 vg/kg)
AAV8-hFIX (1x10^12 vg/kg)
AAV8-hFIX (1x10^12 vg/kg EC)
AAV8-hFIX (2x10^12 vg/kg)
AAV8-hFIX (2x10^12 vg/kg)
AAV8-hFIX (2x10^12 vg/kg)
AAV8-hFIX (2x10^12 vg/kg EC)
AAV8-hFIX (2x10^12 vg/kg EC)
AAV8-hFIX (2x10^12 vg/kg EC)
AAVrh74-hFIX (2x10^12 vg/kg)
AAVrh74-hFIX (2x10^12 vg/kg)

Figure 5



RHM4_1	G195A-L199V- S201P-G202N
RHM15_2	G195A-L199V- S201P-G202N K(137/259/333/530/552/569/38/51/77/163/169)R
RHM15_3	G195A-L199V- S201P-G202N K(137/259/333/530/552/569/38/51/77/163/547)R
RHM15_4	G195A-L199V- S201P-G202N K(137/259/333/530/552/569/38/51/77/163/668)R
RHM15_5	G195A-L199V- S201P-G202N K(137/259/333/530/552/569/38/51/77/547/163)R
RHM15_6	G195A-L199V- S201P-G202N K(137/259/333/530/552/569/38/51/77/547/688)R

Figure 6


1500
1000
500
0
Plasma hF.IX (ng ml-1)
0
20
40
60
Days Post-Injection
AAV8 - 1001
AAV8 - 1202
RHM4_1 - 3001
RHM4_1 - 3002