FIGURE 1

A – VK SEQUENCES

77E11 DIVLTQSPASLAVSLGQRATMSCRASENIDNSGISFMNWFQQKPGQPPKLLIY

PD1-1 EIVLTQSPATLSLSPGERATMSCRASENIDTSGISFMNWYQQKPGQAPKLLIY

PD1-2 EIVLTQSPATLSLSPGERATMSCRASENIDTSGISFMNWYQQKPGQAPKLLIY

PD1-3 EIVLTQSPATLSLSPGERATMSCRASENIDVSGISFMNWYQQKPGQAPKLLIY

PD1-4 EIVLTQSPATLSLSPGERATMSCRASENIDVSGISFMNWYQQKPGQAPKLLIY

PD1-5 EIVLTQSPATLSLSPGERATMSCRASENIDVSGISFMNWYQQKPGQAPKLLIY

A – VK SEQUENCES

77E11 VASNQGSGVPARFSGSGSGTDFRLTIHPLEEDDTAMYFCQQSKEVPWTFGGGTKLEIK

PD1-1 VASNQGSGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQSKEVPWTFGQGTKLEIK

PD1-2 VASNQGSGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQSKEVPWTFGQGTKLEIK

PD1-3 VASNQGSGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQSKEVPWTFGQGTKLEIK

PD1-4 VASNQGSGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQSKEVPWTFGQGTKLEIK

PD1-5 VASNQGSGIPARFSGSGSGTDFTLTISRLEPEDFAVYYCQQSKEVPWTFGQGTKLEIK

FIGURE 1 (continued)

B – VH SEQUENCES

77E11 EVMLVESGGGLVKPGGSLKLSCTASGFTFSNSAMSWVRQTPERRLEWVA

PD1-1 EVMLVESGGGLVQPGGSLRLSCTASGFTFSASAMSWVRQAPGKGLEWVA

PD1-2 EVMLVESGGGLVQPGGSLRLSCTASGFTFSASAMSWVRQAPGKGLEWVA

PD1-3 EVMLVESGGGLVQPGGSLRLSCTASGFTFSKSAMSWVRQAPGKGLEWVA

PD1-4 EVMLVESGGGLVQPGGSLRLSCTASGFTFSKSAMSWVRQAPGKGLEWVA

PD1-5 EVMLVESGGGLVQPGGSLRLSCTASGFTFSKSAMSWVRQAPGKGLEWVA

B – VH SEQUENCES

77E11 YISGGGGDTYYSDSVKGRFTISRDNAKDTLYLHMSSLRSEDTALHYCARHSNSNYYAMDYWGQGTSVTVSS

PD1-1 YISGGGGDTYYSSSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSNVNYYAMDYWGQGTLVTVSS

PD1-2 YISGGGGDTYYSSSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSNPNYYAMDYWGQGTLVTVSS

PD1-3 YISGGGGDTYYSSSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSNVNYYAMDYWGQGTLVTVSS

PD1-4 YISGGGGDTYYSSSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSNVNYYAMDYWGQGTLVTVSS

PD1-5 YISGGGGDTYYSSSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHSNVNYYAMDYWGQGTLVTVSS

FIGURE 2

A)

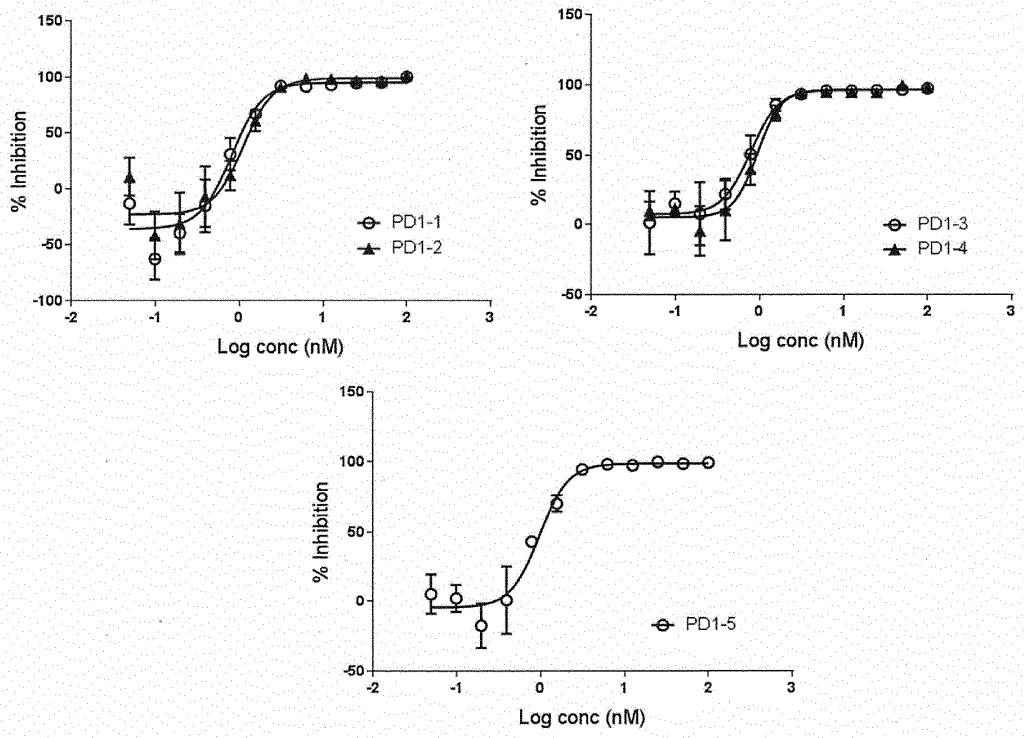


FIGURE 2 (continued)

B)

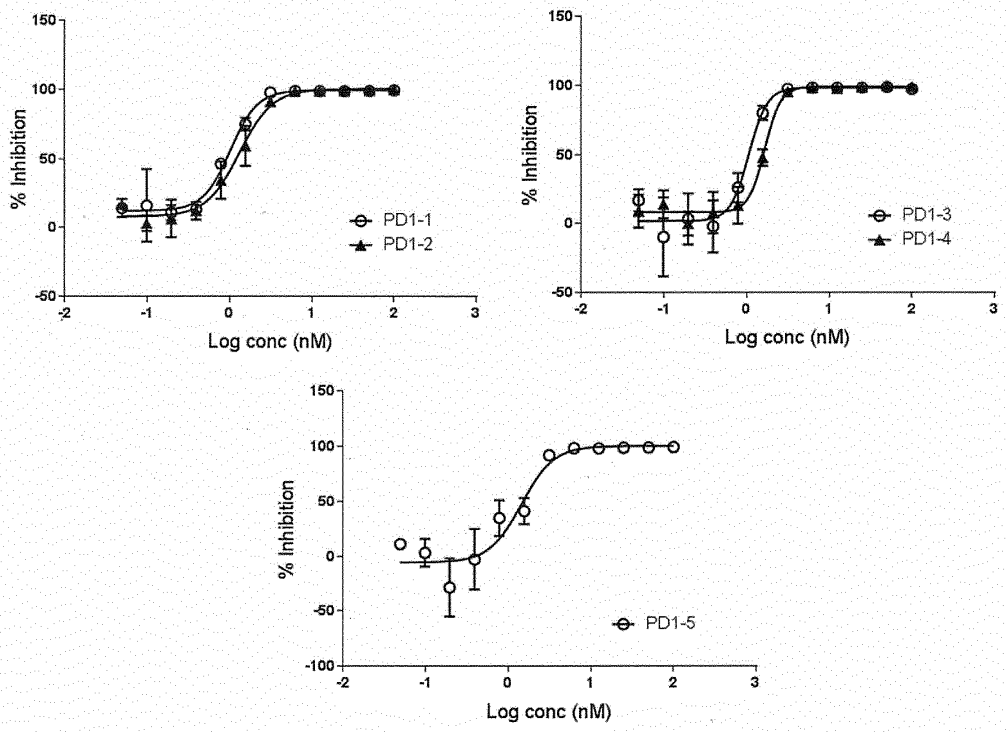


FIGURE 3

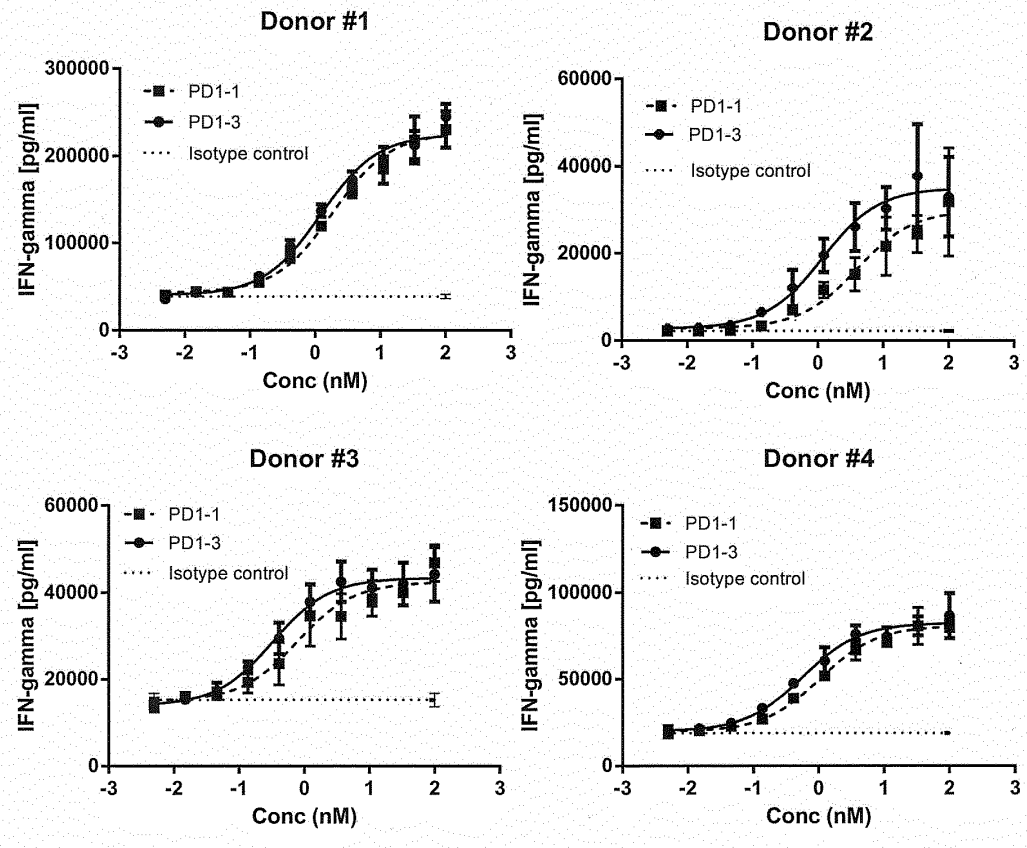

Donor #1
IFN-gamma [pg/ml]
300000
200000
100000
0
PD1-1
PD1-3
Isotype control
-3 -2 -1 0 1 2 3
Conc (nM)
Donor #2
IFN-gamma [pg/ml]
60000
40000
20000
0
PD1-1
PD1-3
Isotype control
-3 -2 -1 0 1 2 3
Conc (nM)
Donor #3
IFN-gamma [pg/ml]
60000
40000
20000
0
PD1-1
PD1-3
Isotype control
-3 -2 -1 0 1 2 3
Conc (nM)
Donor #4
IFN-gamma [pg/ml]
150000
100000
50000
0
PD1-1
PD1-3
Isotype control
-3 -2 -1 0 1 2 3
Conc (nM)

FIGURE 4

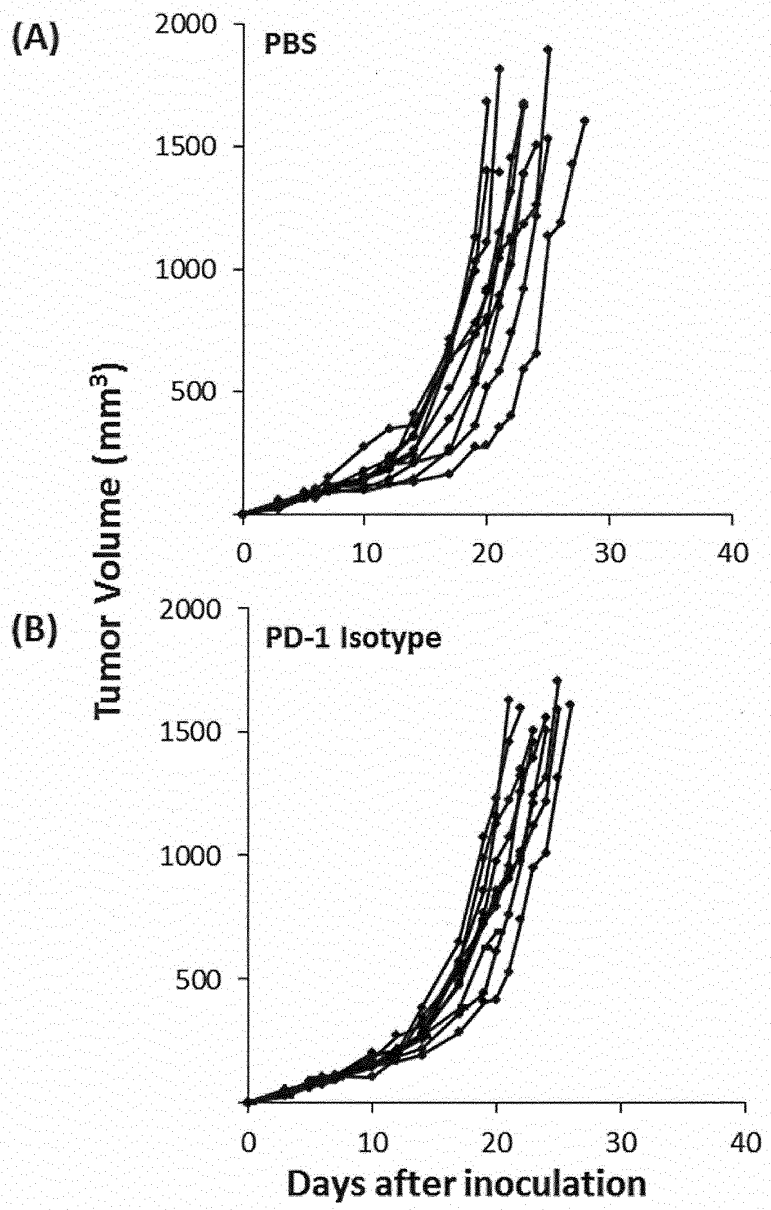

(A)
PBS
2000
1500
1000
500
0
10
20
30
40
(B)
PD-1 Isotype
2000
1500
1000
500
0
10
20
30
40
Tumor Volume (mm3)
Days after inoculation

FIGURE 4 (continued)

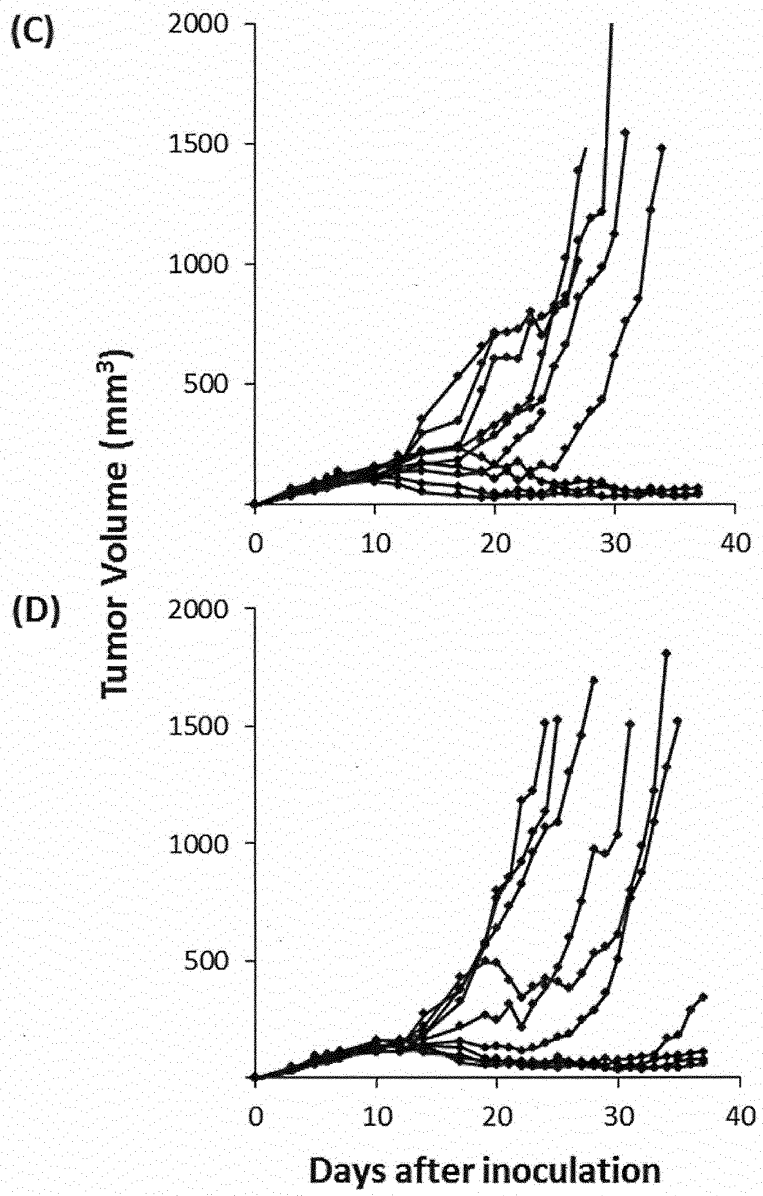


FIGURE 5

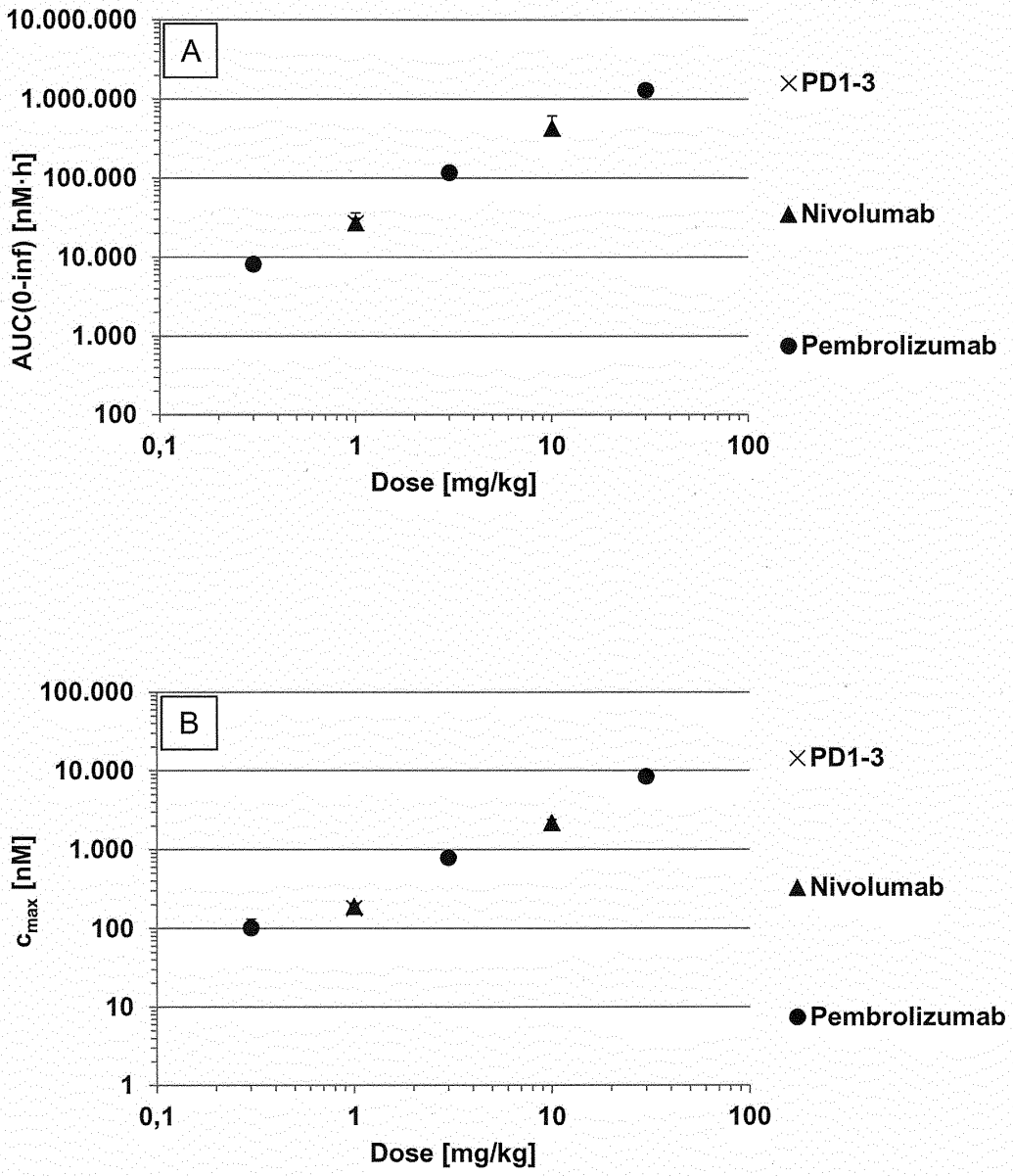
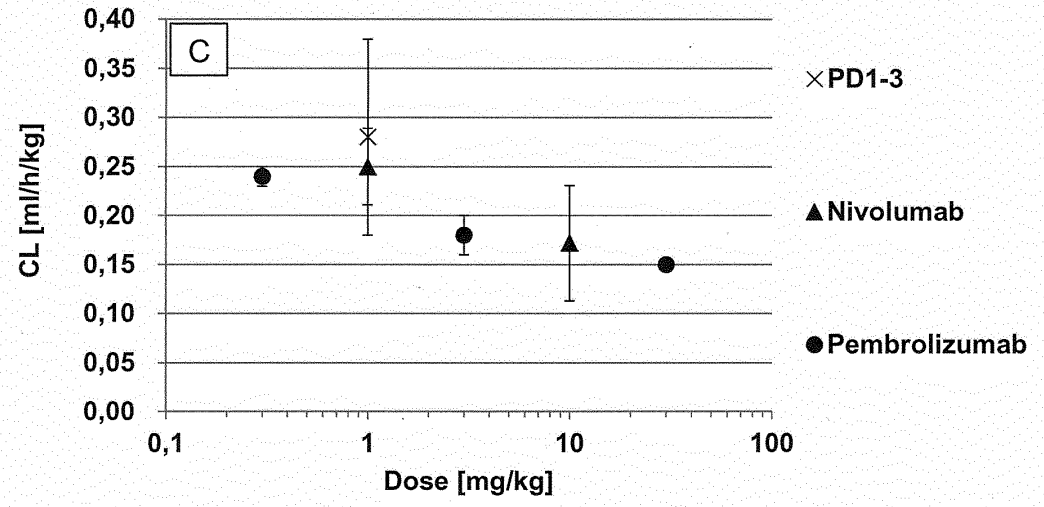

A
10.000.000
1.000.000
100.000
10.000
1.000
100
AUC(0-inf) [nM·h]
0,1
1
10
100
Dose [mg/kg]
×PD1-3
▲Nivolumab
●Pembrolizumab
B
100.000
10.000
1.000
100
10
1
c_{max} [nM]
0,1
1
10
100
Dose [mg/kg]
×PD1-3
▲Nivolumab
●Pembrolizumab

FIGURE 5 (continued)



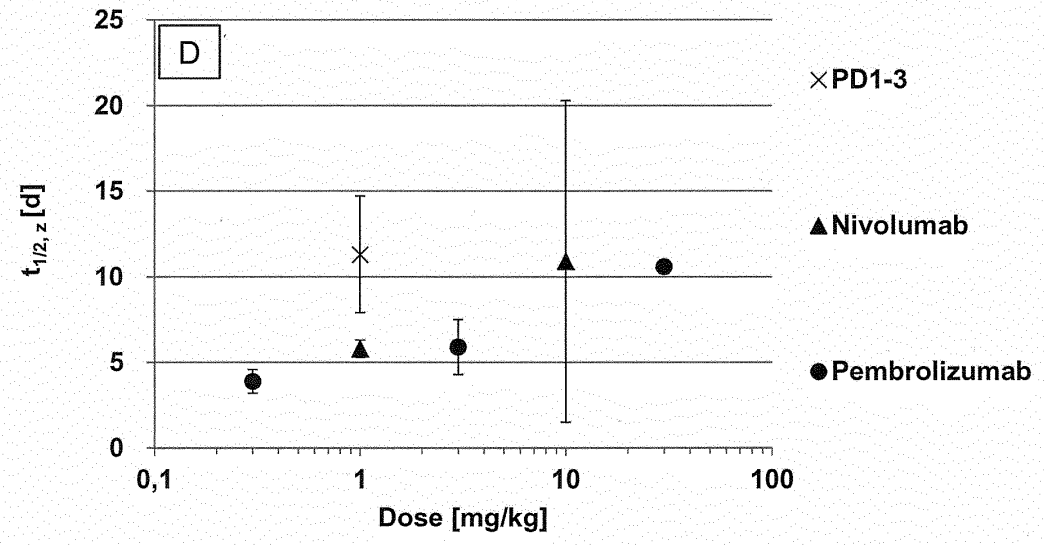


FIGURE 6

A – VK SEQUENCES

```
496G6   DIVMTQSHKFMSTSVGDRVSFTCKASQDVNTAVAWYQQKPGQSPKLLIY
LAG3-1  DIQMTQSPSFLSASVGDRVSITCKASQDVSTAVAWYQQKPGKAPKLLIY
LAG3-2  DIQMTQSPSFLSASVGDRVTFTCKASQDVSTAVAWYQQKPGKAPKLLIY
LAG3-3  DIQMTQSPSFLSASVGDRVTITCKASQDVSTAVAWYQQKPGKAPKLLIY
LAG3-4  DIVMTQSPSFLSASVGDRVTITCKASQDVSTAVAWYQQKPGKAPKLLIY
LAG3-5  DIQMTQSPSFLSASVGDRVSITCKASQDVSTAVAWYQQKPGKAPKLLIY
```

A – VK SEQUENCES

```
496G6   SASYRYTGVPDRFTGSGSGTDFTFTISSVQAEDLALYYCQQHYSIPLTFGAGTKLELK
LAG3-1  SASYRYTGVPDRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSIPLTFGQGTKLEIK
LAG3-2  SASYRYTGVPDRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSIPLTFGQGTKLEIK
LAG3-3  SASYRYTGVPDRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSIPLTFGAGTKLEIK
LAG3-4  SASYRYTGVPDRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSIPLTFGQGTKLEIK
LAG3-5  SASYRYTGVPDRFSGSGSGTDFTLTISSLQPEDFAVYYCQQHYSIPLTFGQGTKLEIK
```

FIGURE 6 (continued)

B – VH SEQUENCES

```
496G6   QVTLKESGPGILQPSQTLSLTCSFSGFSLSTSDMGVGWIRQPSGKGLEWLA
LAG3-1  QVTLVESGGGVVQPGRSLRLSCAFSGFSLSTSDMGVGWIRQAPGKGLEWVA
LAG3-2  QVTLKESGPTLVKPTQTLTLTCSFSGFSLSTSDMGVGWIRQPPGKALEWLA
LAG3-3  QVTLVESGGGVVQPGRSLSLSCAFSGFSLSTSDMGVGWVRQPPGKGLEWVA
LAG3-4  QVTLVESGGGVVQPGRSLRLSCAFSGFSLSTSDMGVGWIRQAPGKGLEWVA
LAG3-5  QVTLKESGPTLVKPTQTLTLTCSFSGFSLSTSDMGVGWIRQPPGKALEWLA
```

B – VH SEQUENCES

```
496G6   HIWWDDVKRYNPALKSRLTISKDTSSSQVFLMIASVDTADTATYFCARIEDYGVSYYFDYWGQGTTLTVSS
LAG3-1  HIWWDDVKRYNPALKSRFTISRDNSKNTLYLQMNSLRAEDTAVYFCARIEDYGVSYYFDYWGQGTTVTVSS
LAG3-2  HIWWDDVKRYNPALKSRLTITKDTSKNQVVLTMTNMDPVDTATYFCARIEDYGVSYYFDYWGQGTTVTVSS
LAG3-3  HIWWDDVKRYNPALKSRFTISRDNSKNTLYLQMNSLRAEDTATYYCARIEDYGVSYYFDYWGQGTTVTVSS
LAG3-4  HIWWDDVKRYNPALKSRFTISRDNSKNTLYLQMNSLRAEDTATYFCARIEDYGVSYYFDYWGQGTTVTVSS
LAG3-5  HIWWDDVKRYNPALKSRLTITKDTSKNQVVLTMTNMDPVDTATYFCARIVDYGVSYYFDYWGQGTTVTVSS
```

FIGURE 7

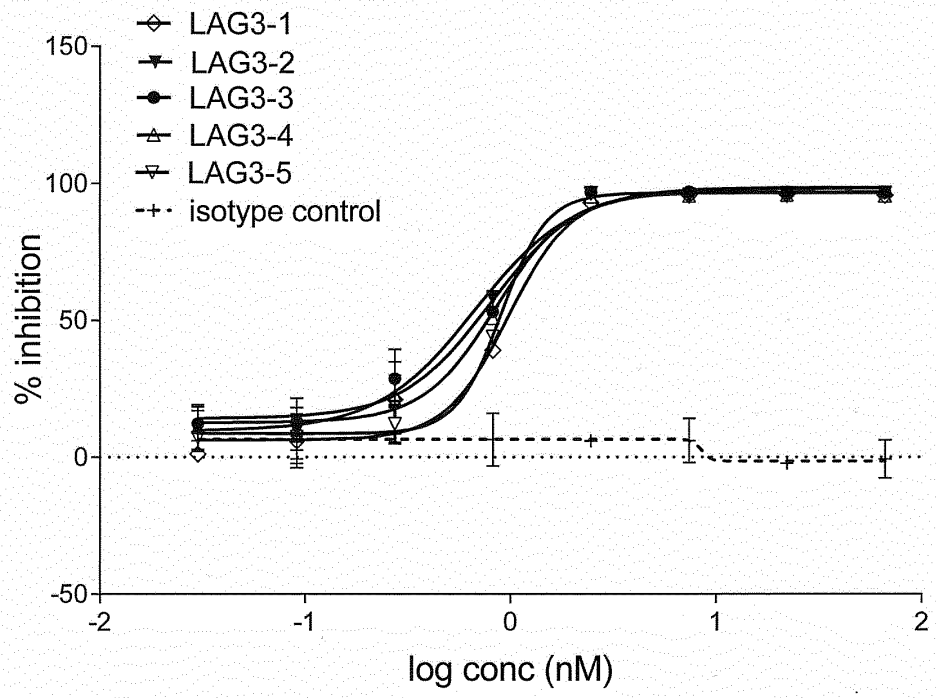
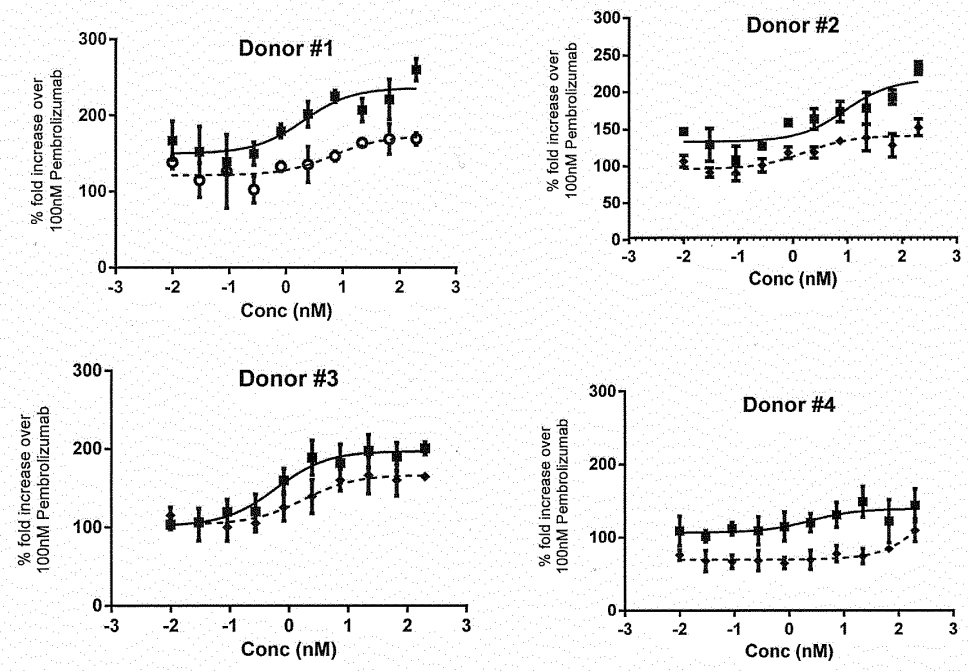

LAG3-1
LAG3-2
LAG3-3
LAG3-4
LAG3-5
isotype control
% inhibition
150
100
50
0
-50
-2
-1
0
1
2
log conc (nM)

FIGURE 8

A)


Donor #1
Donor #2
Donor #3
Donor #4
% fold increase over 100nM Pembrolizumab
Conc (nM)

B)

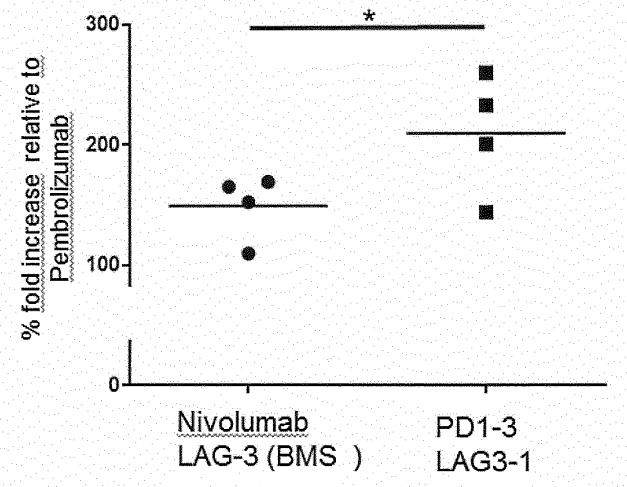

*
% fold increase relative to Pembrolizumab
Nivolumab
LAG-3 (BMS)
PD1-3
LAG3-1

FIGURE 9

A

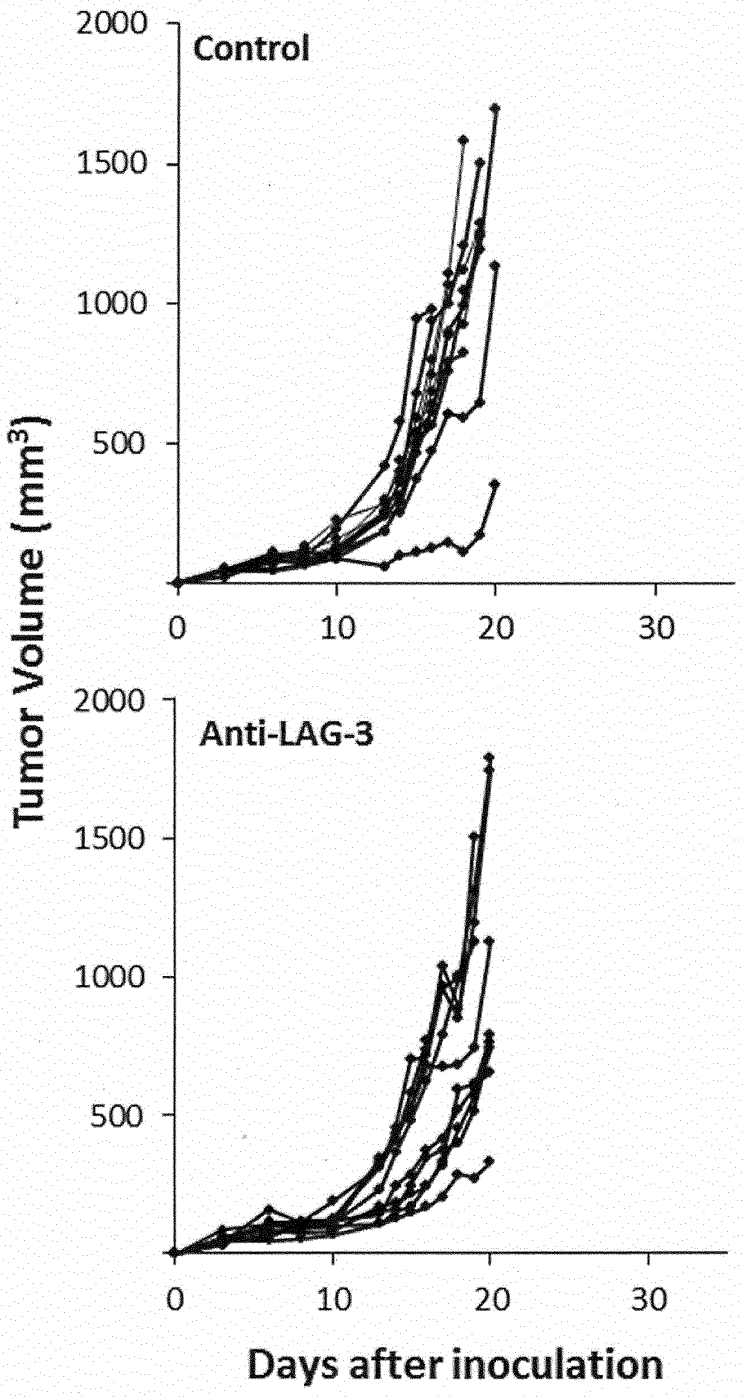

Control
Anti-LAG-3
Tumor Volume (mm³)
2000
1500
1000
500
0
10
20
30
Days after inoculation

FIGURE 9 (continued)

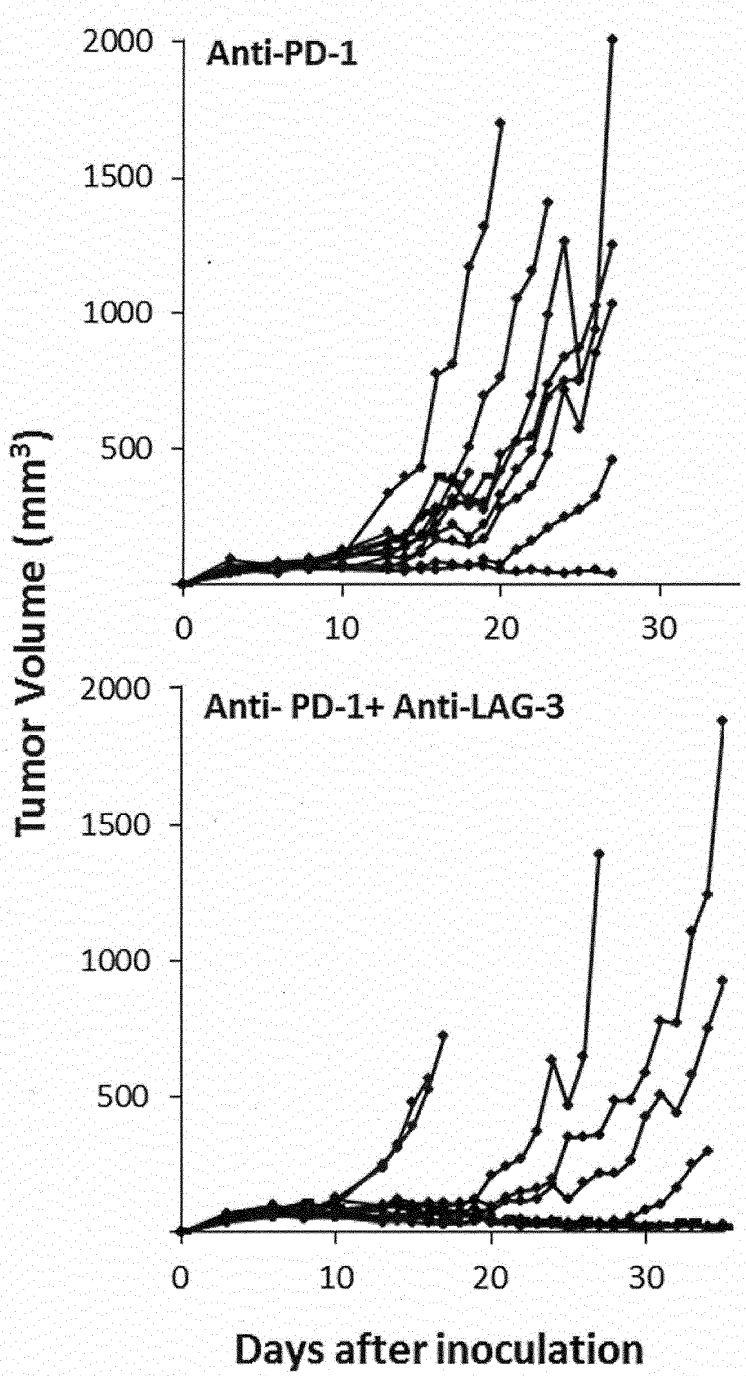


FIGURE 9 (continued)

B

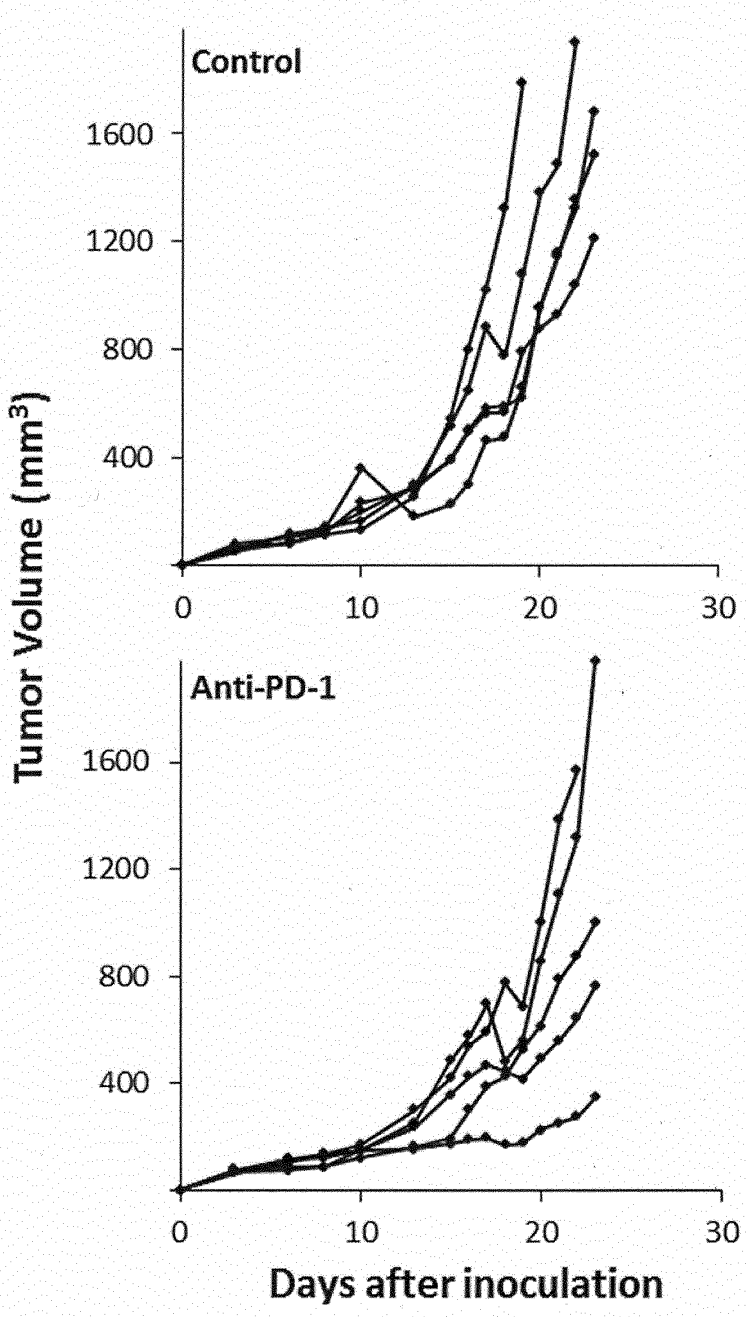


FIGURE 9 (continued)

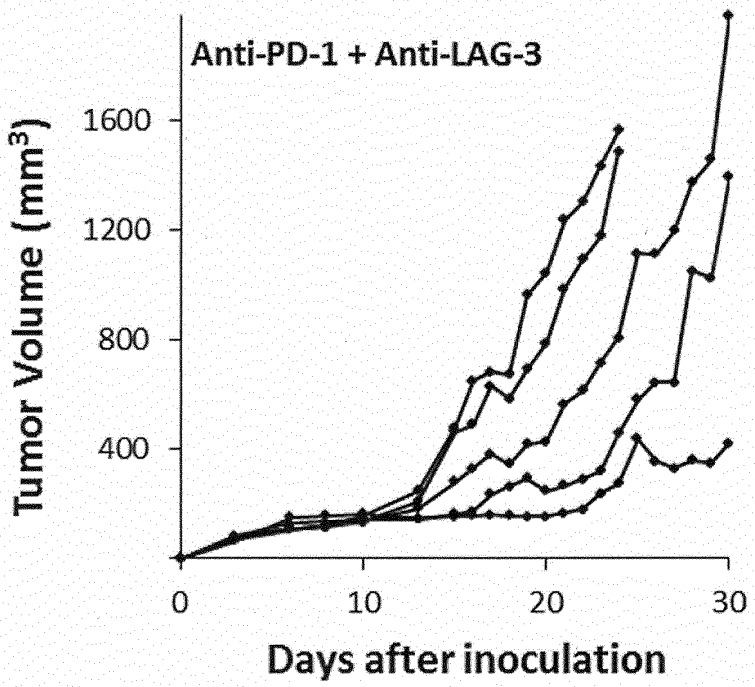


FIGURE 9 (continued)

C

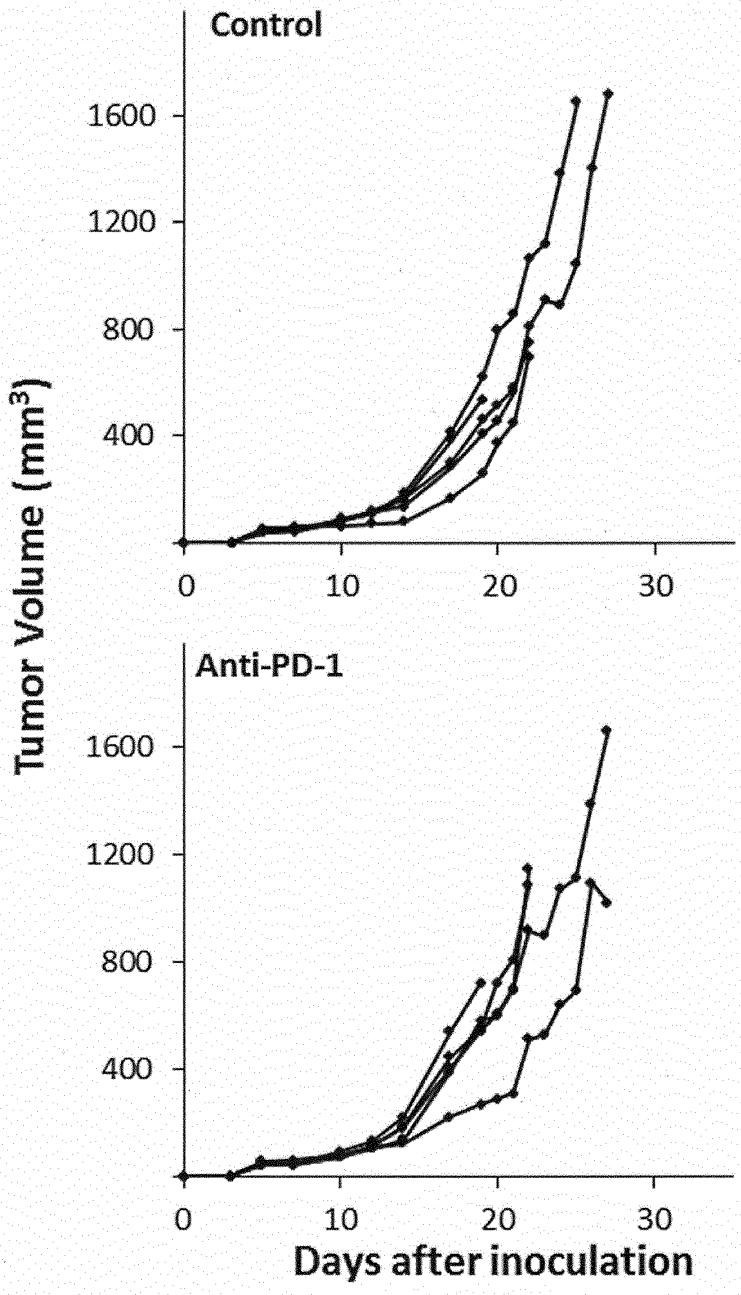


FIGURE 9 (continued)

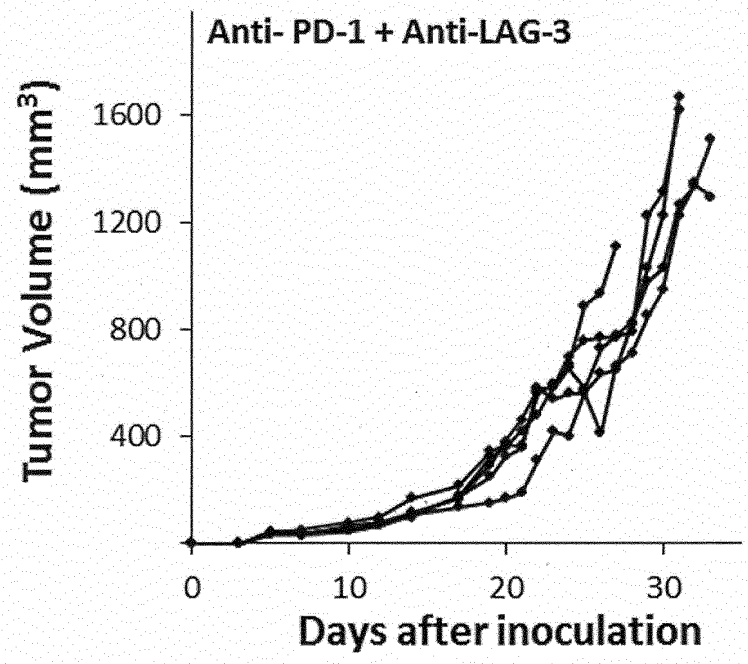


FIGURE 9 (continued)

D

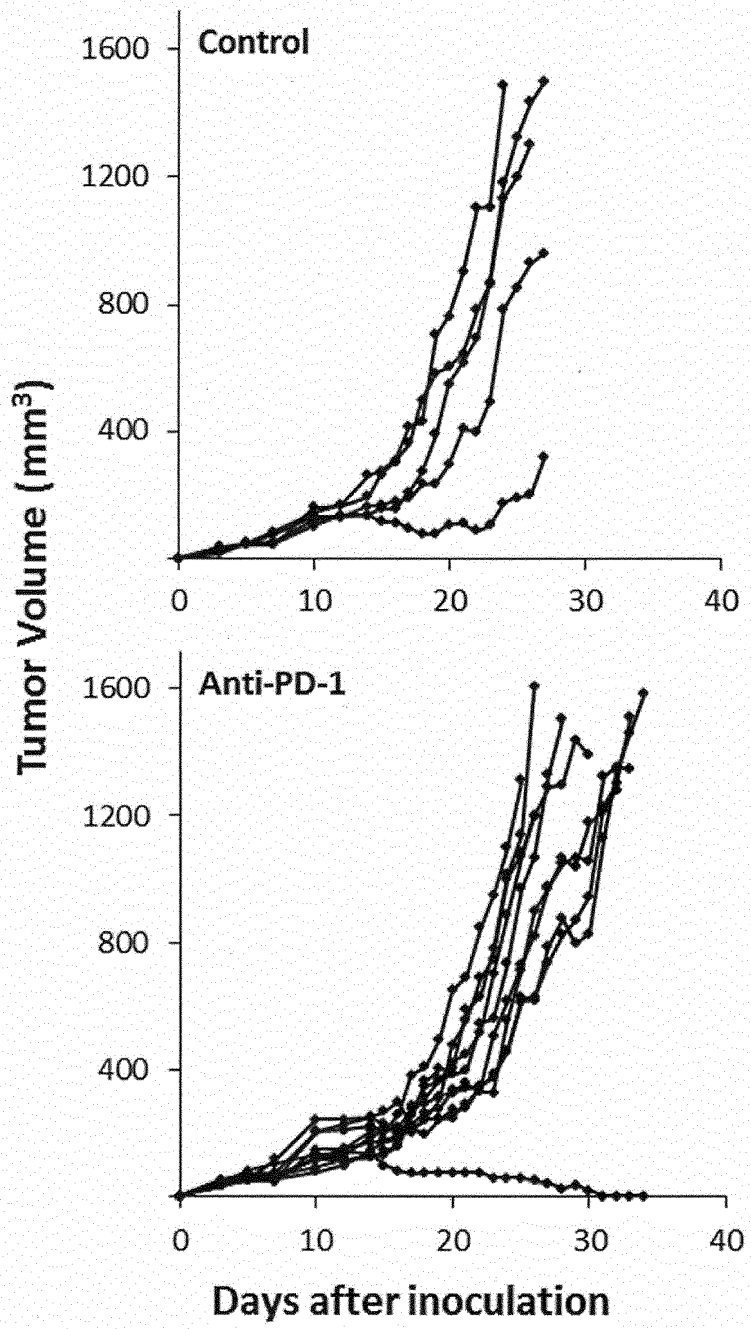


FIGURE 9 (continued)

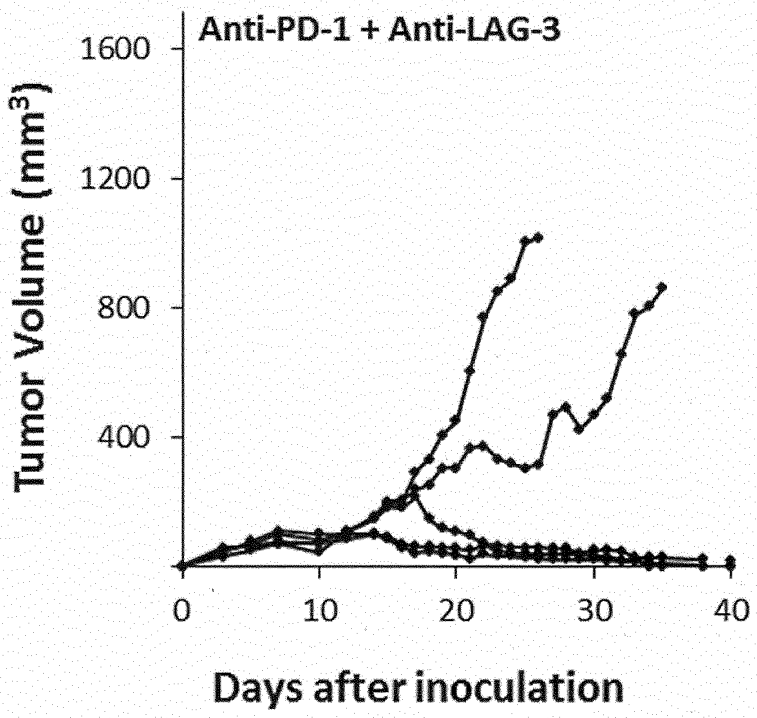


FIGURE 9 (continued)

E

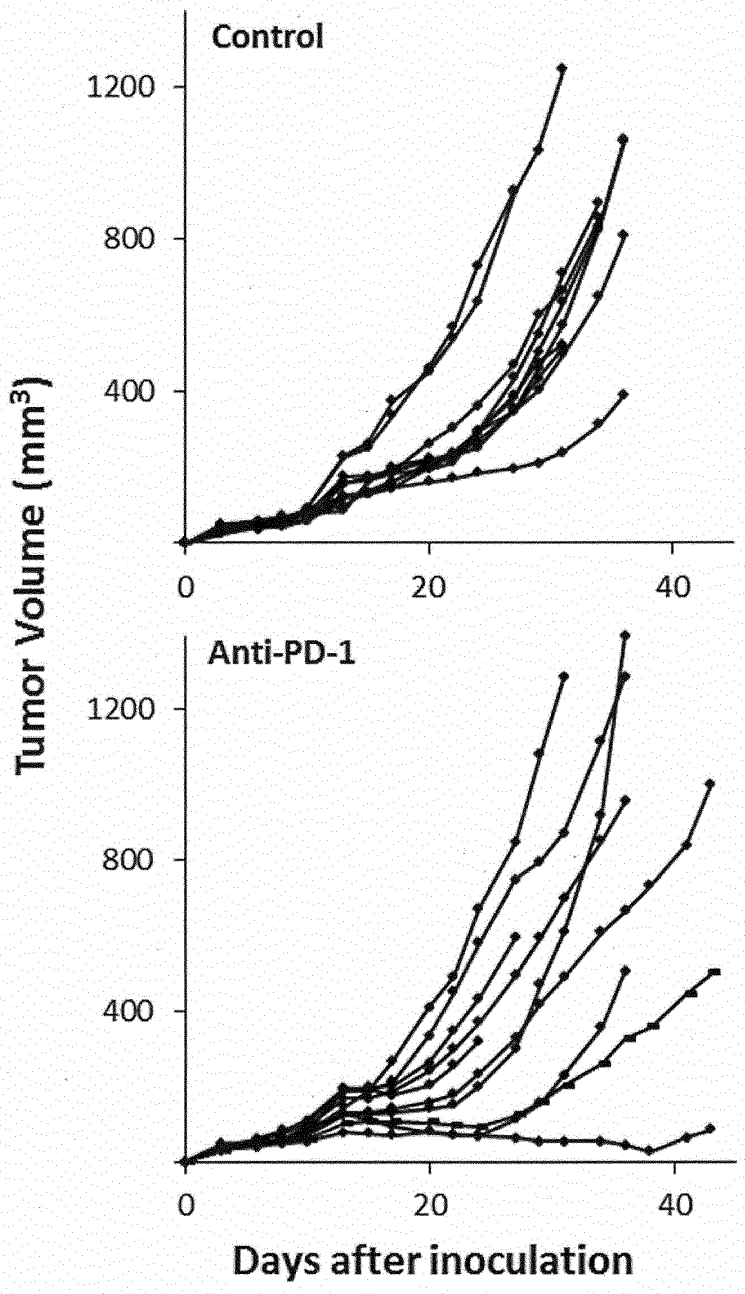
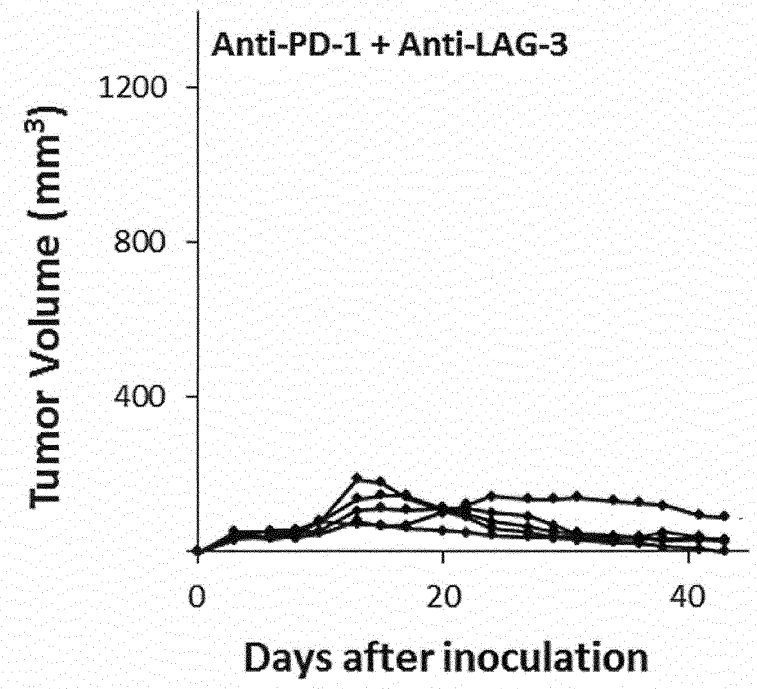



FIGURE 9 (continued)