

FIG. 1A: The cDNA (SEQ ID NO:1) and amino acid sequence (SEQ ID NO:2) of 191P4D12. The start methionine is underlined. The open reading frame extends from nucleic acid 264-1796 including the stop codon.

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1  ggccgctcgttggttgccacagcgtgggaagcagctctgggggagctcggagctcccgatc
61  acggcttcttgggggtagctacggctgggtgtgtagaacggggccggggctggggctggg
121  tcccctagtggagaccaagtgcgagaggcaagaactctgcagcttctgccttctgggt
181  cagttccttattcaagtctgcagccggtcccaggagatctcggtggaacttcagaaac
1      M P L S L G A E M W G P E
241  gctgggcagctctgcctttcaaccATGCCCCCTGTCCCTGGGAGCCGAGATGTGGGGGCCTG
14   A W L L L L L L L A S F T G R C P A G E
301  AGGCCTGGCTGCTGCTGCTGCTACTGCTGGCATCATTTACAGGCCGGTGGCCCGGGTG
34   L E T S D V V T V V L G Q D A K L P C F
361  AGCTGGAGACCTCAGACGTGGTAAGTGTGGTGCTGGGCCAGGACGCAAACTGCCCTGCT
54   Y R G D S G E Q V G Q V A W A R V D A G
421  TCTACCGAGGGGACTCCGGCGAGCAAGTGGGGCAAGTGGCATGGGCTCGGTGGACGCGG
74   E G A Q E L A L L H S K Y G L H V S P A
481  GCGAAGGCGCCCAGGAAGTAGCGCTACTGCACTCCAATACGGGCTTCATGTGAGCCCGG
94   Y E G R V E Q P P P P R N P L D G S V L
541  CTTACGAGGGCCGCGTGGAGCAGCCGCCGCCCCACGCAACCCCTGGACGGCTCAGTGC
114  L R N A V Q A D E G E Y E C R V S T F P
601  TCCTGCGCAACGCAGTGCAGGCGGATGAGGGCGAGTACGAGTGCCGGGTGAGCACCTTCC
134  A G S F Q A R L R L R V L V P P L P S L
661  CCGCCGGCAGCTTCCAGGCGCGGCTGCGGCTCCGAGTGCTGGTGCCTCCCCTGCCCTCAC
154  N P G P A L E E G Q G L T L A A S C T A
721  TGAATCCTGGTCCAGCACTAGAAGAGGGCCAGGGCCTGACCCTGGCAGCCTCCTGCACAG
174  E G S P A P S V T W D T E V K G T T S S
781  CTGAGGGCAGCCCAGCCCCAGCGTGACCTGGGACACGGAGGTCAAAGGCACAACGTCCA
194  R S F K H S R S A A V T S E F H L V P S
841  GCCGTTCTTCAAGCACTCCCGCTCTGCTGCCGTCACCTCAGAGTTCCACTTGGTGCCTA
214  R S M N G Q P L T C V V S H P G L L Q D
901  GCCGCAGCATGAATGGGCAGCCACTGACTTGTGTGGTGTCCCATCCTGGCCTGCTCCAGG
234  Q R I T H I L H V S F L A E A S V R G L
961  ACCAAAGGATCACCCACATCCTCCACGTGTCCTTCCTTGCTGAGGCCTCTGTGAGGGGCC
254  E D Q N L W H I G R E G A M L K C L S E
1021 TTGAAGACCAAAATCTGTGGCACATTGGCAGAGAAGGAGCTATGCTCAAGTGCCTGAGTG
274  G Q P P P S Y N W T R L D G P L P S G V
1081 AAGGGCAGCCCCCTCCCTCATACAACTGGACACGGCTGGATGGGCCTCTGCCCAGTGGGG
294  R V D G D T L G F P P L T T E H S G I Y
1141 TACGAGTGGATGGGGACACTTTGGGCTTTCCCCCACTGACCACTGAGCACAGCGGCATCT
314  V C H V S N E F S S R D S Q V T V D V L
1201 ACGTCTGCCATGTCTAGCAATGAGTTCTCCTCAAGGGATTCTCAGGTCACTGTGGATGTTT
334  D P Q E D S G K Q V D L V S A S V V V V

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[illegible]

FIG. 1A
(Continued)

FIG. 1B: The cDNA (SEQ ID NO:3) and amino acid sequence (SEQ ID NO:4) of Ha22-2(2,4)6.1 heavy chain. Double-underlined is the leader sequence, underlined is the heavy chain variable region, and underlined with a dashed line is the human IgG1 constant region.

M E L G L C W V F L V A I L E

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1  GGTGATCAGCACTGAACACAGAGGACTCACCATGGAGTTGGGGCTGTGCTGGGTTTTCCTTGTGCTATTTTAGA
   · G V Q C E V Q L V E S G G G L V Q P G G S L R L S
76  AGGTGTCCAGTGTGAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAGACTCTC
   · C A A S G F T F S S Y N M N W V R Q A P G K G L E
151 CTGTGCAGCCTCTGGATTACCTTCAGTAGCTATAACATGAAGTGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
   · W V S Y I S S S S S T I Y Y A D S V K G R F T I S
226 GTGGGTTTCATACATTAGTAGTAGTAGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTACCATTCTC
   · R D N A K N S L S L Q M N S L R D E D T A V Y Y C
301 CAGAGACAATGCCAAGAACTCACTGTCTCTGCAAATGAACAGCCTGAGAGACGAGGACACGGCTGTGTATTACTG
   · A R A Y Y Y G M D V W G Q G T T V T V S S A S T K
376 TGCGAGAGCATACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGCCTCCACCAA
   · G P S V F P L A P S S K S T S G G T A A L G C L V
451 GGGCCCATCGGTCTTCCCCCTGGCACCCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT
   · K D Y F P E P V T V S W N S G A L T S G V H T F P
526 CAAGACTCACTTCCCCGAACCGGTGACGGTGTCTGGAAGTCAAGCGCCCTGACAGCGCGGTGCACACTTCCC
   · A V L Q S S G L Y S L S S V V T V P S S S L G T Q
601 GGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCA
   · T Y I C N V N H K P S N T R V D K R V E P K S C D
676 GACCTACATCTGCAACGTGAATCACAAGCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAATCTTGTGA
   · K T H T C P P C P A P E L L G G P S V F L F P P K
751 CAAAACTCACACATGCCCACCGTGGCCAGCACCTGAAGTCTTGGGGGGACCGTCAGTCTTCTTCCCCCAAA
   · P K D T L M I S R T P E V T C V V V D V S H E D P
826 ACCCAAGGACACCCCTCATGATCTCCCGGACCCCTGAGGTACATGCGTGGTGGTGGACGTGAGCCACGAAGACCC
   · E V K F N W Y V D G V E V H N A K T K P R E E Q Y
901 TGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTA
   · N S T Y R V V S V L T V L H Q D W L N G K E Y K C
976 CAACAGCACGTACCGTGTGGTCAGCGTCTCTCACCTGCTGCACCAAGGACTGGCTGAATGGCAAGGATCAAGTG
   · K V S N K A L P A P I E K T I S K A K G Q P R E P
1051 CAAGGTCTCCAACAAAGCCCTCCAGCCCCATCGAGAAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAACC
   · Q V Y T L P P S R E E M T K N Q V S L T C L V K G
1126 ACAGGTGTACACCTTCCCCCGGAGGAGATGACCAAGAACAGGTGACCTGACCTGCCTGGTCAAAGG
   · F Y P S D I A V E W E S N G Q P E N N Y K T T P P
1201 CTTCTATCCCGGACATCGCGGTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACACGCTCC
   · V L D S D G S F F L Y S K L T V D K S R W Q Q G N
1276 CGTGTGACTCCGACGGCTCCTTCTCTCTATAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAA
   · V F T S C S V M H E A L H N H Y T Q K S L S L S P G
1351 CGTCTTCTCATGCTCCGTGATGCATGAGGTCTGCACAACCACTACACGAGAAGAGCTCTCCCTGTCCCCGGG
   · K *
1426 TAAATGA

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FIG. 1C: The cDNA (SEQ ID NO:5) and amino acid sequence (SEQ ID NO:6) of Ha22-2(2,4)6.1 light chain. Double-underlined is the leader sequence, underlined is the light chain variable region, and underlined with a dashed line is the human kappa constant region.

M D M R V P A Q L L G L L L L W F

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1  AGTCAGACCCAGTCAGGACACAGCATGGACATGAGGGTCCCCGCTCAGCTCCTGGGGCTCCTGCTGCTCTGGTTTC
   P G S R C D I Q M T Q S P S S V S A S V G D R V T
76  CCAGGTTCCAGATGCGACATCCAGATGACCCAGTCTCCATCTTCCGTGTCTGCATCTGTTGGAGACAGAGTCACC
   I T C R A S Q G I S G W L A W Y Q Q K P G K A P K
151 ATCACTTGTCTGGGCGAGTCAGGGTATTAGCGGTGGTTAGCCTGGTATCAGCAGAAACAGGGAAAGCCCTAAG
   F L I Y A A S T L Q S G V P S R F S G S G T D
226 TTCCTGATCTATGCTGCATCCACTTTGCAAAGTGGGGTCCCATCAAGGTTACAGCGGAGTGGATCTGGGACAGAT
   F T L T I S S L Q P E D F A T Y Y C Q Q A N S F P
301 TTCACTCTCACCATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTACTATTGTCAACAGGCTAACAGTTTCCCT
   P T F F G G G T K V E I K R T V A A P S V F I F P P
376 CCCCTTTCGGCGGAGGACCAAGGTGGAGATCAAACGAAGTGTGGCTGCACCATCTGTTCTCATCTTCCGCGCA
   S D E Q Q L K S G T A S V V C L L N N F Y P R E A K
451 TCTGATGAGCAGTTGAAATCTGGAAGTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAA
   V Q W K V D N A L Q S G N S Q E S V T E Q D S K D
526 GTACAGTGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCAGGAGAGTGTACAGAGCAGGACAGCAAGGAC
   S T Y S L S S T L T L S K A D Y E K H K V Y A C E
601 AGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAA
   V T H Q G L S S P V T K S F N R G E C *
676 GTACCCCATCAGGGCCTGAGCTCGCCGTCACAAAGAGCTTCAACAGGGGAGAGTGTAG

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FIG. 1D: The amino acid sequence (SEQ ID NO:7) of Ha22-2(2,4)6.1 heavy chain. Double-underlined is the leader sequence, underlined is the heavy chain variable region, (SEQ ID NO:22, which is the sequence ranging from the 20th to the 136th amino acid of SEQ ID NO:7) and underlined with a dashed line is the human IgG1 constant region.

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1  MELGLCWVFLVAILEGVOCEVOLVESGGGLVOPGGSLRLSCAASGFTFSS
51  YNMNWVRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISRDAKNSLSL
101 QMNSLRDEDTAVYYCARAYYYGMDVWGQGTTVTVSSASTKGPSVFPLAPS
151 SKSTSGGTAALGCLVKDYFPEPVTSVNSGALTSGVHTFPAVLQSSGLYS
201 LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPA
251 PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG
301 VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
351 IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
401 ESNGQOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCSVMHEA
451 LHNHYTQKSLSLSPGK

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FIG. 1E: The amino acid sequence (SEQ ID NO:8) of Ha22-2(2,4)6.1 light chain. Double-underlined is the leader sequence, underlined is the light chain variable region (SEQ ID NO:23, which is the sequence ranging from the 23rd to the 130th amino acid of SEQ ID NO:8), and underlined with a dashed line is the human kappa constant region.

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1  MDMRVPAQLLGLLLLWFPGSRCDIQMTQSPSSVSASVGDRVTITCRASQG
51  ISGWLAWYQQKPGKAPKFLIYAASTLQSGVPSRFSSGSGSGTDFTLTISSL
101 QPEDFATYYCQQANSFPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSG
151 TASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYLSLSST
201 LTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

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FIG. 2: Efficacy of Ha22-2(2,4)6.1-vcMMAE in subcutaneous established human lung cancer xenograft AG-L4 in SCID mice

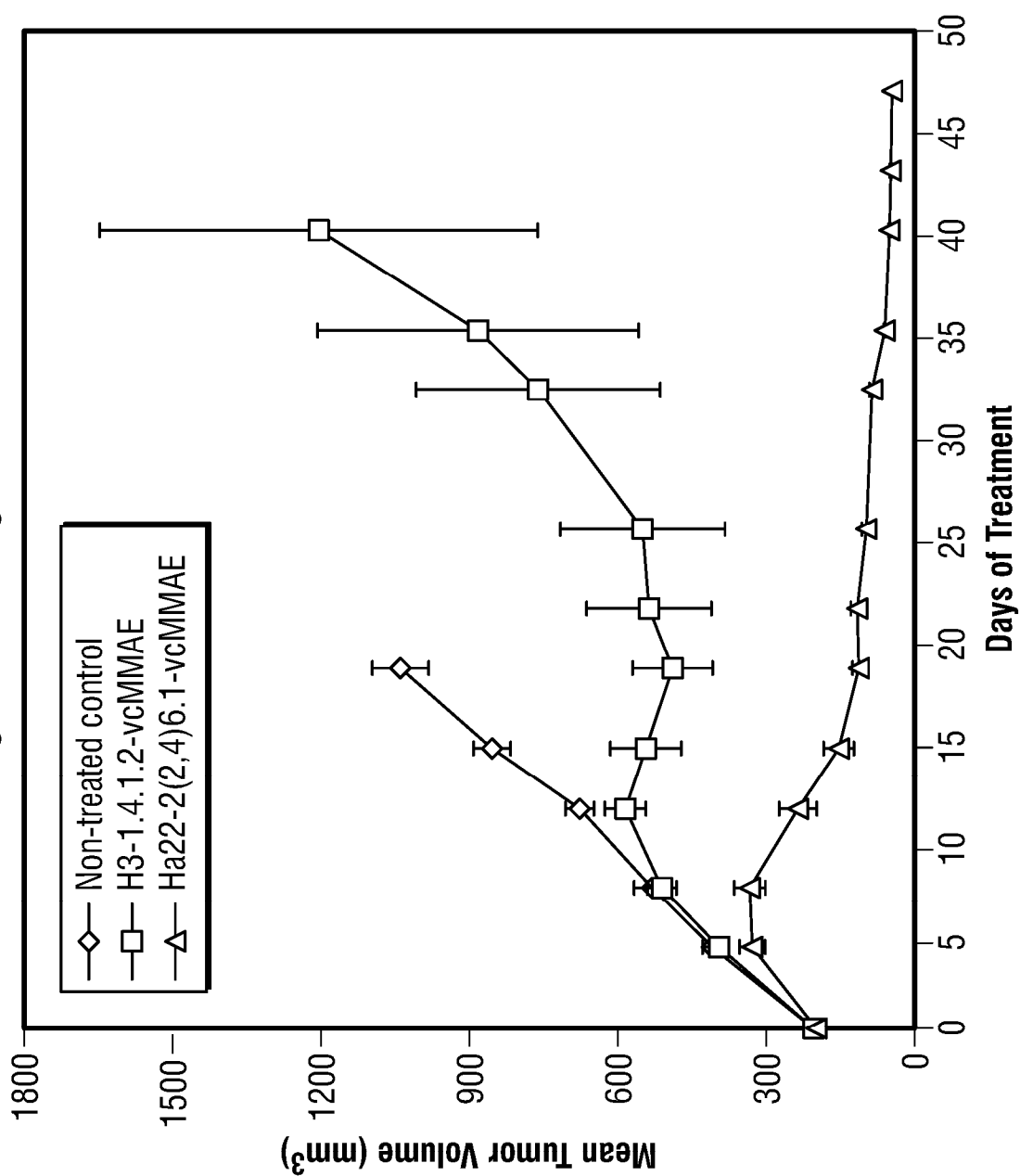
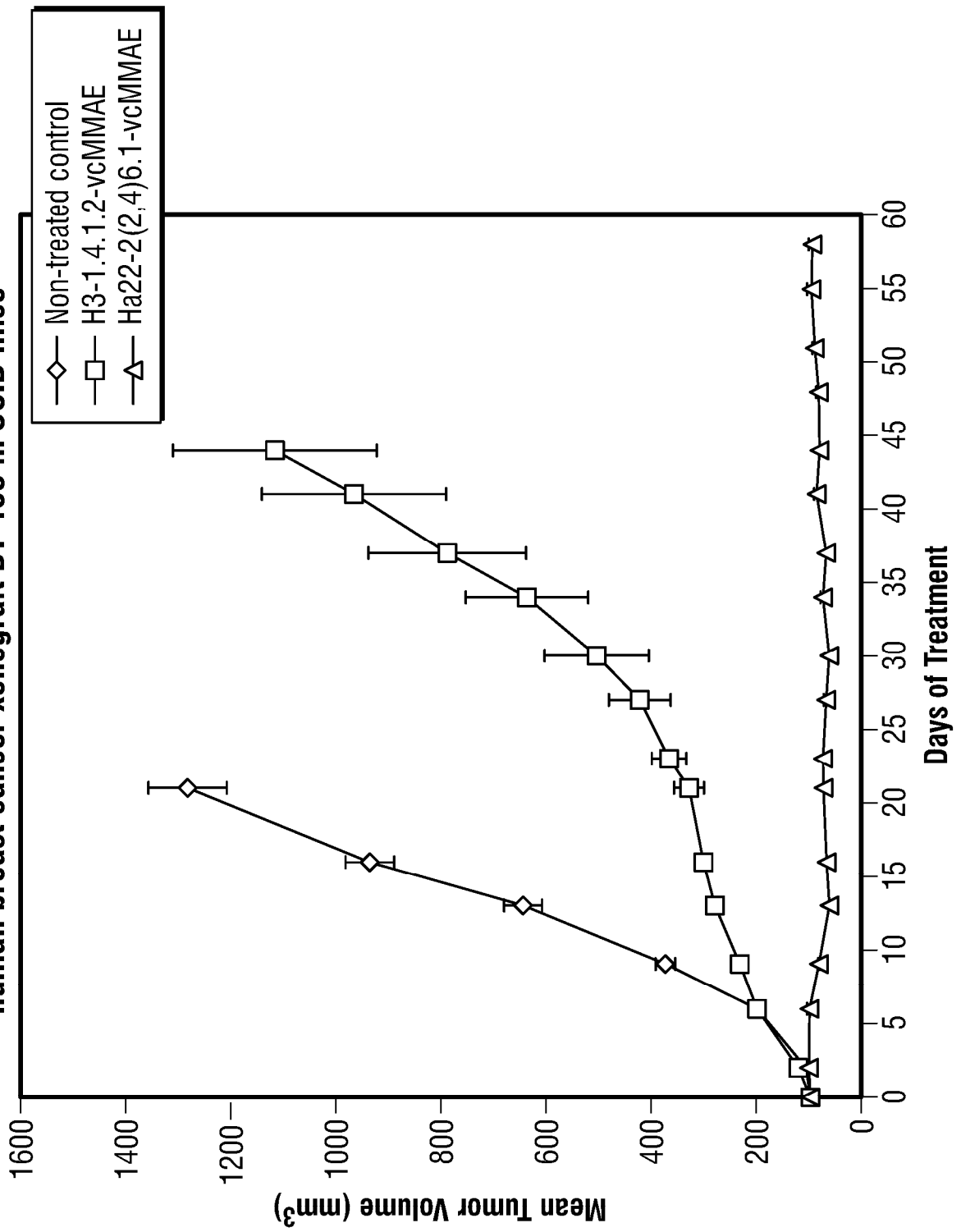


FIG. 3: Efficacy of Ha22-2(2,4)6.1-vcMMAE in subcutaneous established human breast cancer xenograft BT-483 in SCID mice



Breast cancer specimen

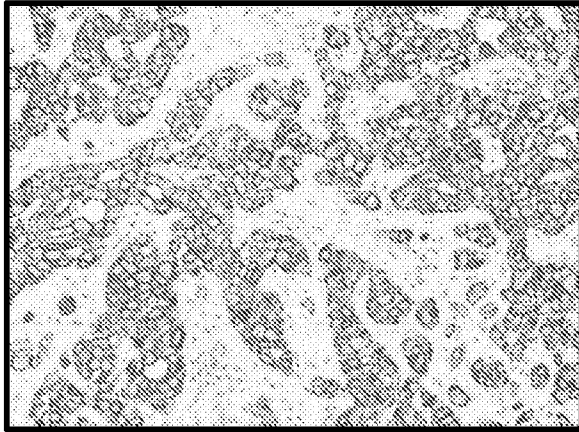


FIG. 4A

Breast cancer specimen

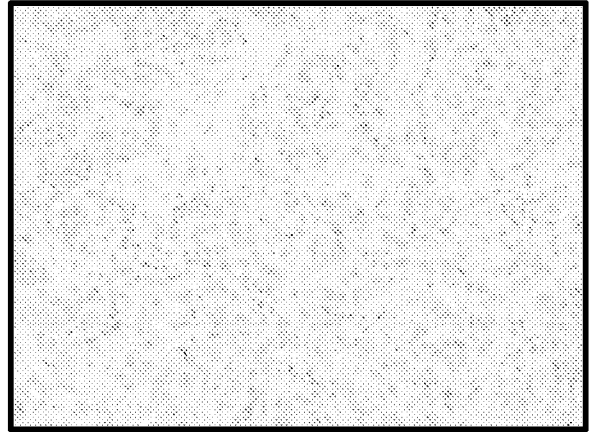


FIG. 4B

Lung cancer specimen



FIG. 4C

Lung cancer specimen



FIG. 4D

Esophageal cancer specimens



FIG. 4E

Esophageal cancer specimens



FIG. 4F

Head and neck cancer specimens

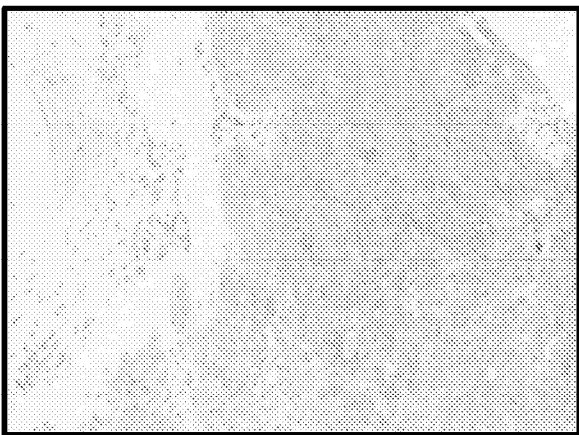


FIG. 4G

Head and neck cancer specimens

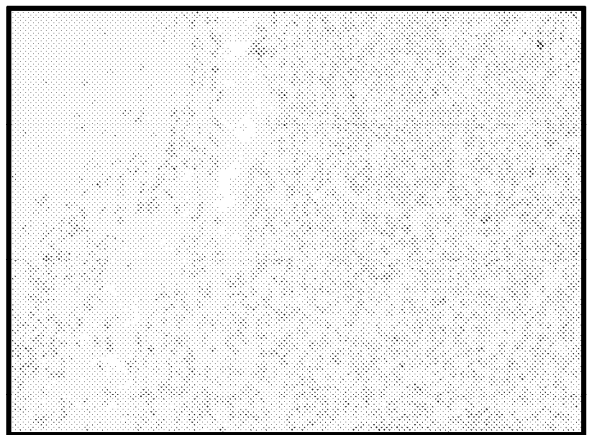


FIG. 4H

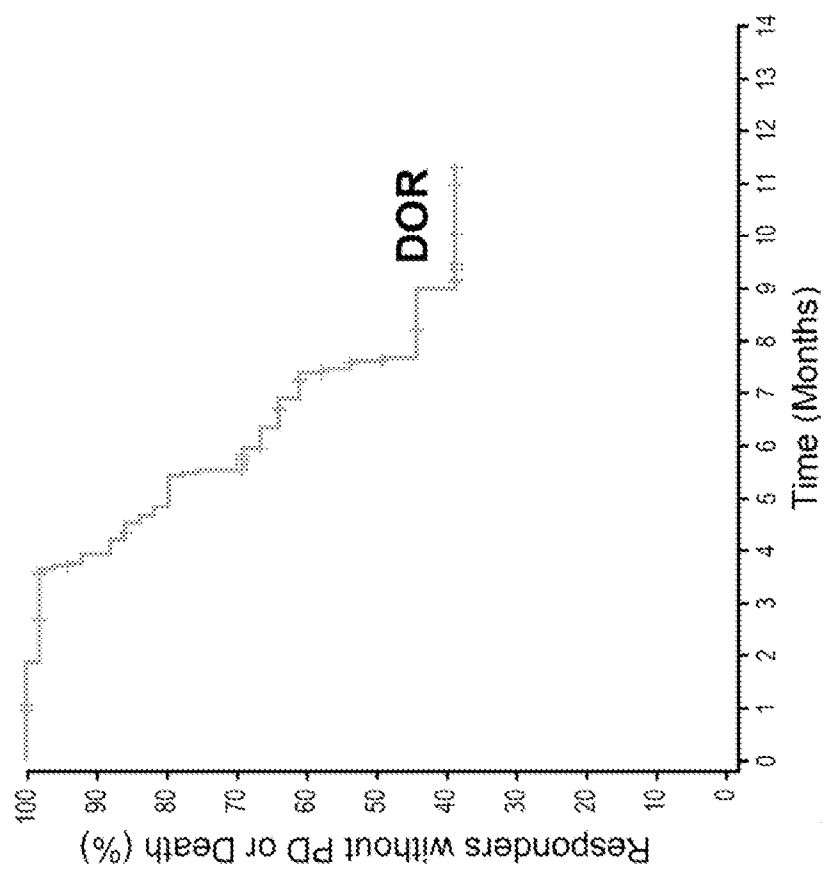


FIG. 5