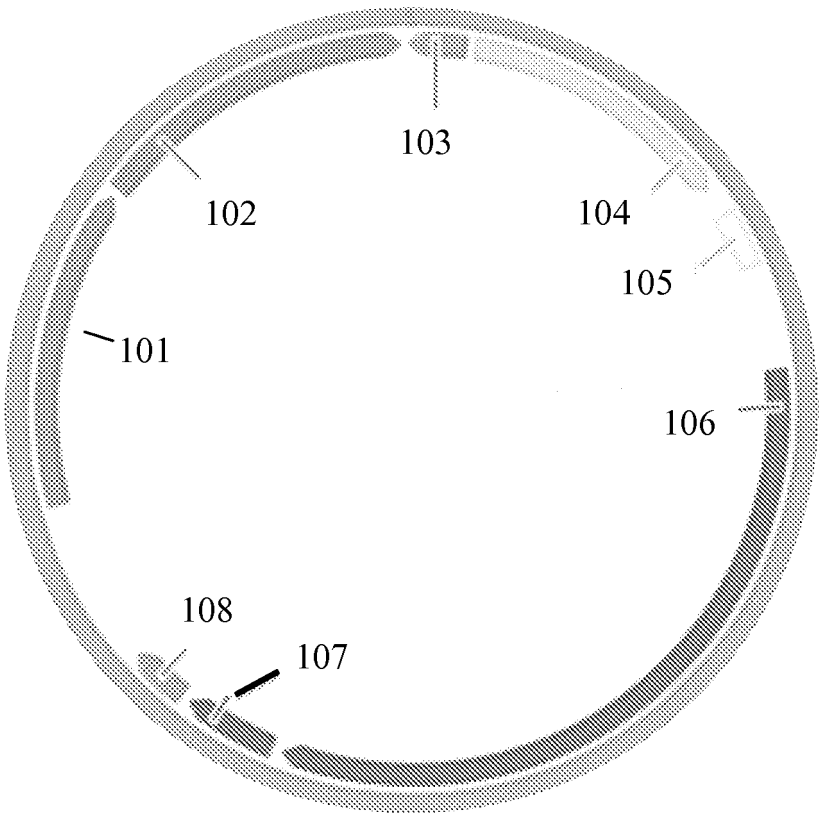


FIG. 1

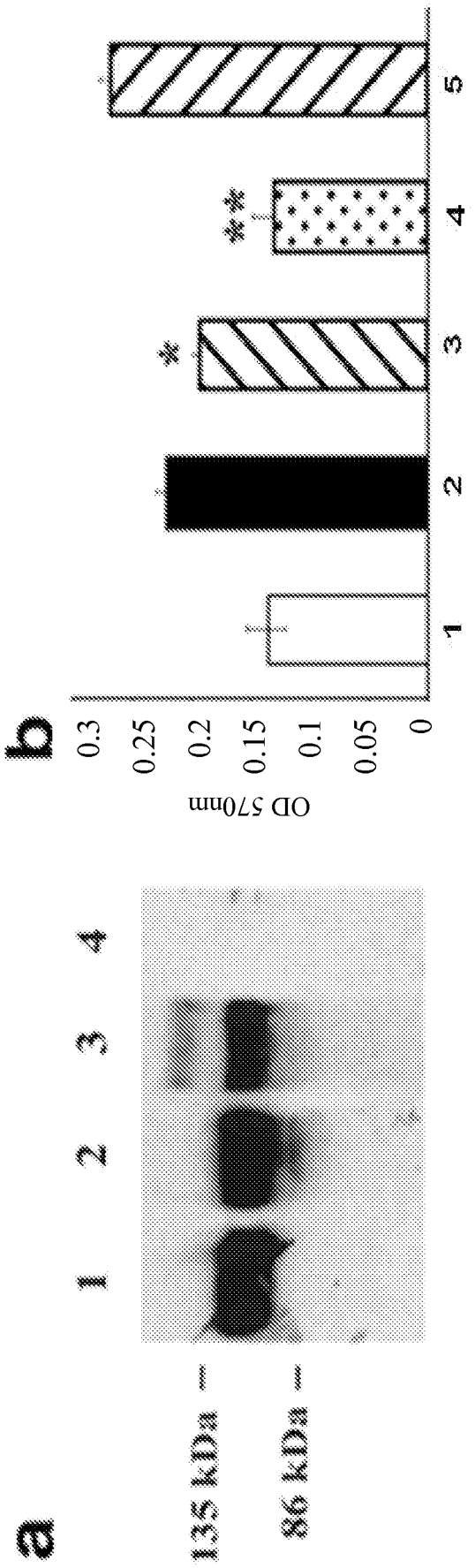


FIG. 2

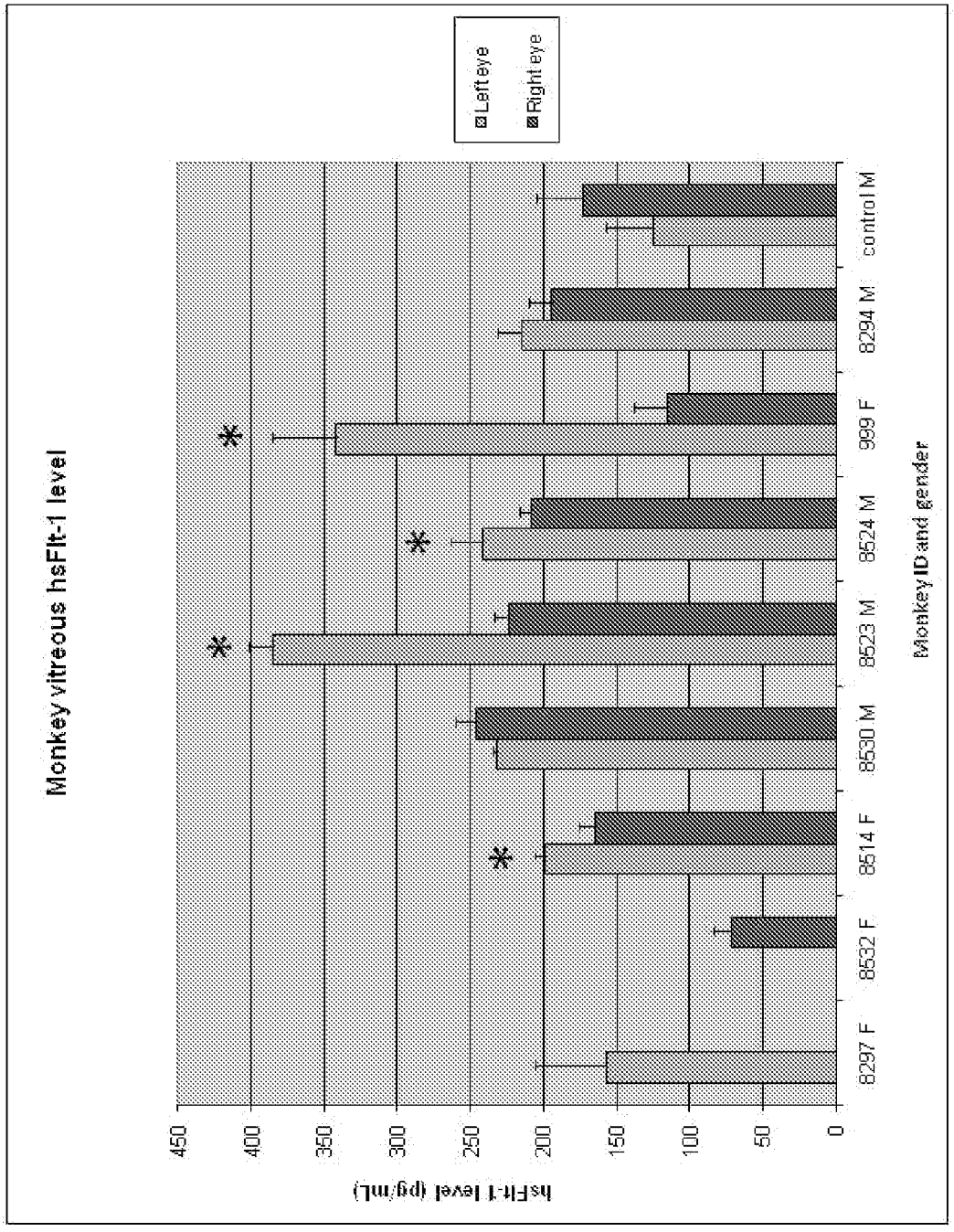

Monkey vitreous hsFlt-1 level
Left eye
Right eye
hsFlt-1 level (pg/mL)
0
50
100
150
200
250
300
350
400
450
8297 F
8532 F
8514 F
8530 M
8523 M
8524 M
999 F
8294 M
control M
Monkey ID and gender
*
*
*
*

FIG. 3A

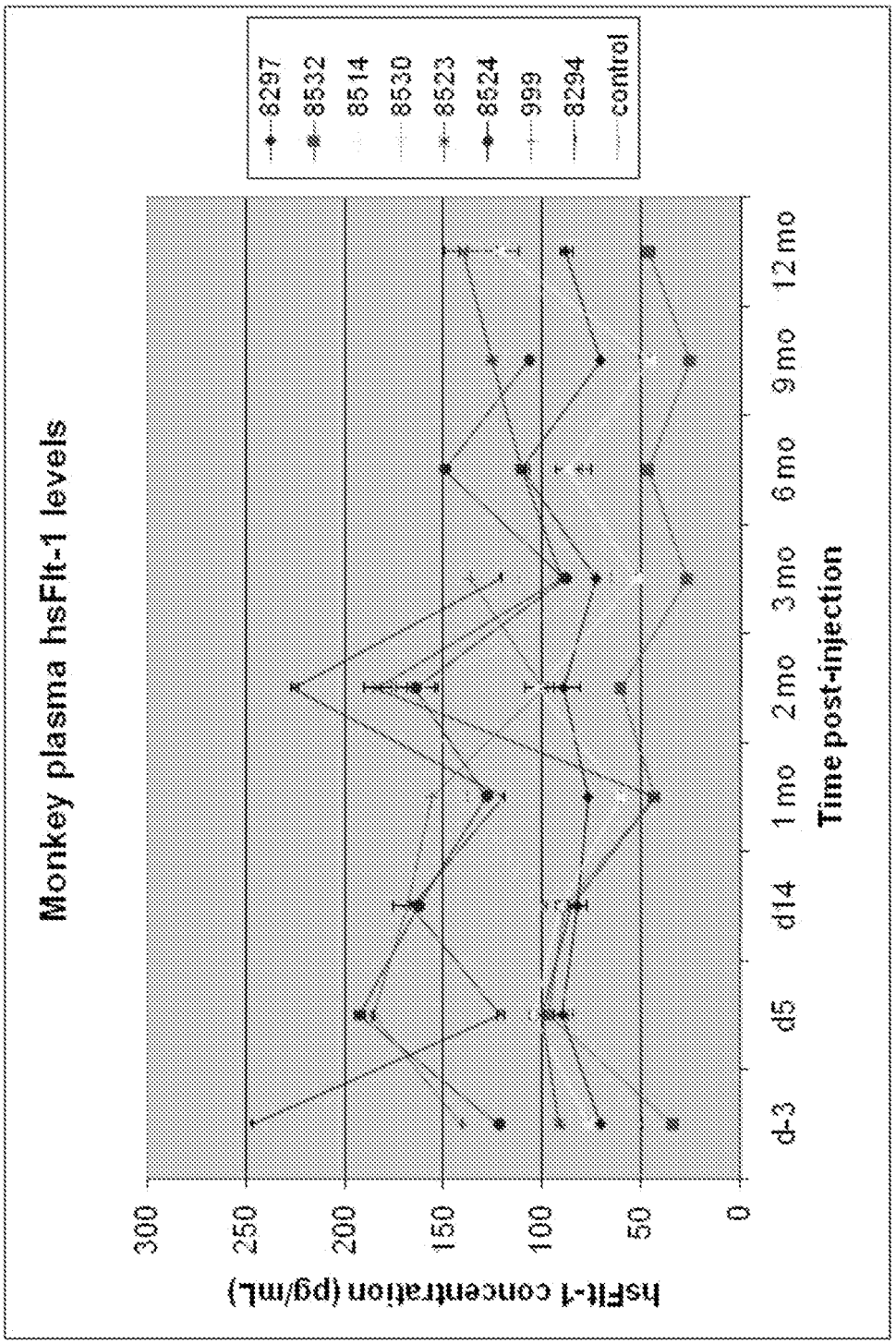

Monkey plasma hsFlt-1 levels
hsFlt-1 concentration (pg/mL)
300
250
200
150
100
50
0
d-3
d5
d14
1 mo
2 mo
3 mo
6 mo
9 mo
12 mo
Time post-injection
8297
8532
8514
8530
8523
8524
999
8294
control

FIG. 3B

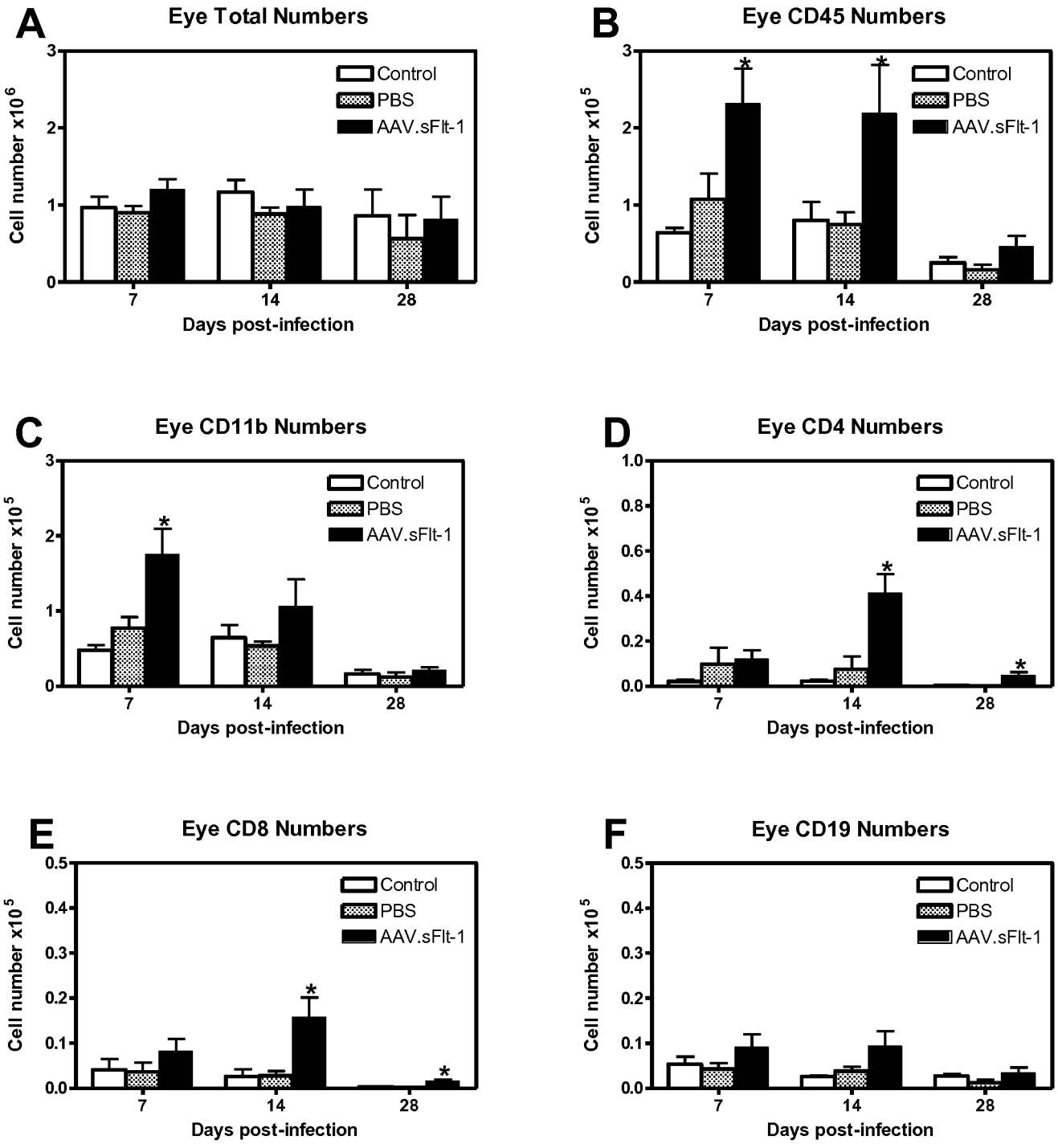

A
Eye Total Numbers
Cell number x10^6
Control
PBS
AAV.sFlt-1
Days post-infection
B
Eye CD45 Numbers
Cell number x10^5
C
Eye CD11b Numbers
D
Eye CD4 Numbers
E
Eye CD8 Numbers
F
Eye CD19 Numbers
7
14
28

FIG. 4

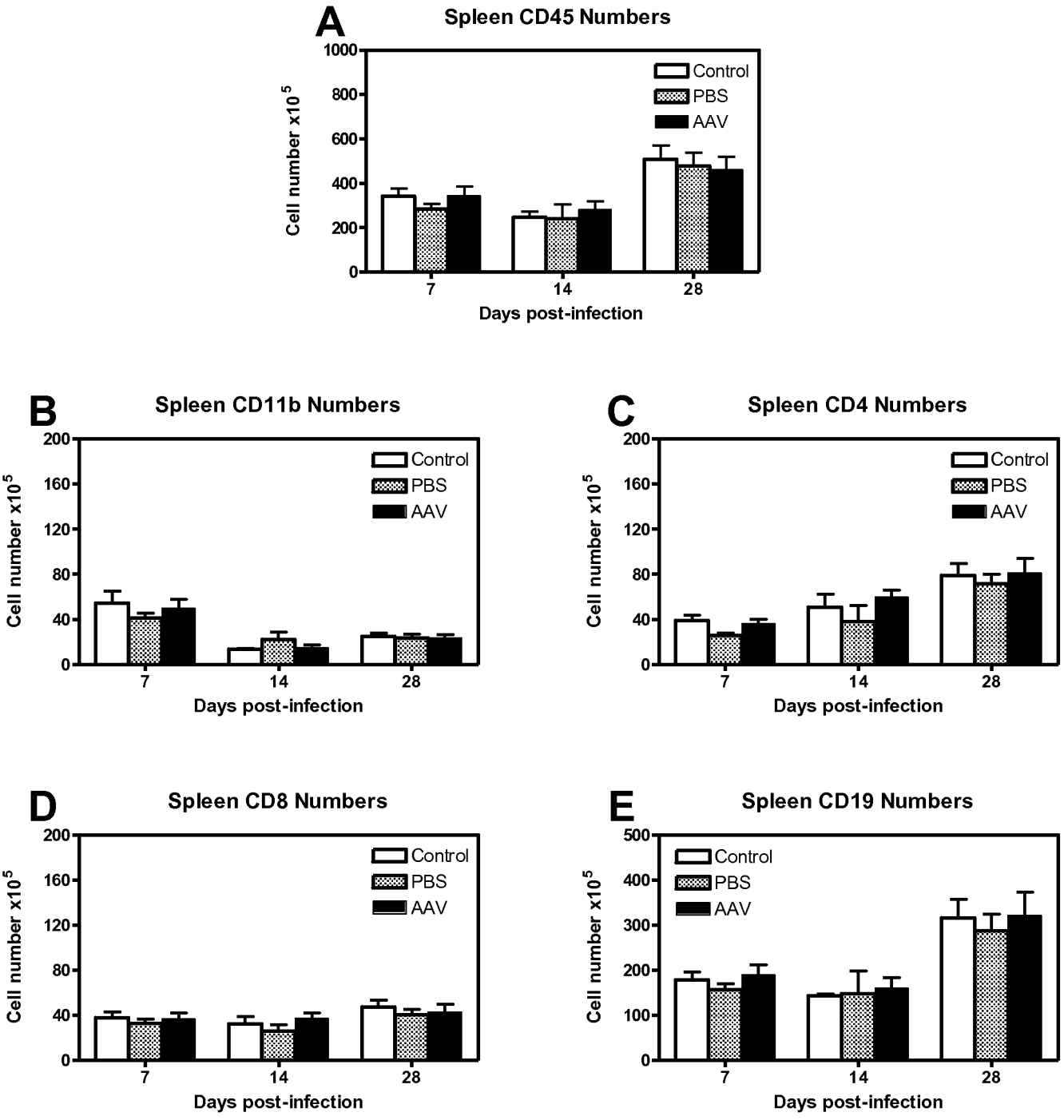

A
Spleen CD45 Numbers
Cell number x10^5
1000
800
600
400
200
0
Control
PBS
AAV
7
14
28
Days post-infection
B
Spleen CD11b Numbers
Cell number x10^5
200
160
120
80
40
0
Control
PBS
AAV
7
14
28
Days post-infection
C
Spleen CD4 Numbers
Cell number x10^5
200
160
120
80
40
0
Control
PBS
AAV
7
14
28
Days post-infection
D
Spleen CD8 Numbers
Cell number x10^5
200
160
120
80
40
0
Control
PBS
AAV
7
14
28
Days post-infection
E
Spleen CD19 Numbers
Cell number x10^5
500
400
300
200
100
0
Control
PBS
AAV
7
14
28
Days post-infection

FIG. 5

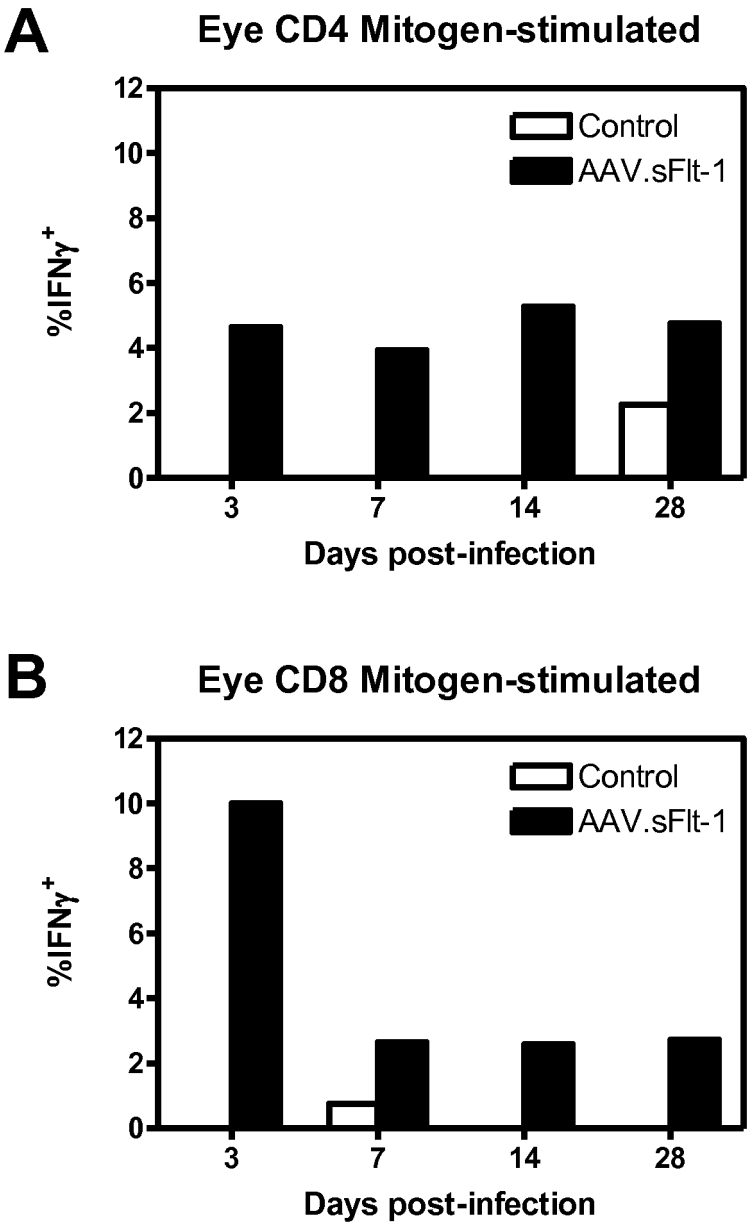

A
Eye CD4 Mitogen-stimulated
%IFNγ+
12
10
8
6
4
2
0
Control
AAV.sFlt-1
3
7
14
28
Days post-infection
B
Eye CD8 Mitogen-stimulated
%IFNγ+
12
10
8
6
4
2
0
Control
AAV.sFlt-1
3
7
14
28
Days post-infection

FIG. 6

Origin 1

ATGGAAAAACGCCAGCAACG (SEQ ID NO: 1)

Origin 2

AAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTTCCACTGAGCGTCAGACCCCGTAGAAA
AGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCC
GGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGG
CCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTT
ACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAA
CGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAG
CGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGAC
TTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCT
GGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGC
CGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGA (SEQ ID NO: 2)

Origin 3

GCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGG
GGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTA
TGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGT
GGATAACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAA (SEQ ID
NO: 3)

Origin 4

AAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATC
AAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTTCTTCTAGTGTAGCCGTAGTTAGGCCACCA
CTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGG
TTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCT
ACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAG
GGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGC
GTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCG (SEQ ID NO: 4)

FIG. 7A

Origin 5

TGTTGTTTGTCGGTTAACGTCGACCTAGAGCTGCCTCGCGCGTTTCGGTGATGACGGTGAAAACCTCTGACACATGCAGCTCCCGGAGACGGT
CACAGCTTGTCTGTAAGCGGATGCCGGGAGCAGACAAGCCCGTCAGGGCGCGTCAGCGGGTGTTGGCGGGTGTCGGGGCGCAGCCATGACC
CAGTCACGTAGCGATAGCGGAGTGTATACTGGCTTAACTATGCGGCATCAGAGCAGATTGTACTGAGAGTGCACCATATGCGGTGTGAAATA
CCGCACAGATGCGTAAGGAGAAAATACCGCATCAGGCGCTCTTCCGCTTCCTCGCTCACTGACTCGCTGCGCTCGGTCGTTCGGCTGCGGCGA
GCGGTATCAGCTCACTCAAAGGCGGTAATACGGTTATCCACAGAATCAGGGGATAACGCAGGAAAGAACATGTGAGCAAAAGGCCAGCAAA
AGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCACAAAAATCGACGCTCAAGTCAG
AGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCCTGTTCCGACCCTGCCGCTTACC
GGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCAATGCTCACGCTGTAGGTATCTCAGTTCGGTGTAGGTCGTTCGCTCCA
AGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTCCAACCCGGTAAGACACGACT
TATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCTTGAAGTGGTGGCCTAACTAC
GGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTAGCTCTTGATCCGGCAAACAA
ACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAAGATCCTTTGATCTTTTCTACG
GGGTCTGACGCTCAGTGGAACGAAAACTCACGTTAAGGGATTTTGGTCATGAGATTATCAAAAAGGATCTTCACCTAGATCCTTTTAAATTAA
AAATGAAGTTTTAAATCAATCTAAAGTATATATGAGTAAACTTGGTCTGACAGTT (SEQ ID NO: 5)

Origin 6

CCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGG
TTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCC
GTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAG
TCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTT
GGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCATTGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTAT
CCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCC
ACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGG
CCTTTTGCTGGCCTTTTGCTCACAT (SEQ ID NO: 6)

Origin 7

ATGTGAGCAAAAGGCCAGCAAAAGGCCAGGAACCGTAAAAAGGCCGCGTTGCTGGCGTTTTTCCATAGGCTCCGCCCCCCTGACGAGCATCA
CAAAAATCGACGCTCAAGTCAGAGGTGGCGAAACCCGACAGGACTATAAAGATACCAGGCGTTTCCCCCTGGAAGCTCCCTCGTGCGCTCTCC
TGTTCCGACCCTGCCGCTTACCGGATACCTGTCCGCCTTTCTCCCTTCGGGAAGCGTGGCGCTTTCTCATAGCTCACGCTGTAGGTATCTCAGTT
CGGTGTAGGTCGTTCGCTCCAAGCTGGGCTGTGTGCACGAACCCCCCGTTCAGCCCGACCGCTGCGCCTTATCCGGTAACTATCGTCTTGAGTC
CAACCCGGTAAGACACGACTTATCGCCACTGGCAGCAGCCACTGGTAACAGGATTAGCAGAGCGAGGTATGTAGGCGGTGCTACAGAGTTCT
TGAAGTGGTGGCCTAACTACGGCTACACTAGAAGGACAGTATTTGGTATCTGCGCTCTGCTGAAGCCAGTTACCTTCGGAAAAAGAGTTGGTA
GCTCTTGATCCGGCAAACAAACCACCGCTGGTAGCGGTGGTTTTTTTGTTTGCAAGCAGCAGATTACGCGCAGAAAAAAAGGATCTCAAGAA
GATCCTTTGATCTTTTCTACGGG (SEQ ID NO: 7)

FIG. 7B

Origin 8

TTAATAAGATGATCTTCTTGAGATCGTTTTGGTCTGCGCGTAATCTCTTGCTCTGAAAACGAAAAAACCGCCTTGCAGGGCGGTTTTTCGAAGG
TTCTCTGAGCTACCAACTCTTTGAACCGAGGTAACTGGCTTGGAGGAGCGCAGTCACCAAAACTTGTCCTTTCAGTTTAGCCTTAACCGGCGCA
TGACTTCAAGACTAACTCCTCTAAATCAATTACCAGTGGCTGCTGCCAGTGGTGCTTTTGCATGTCTTTCCGGGTTGGACTCAAGACGATAGTT
ACCGGATAAGGCGCAGCGGTCGGACTGAACGGGGGGTTCGTGCATACAGTCCAGCTTGGAGCGAACTGCCTACCCGGAACTGAGTGTCAGG
CGTGGAATGAGACAAACGCGGCCATAACAGCGGAATGACACCGGTAAACCGAAAGGCAGGAACAGGAGAGCGCACGAGGGAGCCGCCAG
GGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCACTGATTTGAGCGTCAGATTTCGTGATGCTTGTCAGGGGGGCGGAGCC
TATGGAAAAACGGCTTTGCCGCGGCCCTCTCACTTCCCTGTTAAGTATCTTCCTGGCATCTTCCAGGAAATCTCCGCCCCGTTCGTAAGCCATTT
CCGCTCGCCGCAGTCGAACGACCGAGCGTAGCGAGTCAGTGAGCGAGGAAGCGGAATATATCCTGTATCACATATTCTGCTGACGCACCGGT
GCAGCCTTTTTTCTCCTGCCACATGAAGCACTTCACTGACACCCTCATCAGTGCCAACATAGTAAGCCAGTATACACTCCGCTAGCGC (SEQ ID NO: 8)

Origin 9

AAACGCCAGCAACGCGGCCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATA
ACCGTATTACCGCCTTTGAGTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCG
CCCAATACGCAAACCGCCTCTCCCCGCGCGTTGGCCGATTCATTAATGCAG (SEQ ID NO: 9)

Origin 10

AAATTGTAAACGTTAATATTTTGTTAAAATTCGCGTTAAATATTTGTTAAATCAGCTCATTTTTTAACCAATAGGCCGAAATCGGCAAAATCCCT
TATAAATCAAAAGAATAGACCGCGATAGGGTTGAGTGTTGTTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACGTGGACTCCAACGTCAAA
GGGCGAAAAACCGTCTATCAGGGCGATGGCCCACTACGTGAACCATCACCCAAATCAAGTTTTTTGCGGTCGAGGTGCCGTAAAGCTCTAAAT
CGGAACCCTAAAGGGAGCCCCCGATTTAGAGCTTGACGGGGAAAGCCGGCGAACGTGGCGAGAAAGGAAGGGAAGAAAGCGAAAGGAGC
GGGCGCTAGGGCGCTGGCAAGTGTAGCGGTCACGCTGCGCGTAACCACCACACCCGCCGCGCTTAATGCGCCGCTACAGGGCGCGT (SEQ ID NO: 10)

Origin 11

GGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCTTTCGCTTTCTTCCCT
TCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTACGGCACCTCGACCC
CAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAGTCCACGTTCTTTAAT
AGTGGACTCTTGTTCCAAACTGGAA (SEQ ID NO: 11)

Origin 12

ACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCTCCT
TTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCTTTA
CGGCACCTCGACCCCAAAAAACTTGATTAGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGGAG
TCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTGGAACAACACTCAACCCTATCTCGGTCTATTCTTTTGATTTATAAGGGATTTTGCCGATT
TCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTTTAACAAAATATTAACGCTTACAATTT (SEQ ID NO: 12)

Origin 14

AATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAAGTAGTGAGG (SEQ ID NO: 13)

FIG. 7C

Origin 15

TGGACAGCGAACGCACACTACAACCTTGGATAGAGTTAGGAATTAGTAGACGGACATACTACAGGGATTTAAATGATAATCATTCTCAAAAAT
GACACCAGATAAGCCTAAATCAGATAACAGCCCCAAAAGCGAGCTTTTGGGGTGCCTTTTAGACGGTGCTAGGTTTTTGACAGCAGATAAGCC
TAAATCAGATAACAGCCGAATCGATAAGCCTTAGTTGGTTAAGGGGGCAGGAAATTCATATTGAACAAATGTTTAGTTAAGTGTAGAATAATC
ATACATCCTTATTAAGGGCAAGCATACTCAAGCCCCACAAAGTGTGCTTGAAATCCTTGTAAGGGGAAATCCCCCTTAACCCC (SEQ ID NO:
14)

Origin 16

TTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCACCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTACCA
ACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACTGTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACT
CTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGCTGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAG
ACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCGTGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTG
AGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAGAAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACA
GGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAGTCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTG
TGATGCTCGTCAGGGGGGCGGAGCCTATGGAAA (SEQ ID NO: 15)

Origin 17

TTTACGCGCCCTGTAGCGGCGCATTAAGCGCGGCGGGTGTGGTGGTTACGCGCAGCGTGACCGCTACACTTGCCAGCGCCCTAGCGCCCGCT
CCTTTCGCTTTCTTCCCTTCCTTTCTCGCCACGTTCGCCGGCTTTCCCCGTCAAGCTCTAAATCGGGGGCTCCCTTTAGGGTTCCGATTTAGTGCT
TTACGGCACCTCGACCCCAAAAAACTTGATTTGGGTGATGGTTCACGTAGTGGGCCATCGCCCTGATAGACGGTTTTTCGCCCTTTGACGTTGG
AGTCCACGTTCTTTAATAGTGGACTCTTGTTCCAAACTTGAACAACACTCAACCCTATCTCGGGCTATTCTTTTGATTTATAAGGGATTTTGCCG
ATTTCGGCCTATTGGTTAAAAAATGAGCTGATTTAACAAAAATTTAACGCGAATTTTAACAAAATATTAACGTTTACAATTT (SEQ ID NO: 16)

FIG. 7D

Promoter 1

ATGCATTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCG
CCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAAT
GGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAAT
GGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGAT
GCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTT
TTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCT
ATATAAGCAGAGCTGGTTTAGTGAACCGTCAGATCCGCTAGC (SEQ ID NO: 17)

Promoter 2

TCAATATTGGCCATTAGCCATATTATTCATTGGTTATATAGCATAAATCAATATTGGCTATTGGCCATTGCATACGTTGTATCTATATCATAATAT
GTACATTTATATTGGCTCATGTCCAATATGACCGCCATGTTGGCATTGATTATTGACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTC
ATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAAT
GACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCA
AGTGTATCATATGCCAAGTCCGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTACGGGACTTT
CCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTTTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACT
CACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAATAACCC
CGCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGAT (SEQ ID NO:
18)

Promoter 3

ACGCGTACTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCC
CGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGTCAATAGGGACTTTCCATTGACGTCA
ATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAA
ATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTG
ATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTG
TTTTGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCT
ATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCA
GCCTCCGTAC (SEQ ID NO: 19)

Promoter 4

ACGCGTGGAGCTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATG
GCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGTCAATAGGGACTTTCCATTGACG
TCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGG
TAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGG
TGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTT
TGTTTTGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGG
TCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGAT
CCAGCCTCC (SEQ ID NO: 20)

FIG. 8A

Promoter 5

TAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTACGGTAAATGGCCCGCCTGGC
TGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTG
GAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCC
GCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCGGTT
TTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCA
CCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAA
GCAGAGCTGGTTTAGTGAACCGTCAGATC (SEQ ID NO: 21)

Promoter 6

GCGGCCGCACGCGTGGAGCTAGTTATTAATAGTAATCAATTACGGGGTCATTAGTTCATAGCCCATATATGGAGTTCCGCGTTACATAACTTAC
GGTAAATGGCCCGCCTGGCTGACCGCCCAACGACCCCCGCCCATTGACGTCAATAATGACGTATGTTCCCATAGTAACGTCAATAGGGACTTT
CCATTGACGTCAATGGGTGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTC
AATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATGACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTA
TTACCATGGTGATGCGGTTTTGGCAGTACATCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCA
ATGGGAGTTTGTTTTGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAACAACTCCGCCCCATTGACGCAAATGGGCGGTAGGCGTGTACG
GTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGTCAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCG
GGACCGATCCAGCCTC (SEQ ID NO: 22)

Promoter 7

GGCGACCGCCCAGCGACCCCCGCCCGTTGACGTCAATAGTGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGG
TGGAGTATTTACGGTAAACTGCCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTCCGCCCCCTATTGACGTCAATGACGGTAAATGGC
CCGCCTAGCATTATGCCCAGTACATGACCTTACGGGAGTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTGATGCG
GTTTTGGCAGTACACCAATGGGCGTGGATAGCGGTTTGACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTG
GCACCAAAATCAACGGGACTTTCCAAAATGTCGTAATAACCCCGCCCCGTTGACCCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATA
TAGCAGAGCTCGTTTAGTGAACCGT (SEQ ID NO: 23)

Promoter 8

TTAGTCATATGTTACTTGGCAGAGGCCGCATGGAAAGTCCCTGGACGTGGGACATCTGATTAATACGTGAGGAGGTCAGCCATGTTCTTTTTG
GCAAAGGACTACGGTCATTGGACGTTTGATTGGCATGGGATAGGGTCAGCCAGAGTTAACAGTGTTCTTTTGGCAAAGGGATACGTGGAAAG
CCCCGGGCCATTTACAGTAAACTGATACGGGGACAAAGCACAGCCATATTTAGTCATGTACTGCTTGGCAGAGGGTCTATGGAAAGTCCCTG
GACGTGGGACGTCTGATTAATATGAAAGAAGGTCAGCCAGAGGTAGCTGTGTCCTTTTTGGCAAAGGGATACGGTTATGGGACGTTTGATTG
GACTGGGATAGGGTCAGCCAGAGTTAACAGTGTTCTTTTGGCAAAGGAAACGTGGAAAGTCCCGGGCCATTTACAGTAAACTGATACTGGGA
CAAAGTACACCCATATTTAGTCATGTTCTTTTTGGCAAAGAGCATCTGGAAAGTCCCGGGCAGCATTATAGTCACTTGGCAGAGGGAAAGGGT
CACTCAGAGTTAAGTACATCTTTCCAGGGCCAATATTCCAGTAAATTACACTTAGTTTTATGCAAATCAGCCACAAAGGGGATTTTCCCGGTCA
ATTATGACTTTTTCCTTAGTCATGCGGTATCCAATTACTGCCAAATTGGCAGTACATACTAGGTGATTCACTGACATTTGGCCGTCCTCTGGAAA
GTCCCTGGAAACCGCTCAAGTACTGTATCATGGTGACTTTGCATTTTTGGAGAGCACGCCCCACTCCACCATTGGTCCACGTACCCTATGGGGG
AGTGGTTTATGAGTATATAAGGGGCTCCGGTTTAGAAGCCGGGCAGAGCG (SEQ ID NO: 24)

FIG. 8B

Promoter 9

ATTGACGTCAATAATGACGTATGTTCCCATAGTAACGCCAATAGGGACTTTCCATTGACGTCAATGGGTGGACTATTTACGGTAAACTGCCCAC
TTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCCCTATTGACGTCAATGACGGTAAATGGCCCGCCTGGCATTATGCCCAGTACATG
ACCTTATGGGACTTTCCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTCGAGGTGAGCCCCACGTTCTGCTTCACTCTCCC
CATCTCCCCCCCCTCCCCACCCCCAATTTTGTATTTATTTATTTTTTAATTATTTTGTGCAGCGATGGGGGCGGGGGGGGGGGGGGGCGCGC
GCCAGGCGGGGCGGGGCGGGGCGAGGGGCGGGGCGGGGCGAGGCGGAGAGGTGCGGCGGCAGCCAATCAGAGCGGCGCGCTCCGAAA
GTTTCCTTTTATGGCGAGGCGGCGGCGGCGGCCCTATAAAAAGCGAAGCGCGCGGCGGGCGGGAGTCGCTGCGACGCTGCCTTCGCCC
CGTGCCCCGCTCCGCCGCCGCCTCGCGCCGCCCGCCCCGGCTCTGACTGACCGCGTTACTCCCACAGGTGAGCGGGCGGGACGGCCCTTCTCC
TCCGGGCTGTAATTAGCGCTTGGTTTAATGACGGCTTGTTTCTTTTCTGTGGCTGCGTGAAAGCCTTGAGGGGCTCCGGGAGGGCCCTTTGTG
CGGGGGGAGCGGCTCGGGGCTGTCCGCGGGGGGACGGCTGCCTTCGGGGGGGACGGGGCAGGGCGGGGTTCGGCTTCTGGCGTGTGACC
GGCGGCTCTAGAGCCTCTGCTAACCATGTTCATGCCTTCTTCTTTTTCCTACAGCTCCTGGGCAACGTGCTGGTTATTGTGCTGTCTCATCATTTT
GGCAAAGAATT (SEQ ID NO: 25)

Promoter 10

GTCGAGGTGAGCCCCACGTTCTGCTTCACTCTCCCCATCTCCCCCCCCTCCCCACCCCCAATTTTGTATTTATTTATTTTTTAATTATTTTGTGCAG
CGATGGGGGCGGGGGGGGGGGGGGGCGCGCGCCAGGCGGGGCGGGGCGGGGCGAGGGGCGGGGCGGGGCGAGGCGGAGAGGTGCGGC
GGCAGCCAATCAGAGCGGCGCGCTCCGAAAGTTTCCTTTTATGGCGAGGCGGCGGCGGCGGCGGCCCTATAAAAAGCGAAGCGCGCGGCG
GGCGGGAGTCGCTGCGTTGCCTTCGCCCCGTGCCCCGCTCCGCGCCGCCTCGCGCCGCCCGCCCCGGCTCTGACTGACCGCGTTACTCCCACA
G (SEQ ID NO: 26)

Promoter 11

TCGAGGTGAGCCCCACGTTCTGCTTCACTCTCCCCATCTCCCCCCCCCTCCCCACCCCCAATTTTGTATTTATTTATTTTTTAATTATTTTGTGCAGC
GATGGGGGCGGGGGGGGGGGGGGGGCGCGCGCCAGGCGGGGCGGGGCGGGGCGAGGGGCGGGGCGGGGCGAGGCGGAGAGGTGCGG
CGGCAGCCAATCAGAGCGGCGCGCTCCGAAAGTTTCCTTTTATGGCGAGGCGGCGGCGGCGGCGGCCCTATAAAAAGCGAAGCGCGCGGCG
GGCG (SEQ ID NO: 27)

Promoter 12

CCAGAAAAAGTCAACACACTTGTCATAAAGTCCCGACGAAGTAAAACAAGCGGAATTAATTCAATTTGGCCAAAAAACCTAGTATAAAGACGT
GCATAGTGTCGGGAAT (SEQ ID NO: 28)

Promoter 13

CTTCCTCACGCTGAACCCCTTTAACCGTTTCAGTGGTCGTGAGTCTTCTAATCTGACTGTGTGACGATGTTTTAAGGATTTGGAGGATTGAGGA
GGATCACCTGGTCAGGTAAATCTGAAATATCCGGATTACATCGGAAGTTGAGCACACGGAAAAACAAAAGACTCTTATTGGATTTAGATCCGT
CAGCCACCTGCTGCTGCTCTTCATCATCAGGCGTCTTCATCGCCCTGCAGTGGGCCTGACAACAGCTTGTGTTTATTACACTAAAAACTTTATAA
ACCCATCACAAACCATATCACACAGCAGGGACTTACCTCTTCATCTGTAAGAAGGATTTTTAGAGTTGGCAGCAGAGCAACAGTCAGCTCTGTT
GCCTCACTAAAAGAGATCTTTGTTTGAATCTGTGACCTGTCCAAGTGTACCTCGCTTCTCACCCACTGACCTCTCCACAACAGTGAGCTGGTTG
GCGGGATGCTAATGTTTCTAGTTATTACGTGTAACCAAACTTAAAGAGTACAGATAAATCATTTAGCATAATTAAAGTTTTACTGTCATGTTATT
GGCTGTTAATATGATTGCTGTTGTAAGTATGTGTTGATCACTAACAATTTAATTAATTAAATCAATCATTAAATTAAGTTTGTTTGGAAAAAGAG
GGAAAACTCATCCACTGACCACATGGTTCTAGGTTCAATTCCTTGGAGTTAAAGGGCTAATCCCAGAGCCATTTACCAAAATAATAAATAAATA
TTTAAATAAGACGTGCATGCGACTGCGGTCACCTTTAAAGCACAAAGTTTTTTTTGAGCAGTGAGGTGAACTCGGGTGGATCTGTGTGTTCAC
AGAGAAAACCTTCTGTAAGCAGATTAAGGAGTCAGAAGTTCTTAATCCTGAAAGTTTAGAAAAATCCCAGCAGCATAATCTTTGCTGTAAGTG
GTTTACGAGCGTATATAAGAGGCTGACACAGCGGCAGCGGCAAAGAGCTCAGGGTCACA (SEQ ID NO: 29)

FIG. 8C

Promoter 14

AAATCAAAAGTCCTCAACCTGGTTGGAAGAATATTGGCACTGAATGGTATCAATAAGGTTGCTAGAGAGGGTTAGAGGTGCACAATGTGCTT
CCATAACATTTTATACTTCTCCAATCTTAGCACTAATCAAACATGGTTGAATACTTTGTTTACTATAACTCTTACAGAGTTATAAGATCTGTGAAG
ACAGGGACAGGGACAATACCCATCTCTGTCTGGTTCATAGGTGGTATGTAATAGATATTTTTAAAAATAAGTGAGTTAATGAATGAGGGTGAG
AATGGAGGCACAGAGGTATTAGGGGGAGGTGGGCCCCAGAGAATGGTGCCAAGGTCCAGTGGGGTGACTGGGATCAGCTCAGGCCTGACG
CTGGCCACTCCCACCTAGCTCCTTTCTTTCTAATCTGTTCTCATTCTCCTTGGGAAGGATTGAGGTCTCTGGAAAACAGCCAAACAACTGTTATG
GGAACAGCAAGCCCAAATAAAGCCAAGCATCAGGGGGATCTGAGAGCTGAAAGCAACTTCTGTTCCCCCTCCCTCAGCTGAAGGGGTGGGG
AAGGGCTCCCAAAGCCATAACTCCTTTTAAGGGATTTAGAAGGCATAAAAAGGCCCCTGGCTGAGAACT (SEQ ID NO: 30)

Promoter 15

ACTCACGGGGATTTCCAAGTCTCCACCCCATTGACGTCAATGGGAGTTTGTTTTGGCACCAAAATCAACGGGACTTTCCAAAATGTCGTAATAA
CCCCGCCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGCAGAGCTCGTTTAGTGAACCGT (SEQ ID NO: 31)

Promoter 16

AAAATCAACGGGACTTTCCAAAATGTCGTAATAACCCCGCCCCGTTGACGCAAATGGGCGGTAGGCGTGTACGGTGGGAGGTCTATATAAGC
AGAGCTCGTTTAGTGAACCGT (SEQ ID NO: 32)

Promoter 17

GTAATACGACTCACTATAGGG (SEQ ID NO: 33)

Promoter 18

TAATACGACTCACTATAGG (SEQ ID NO: 34)

Promoter 19

CCGATTAATCATAAATATGAAAAATAATTGTTGCATCACCCGCCAATGCGTGGCTTAATGCACATCA (SEQ ID NO: 35)

Promoter 20

ATTAACCCTCACTAAAGGG (SEQ ID NO: 36)

Promoter 21

ATTAACCCTCACTAAAGGG (SEQ ID NO: 36)

FIG. 8D

Promoter 22

CTAGACAAGGTCGAACGAGGGGCATGACCCGGTGCGGGGCTTCTTGCACTCGGCATAGGCGAGTGCTAAGAATAACGTTGGCACTCG (SEQ ID NO: 37)

Promoter 23

TATTAGGCGAAGAGGCATCTAGTAGTAGTGGCAGTGGTGAGAACGTGGGCGCTGCTATAGTGAACAATCTCCAGTCGATGGTTAAGAAGAA
GAGTGACAAACCAGCAGTGAATGACTTGTCTGGGTCCGTGAGGAAAAGAAAGAAGCCCGACACAAAGGACAGTAACGTCAAGAAACCCAAG
AAATAGGGGGGACCTGTTTAGATGTATAGGAATAAAAACTCCGAGATGATCTCAATGTGTAATGGAGTTGTAATATTGCAAAGGGGGAAAAT
CAAGACTCAAACGTGTGTATGAGTGAGCGTACGTATATCTCCGAGAGTAGTATGACATAATGATGACTGTGAATCATCGTAATCTCACACAAA
AACCCCATTGTCGGCCATATACCACACCAAGCAACACCACATATCCCCCGGAAAAAAAAAACGTGAAAAAAAGAAACAATCAAAACTACAACCT
ACTCCTTGATCACACAGTCATTGATCAAGTTACAGTTCCTGCTAGGGAATGACCAAGGTACAAATCAGCACCTTAATGGTTAGCACGCTCTCTT
ACTCTCTCTCACAGTCTTCCGGCCCCTATTCAAAATTCTGCACTTCCATTTGACCCCAGGGTTGGGAAACAGGGCCACAAAAGAAAAACCCGAC
GTGAATGAAAAAACTAAGAAAAGAAAAAAAATTATCACACCAGAAATTTACCTAATTGGGTAATTCCCATCGGTGTTTTTCCTGGATTGTCGCA
CGCACGCATGCTGAAAAAAGTGTTCGAGTTTTGCTTTTGCCTCGGAGTTTCACGCAAGTTTTTCGATCTCGGAACCGGAGGGCGGTCGCCTTG
TTGTTTGTGATGTCGTGCTTTGGGTGTTCTAATGTGCTGTTATTGTGCTCTTTTTTTTTCTTCTTTTTTTGGTGATCATATGATATTGCTCGGTAGA
TTACTTTCGTGTGTAGGTATTCTTTTAGACGTTTGGTTATTGGGTAGATATGAGAGAGAGAGAGTGGGTGGGGGAGGAGTTGGTTGTAGGAG
GGACCCCTGGGAGGAAGTGTAGTTGAGTTTTCCCTGACGAATGAAAATACGTTTTTGAGAAGATAATACAGGAAAGGTGTGTCGGTGAATTT
CCATCTATCCGAGGATATGAGTGGAGGAGAGTCGTGTGCGTGTGGTTAATTTAGGATCAGTGGAACACACAAAGTAACTAAGACAGAGAGA
CAGAGAGAAAAATCTGGGGAAGAGACAAAGAGTCAGAGTGTGTGAGTTATTCTGTATTGTGAAATTTTTTTGCCCAACTACATAATATTGCTG
AAACTAATTTTACTTAAAAAGAAAAGCCAACAACGTCCCCAGTAAAACTTTTCTATAAATATCAGCAGTTTTCCCTTTCCTCCATTCCTCTTCTTG
TCTTTTTTCTTACTTTCCCTTTTTTATACCTTTTCATTATCATCCTTTATAATTGTCTAACCAACAACTATATATCTATCAA (SEQ ID NO: 38)

Promoter 24

CCCACACACCATAGCTTCAAAATGTTTCTACTCCTTTTTTACTCTTCCAGATTTTCTCGGACTCCGCGCATCGCCGTACCACTTCAAAACACCCAA
GCACAGCATACTAAATTTTCCCTCTTTCTTCCTCTAGGGTGTCGTTAATTACCCGTACTAAAGGTTTGGAAAAGAAAAAAGAGACCGCCTCGTT
TCTTTTTCTTCGTCGAAAAAGGCAATAAAAATTTTTATCACGTTTCTTTTTCTTGAAATTTTTTTTTTTAGTTTTTTTCTCTTTCAGTGACCTCCATT
GATATTTAAGTTAATAAACGGTCTTCAATTTCTCAAGTTTCAGTTTCATTTTTCTTGTTCTATTACAACTTTTTTTACTTCTTGTTCATTAGAAAGA
AAGCATAGCAATCTAATCTAAGGGGCG (SEQ ID NO: 39)

Promoter 25

TTGACAATTAATCATCGGCTCGTATAAT (SEQ ID NO: 40)

Promoter 26

TTCAAATATGTATCCGCTCATGAGACA (SEQ ID NO: 41)

Promoter 27

AACTACCCGTAGGTGTAGTTGGCGCAAGCGTCCGATTAGCTCAGGTTTAAGATGTCGAGAGTGAGAGTGGGCGGCTTAACTTTCTCAGTTAG
GCATAAAATTACGTCTTAAATCTCGTAGCGACTAATTTAATAAAAATTGGA (SEQ ID NO: 42)

FIG. 8E

Promoter 28

GCGCAGCACCATGGCCTGAAATAACCTCTGAAAGAGGAACTTGGTTAGGTACCTTCTGAGGCGGAAAGAACCAGCTGTGGAATGTGTGTCAG
TTAGGGTGTGGAAAGTCCCCAGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCAGGTGTGGAAAGTCCCC
AGGCTCCCCAGCAGGCAGAAGTATGCAAAGCATGCATCTCAATTAGTCAGCAACCATAGTCCCGCCCCTAACTCCGCCCATCCCGCCCCTAACT
CCGCCCAGTTCCGCCCATTCTCCGCCCCATGGCTGACTAATTTTTTTTATTTATGCAGAGGCCGAGGCCGCCTCGGCCTCTGAGCTATTCCAGAA
GTAGTGAGGAGGCTTTTTTGGAGGCCTAGGCTTTTGCAAAAAGCTT (SEQ ID NO: 43)

Promoter 29

GACGCTTTTTATCGCAACTCTCTACTGT (SEQ ID NO: 44)

Promoter 30

CATGACAAAAACGCGTAACAAAAGTGTCT (SEQ ID NO: 45)

Promoter 31

AGCCGAATTCCTCCTCATTCTTCTCCAAACCTTTATTGAGTACCTACTGTGTGCTGGAATAAGACAGGCAGGGCCATGCCCTCATGAAGCTGAC
AATCCTATTGGTGTGACCATCCCCAGGTGTGTCCCAGGTGTGTTGCAGGTGTGTCCGAGGTATGCCCCAGCTGTCCCAGGTGTGCCCCAGCTG
TCTCAGATGTGCCCCAGCTGTCCCAGGTGTGTCACAGCTGCATTGCAGGTGTGCCCCAGTTGCATTCCATGTGTGCTCCAAGTGTGTACCAGCT
GTCCCAGGTGTGTCTCAGGTGTGCCCCAGCTGTATCCCAGGTGTGCCTCAGCTGTCTTAGGTGTGTCTCAGGTGCATCCCAGGTGTGTCTCAG
ATGTGCCCCAGCTGTCCCAGGTGTGCCCCAGCTGTCCCAGGTGTGCCCCAGCTGTCTCCAGTGTGTCCCAGCTGTGCCCCAGGTGTGTGTCCTA
GGTGTGCCTCAGCTGTCTCAGGTGTGCCCCAGGCATATCCCAGGTGTGCCCCAGCTGTCCCAGGTGTGTCCTACGTGTGCACCAGCTGTATCC
CAGGTGTGCCCCAGGTGTGTCTCAGATGGGTCCCAAGTGTTCCCCAACTGCATTTCAGGTGTCTCAGGTGTGCCCAAGCTGTCCCAGGTGTGT
CCAAGATGTGCCCCAGGTGTGTCTCAGGTGGGTCTCAAGTGCCCCAGCTGCATTTCAGGTGTCTCAGGTGTGCCCCCCAGTGCATCCCAGGTG
TGTCCCAGGTGTGCCCCAGGTGCATCCCAGGTGTGTCCCAGGTGTGCCCCAGCTGTCTCAGGTGTCTCAGGTGTGCCCCAGGCATATCCCAGG
TGTGCCTCAGCTCTCCCAGGTGTGTCCTACATGTGCACCAGCTGTATCTCAGGTGTGTCTCAGGTGTGCCCCAGATGTGCCCCCGGTGTGTCTC
AGGTGGGTCCCAAGTGTTCCCCAGCTGCATTTCAAGTGTCTCAGGTGTGCCCCAGGTGTGCCCCCGCTGTCCCAGGTGTGTCCAAGATGTACC
CCAGGTGTGTCCCAGCTGTCCCAAGTGTGTCTCAGGTGTGCCCCAGGTGTGTTCCAGGTGTTCCCCAGCTGTCCCAGCTGTCCCAGGTCTCAG
GTGTGCCCCAGGTGTGTTCCAGGTGTTCACCAGCTGTCCCAGCTGTCCCAGGTCTCAGGTGTGCCCCAGGTATGTTGCAGGTGTTCCCCAGCT
GTCCCAGCTGTCCCAGGTGTGTCCCAGGTGTTCCCCAGGTGTGTCCCAGCTGTCCCAGGTGTGTCCCAGATGTGCCCCAGGTGTACCCCAGGT
GTTTCTCAGGTGGATTCCAGGTGTGTCCCAGGTGAGCCCCAGCTGTATTCCATATGCGTCCCTCTGAGTGGGGCCTTGGTTTGATGTAGCTCCG
GGGATCTTCTGCTCCCTGGTCCTGGTGTCACCAGCAACTGCCTCTTGACAATCCTGCCTTGCCTGCAAACCCCAGGTGAGAAGAAGACAAATG
ACTGGGAACTGACCCCTCAGTAAGCGCTGGTGGTCTCACCTACAGACCCCCAGGAAGCTGGTCACTGTGGGCTTCTTTTCCTCTCTAAATTCCT
ATTATCAGGTGGTTTTCTTTCTCATTTGCTATTTTCTTAAAAATAAAAATAGGGAAAAACAGCCTTTGTAAATTACGGTTTCTTCCGGCTCCATCC
TCTCCGTCAGGCCCACATCCCAAGGAAACAGCAGGCTTGAGCCTGGCTGCTGAAGCCAGGGGCTGGATGGAGCAGCTCAGAACAGAGCTTTG
AGTGCCTCTCCAGCCAGGGGCCCCAGAAGCCTGGTGGTTGTTTGTCCTTCTCAGGGGAAAAGTGAGGCGGCCCCTTGGAGGAAGGGGCCGG
GCAGAATGATCTAATCGGATTCCAAGCAGCTCAGGGGA (SEQ ID NO: 46)

Promoter 32

CTCTGAGCTGCTTCCCTACTCACACTCTGTCCACAACCCCATTTTCCTGATCATGTAGTAGAAAGAAATGGAACACAATCTTTGTAAATAAGCCC
TTGTAAACAAGCAAGAGCTACAGTGCTTCCACAAGCCCTACTGCAAGCCAGGAATGGGAACAGTGGTGTGTGTGCAGCAAATGCCCTGAGCA
CCCCTGTGGATTGGACTCAGAAACATGGAAGTGAGGGTAGGAGGGGATGATCTAAGTCCTGGGCCCAATTAAGAGATCAGATGGTGAAGGG
TTTGGGGGCCTTTAAGGTAAGGAGGCCTGGGCTGATCCTGCAGGCTGATATAAAGTCCTGTAACCCCATAGGCA (SEQ ID NO: 47)

FIG. 8F

Intron 1

GTAAGTATCAAGGTTACAAGACAGGTTTAAGGAGACCAATAGAAACTGGGCTTGTCGAGACAGAGAAGACTCTTGCGTTTCTGATAGGCACC
TATTGGTCTTACTGACATCCACTTTGCCTTTCTCTCCACAG (SEQ ID NO: 48)

Intron 2

GTAAGTTTAGTCTTTTTGTCTTTTATTTCAGGTCCCGGATCCGGTGGTGGTGCAAATCAAAGAACTGCTCCTCAGTGGATGTTGCCTTTACTTCT
AG (SEQ ID NO: 115)

Poly A Region 1

AGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGC
TTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGATGTGGGAGGTT
TTTTAAAGCAAGTAAAACCTCTACAAATGTGGTA (SEQ ID NO: 49)

Poly A Region 2

CAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTG
CTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGATGTGGGAGGT
TTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTA (SEQ ID NO: 50)

Poly A Region 3

GGCCGCTTCGAGCAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTT
GTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGA
GATGTGGGAGGTTTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTAAAATC (SEQ ID NO: 51)

Poly A Region 4

TAATCAGCATACCACATTTGTAGAGGTTTTACTTGCTTTAAAAAACCTCCCACACCTCCCCCTGAACCTGAAACATAAAATGAATGCAATTGTTG
TTGTTAACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTT
GTGGTTTGTCCAAACTCATCAATGTATCTTA (SEQ ID NO: 52)

Poly A Region 5

AGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTGC
TTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGATGTGGGAGGTT
TTTTAAAGCAAGTAAAACCTCTACAAATGTGGTA (SEQ ID NO: 49)

Poly A Region 6

CAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTG
CTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGATGTGGGAGGT
TTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTA (SEQ ID NO: 50)

FIG. 9A

Poly A Region 7

AACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGG
TTTGTCCAAACTCATCAATGTATCTTATCACGTCTGGTCAGGTGGCA (SEQ ID NO: 53)

Poly A Region 8

AACTTGTTTATTGCAGCTTATAATGGTTACAAATAAAGCAATAGCATCACAAATTTCACAAATAAAGCATTTTTTTCACTGCATTCTAGTTGTGG
TTTGTCCAAACTCATCAATGTATCTTATCACGTCTGG (SEQ ID NO: 54)

Poly A Region 9

CAGACATGATAAGATACATTGATGAGTTTGGACAAACCACAACTAGAATGCAGTGAAAAAAATGCTTTATTTGTGAAATTTGTGATGCTATTG
CTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAACAACAACAATTGCATTCATTTTATGTTTCAGGTTCAGGGGGAGATGTGGGAGGT
TTTTTAAAGCAAGTAAAACCTCTACAAATGTGGTA (SEQ ID NO: 50)

Poly A Region 10

AATAAAATATCTTTATTTTCATTACATCTGTGTGTTGGTTTTTTGTGTG (SEQ ID NO: 55)

ITR Region 1 – Interval 1

CTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGAGCGC
GCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGTTAATGATTAACCCGCCATGCTACTTATCTACGCGTAGATAAGTAGCAT
GGCGGGTTAATCATTAACTACAAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCA
AAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGCCTTA (SEQ ID NO: 56)

ITR Region 1 – Interval 2

CTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGAGCGC
GCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGTTAATGATTAACCCGCCATGCTACTTATCTACGCGTAGATAAGTAGCAT
GGCGGGTTAATCATTAACTACAAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCA
AAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGCCTTA (SEQ ID NO: 56)

ITR Region 2 – Interval 1

AGGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGAG
CGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGTTAATGATTAACCCGCCATGCTACTTATCTACGCGTAGATAAGTAG
CATGGCGGGTTAATCATTAACTACAAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGA
CCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGCCTTA (SEQ ID NO: 57)

FIG. 9B

ITR Region 2 – Interval 2

AGGCTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACCTTTGGTCGCCCGGCCTCAGTGAGCGAGCGAG
CGCGCAGAGAGGGAGTGGCCAACTCCATCACTAGGGGTTCCTTGTAGTTAATGATTAACCCGCCATGCTACTTATCTACGCGTAGATAAGTAG
CATGGCGGGTTAATCATTAACTACAAGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGA
CCAAAGGTCGCCCGACGCCCGGGCTTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAGCCTTA (SEQ ID NO: 57)

ITR Region 3 – Interval 1

AGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGC
TTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGC (SEQ ID NO: 58)

ITR Region 3 – Interval 2

AGGAACCCCTAGTGATGGAGTTGGCCACTCCCTCTCTGCGCGCTCGCTCGCTCACTGAGGCCGGGCGACCAAAGGTCGCCCGACGCCCGGGC
TTTGCCCGGGCGGCCTCAGTGAGCGAGCGAGCGCGCAG (SEQ ID NO: 59)

Intron 3

TCGAATCCCGGCCGGGAACGGTGCATTGGAACGCGGATTCCCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCCACAAA
AAATGCTTTCTTCTTTTAATATACTTTTTTGTTTATCTTATTTCTAATACTTTCCCTAATCTCTTTCTTTCAGGGCAATAATGATACAATGTATCATG
CCTCTTTGCACCATTCTAAAGAATAACAGTGATAATTTCTGGGTTAAGGCAATAGCAATATTTCTGCATATAAATATTTCTGCATATAAATTGTA
ACTGATGTAAGAGGTTTCATATTGCTAATAGCAGCTACAATCCAGCTACCATTCTGCTTTTATTTTATGGTTGGGATAAGGCTGGATTATTCTGA
GTCCAAGCTAGGCCCTTTTGCTAATCATGTTCATACCTCTTATCTTCCTCCCACAGCTCCTGGGCAACGTGCTGGTCTGTGTGCTGGCCCATCAC
TTTGGCAAAGAATTGGGA (SEQ ID NO: 116)

Intron 4

GTAAGTTTAGTCTTTTTGTCTTTTATTTCAGGTCCCGGATCCGGTGGTGGTGCAAATCAAAGAACTGCTCCTCAGTGGATGTTGCCTTTACTTCT
AG (SEQ ID NO: 117)

Intron 5

GTAAGTTTAGTCTTTTTGTCTTTTATTTCAG (SEQ ID NO: 118)

Intron 6

ACTTACCATACTTTACCCGGAAACTAATCGTCCCACTCTCACATCCTTCATTGCAG (SEQ ID NO: 119)

Intron 7

AAAAGTTCCCCAGCCAGAAGCAGAGAAGATGATGTCAAGAAATCAAGGGGGATAAATGGCCATAGCTGCTGCAAATAGCTTATTGCAGTCTC
TAGAGTGTGGTAAACAGGTTTCCAGTGCCAGCTGTGGAGGTGACAGCGGCAGGGAA (SEQ ID NO: 120)

FIG. 9C

LINKER SEQUENCE 1

TTATGAAGATCCCTCGACCTGCAGCCCAAGCTTGGCGTAATCATG (SEQ ID NO: 60)

LINKER SEQUENCE 2

GATAAGGATCTTCCTAGAGCATGGCTA (SEQ ID NO: 61)

LINKER SEQUENCE 3

ATGTCTGCCCGTATTTCGCGTAAGGAAATCCATTATGTACTATTTAAAAAACACAAACTTTTGGATGTTCGGTTTATTCTTTTTCTTTTACTTTTTT
ATCATGGGAGCCTACTTCCCGTTTTTCCCGATTTGGCTACATGACATCAACCATATCAGCAAAAGTGATACGGGTATTATTTTTGCCGCTATTTC
TCTGTTCTCGCTATTATTCCAACCGCTGTTTGGTCTGCTTTCTGACAAACTCGGCCTCGACTCTAGGCGGCCGCGGGGATC (SEQ ID NO: 62)

LINKER SEQUENCE 4

GGAGGGGTGGAGTCGTGACGTGAATTACGTCATAGGGTTAGGGAGGTCCTGTATTAGAGGTCACGTGAGTGTTTTGCGACATTTTGCGACAC
CATGTGGTCACGCTGGGTATTTAAGCCCGAGTGAGCACGCAGGGTCTCC (SEQ ID NO: 63)

LINKER SEQUENCE 5

GGATCCACTCGAGTGGAGCTCGCGACTAGTCGATTCGAATTCGATATCAAGCTTATCGAT (SEQ ID NO: 64)

LINKER SEQUENCE 6

GCCTGTACGGAAGTGTTACTTCTGCTCTAAAAGCTGCGGAATTGTACCCGCGGCCGCAATTCCCGGGGATCGAAAGAGCCTGCTAAAGCAAA
AAAGAA (SEQ ID NO: 65)

LINKER SEQUENCE 7

CCGAACCCGAATTCTGCAGATATCCAGCACAGTGGCGGCCGCTTCGAG (SEQ ID NO: 66)

LINKER SEQUENCE 8

TAGTTTCCATGGCTACGTAGATAAGTAGCATGGCGGGTTAATCATTAACTACA (SEQ ID NO: 67)

LINKER SEQUENCE 9

TGTAGTTAATGATTAACCCGCCATGCTACTTATCTACGTAGCCATGCTCGATCTGAATTCGGTA (SEQ ID NO: 68)

LINKER SEQUENCE 10

GGCCGCGGGGATCC (SEQ ID NO: 69)

LINKER SEQUENCE 11

GGTTCGAACAG (SEQ ID NO: 70)

FIG. 9D

LINKER SEQUENCE 12

CATGTTCATGCCTTCTTCTTTTTCCTACAGCTCCTGGGCAACGTGCTGGTTATTGTGCTGTCTCATCATTTTGGCAAAGAATTCTGCAGTCGACG GTACCGCGGGCCCGGGATCCACCGG (SEQ ID NO: 71)

LINKER SEQUENCE 13

GCGGCCGCACGCGTGTTACTAGTTATTAAT (SEQ ID NO: 72)

LINKER SEQUENCE 14

CACTAGAAGCTTTATTGCGGTAGTTTATCACAGTTAAATTGCTAACGCAGTCAGTGCTTCTGACACAACAGTCTCGAACTTAAGCTGCAGAAGT TGGTCGTGAGGCACTGGGCAG (SEQ ID NO: 73)

LINKER SEQUENCE 15

None

LINKER SEQUENCE 16

GCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGGAC (SEQ ID NO: 74)

LINKER SEQUENCE 17

GGATCCACTCGAGTGGAGCTCGCGACTAGTCGATTCGAATTCGATATCAAGCTTATCGAT (SEQ ID NO: 64)

LINKER SEQUENCE 18

GTGTCCACTCCCAGTTCAATTACAGCTCTTAAGGCTAGAGTACTTAATACGACTCACTATAGGCTAGCCTCGAGAATTCACGCGTGGTACCGAG CTCGGATCCACTAGTCCAGTGTGGTGGAATTCGGGCGGG (SEQ ID NO: 75)

LINKER SEQUENCE 19

TGTATTTAGAAAAATAAACAAATAGGGGTTCCGCGCACATTTCCCCGAAAAGTGCCACCTGGTC (SEQ ID NO: 76)

LINKER SEQUENCE 20

TAGCCATGCTCTAGGAAGATCGTACC (SEQ ID NO: 77)

LINKER SEQUENCE 21

GAATTCGAGCTTGCATGCCTGCAGGT (SEQ ID NO: 78)

LINKER SEQUENCE 22

GTGTCCACTCCCAGTTCAATTACAGCTCTTAAGGCTAGAGTACTTCTAGCCTCGAG (SEQ ID NO: 79)

LINKER SEQUENCE 23

AAATCGATAAGGATCCTAGAGCATGGCTACGTAGATAAGTAGCATGGCGGGTTAATCATTAACTACA (SEQ ID NO: 80)

LINKER SEQUENCE 24

GGCCCGGGATCCA (SEQ ID NO: 81)

FIG. 9E

LINKER SEQUENCE 25

GTTGAATTCGATATCGGATCCATCGATACCGTCGACCTCGAGGGGGGGCCCGGTACC (SEQ ID NO: 82)

LINKER SEQUENCE 26

CAATTCGCCCTATAGTGAGTCGTATTACGCGCGCAGCGGCCGAC (SEQ ID NO: 83)

LINKER SEQUENCE 27

TTCGAG

LINKER SEQUENCE 28

TGTAGTTAATGATTAACCCGCCATGCTACTTATCTACGTAGCCATGCTCTAGATCT (SEQ ID NO: 84)

LINKER SEQUENCE 29

AGCGGCCGCACTCCTCAG (SEQ ID NO: 85)

LINKER SEQUENCE 30

ATCGATACCGTCGACCCGGGC (SEQ ID NO: 86)

LINKER SEQUENCE 31

AACC

LINKER SEQUENCE 32

CAGATCGCCTGGAGACGCCATCCACGCTGTTTTGACCTCCATAGAAGACACCGGGACCGATCCAGCCTCCGGACTCTAGAGGATCCGGTACTC GAGGAACTGAAAAACCAGAAAGTTAACTG (SEQ ID NO: 87)

LINKER SEQUENCE 33

CCGGACCACGTGCGGACCGAGCGGCCGC (SEQ ID NO: 88)

LINKER SEQUENCE 34

GTGTCCACTCCCAGTTCAATTACAGCTCTTAAGGCTAGAGTACTTCTAGCCTCGAGAATTCACGCGTGGTACCGAGCTCGGATCCACTAGTCCA GTGTGGTGGAATTCGGGCGGG (SEQ ID NO: 89)

LINKER SEQUENCE 35

AAATCGATAAGGATCCTAGAGCATGGCTACGTAGATAAGTAGCATGGCGGGTTAATCATTAACTACA (SEQ ID NO: 80)

LINKER SEQUENCE 36

TTATTTGTGAAATTTGTGATGCTATTGCTTTATTTGTAACCATTATAAGCTGCAATAAACAAGTTAA (SEQ ID NO: 90)

FIG. 9F

UTR SEQUENCE 1
TAATAATAACCGGGCAGGCC (SEQ ID NO: 91)

UTR SEQUENCE 2

AGCCGCGAGACGGGCGCTCAGGGCGCGGGGCCGGCGGCGGCGAACGAGAGGACGGACTCTGGCGGCCGGGTCGTTGGCCGCGGGGAGCG
CGGGCACCGGGCGAGCAGGCCGCGTCGCGCTCACC (SEQ ID NO: 92)

UTR SEQUENCE 3

GGGGCTCGGGTGCAGCGGCCAGCGGGCCTGGCGGCGAGGATTACCCGGGGAAGTGGTTGTCTCCTGGCTGGAGCCGCGAGACGGGCGCTC
AGGGCGCGGGGCCGGCGGCGGCGAACGAGAGGACGGACTCTGGCGGCCGGGTCGTTGGCCGGGGGAGCGCGGGCACCGGGCGAGCAGG
CCGCGTCGCGCTCACC (SEQ ID NO: 93)

UTR SEQUENCE 4

AGGACTCATTAAAAAGTAAC (SEQ ID NO: 94)

UTR SEQUENCE 5

GGGGCTCGGGTGCAGCGGCCAGCGGGCGCCTGGCGGCGAGGATTACCCGGGGAAGTGGTTGTCTCCTGGCTGGAGCCGCGAGACGGGCGC
TCAGGGCGCGGGGCCGGCGGCGGCGAACGAGAGGACGGACTCTGGCGGCCGGGTCGTTGGCCGCGGGGAGCGCGGGCACCGGGCGAGCA
GGCCGCGTCGCGCTCACC (SEQ ID NO: 95)

UTR SEQUENCE 6

AGC

UTR SEQUENCE 7

CCACC

UTR SEQUENCE 8

GTCACC

FIG. 9G

UTR SEQUENCE 9

GGGCGGGTGCATCAATGCGGCCGAAAAAGACACGGACACGCTCCCCTGGGACCTGAGCTGGTTCGCAGTCTTCCCAAAGGTGCCAAGCAAG
CGTCAGTTCCCCTCAGGCGCTCCAGGTTCAGTGCCTTGTGCCGAGGGTCTCCGGTGCCTTCCTAGACTTCTCGGGACAGTCTGAAGGGGTCAG
GAGCGGCGGGACAGCGCGGGAAGAGCAGGCAAGGGGAGACAGCCGGACTGCGCCTCAGTCCTCCGTGCCAAGAACACCGTCGCGGAGGC
GCGGCCAGCTTCCCTTGGATCGGACTTTCCGCCCCTAGGGCCAGGCGGCGGAGCTTCAGCCTTGTCCCTTCCCCAGTTTCGGGCGGCCCCCAG
AGCTGAGTAAGCCGGGTGGAGGGAGTCTGCAAGGATTTCCTGAGCGCGATGGGCAGGAGGAGGGGCAAGGGCAAGAGGGCGCGGAGCAA
AGACCCTGAACCTGCCGGGGCCGCGCTCCCGGGCCCGCGTCGCCAGCACCTCCCCACGCGCGCTCGGCCCCGGGCCACCCGCCCTCGTCGGC
CCCCGCCCCTCTCCGTAGCCGCAGGGAAGCGAGCCTGGGAGGAAGAAGAGGGTAGGTGGGGAGGCGGATGAGGGGTGGGGGACCCCTTG
ACGTCACCAGAAGGAGGTGCCGGGGTAGGAAGTGGGCTGGGGAAAGGTTATAAATCGCCCCCGCCCTCGGCTGCTCTTCATCGAGGTCCGC
GGGAGGCTCGGAGCGCGCCAGGCGGACACTCCTCTCGGCTCCTCCCCGGCAGCGGCGGCGGCTCGGAGCGGGCTCCGGGGCTCGGGTGCA
GCGGCCAGCGGGCGCCTGGCGGCGAGGATTACCCGGGGAAGTGGTTGTCTCCTGGCTGGAGCCGCGAGACGGGCGCTCAGGGCGCGGGGC
CGGCGGCGGCGAACGAGAGGACGGACTCTGGCGGCCGGGTCGTTGGCCGCGGGGAGCGCGGGCACCGGGCGAGCAGGCCGCGTCGCGCT
CACC (SEQ ID NO: 96)

UTR SEQUENCE 10

TTGCTTGTTAATCAATAAACCGTTTAATTCGTTTCAGTTGAACTTTGGTCTCTGCGTATTTCTTTCTTATC (SEQ ID NO: 97)

UTR SEQUENCE 11

ATTTTGAAGCGGGAGGTTTGAACGCGCAGCCGCC (SEQ ID NO: 98)

UTR SEQUENCE 12

CCGGTCGCCACC (SEQ ID NO: 99)

UTR SEQUENCE 13

GGGGCTCGGGTGCAGCGGCCAGCGGGCGCCTGGCGGCGAGGATTACCCGGGGAAGTGGTTGTCTCCTGGCTGGAGCCGCGAGACGGGCGC
TCAGGGCGCGGGGCCGGCGGCGGCGAACGAGAGGACGGACTCTGGCGGCCGGGTCTTTGGCCGCGGGGAGCGCGGGCACCGGGCGAGCA
GGCCGCGTCGCGCTCACC (SEQ ID NO: 100)

UTR SEQUENCE 14

TCGCCACC

UTR SEQUENCE 15

GGGGTGGGGGACCCCTTGACGTCACCAGAAGGAGGTGCCGGGGTAGGAAGTGGGCTGGGGAAAGGTTATAAATCGCCCCCGCCCTCGGCT
GCTCTTCATCGAGGTCCGCGGGAGGCTCGGAGCGCGCCAGGCGGACACTCCTCTCGGCTCCTCCCCGGCAGCGGCGGCGGCTCGGAGCGGG
CTCCGGGGCTCGGGTGCAGCGGCCAGCGGGCGCCTGGCGGCGAGGATTACCCGGGGAAGTGGTTGTCTCCTGGCTGGAGCCGCGAGACGG
GCGCTCAGGGCGCGGGGCCGGCGGCGGCGAACGAGAGGACGGACTCTGGCGGCCGGGTCGTTGGCCGCGGGGAGCGCGGGCACCGGGCG
AGCAGGCCGCGTCGCGCTCACC (SEQ ID NO: 101)

UTR SEQUENCE 16

GCGGCCGC

FIG. 9H

sFLT-1

ATGGTCAGCTACTGGGACACCGGGGTCCTGCTGTGCGCGCTGCTCAGCTGTCTGCTTCTCACAGGATCTAGTTCAGGTTCAAAATTAAAAGAT
CCTGAACTGAGTTTAAAAGGCACCCAGCACATCATGCAAGCAGGCCAGACACTGCATCTCCAATGCAGGGGGGAAGCAGCCCATAAATGGTC
TTTGCCTGAAATGGTGAGTAAGGAAAGCGAAAGGCTGAGCATAACTAAATCTGCCTGTGGAAGAAATGGCAAACAATTCTGCAGTACTTTAA
CCTTGAACACAGCTCAAGCAAACCACACTGGCTTCTACAGCTGCAAATATCTAGCTGTACCTACTTCAAAGAAGAAGGAAACAGAATCTGCAA
TCTATATATTTATTAGTGATACAGGTAGACCTTTCGTAGAGATGTACAGTGAAATCCCCGAAATTATACACATGACTGAAGGAAGGGAGCTCG
TCATTCCCTGCCGGGTTACGTCACCTAACATCACTGTTACTTTAAAAAAGTTTCCACTTGACACTTTGATCCCTGATGGAAAACGCATAATCTGG
GACAGTAGAAAGGGCTTCATCATATCAAATGCAACGTACAAAGAAATAGGGCTTCTGACCTGTGAAGCAACAGTCAATGGGCATTTGTATAA
GACAAACTATCTCACACATCGACAAACCAATACAATCATAGATGTCCAAATAAGCACACCACGCCCAGTCAAATTACTTAGAGGCCATACTCTT
GTCCTCAATTGTACTGCTACCACTCCCTTGAACACGAGAGTTCAAATGACCTGGAGTTACCCTGATGAAAAAAATAAGAGAGCTTCCGTAAGG
CGACGAATTGACCAAAGCAATTCCCATGCCAACATATTCTACAGTGTTCTTACTATTGACAAAATGCAGAACAAAGACAAAGGACTTTATACTT
GTCGTGTAAGGAGTGGACCATCATTCAAATCTGTTAACACCTCAGTGCATATATATGATAAAGCATTCATCACTGTGAAACATCGAAAACAGC
AGGTGCTTGAAACCGTAGCTGGCAAGCGGTCTTACCGGCTCTCTATGAAAGTGAAGGCATTTCCCTCGCCGGAAGTTGTATGGTTAAAAGATG
GGTTACCTGCGACTGAGAAATCTGCTCGCTATTTGACTCGTGGCTACTCGTTAATTATCAAGGACGTAACTGAAGAGGATGCAGGGAATTATA
CAATCTTGCTGAGCATAAAACAGTCAAATGTGTTTAAAAACCTCACTGCCACTCTAATTGTCAATGTGAAACCCCAGATTTACGAAAAGGCCGT
GTCATCGTTTCCAGACCCGGCTCTCTACCCACTGGGCAGCAGACAAATCCTGACTTGTACCGCATATGGTATCCCTCAACCTACAATCAAGTGG
TTCTGGCACCCCTGTAACCATAATCATTCCGAAGCAAGGTGTGACTTTTGTTCCAATAATGAAGAGTCCTTTATCCTGGATGCTGACAGCAACA
TGGGAAACAGAATTGAGAGCATCACTCAGCGCATGGCAATAATAGAAGGAAAGAATAAGATGGCTAGCACCTTGGTTGTGGCTGACTCTAGA
ATTTCTGGAATCTACATTTGCATAGCTTCCAATAAAGTTGGGACTGTGGGAAGAAACATAAGCTTTTATATCACAGATGTGCCAAATGGGTTTC
ATGTTAACTTGGAAAAAATGCCGACGGAAGGAGAGGACCTGAAACTGTCTTGCACAGTTAACAAGTTCTTATACAGAGACGTTACTTGGATTT
TACTGCGGACAGTTAATAACAGAACAATGCACTACAGTATTAGCAAGCAAAAAATGGCCATCACTAAGGAGCACTCCATCACTCTTAATCTTAC
CATCATGAATGTTTCCCTGCAAGATTCAGGCACCTATGCCTGCAGAGCCAGGAATGTATACACAGGGGAAGAAATCCTCCAGAAGAAAGAAA
TTACAATCAGAGGTGAGCACTGCAACAAAAAGGCTGTTTTCTCTCGGATCTCCAAATTTAAAAGCACAAGGAATGATTGTACCACACAAAGTA
ATGTAAAACATTAA (SEQ ID NO: 102)

VEGF-Trap

AAGCTTGGGCTGCAGGTCGATCGACTCTAGAGGATCGATCCCCGGGCGAGCTCGAATTCGCAACCACCATGGTCAGCTACTGGGACACCGGG
GTCCTGCTGTGCGCGCTGCTCAGCTGTCTGCTTCTCACAGGATCTAGTTCCGGAGGTAGACCTTTCGTAGAGATGTACAGTGAAATCCCCGAA
ATTATACACATGACTGAAGGAAGGGAGCTCGTCATTCCCTGCCGGGTTACGTCACCTAACATCACTGTTACTTTAAAAAAGTTTCCACTTGACA
CTTTGATCCCTGATGGAAAACGCATAATCTGGGACAGTAGAAAGGGCTTCATCATATCAAATGCAACGTACAAAGAAATAGGGCTTCTGACCT
GTGAAGCAACAGTCAATGGGCATTTGTATAAGACAAACTATCTCACACATCGACAAACCAATACAATCATAGATGTGGTTCTGAGTCCGTCTC
ATGGAATTGAACTATCTGTTGGAGAAAAGCTTGTCTTAAATTGTACAGCAAGAACTGAACTAAATGTGGGGATTGACTTCAACTGGGAATACC
CTTCTTCGAAGCATCAGCATAAGAAACTTGTAAACCGAGACCTAAAAACCCAGTCTGGGAGTGAGATGAAGAAATTTTTGAGCACCTTAACTA
TAGATGGTGTAACCCGGAGTGACCAAGGATTGTACACCTGTGCAGCATCCAGTGGGCTGATGACCAAGAAGAACAGCACATTTGTCAGGGTC
CATGAAAAGGGCCCGGGCGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCA
AAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAA
CTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTC
ACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCC
AAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCT
GGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTG
GACTCCGACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCAT
GAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAGCGGCCGC (SEQ ID NO: 103)

FIG. 10A

VEGF-Trap

ATGGTCAGCTACTGGGACACCGGGGTCCTGCTGTGCGCGCTGCTCAGCTGTCTGCTTCTCACAGGATCTAGTTCCGGAAGTGATACCGGTAGA
CCTTTCGTAGAGATGTACAGTGAAATCCCCGAAATTATACACATGACTGAAGGAAGGGAGCTCGTCATTCCCTGCCGGGTTACGTCACCTAAC
ATCACTGTTACTTTAAAAAAGTTTCCACTTGACACTTTGATCCCTGATGGAAAACGCATAATCTGGGACAGTAGAAAGGGCTTCATCATATCAA
ATGCAACGTACAAAGAAATAGGGCTTCTGACCTGTGAAGCAACAGTCAATGGGCATTTGTATAAGACAAACTATCTCACACATCGACAAACCA
ATACAATCATAGATGTGGTTCTGAGTCCGTCTCATGGAATTGAACTATCTGTTGGAGAAAAGCTTGTCTTAAATTGTACAGCAAGAACTGAACT
AAATGTGGGGATTGACTTCAACTGGGAATACCCTTCTTCGAAGCATCAGCATAAGAAACTTGTAAACCGAGACCTAAAAACCCAGTCTGGGAG
TGAGATGAAGAAATTTTTGAGCACCTTAACTATAGATGGTGTAACCCGGAGTGACCAAGGATTGTACACCTGTGCAGCATCCAGTGGGCTGAT
GACCAAGAAGAACAGCACATTTGTCAGGGTCCATGAAAAGGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGAC
CGTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACG
AAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCAC
GTACCGTGTGGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAG
CCCCCATCGAGAAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAG
AACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACT
ACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCTACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAAC
GTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGA (SEQ ID NO: 104)

VEGF-Trap

AAGCTTGGGCTGCAGGTCGATCGACTCTAGAGGATCGATCCCCGGGCGAGCTCGAATTCGCAACCACCATGGTCAGCTACTGGGACACCGGG
GTCCTGCTGTGCGCGCTGCTCAGCTGTCTGCTTCTCACAGGATCTAGTTCCGGAGGTAGACCTTTCGTAGAGATGTACAGTGAAATCCCCGAA
ATTATACACATGACTGAAGGAAGGGAGCTCGTCATTCCCTGCCGGGTTACGTCACCTAACATCACTGTTACTTTAAAAAAGTTTCCACTTGACA
CTTTGATCCCTGATGGAAAACGCATAATCTGGGACAGTAGAAAGGGCTTCATCATATCAAATGCAACGTACAAAGAAATAGGGCTTCTGACCT
GTGAAGCAACAGTCAATGGGCATTTGTATAAGACAAACTATCTCACACATCGACAAACCAATACAATCATAGATATCCAGCTGTTGCCCAGGA
AGTCGCTGGAGCTGCTGGTAGGGGAGAAGCTGGTCCTCAACTGCACCGTGTGGGCTGAGTTTAACTCAGGTGTCACCTTTGACTGGGACTAC
CCAGGGAAGCAGGCAGAGCGGGGTAAGTGGGTGCCCGAGCGACGCTCCCAACAGACCCACACAGAACTCTCCAGCATCCTGACCATCCACA
ACGTCAGCCAGCACGACCTGGGCTCGTATGTGTGCAAGGCCAACAACGGCATCCAGCGATTTCGGGAGAGCACCGAGGTCATTGTGCATGAA
AATGGCCCGGGCGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCCAAAACCC
AAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTA
CGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTC
CTGCACCAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCTCCAAAGC
CAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTGACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCA
AAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCC
GACGGCTCCTTCTTCCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAGGCT
CTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGAGCGGCCGC (SEQ ID NO: 105)

Lucentis/ ranibizumab Protein Sequence (hVEGF humanized antibody)

DIQLTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAPKVLIYFTSSLHSGVPS
RFSGSGSGTDFTLTISSLQPEDFATYYCQQYSTVPWTFGQGTKVEIKRTVAAPSVFIFPP
SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT
LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 106)

FIG. 10B

DNA sequence 1 coding for lucentis/ ranibizumab (generated from protein sequence)

GATATTCAGCTGACCCAGAGCCCGAGCAGCCTGAGCGCGAGCGTGGGCGATCGCGTGACCATTACCTGCAGCGCGAGCCAGGATATTAGCA
ACTATCTGAACTGGTATCAGCAGAAACCG
GGCAAAGCGCCGAAAGTGCTGATTTATTTTACCAGCAGCCTGCATAGCGGCGTGCCGAGC
CGCTTTAGCGGCAGCGGCAGCGGCACCGATTTTACCCTGACCATTAGCAGCCTGCAGCCG
GAAGATTTTGCGACCTATTATTGCCAGCAGTATAGCACCGTGCCGTGGACCTTTGGCCAG
GGCACCAAAGTGGAAATTAAACGCACCGTGGCGGCGCCGAGCGTGTTTATTTTTCCGCCG
AGCGATGAACAGCTGAAAAGCGGCACCGCGAGCGTGGTGTGCCTGCTGAACAACTTTTAT
CCGCGCGAAGCGAAAGTGCAGTGGAAAGTGGATAACGCGCTGCAGAGCGGCAACAGCCAG
GAAAGCGTGACCGAACAGGATAGCAAAGATAGCACCTATAGCCTGAGCAGCACCCTGACC
CTGAGCAAAGCGGATTATGAAAAACATAAAGTGTATGCGTGCGAAGTGACCCATCAGGGC
CTGAGCAGCCCGGTGACCAAAAGCTTTAACCGCGGCGAATGC (SEQ ID NO: 107)

DNA sequence 2 coding for lucentis/ ranibizumab (generated from protein sequence)

GATATTCAATTGACTCAATCTCCTTCTTCTTTGTCTGCTTCTGTTGGTGATCGTGTTACTATTACTTGTTCTGCTTCTCAAGATATTTCTAATTATTT
GAATTGGTATCAACAAAAACCTGGTAAAGCTCCTAAAGTTTTGATTTATTTTACTTCTTCTTTGCATTCTGGTGTTCCTTCTCGTTTTTCTGGTTCT
GGTTCTGGTACTGATTTTACTTTGACTATTTCTTCTTTGCAACCTGAAGATTTTGCTACTTATTATTGTCAACAATATTCTACTGTTCCTTGGACTT
TTGGTCAAGGTACTAAAGTTGAAATTAAACGTACTGTTGCTGCTCCTTCTGTTTTTATTTTTCCTCCTTCTGATGAACAATTGAAATCTGGTACTG
CTTCTGTTGTTTGTTTGTTGAATAATTTTTATCCTCGTGAAGCTAAAGTTCAATGGAAAGTTGATAATGCTTTGCAATCTGGTAATTCTCAAGAA
TCTGTTACTGAACAAGATTCTAAAGATTCTACTTATTCTTTGTCTTCTACTTTGACTTTGTCTAAAGCTGATTATGAAAAACATAAAGTTTATGCT
TGTGAAGTTACTCATCAAGGTTTGTCTTCTCCTGTTACTAAATCTTTTAATCGTGGTGAATGT (SEQ ID NO: 108)

FIG. 10C

MVSYWDTGVLLCALLSCLLLTGSSSGSKLKDPELSLKGTQHIAGQTLHLQCRGEAAMQHKWSLPEMVSKESERLSITKSAC
GRNGKQFCSTLTLNTAQANHTGFYSCKYLAVPTSKKKETESAIYIFISDTGRPFVEMYSEIPEIIHMTEGRELVIPCRVTSPNIT
VTLKKFPLDTLIPDGKRIIWDSRKGFIISNATYKEIGLLTCEATVNGHLYKTNYLTHRQTNTIIDVQISTPRPVKLLRGHTLVLNC
TATTPLNTRVQMTWSYPDEKNKRASVRRRIDQSNSHANIFYSVLTIDKMQNKDKGLYTCRVRSGPSFKSVNTSVHIYDKAF
ITVKHRKQQVLETVAGKRSYRLSMKVKAFPSPEVVWLKDGLPATEKSARYLTRGYSLIIKDVTEEDAGNYTILLSIKQSNVFK
NLTATLIVNVKPQIYEKAVSSFPDPALYPLGSRQ (SEQ ID NO: 109)

FIG. 11A

IYIFISDTGRPFVEMYSEIPEIIHMTEGRELVIPCRVTSPNITVTLKKFPLDTLIPDGKRIIWDSRKGFIISNATYKEIGLLTCEATV
NGHLYKTNYLTHRQTNTI (SEQ ID NO: 121)

FIG. 11B

AATCTATATATTTATTAGTGATACAGGTAGACCTTTCGTAGAGATGTACAGTGAAATCCCCGAA
ATTATACACATGACTGAAGGAAGGGAGCTCGTCATTCCCTGCCGGGTTACGTCACCTAACATC
ACTGTTACTTTAAAAAAGTTTCCACTTGACACTTTGATCCCTGATGGAAAACGCATAATCTGGG
ACAGTAGAAAGGGCTTCATCATATCAAATGCAACGTACAAAGAAATAGGGCTTCTGACCTGTG
AAGCAACAGTCAATGGGCATTTGTATAAGACAAACTATCTCACACATCGACAAACCAATACAA
TCA (SEQ ID NO: 122)

FIG. 11C

Zeocin resistance

ATGGCCAAGTTGACCAGTGCCGTTCCGGTGCTCACCGCGCGCGACGTCGCCGGAGCGGTCGAGTTCTGGACCGACCGGCTCGGGTTCTCCCG
GGACTTCGTGGAGGACGACTTCGCCGGTGTGGTCCGGGACGACGTGACCCTGTTCATCAGCGCGGTCCAGGACCAGGTGGTGCCGGACAAC
ACCCTGGCCTGGGTGTGGGTGCGCGGCCTGGACGAGCTGTACGCCGAGTGGTCGGAGGTCGTGTCCACGAACTTCCGGGACGCCTCCGGGC
CGGCCATGACCGAGATCGGCGAGCAGCCGTGGGGGCGGGAGTTCGCCCTGCGCGACCCGGCCGGCAACTGCGTGCACTTCGTGGCCGAGG
AGCAGGACTGA (SEQ ID NO: 110)

Zeocin resistance

ATGTCTAAATTAACCTCTGCTGTTCCAGTGTTAACCGCCCGTGATGTTGCCGGTGCAGTGGAATTTTGGACTGACCGTTTGGGTTTCTCACGTG
ACTTTGTCGAAGATGATTTTGCTGGCGTTGTGCGTGATGACGTCACTTTGTTCATCTCTGCTGTTCAGGATCAGGTCGTCCCAGACAACACTTT
GGCCTGGGTCTGGGTTCGTGGTTTGGACGAATTGTACGCTGAGTGGAGTGAAGTTGTGTCTACAAACTTTCGTGATGCATCAGGTCCAGCTAT
GACCGAAATTGGCGAACAACCTTGGGGCCGTGAGTTCGCTTTACGTGATCCAGCCGGTAATTGCGTGCACTTCGTTGCTGAGGAGCAAGATT
AG (SEQ ID NO: 111)

Amp

ATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAA
GATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACG
TTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACAC
TATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATA
ACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCAT
GTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAAC
GTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACT
TCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCC
AGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTG
CCTCACTGATTAAGCATTGGTAA (SEQ ID NO: 112)

Amp

ATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTCCTGTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAA
GATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGCGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACG
TTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTATTGACGCCGGGCAAGAGCAACTCGGTCGCCGCATACAC
TATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGATGGCATGACAGTAAGAGAATTATGCAGTGCTGCCATA
ACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTTTGCACAACATGGGGGATCAT
GTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGACGAGCGTGACACCACGATGCCTGTAGCAATGGCAACAAC
GTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAATAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACT
TCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGTGAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCC
AGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACAGATCGCTGAGATAGGTG
CCTCACTGATTAAGCATTGGTAA (SEQ ID NO: 112)

FIG. 12A

Neomycin

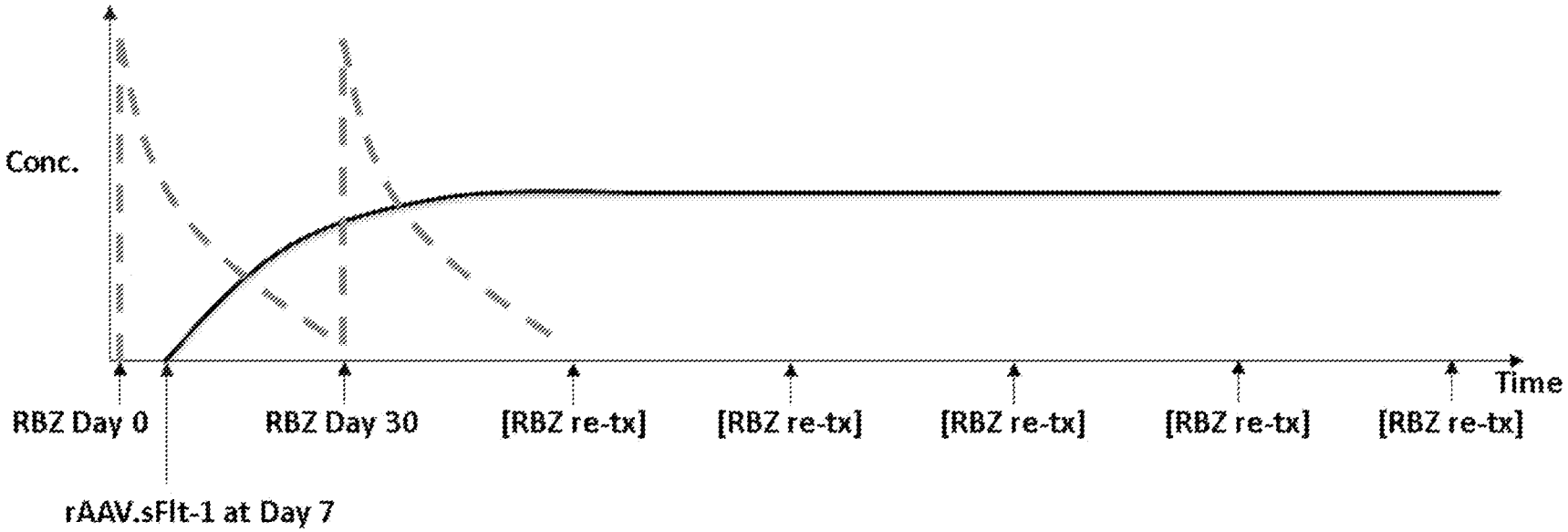
ATGATTGAACAAGATGGATTGCACGCAGGTTCTCCGGCCGCTTGGGTGGAGAGGCTATTCGGCTATGACTGGGCACAACAGACAATCGGCTG
CTCTGATGCCGCCGTGTTCCGGCTGTCAGCGCAGGGGCGCCCGGTTCTTTTTGTCAAGACCGACCTGTCCGGTGCCCTGAATGAACTGCAGGA
CGAGGCAGCGCGGCTATCGTGGCTGGCCACGACGGGCGTTCCTTGCGCAGCTGTGCTCGACGTTGTCACTGAAGCGGGAAGGGACTGGCTG
CTATTGGGCGAAGTGCCGGGGCAGGATCTCCTGTCATCTCACCTTGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCGGCTG
CATACGCTTGATCCGGCTACCTGCCCATTCGACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGTCTTGTCGAT
CAGGATGATCTGGACGAAGAGCATCAGGGGCTCGCGCCAGCCGAACTGTTCGCCAGGCTCAAGGCGCGCATGCCCGACGGCGAGGATCTCG
TCGTGACCCATGGCGATGCCTGCTTGCCGAATATCATGGTGGAAAATGGCCGCTTTTCTGGATTCATCGACTGTGGCCGGCTGGGTGTGGCG
GACCGCTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGGCGAATGGGCTGACCGCTTCCTCGTGCTTTACGGTATC
GCCGCTCCCGATTCGCAGCGCATCGCCTTCTATCGCCTTCTTGACGAGTTCTTCTGA (SEQ ID NO: 113)

Ampicillin Resistance

AGGTGGCACTTTTCGGGGAAATGTGCGCGGAACCCCTATTTGTTTATTTTTCTAAATACATTCAAATATGTATCCGCTCATGAGACAATAACCCT
GATAAATGCTTCAATAATATTGAAAAAGGAAGAGTATGAGTATTCAACATTTCCGTGTCGCCCTTATTCCCTTTTTTGCGGCATTTTGCCTTCCT
GTTTTTGCTCACCCAGAAACGCTGGTGAAAGTAAAAGATGCTGAAGATCAGTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAG
CGGTAAGATCCTTGAGAGTTTTCGCCCCGAAGAACGTTTTCCAATGATGAGCACTTTTAAAGTTCTGCTATGTGGCGCGGTATTATCCCGTGTT
GACGCCGGGCAAGAGCAACTCGGTCGCCGCATACACTATTCTCAGAATGACTTGGTTGAGTACTCACCAGTCACAGAAAAGCATCTTACGGAT
GGCATGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGTGATAACACTGCGGCCAACTTACTTCTGACAACGATCGGAGGACCGAA
GGAGCTAACCGCTTTTTTGCACAACATGGGGGATCATGTAACTCGCCTTGATCGTTGGGAACCGGAGCTGAATGAAGCCATACCAAACGACG
AGCGTGACACCACGATGCCTGCAGCAATGGCAACAACGTTGCGCAAACTATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAATTAA
TAGACTGGATGGAGGCGGATAAAGTTGCAGGACCACTTCTGCGCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGCCGGT
GAGCGTGGGTCTCGCGGTATCATTGCAGCACTGGGGCCAGATGGTAAGCCCTCCCGTATCGTAGTTATCTACACGACGGGGAGTCAGGCAAC
TATGGATGAACGAAATAGACAGATCGCTGAGATAGGTGCCTCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTTACTCATATATACTTTA
GATTGATTTAAAACTTCATTTTTAATTTAAAAGGATCTAGGTGAAGATCCTTTTTGATAATCTCATGACCAAAATCCCTTAACGTGAGTTTTCGTT
CCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTTCTTGAGATCCTTTTTTTCTGCGCGTAATCTGCTGCTTGCAAACAAAAAAACCA
CCGCTACCAGCGGTGGTTTGTTTGCCGGATCAAGAGCTACCAACTCTTTTTCCGAAGGTAACTGGCTTCAGCAGAGCGCAGATACCAAATACT
GTCCTTCTAGTGTAGCCGTAGTTAGGCCACCACTTCAAGAACTCTGTAGCACCGCCTACATACCTCGCTCTGCTAATCCTGTTACCAGTGGCTGC
TGCCAGTGGCGATAAGTCGTGTCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGGTCGGGCTGAACGGGGGGTTCG
TGCACACAGCCCAGCTTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCCGAAGGGAG
AAAGGCGGACAGGTATCCGGTAAGCGGCAGGGTCGGAACAGGAGAGCGCACGAGGGAGCTTCCAGGGGGAAACGCCTGGTATCTTTATAG
TCCTGTCGGGTTTCGCCACCTCTGACTTGAGCGTCGATTTTTGTGATGCTCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAACGCGG
CCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCTTTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGA
GTGAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCTGATGCGGTATTTTCTC
CTTACGCATCTGTGCGGTATTTCACACCGCATATGGTGCACTCTCAGTACAATCTGCTCTGATGCCGCATAGTTAAGCCAGTAT (SEQ ID NO:
114)

FIG. 12B

AAV expression kinetics inform dosing schedule for clinical study



- Protocol for study of safety and efficacy of rAAV.sFlt-1 in humans with wet AMD is informed by expression kinetics
- rAAV.sFlt-1 reaches optimal expression of anti-VEGF protein sFLT-1 at 6-8 weeks
- Subjects in all arms receive two mandatory injections of 0.5 mg ranibizumab on day 0 and day 30
- Expect greater need for re-treatment or rescue treatment in control arm

FIG. 13

Subject	Visit	Study Eye				Fellow Eye			
		AC-cells	AC-flare	VC-BE	VC-IOE	AC-cells	AC-flare	VC-BE	VC-IOE
R1001	SCR	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Baseline	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 8	0	0	Trace	Trace	0	0	Unrem.	Unrem.
	Day 11	0	0	Unrem.	Trace	0	0	Unrem.	Unrem.
	Day 21	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 30	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 60	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
R1002	SCR	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Baseline	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 8	0	0	Unrem.	Unrem.	0	0	Unrem.	
	Day 11	0	0	Trace	Trace				
	Day 21	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 30	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 60	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
R1003	SCR	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Baseline	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 7	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 30	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 60	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
R1004	SCR	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 8	0	0	Unrem.	Trace	0	0	Unrem.	
	Day 11	0	0	Unrem.	Unrem.				
	Day 21	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 30	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.
	Day 60	0	0	Unrem.	Unrem.	0	0	Unrem.	Unrem.

FIG. 14

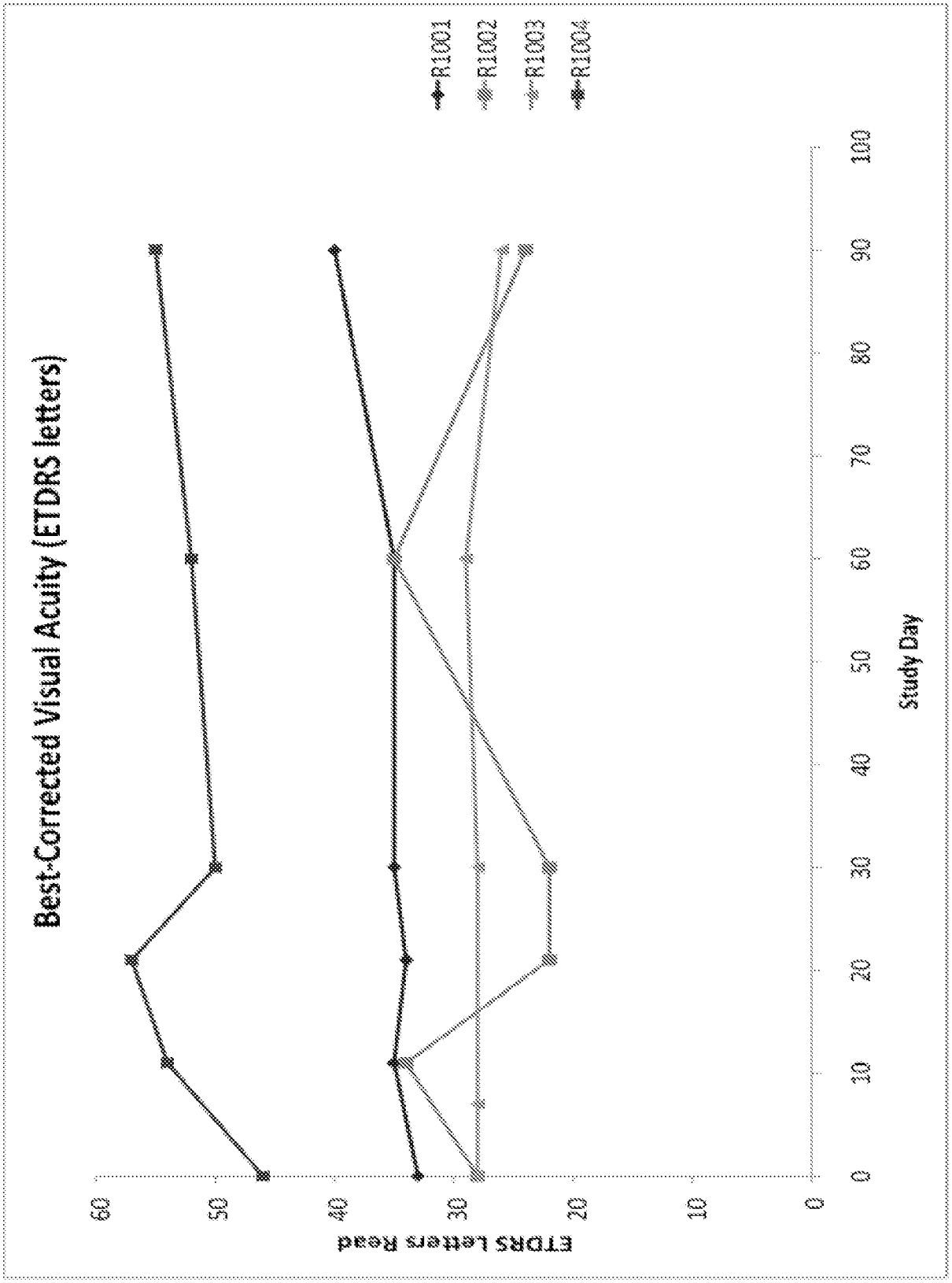

Best-Corrected Visual Acuity (ETDRS letters)
R1001
R1002
R1003
R1004
ETDRS Letters Read
Study Day
0
10
20
30
40
50
60
0
10
20
30
40
50
60
70
80
90
100

FIG. 15A

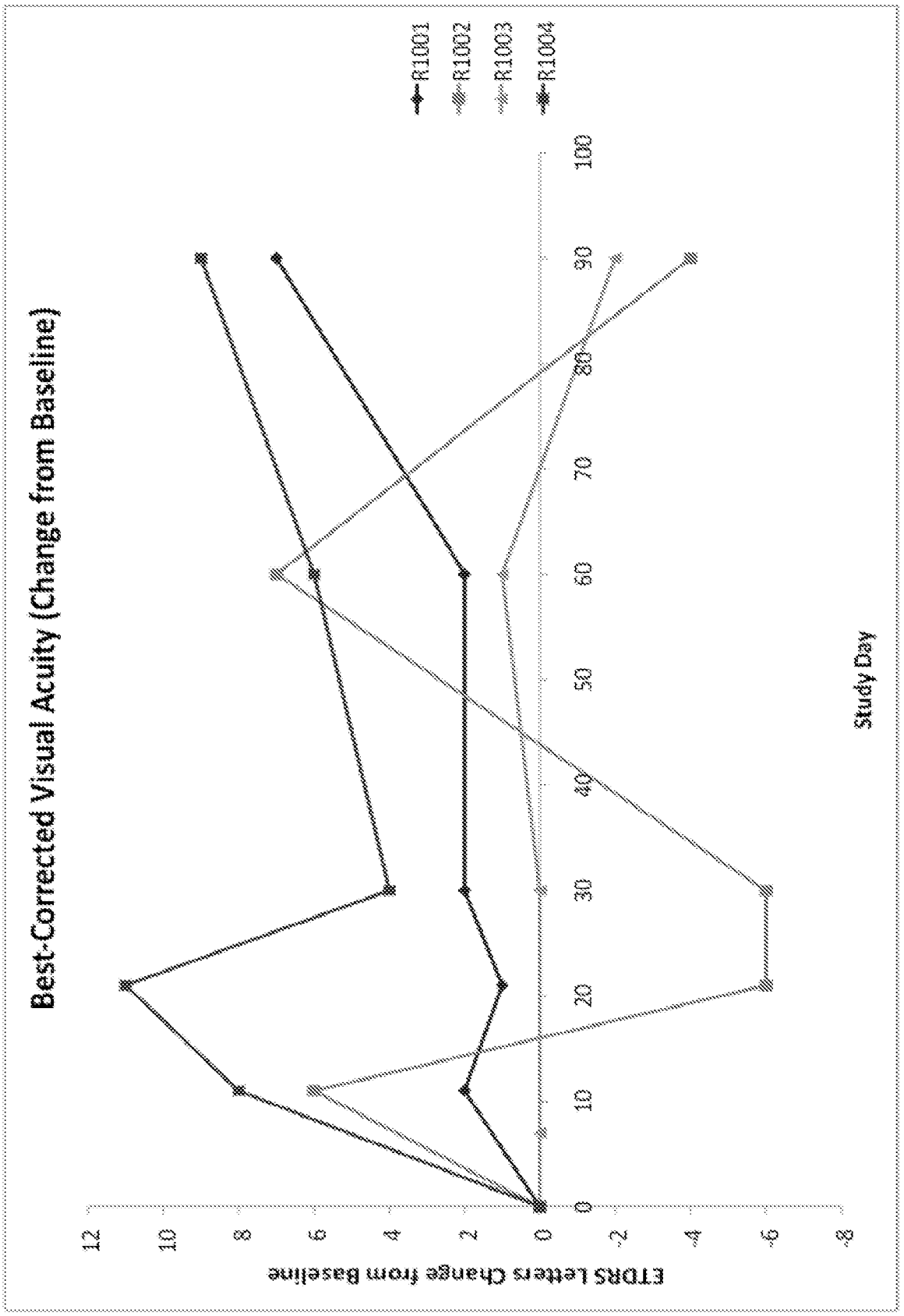
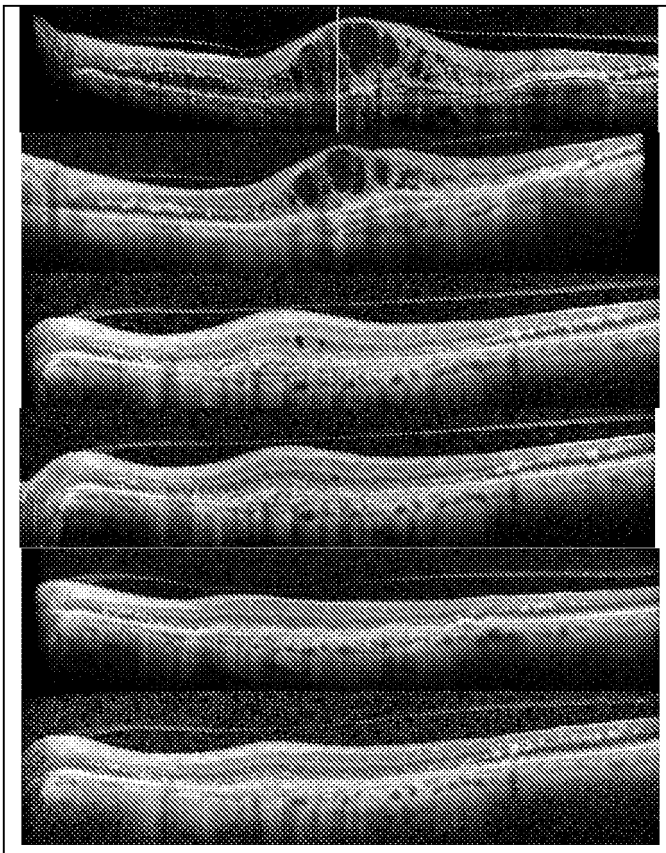

Best-Corrected Visual Acuity (Change from Baseline)
ETDRS letters change from baseline
Study Day
R1001
R1002
R1003
R1004
12
10
8
6
4
2
0
-2
-4
-6
-8
0
10
20
30
40
50
60
70
80
90
100

FIG.15B



Date	OCT CPT	BCVA Snellen Eq
December 2011	704 µm	20/320
Baseline	642 µm	20/250
Day 21	472 µm	20/400
Day 30	498 µm	20/400
Day 60	393 µm	20/200
Day 90	361 µm	20/400

FIG. 16

Subject	Visit Day	Blood	Tear (Study)	Tear (Fellow)	Saliva	Urine
R1005	SCR	0	0	0	0	0
	Day 8	0	35,000*	0	0	0
	Day 30	0	0	0	0	0
R1006	SCR	0	0	0	0	0
	Day 8	0	0	0	0	0
	Day 30	0	0	0	0	0
R1007	SCR	0	0	0	0	0
	Day 8	0	0	0	0	0
	Day 30	0	0	0	0	0
R1008	SCR	0	0	0	0	0
	Day 8	0	0	0	0	0
	Day 30	0	0	0	0	0

FIG. 17

Subject	Visit Day	Serum	Tear (Study)	Tear (Fellow)	Saliva	Urine
R1001	SCR	0	ND	ND	ND	0
	Day 8	0	ND	ND	ND	0
	Day 21	0	ND	ND	0	0
	Day 30	0	ND	ND	0	0
	Day 60	0	ND	ND	0	0
R1002	SCR	0	ND	ND	ND	ND
	Day 8	0	ND	ND	0	0
	Day 21	0	ND	ND	0	0
	Day 30	0	ND	ND	0	0
	Day 60	0	ND	ND	0	0
R1003	SCR	0	ND	ND	0	0
	Day 30	0	ND	ND	0	0
R1004	SCR	0	ND	ND	0	0
	Day 8	0	ND	ND	ND	0
	Day 21	0	ND	ND	ND	0
	Day 30	0	ND	ND	0	0
	Day 60	0	ND	ND	0	0

FIG. 18

Subject	Visit Day	Serum	Tear (Study)	Tear (Fellow)	Saliva	Urine
R1001	SCR	85.51±9.28	ND	ND	ND	0
	Day 8	76.67±24.46	ND	ND	0	0
	Day 21	46.19±11.65	ND	ND	875.27±99.44	0
	Day 30	60.19±10.61	ND	ND	0	0
	Day 60	14.89±20.97	ND	ND	0	0
	Day 90	9.24±1.13	ND	ND	438.58±210.88	0
R1002	SCR	35.82±37.12	ND	ND	ND	ND
	Day 8	46.19±6.99	ND	ND	1680.55±104.84	149.16±3.49
	Day 21	12.42±5.82	ND	ND	407.93±17.47	102.03±26.79
	Day 30	79.88±21.21	ND	ND	2337.78±123.30	0
	Day 60	9.95±9.32	ND	ND	1607.72±314.52	0
	Day 90	58.15+11.33	ND	ND	571.66+36.28	0
R1003	SCR	55.51±22.54	ND	ND	1105.90±83.53	0
	Day 30	79.88±14.58	ND	ND	1915.90±83.53	0
	Day 90	34.90+15.31	ND	ND	892.35+54.42	0
R1004	SCR	331.13±216.11	ND	ND	17.46±7.95	60.20±3.49
	Day 8	62.67±4.66	ND	ND	ND	140.92±45.43
	Day 21	4.19±5.82	ND	ND	ND	134.33±15.14
	Day 30	62.07±7.95	ND	ND	1834.44±198.87	37.13±47.66
	Day 60	9.13±15.14	ND	ND	92.77±50.67	25.60±15.14
	Day 90	20.47+5.55	ND	ND	ND	0

FIG. 19

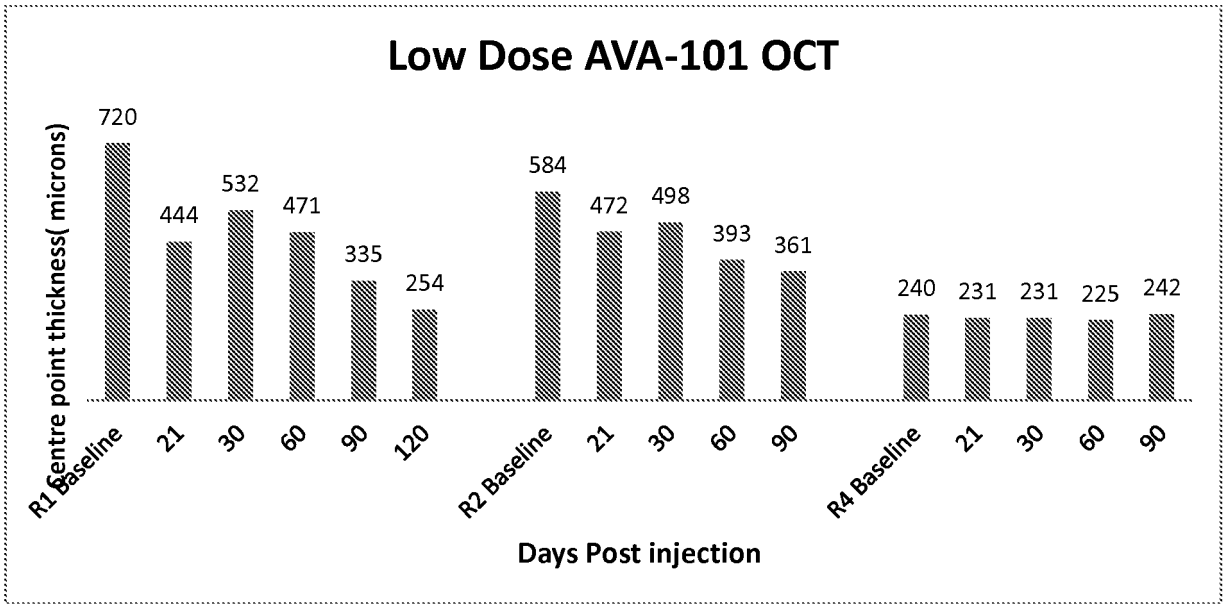


FIG. 20A

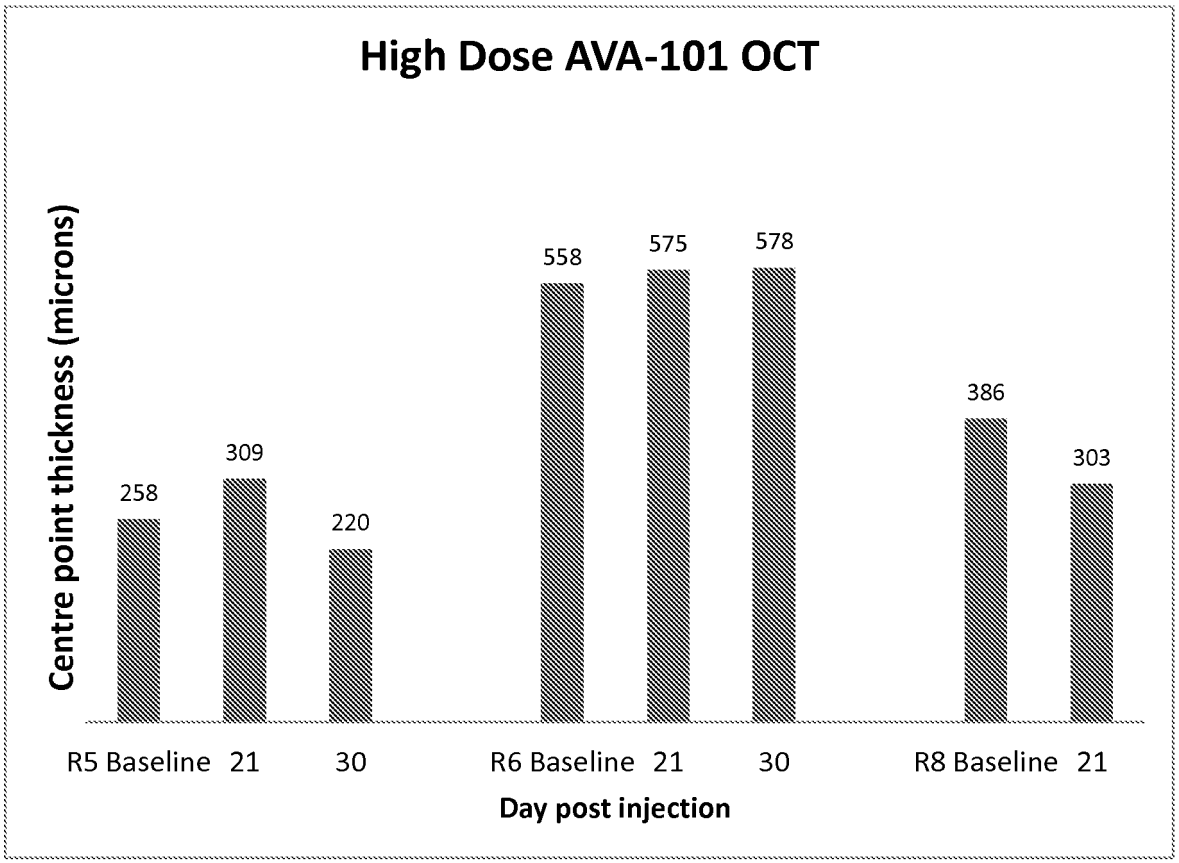


FIG. 20B

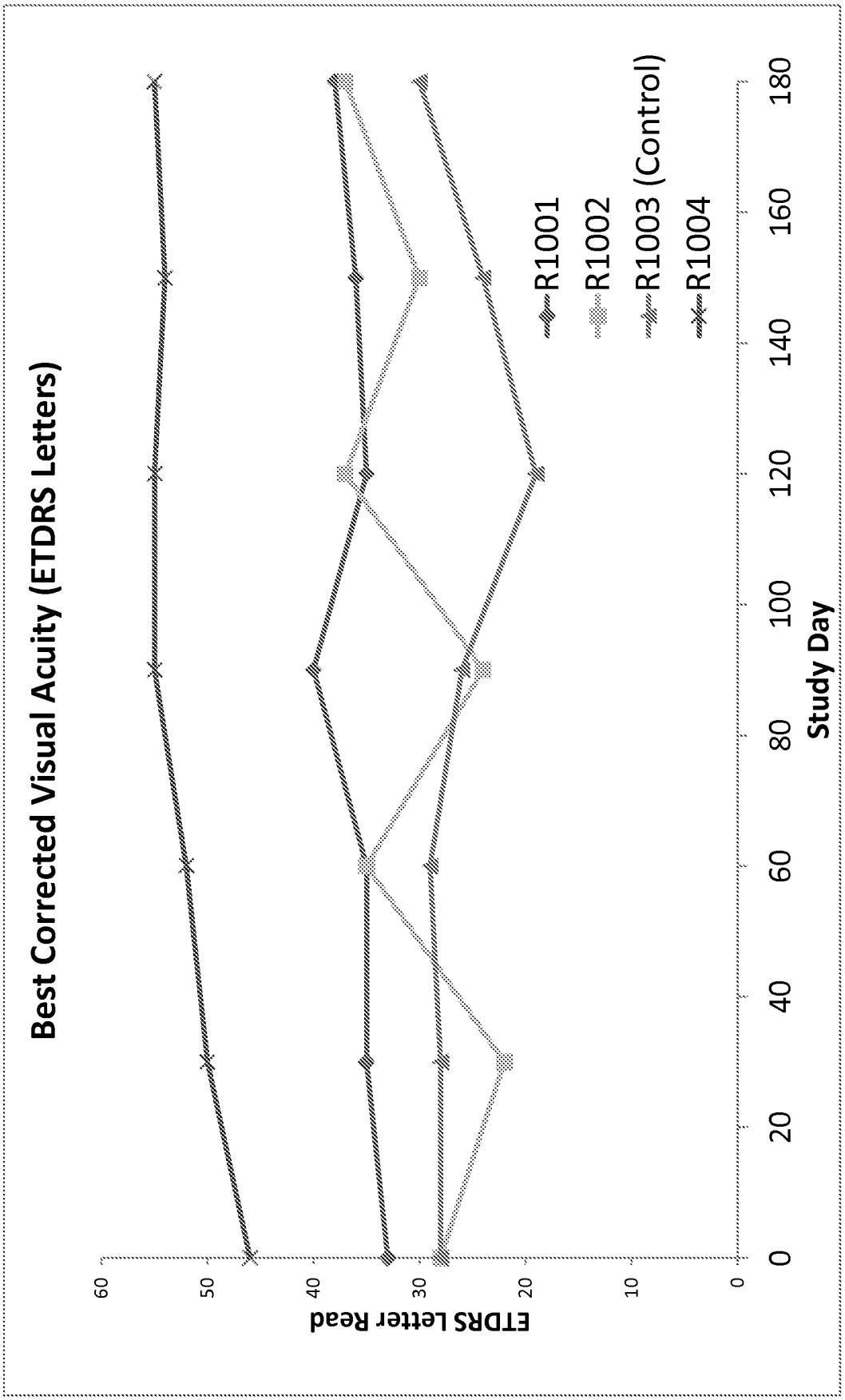

Best Corrected Visual Acuity (ETDRS Letters)
ETDRS Letter Read
60
50
40
30
20
10
0
0
20
40
60
80
100
120
140
160
180
Study Day
R1001
R1002
R1003 (Control)
R1004

FIG. 21A

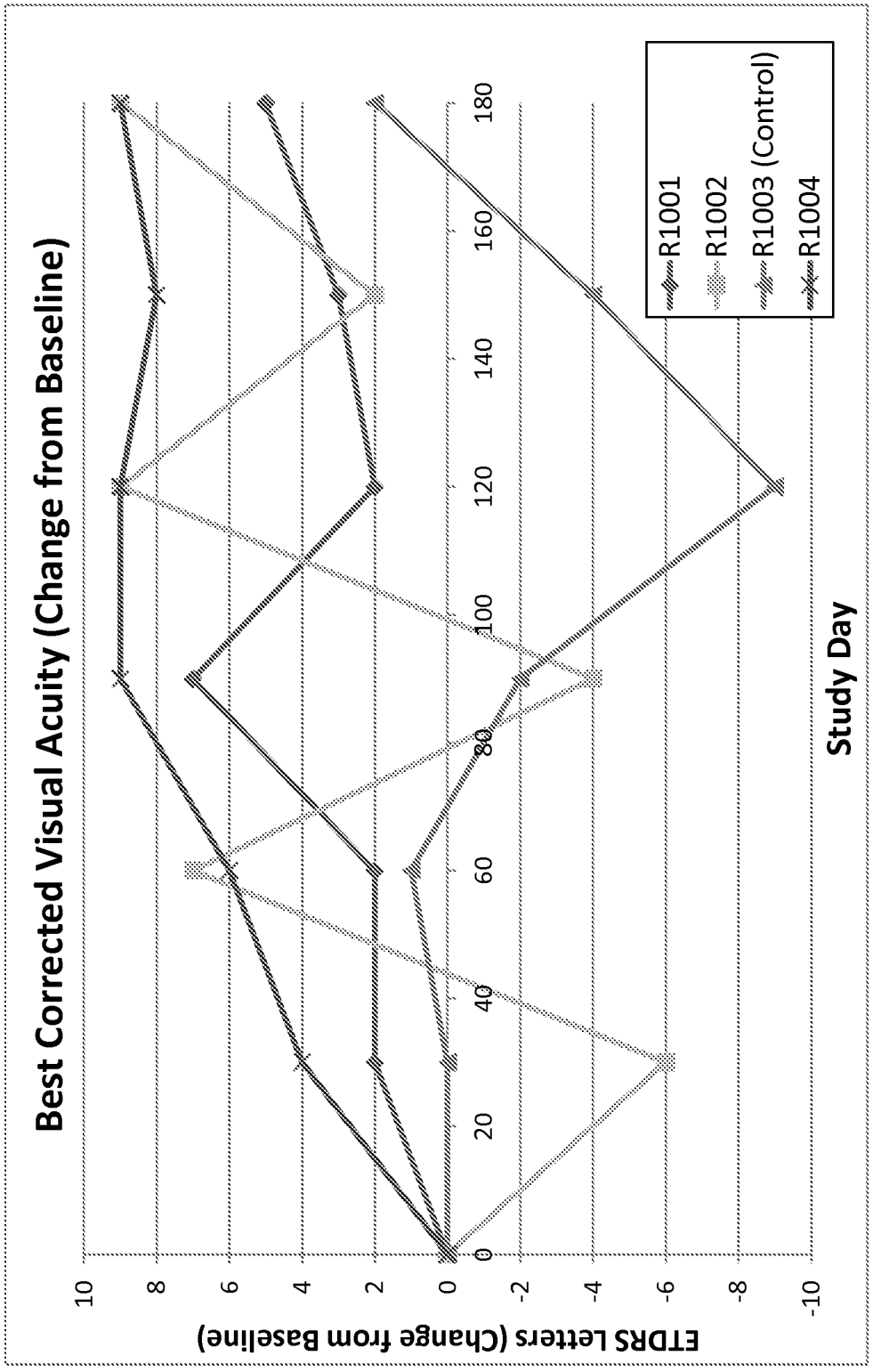

Best Corrected Visual Acuity (Change from Baseline)
ETDRS Letters (Change from Baseline)
Study Day
10
8
6
4
2
0
-2
-4
-6
-8
-10
0
20
40
60
80
100
120
140
160
180
R1001
R1002
R1003 (Control)
R1004

FIG. 21B

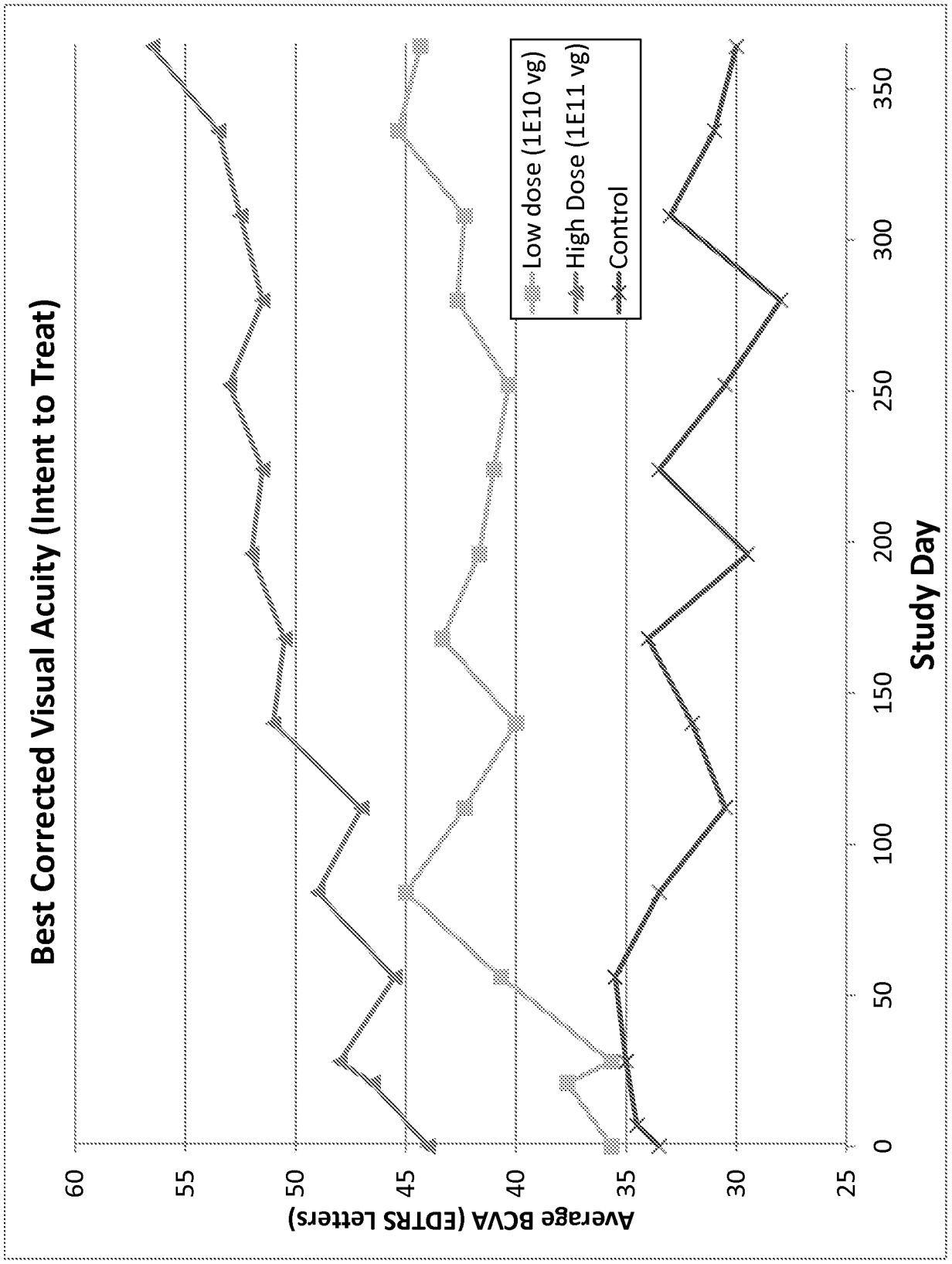

Best Corrected Visual Acuity (Intent to Treat)
Average BCVA (EDTRS Letters)
Study Day
Low dose (1E10 vg)
High Dose (1E11 vg)
Control
60
55
50
45
40
35
30
25
0
50
100
150
200
250
300
350

FIG. 22A

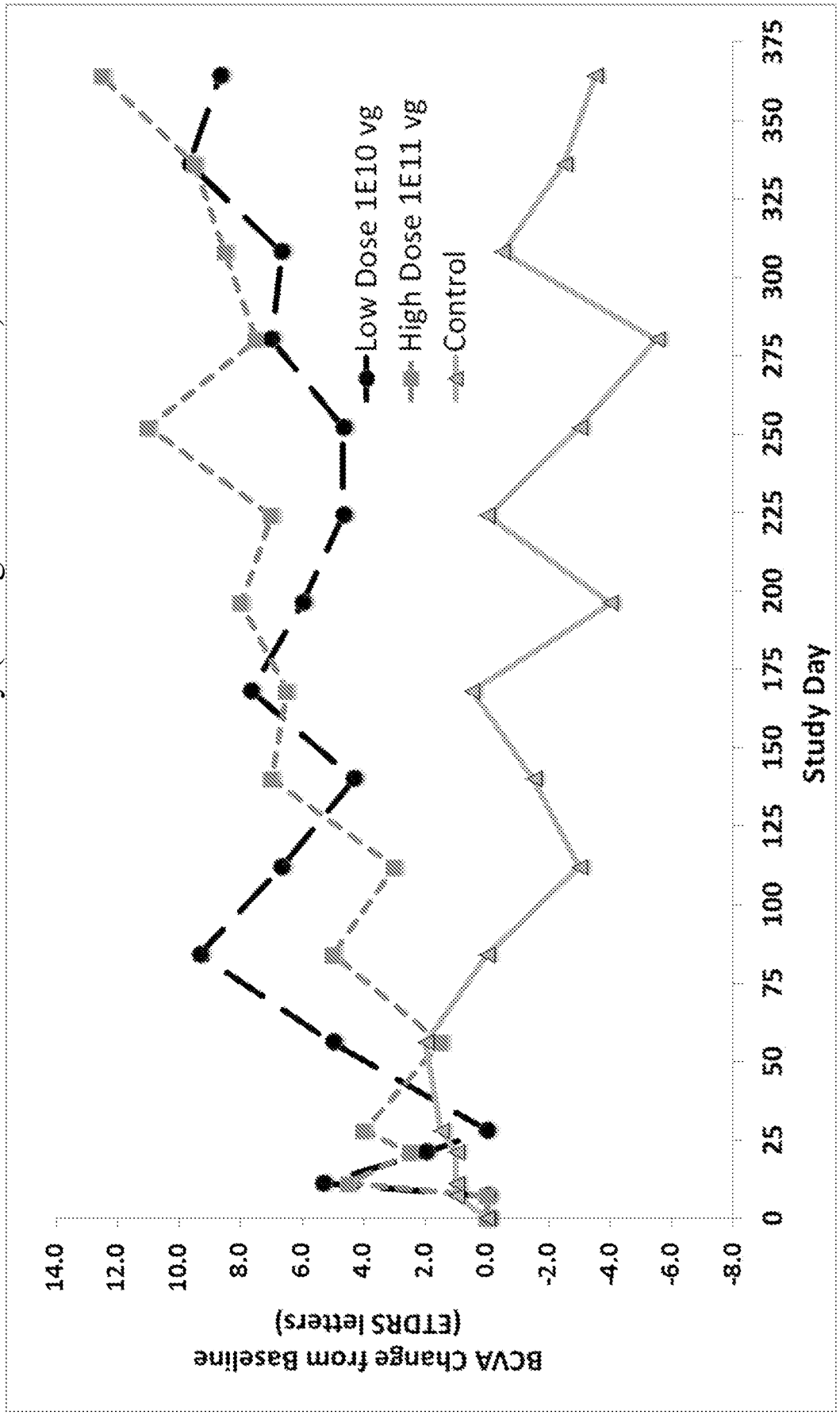

Best Corrected Visual Acuity (Change from Baseline)
BCVA change from baseline (ETDRS letters)
14.0
12.0
10.0
8.0
6.0
4.0
2.0
0.0
-2.0
-4.0
-6.0
-8.0
0
25
50
75
100
125
150
175
200
225
250
275
300
325
350
375
Study Day
Low Dose 1E10 vg
High Dose 1E11 vg
Control

FIG. 22B

Anti-VEGF reinjections for patients in rAAV.sFlt-1 clinical study

Week	8	12	16	20	24	28	32	36	40	44	48	52	(Month) 15
R1003 Control	0	X	X	0	0	X	0	X	0	0	X	0	
R1007 Control	0	0	0	X	0	0	0	0	0	0	0	0	
R1001	0	0	0	0	0	0*	0*	0	0	0	0	0	0
R1002	0	0	0	0	0	0	0	0*	0	0	0	0	
R1004	0	0	0	0	0	0	0	0	0	0	0	X	
R1005	0	0	0	0	0	0*	0	0	0	0	0	0	
R1006	0	X	0*	0	0	0	0	0	0	0	0	0	
R1008	0	0	0	0	0*	0	0	0	0	0	0	0	

- * Missed visit (no injection)The table above shows partial results from a clinical study of the safety and efficacy of rAAV.sFlt-1 in patients with wet AMD.
- According to study protocol, patients initially received intravitreal injections of anti-VEGF at 0 and 30 days vision after which were monitored for disease activity every 4 weeks.
- Additional intravitreal injections of anti-VEGF therapy were administered to patients if exhibited other signs of disease activity as defined in the study protocol.
- " X" indicates patient received an intravitreal injection of anti-VEGF therapy (Lucentis) during a monitoring visit in the listed week.

FIG 23

Visual Acuity and SD-OCT images by Week for Human Subject Treated with rAAV.sFlt-1

Week	BCVA
scr	26
bsl	28
4	22
8	35
12	40
16	37
20	38

Week	BCVA
24	37
28	42
32	40
36	
40	35
44	43
48	44
52	41

FIG 24

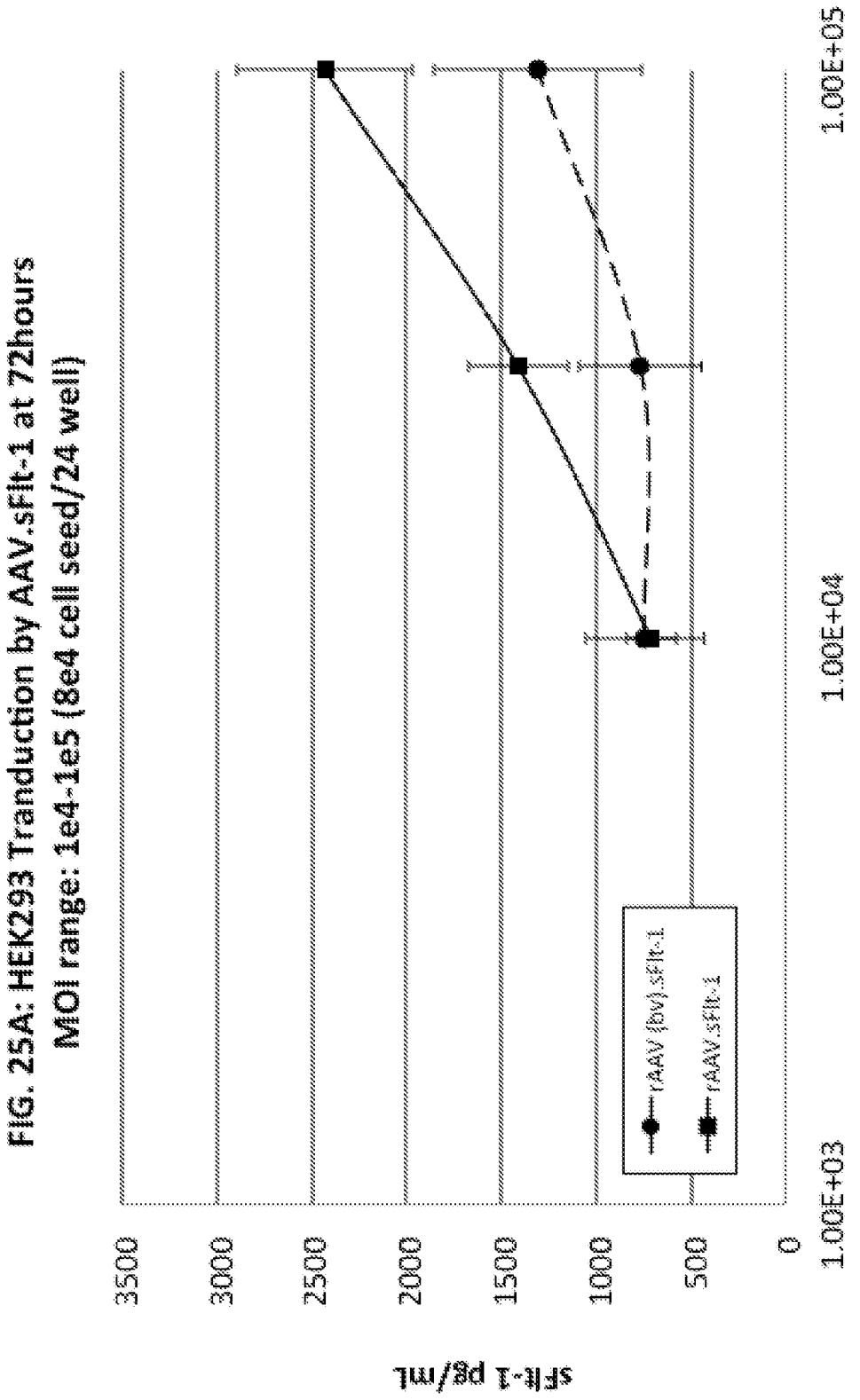

FIG. 25A: HEK293 Tranduction by AAV.sFlt-1 at 72hours
MOI range: 1e4-1e5 (8e4 cell seed/24 well)
sFlt-1 pg/mL
3500
3000
2500
2000
1500
1000
500
0
1.00E+03
1.00E+04
1.00E+05
MOI
rAAV (bv).sFlt-1
rAAV.sFlt-1

FIG 25A

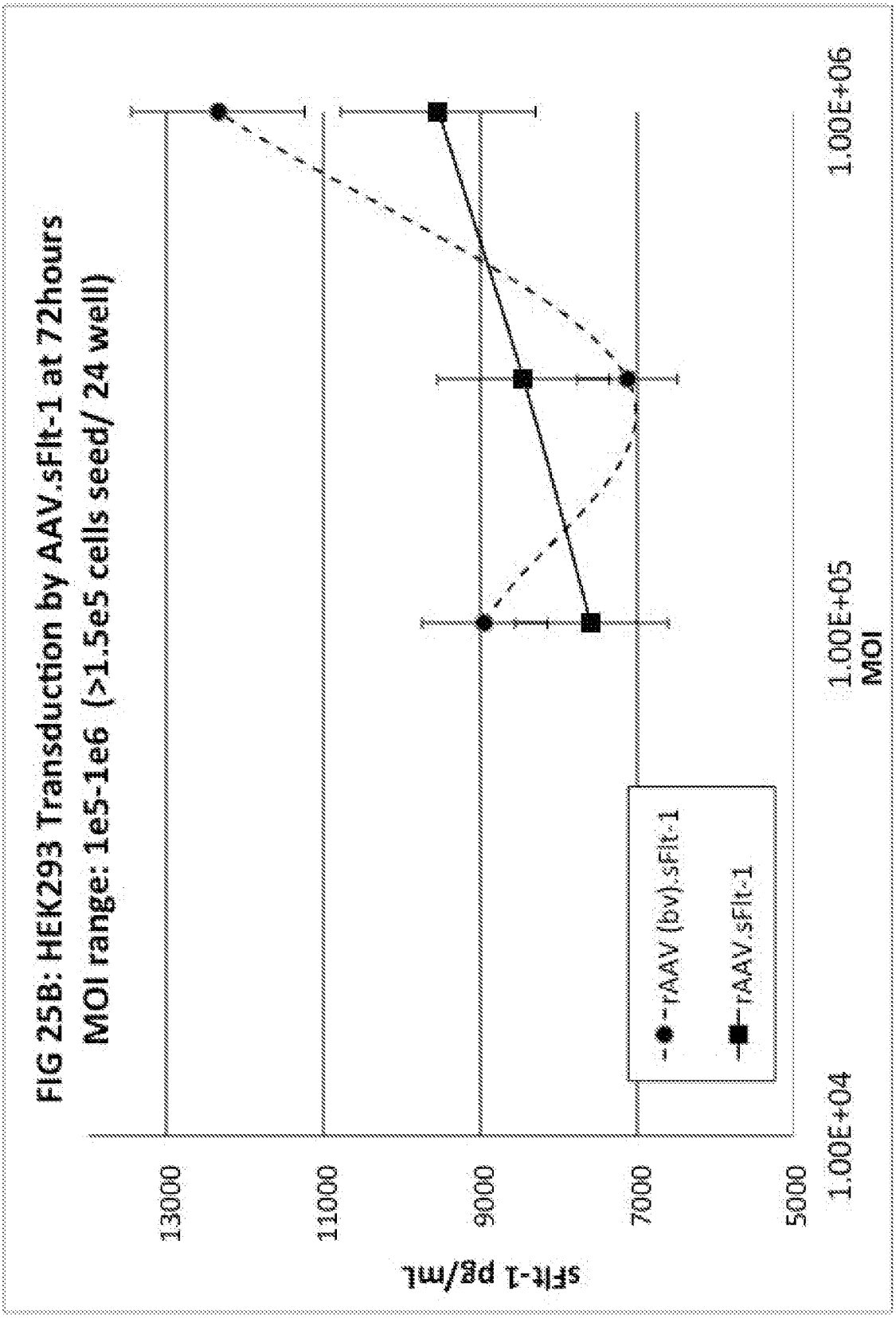

FIG 25B: HEK293 Transduction by AAV.sFlt-1 at 72hours
MOI range: 1e5-1e6 (>1.5e5 cells seed/ 24 well)
sFlt-1 pg/mL
13000
11000
9000
7000
5000
1.00E+04
1.00E+05
1.00E+06
MOI
rAAV (bv).sFlt-1
rAAV.sFlt-1

FIG 25B