

FIG.1
VH Variant 1

10	20	30	40	50	60	70	80	90	100
QAGGTCAGCTGGTGGCTGAGCTTAAAGAGCCAGGGCCCTCAGTCAAGTTCCTGACACAGCTTCGGCTTTAACATTAAAGACCGACTATA									
E V Q L V Q G G A E L K K P G A G V K L S C T A S G F N I K G Y									
10	20	30	40	50	60	70	80	90	100
YACACTGGGTGAAGCAGGCCCTGGACAGGCCCTGGAGTGGATTGGAGGGATTGATCCCTGGGATGGTCATCTAATAATATGCCCGAAGTTCGAGTCAA									
I H W V K Q A P G A P G Q G L E W I G R I D P A D G H T E Y A P K P Q Y K									
40	50	60	70	80	90	100	110	120	130
GGCCACTATACTGCAGACACATCCACACACACACAGCCCTACCTGCAGCCCTGACATCTGAGGACACTGCGGTCTATTACTGTGTAGATATGGT									
A T I T A D T S T N T A Y L Q L S S L T S E D T A V Y Y C A R Y G									
70	80	90	100	110	120	130	140	150	160
YACGGGAGGGAGGTCCTTTGACTACTGGGCGCCAGCCAGCCACTGTCTACAGTCTCTCA									
Y G R E V P Q Y W G Q G T T V T V S S									
100	110	120	130	140	150	160	170	180	190
100 a b	110	120	130	140	150	160	170	180	190

FIG.2
VH Variant 2

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10      20      30      40      50      60      70      80      90     100
QAGGTTCAAGCTGGTGGGCTGAGGTGAAGAGCCAGGGCCCTCAATCAAGTTGTCTCCACAGCTTCTGGCTTTAACATTAAAGGAGGACTATA
E V Q L V Q S G A E V K K P G A G V K L S C T A S G F N I K D D Y
10

110     120     130     140     150     160     170     180     190     200
TACACTGGGTGAAGSCAGGCCCTGGACAGGGCCCTGGAGTGGATTGGAGGATTCCTGGGATGGTCATACATAATATGCCCAGAGTCCAGGTCAA
I R W V K Q A P Q Q G L E W I G R I Q P A Q G H T K Y A P K F Q V K
40      60      80      100      120      140      160      180      200
GGCCACTATAACTGCAGACACATCCACCACACAGCCCTACCTGGAGCTCAGSCAGCCCTGAGATCTGAGGACACTGCCGCTCTATTACTGTGCTAGATATGGT
A Y I T A D T S T N T A Y L E L S S L R S E D T A V Y Y D A R Y G
70      90      110      130      150      170      190      210      230      250
TACGGGAGGAGGAGGTCTTTGACTACTGGGSCCAGGCGCCACGTCGTGACAGTCTGCTCA
Y G R E V P Q Y W G Q G T T V T V S S
100 120 140 160 180 200 220 240 260 280 300

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FIG. 5
VH Variant 5

10	20	30	40	50	60	70	80	90	100
CAGGTTCAAGCTGGTGCACGTCCTGGGCGTGAAGAGCCAGCGGCGCTCAGTCAAGGTCCTGCTGCGCAGCTTCGCTTAAACATTAAAGACGACTATA									
Q V Q L V Q S Q A E V X K P Q A S V K V S C A A S Q F N I K D D Y									
110	120	130	140	150	160	170	180	190	200
TACACTGGGTCGCGCCGCTGGACAGGGCGCTGGAGTGGATTGGAAAGGATTGATCGTGGGATGGTCATACATAATATGCCCCGAACTTGGAAATCAA									
I H W V R Q A P Q Q G L E W I Q R I D P A D Q H T K Y A P K F Q V K									
210	220	230	240	250	260	270	280	290	300
AGTCACATAACTGCAGACACATCCACGACGACAGCCCTACATGGAGGCTCAGCAGGCTGAGATCTGAGGACACTGCGGCTCTATTACTGTGCTAGATATGGT									
V T I T A D T S T S T A Y M E L S S L R S E D T A V Y Y C A R Y Q									
310	320	330	340	350					
TACGGAGGAGGAGGTCCTTTCACACTGCGGCGCAAGGCAACCACTGTCTCACTCTCTCA									
Y G R E V F D Y W Q Q Q T T V T V Q S									
100 a b	110	113							

FIG. 7

VK Variant 2

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10      20      30      40      50      60      70      80      90     100
GACATTCCTGACCCAAATCTCCAGACTCTTGGCTGTCTCTCCGGGAGAGGGCCACCATCTCCTGCAGGCCCAAGTCGTTGATTATGATGGTGG
D I V L T Q S P Q S L A V S L Q E R A T I S C K A S Q S Y Q Y Q S
10      20      30      40      50      60      70      80      90     100
ATAGTTATATGAACCTGATACCAACAAACCCAGGACAGCCACCCCAAAATCCTCATTTTATGATGCATCCGAACTTGGAAATCTGGCATCCGAGCCAGGTTTAG
D S Y R N W Y Q Q K P Q Q P P K I L I Y D A S R L E S G I P A R F S
10      20      30      40      50      60      70      80      90     100
TGGCAGTGGTCTGGGACAGACTTCACCGTCCACCATCAGCCAGCCCTGGAGCCCTGGAGCCCTGCAATCTTCCAACTATTACTGTGAGCAAAAGTAATGAAGACCCGTGG
G S G S G T Q F T L T I S S L E P E D F A I Y Y C Q Q S N E Q P W
10      20      30      40      50      60      70      80      90     100
ACGTTGGGTGGAGGCACCAAGGTGGAAATCAAA
T F G G G T K V E I K
100

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FIG. 9**VH Variants**

Amino Acid Position	TN1005 (Parental Antibody)	VH Variant 1	VH Variant 2	VH Variant 3	VH Variant 4	VH Variant 5
1	E	E	E	Q	Q	Q
5	Q	V	V	V	V	V
11	L	L	V	V	V	V
12	V	K	K	K	K	K
13	R	K	K	K	K	K
20	L	L	L	L	V	V
23	T	T	T	T	T	A
38	K	K	K	K	R	R
40	R	A	A	A	A	A
42	E	G	G	G	G	G
67	A	A	A	V	V	V
75	S	T	T	T	T	T
76	N	N	N	S	S	S
80	L	L	L	L	K	K
81	Q	Q	E	E	E	E
83	T	T	R	R	R	R
109	L	V	V	V	V	V

FIG. 10

VK Variants

Amino Acid Position	TNT005 (Parental Antibody)	VK Variant 1	VK Variant 2	VK Variant 5
9	A	D	D	D
17	Q	E	E	E
40	T	T	P	P
46	I	I	I	L
74	N	T	T	T
76	H	S	S	S
77	P	S	S	S
78	V	L	L	L
80	E	E	P	P
83	A	P	E	F
85	I	I	I	V
104	L	V	V	V

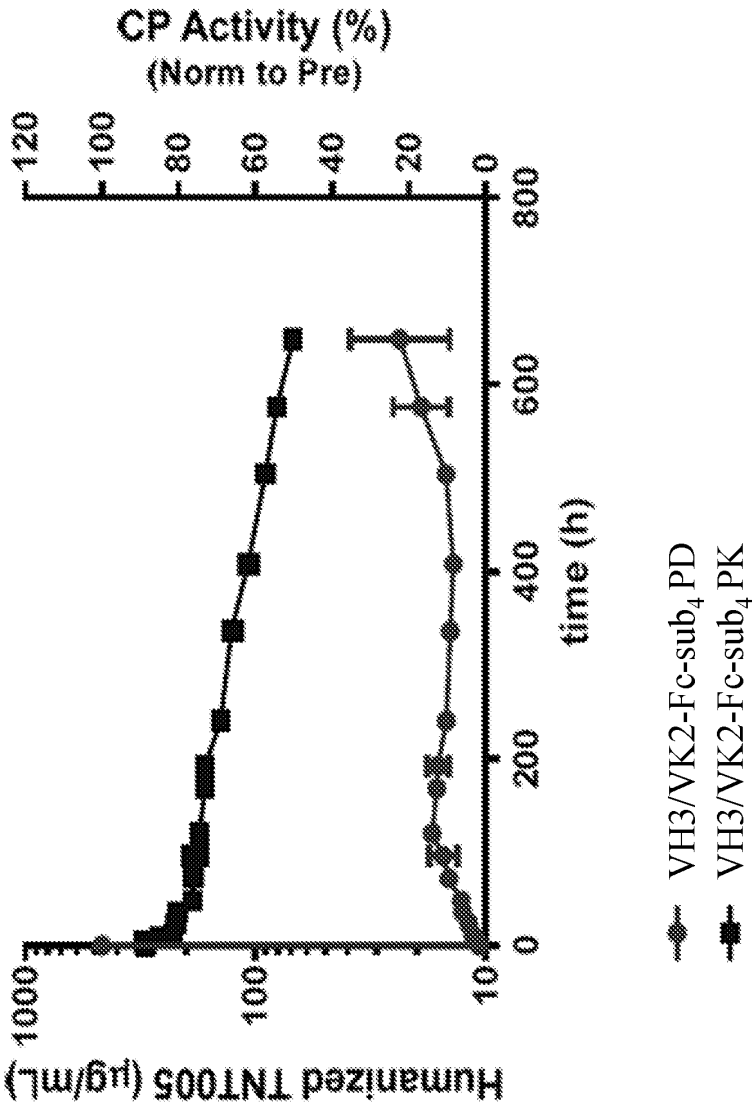
FIG. 11

antibody	Direct Binding Ab to aC1s EC50 (M)	Competition Binding w/ 50pM Biot-005 IC50 (M)	Classical Pathway Inhibition IC50 (M)
TNT005.001	5.536E-11	3.952E-11	1.061E-09
biotin-TNT005.001	8.28E-11	Not Tested	Not Tested
humanized VH1/Vk1	2.007E-10	1.238E-10	1.2E-09
humanized VH1/Vk2	8.797E-11	5.565E-11	1.137E-09
humanized VH1/Vk5	1.074E-10	1.288E-10	1.257E-09
humanized VH2/Vk1	1.374E-10	1.44E-10	1.234E-09
humanized VH2/Vk2	1.335E-10	1.576E-10	1.259E-09
humanized VH2/Vk5	1.239E-10	1.678E-10	1.272E-09
humanized VH3/Vk1	1.68E-10	1.79E-10	1.27E-09
humanized VH3/Vk2	1.63E-10	1.83E-10	1.26E-09
humanized VH3/Vk5	1.38E-10	1.85E-10	1.38E-09
humanized VH4/Vk1	1.52E-10	1.5E-10	1.35E-09
humanized VH4/Vk2	1.19E-10	1.58E-10	1.31E-09
humanized VH4/Vk5	2.05E-10	1.56E-10	1.54E-09
humanized VH5/Vk1	1.13E-10	4.49E-11	1.08E-09
humanized VH5/Vk2	1.64E-10	1.48E-10	1.31E-09
humanized VH5/Vk5	1.55E-10	1.37E-10	1.33E-09

FIG. 12

Humanized TNT005 Variant	K _D (M)	K _{cat} (1/Ms)	k _{obs} (1/s)	R ²
VH1/VK1	2.277E-10	8.641E+05	1.967E-04	0.996
VH1/VK2	2.078E-10	8.177E+05	1.699E-04	0.996
VH1/VK5	2.169E-10	7.763E+05	1.684E-04	0.996
VH2/VK1	2.508E-10	8.294E+05	2.080E-04	0.996
VH2/VK2	2.059E-10	8.354E+05	1.720E-04	0.997
VH2/VK5	2.080E-10	7.979E+05	1.660E-04	0.996
VH3/VK2	5.850E-10	8.379E+05	4.902E-04	0.997
VH5/VK1	4.572E-10	1.030E+06	4.710E-04	0.996

FIG. 13



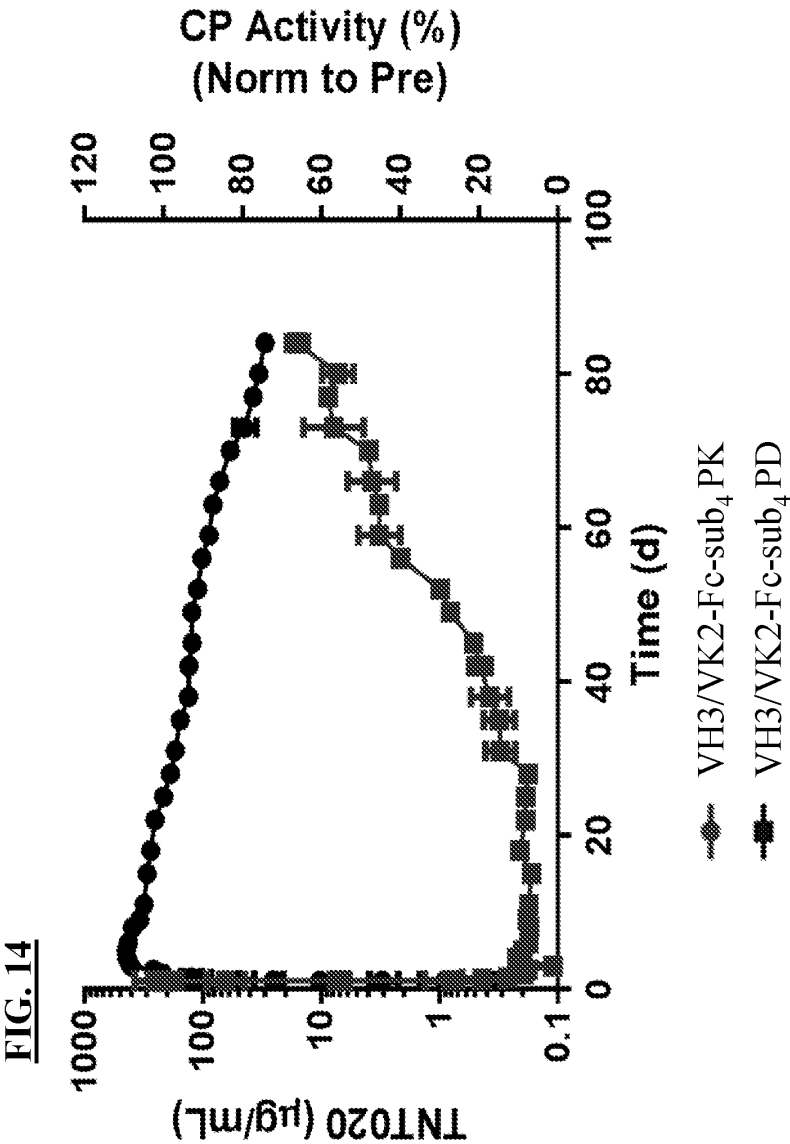


FIG. 15A

ASTKGPSVFP LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTKT
YTCNVDPKPSNTKVDKRVESKYGPPCPCPAPEFEGGPSVFLFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVD
GVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI SKAKGQPREPQVYITLPPSQEEMTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSGDSFFLYSRLLTVDKSRWQEGNVFSCSVLHEALHSHYTQKS
LSLSLGK (SEQ ID NO: 28)

FIG. 15B

QVQLVQSGAEVKKPGASVKLSCTASGFNIKDDYIHWVKQAPGQGLEWIGRIDPADGHTKYAPKFQKVTTITADTSTSTAY
LELSSLRSEDTAVYYCARYGYGREVEDYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSW
NSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTKITYTCNVDPKPSNTKVDKRVESKYGPPCPCPAPEFEGGPSVF
LFPPKPKDTLMI SRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKC
KVSNGKGLPSSIEKTI SKAKGQPREPQVYITLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDS
GSFFLYSRLLTVDKSRWQEGNVFSCSVLHEALHSHYTQKSLSLGK (SEQ ID NO: 29)

FIG. 15C

DIVLTQSPDLSLAVSLGERATISCKASQSDYDGDSYMNWYQQKPGQPPKILIIYDASNLESGIPARFSGSGGTDFTLTIS
SLEPEDFAIYYCQQSNEDPWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
GNSQESVTEQDSKDSSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 30)

FIG. 16A

MGWSLILLFLVAVATRVHSQVQLVQSGAEVKKPGASVKLSCTASGFNIKDDYIHVVKQA
PGQGLEWIGRIDPADGHTKYAPKFQVKVTITADTSTSTAYLELSLSRSEDTAVYYCARY
GYGREVFDYWGQTTVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTV
SWNSGALTSGVHTFPAVLQSSGLYSLSSVTPSSSLGKTYTCNVDHKPSNTKVDKRV
ESKYGPCPCPAPEFEGGPSVFLFPPKPKDTIMISRTPEVTCVVVDVSQEDPEVQFNW
YVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTI
SKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP
PVLDSGGSFFLYSRLTVDKSRWQEGNVFSCSVLHEALHSHYTQKSLSLGK
(SEQ ID NO: 31)

FIG. 16B

MRVPAQLLGLLLWLPGARCDIVLTQSPDLSAVSLGERATISCKASQSVDDYDGDSYMNW
YQQPGQPPKILIIYDASNLESGIPARFSGSGGTDTLTISSLEPEDFAIYYCQQSNED
PWTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA
LQSGNSQESVTEQDSKDSITYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRG
EC (SEQ ID NO: 32)

FIG. 17A

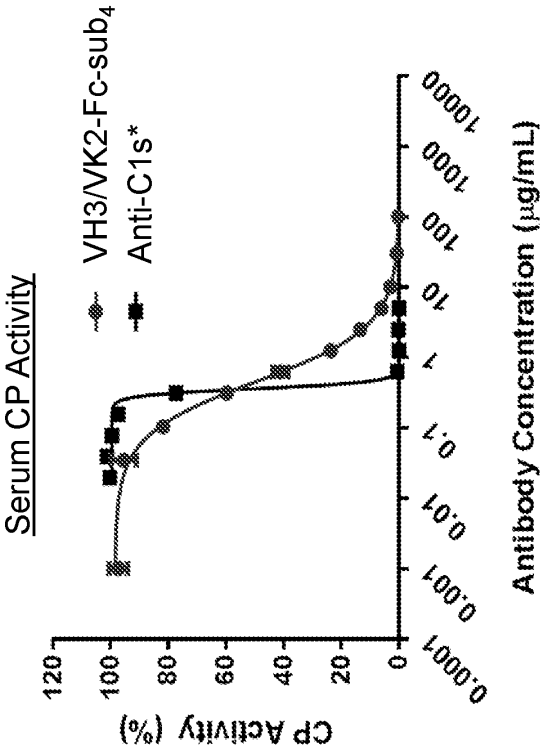


FIG. 17B

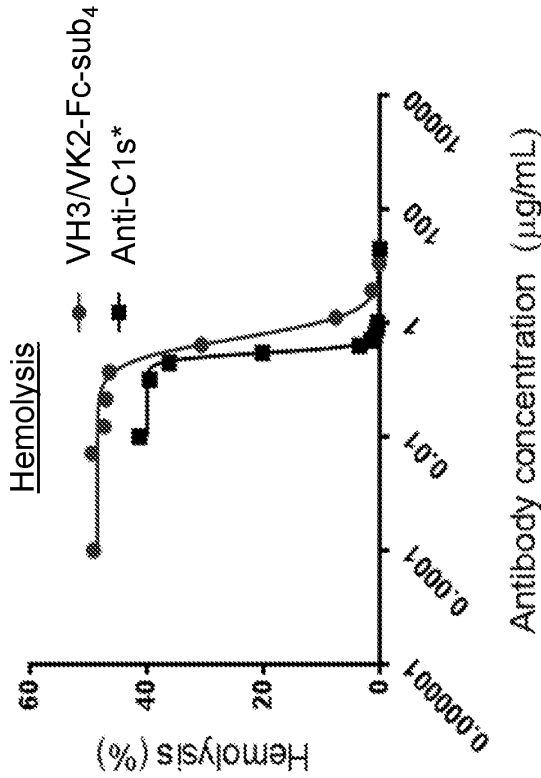


FIG. 18B

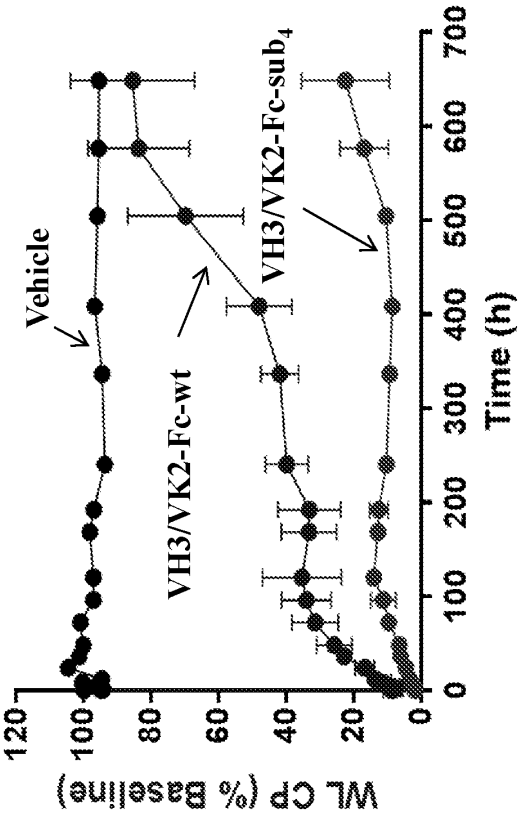


FIG. 18A

