

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.

```

1  ggccgtcgttgttggccacagcgtgggaagcagctctgggggagctcggagctcccgatc
61  acggcttcttgggggtagctacggctgggtgtgtagaacggggccggggctggggctggg
121  tcccctagtggagaccaagtgcgagaggcaagaactctgcagcttctgccttctgggt
181  cagttccttattcaagtctgcagccggctcccagggagatctcgtggaacttcagaaac
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  AGGCCTGGCTGCTGCTGCTGCTACTGCTGGCATCATTTACAGGCCGGTGCCCCGCGGGTG
34   L E T S D V V T V V L G Q D A K L P C F
361  AGCTGGAGACCTCAGACGTGGTAACTGTGGTGCTGGGCCAGGACGAAAACCTGCCCTGCT
54   Y R G D S G E Q V G Q V A W A R V D A G
421  TCTACCGAGGGGACTCCGGCGAGCAAGTGGGGCAAGTGGCATGGGCTCGGGTGGACGCGG
74   E G A Q E L A L L H S K Y G L H V S P A
481  GCGAAGGCGCCCAGGAACTAGCGCTACTGCACTCCAAATACGGGCTTCATGTGAGCCCGG
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 ACGTCTGCCATGTCAGCAATGAGTTCTCCTCAAGGGATTCTCAGGTCACTGTGGATGTTT
334  D P Q E D S G K Q V D L V S A S V V V V

```

1261 TTGACCCCCAGGAAGACTCTGGGAAGCAGGTGGACCTAGTGTCAGCCTCGGTGGTGGTGG
 354 G V I A A L L F C L L V V V V V L M S R
 1321 TGGGTGTGATCGCCGCACTCTTGTCTGCCTTCTGGTGGTGGTGGTGGTGCATGTCCC
 374 Y H R R K A Q Q M T Q K Y E E E L T L T
 1381 GATACCATCGGCGCAAGGCCAGCAGATGACCCAGAAATATGAGGAGGAGCTGACCCTGA
 394 R E N S I R R L H S H H T D P R S Q P E
 1441 CCAGGGAGAACTCCATCCGGAGGCTGCATTCCCATCACACGGACCCAGGAGCCAGCCGG
 414 E S V G L R A E G H P D S L K D N S S C
 1501 AGGAGAGTGTAGGGCTGAGAGCCGAGGGCCACCCTGATAGTCTCAAGGACAACAGTAGCT
 434 S V M S E E P E G R S Y S T L T T V R E
 1561 GCTCTGTGATGAGTGAAGAGCCCCGAGGGCCGAGTTACTCCACGCTGACCACGGTGAGGG
 454 I E T Q T E L L S P G S G R A E E E E D
 1621 AGATAGAAACACAGACTGAACTGCTGTCTCCAGGCTCTGGGCGGGCCGAGGAGGAGGAAG
 474 Q D E G I K Q A M N H F V Q E N G T L R
 1681 ATCAGGATGAAGGCATCAAACAGGCCATGAACCATTTTGTTCAGGAGAATGGGACCCTAC
 494 A K P T G N G I Y I N G R G H L V *
 1741 GGGCCAAGCCCACGGGCAATGGCATCTACATCAATGGGCGGGACACCTGGTCTGA^{ccca}
 1801 ggcctgcctcccttcccttaggcctggctccttctgttgacatgggagat^{tttagctcatc}
 1861 ttgggggcctccttaaacacccccatttcttgcggaagatgctcccatcccactgactg
 1921 cttgacctttacctccaaccccttctgttcacgcgggagggctccaccaattgagtctctcc
 1981 caccatgcatgcaggctcactgtgtgtgtgcatgtgtgcctgtgtgagtgttgactgactg
 2041 tgtgtgtgtggaggggtgactgtccgtggaggggtgactgtgtccgtggtgtgtattatg
 2101 ctgtcatatcagagtcaagtgaactgtggtgtatgtgccacgggatttgagtgggtgcgt
 2161 gggcaacactgtcagggtttggcgtgtgtgtcatgtggctgtgtgtgacctctgcctgaa
 2221 aaagcaggtat^{tttctcagacccagagcag}tattaatgatgcagaggttgaggagaga
 2281 ggtggagactgtggctcagacccagggtgtgcgggcatagctggagctggaatctgcctcc
 2341 ggtgtgagggaaacctgtctcctaccacttcggagccatgggggcaagtgtgaagcagcca
 2401 gtccctgggtcagccagaggcttgaactgttacagaagccctctgccctctggtggcctc
 2461 tgggcctgctgcatgtacatat^{tttctgtaaatatacatgcgcgggagcttcttg}cagg
 2521 aatactgctccgaatcact^{tttaatttttttcttttttttcttgccctttccattag}t
 2581 tgtat^{ttttttat}ttttttat^{tttttttttttag}agatggagtctcactatgttgc
 2641 tcaggctggccttgaactcctgggctcaagcaatcctcctgcctcagcctccctagtagc
 2701 tgggact^{tttaagtgtacaccactgtgcctgctttgaatcctttacgaagagaaaaaaa}
 2761 attaaagaaagcctttagatttatccaatgtttactactgggattgcttaaagtgaggcc
 2821 cctccaacaccaggggttaattcctgtgattgtgaaaggggctacttccaaggcatcct
 2881 catgcaggcagccccttgggagggcacctgagagctggtagagtctgaaattagggatgt
 2941 gagcctcgtggttactgagtaaggtaaaattgcatccaccattgtttgtgataccttagg
 3001 gaattgcttgacctggtgacaagggctcctgttcaatagtgggtgttggggagagagaga
 3061 gcagtgattatagaccgagagagtaggagttgaggtgaggtgaaggaggtgctgggggtg
 3121 agaatgtcgcctttccccctgggttttgatcactaattcaaggctccttctggatgttcc
 3181 tctgggttggggctggagttcaatgaggtttat^{tttttagctggcccaccagatacactc}
 3241 agccagaatacctagatttagtacccaaactcttcttagtctgaaatctgctggatttct
 3301 ggcctaaggagagggctcccatccttctgttccccagccagcctaggacttccaatgtgga
 3361 gcctgaagatctaagatcctaacatgtacattttatgtaaataatgtgcatatttgcacat
 3421 aaaatgatattctgttttttaataaacagacaaaacttgaaaaa

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

```

1  GGTGATCAGCACTGAACACAGAGGACTCACCATGGAGTTGGGGCTGTGCTGGGTTTTCTCTGTGCTATTTTAGA
   · 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 S G F T F S S Y N M N W V R Q A P G K G L E
151 CTGTGCAGCCTCTGGATTACCTTCAGTAGCTATAACATGAACTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGA
   · 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 GTGGGTTTCATACATTAGTAGTAGTAGTAGTACCATATACTACGCAGACTCTGTGAAGGGCCGATTACCATCTC
   · 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 TGCGAGAGCATACTACGGTATGACGCTCTGGGGCCAAGGGACACGGTCACGGTCTCTCCSAGACTCCACCAA
   · 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 GGGCCCCATCGGTCTTCCCCCTGGCACCCCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCTGCCTGGT
   · 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 CAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGGAACTCAGGCGCCCTGACCAGCGCGTGCACACCTTCCC
   · A V L Q S S G L Y S L S S V V T V P S S L G T Q
601 GGCTGTCTACAGTCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCA
   · T Y I C N V N H K P S N T K 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 CAAAACTCACACATGCCCACCGTGCCCGAGCACCTGAACTCTCTGGGGGACCGTCAGTCTCTCTTCCCCCAAA
   · 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 ACCAAGGACACCCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCC
   · 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 CAACAGCACGTACCGTGTGGTCACGCTCTCACCGTCTCTGCACCAGGACTGGCTGAATGGCAAGGATACAAGTG
   · 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 CAAGGTCTCCAACAAAGCCCTCCAGCCCCATCGAGAAAACCATCTCCAAGCCAAAGGGCAGCCCCGAGAACC
   · 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 ACAGGTGTACACCTTCCCCCATCCCGGGAGGAGATGACCAAGAACCAGGTCAGCCTGACCTGGCTGGTCAAAGG
   · 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 CTTCTATCCAGCGACATCGCCGTGGAGTGGGAGAGCAATGGGCAGCCGAGAACAACTACAAGACACGCCTCC
   · 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 CGTGTCTGACTCCGACGGCTCTCTTCTCTATAGCAAGCTCACCGTGGACAGAGCAGGTGGCAGCAGGGGAA
   · 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 CGTCTTCTCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCCCCGGG
   · K *
1426 TAAATGA

```

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

```

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 ATCACTTGTCGGGCGAGTCAGGGTATTAGCGGTGGTTAGCCTGGTATCAGCAGAAACCAGGGAAAGCCCTAAG
   F L I Y A S T L Q S G V P S R F S G S G S G T D
226 TTCCTGATCTATGCTGCATCCACTTTGCAAAGTGGGGTCCCATCAAGGTTCACGCGCAGTGGATCTGGGACAGAT
   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 G G G T K V E I K R T V A A P S V F I F P P
376 CCCACTTTCGGCGGAGGACCAAGGTGGAGATCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCGCCA
   S D E I Q L K S G T A S V V C L L N N F Y P R E A K
451 TCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTGTGTGCTGCTGAATAACTTCTATCCCAGAGAGGCCAAA
   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 GTACAGTGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCAGGAGAGTGTACAGAGCAGGACAGCAGGAC
   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 AGCACCTACAGCCTCAGCAGCACCTGACCGTGAGCAAAGCAGACTACGAGAAACACAAGTCTACGCCTGCGAA
   V T H Q G L S S P V T K S F N R G E C *
676 GTACCCCTCAGGGCCTGAGCTCGCCCGTCAAAAGAGCTTCAACAGGGGAGAGTGTAG

```

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.

```

1  MELGLCWVFLVAILEGVOCEVOLVESGGGLVOPGGSLRLSCAASGFTFSS
51  YNMNWVRQAPGKGLEWVSYISSSSSTIYYADSVKGRFTISRDNAKNSLSL
101 QMNSLRDEDTAVYYCARAYYYGMDVWGQGTTVTVSSASTKGPSVFPLAPS
151 SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS
201 LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEPKSCDKTHTCPPCPA
251 PELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDG
301 VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAP
351 IEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW
401 ESNGQOPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSCVMHEA
451 LHNHYTQKSLSLSPGK

```

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.

```

1  MDMRVPAQLLGLLLLWFPGSRCDIQMTQSPSSVSASVGDRVTITCRASQG
51  ISGWLAWYQQKPGKAPKFLIYAASTLQSGVPSRFSGSGSGTDFTLTISL
101 QPEDFATYYCQQANSFPPTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSG
151 TASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSLSST
201 LTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

```

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

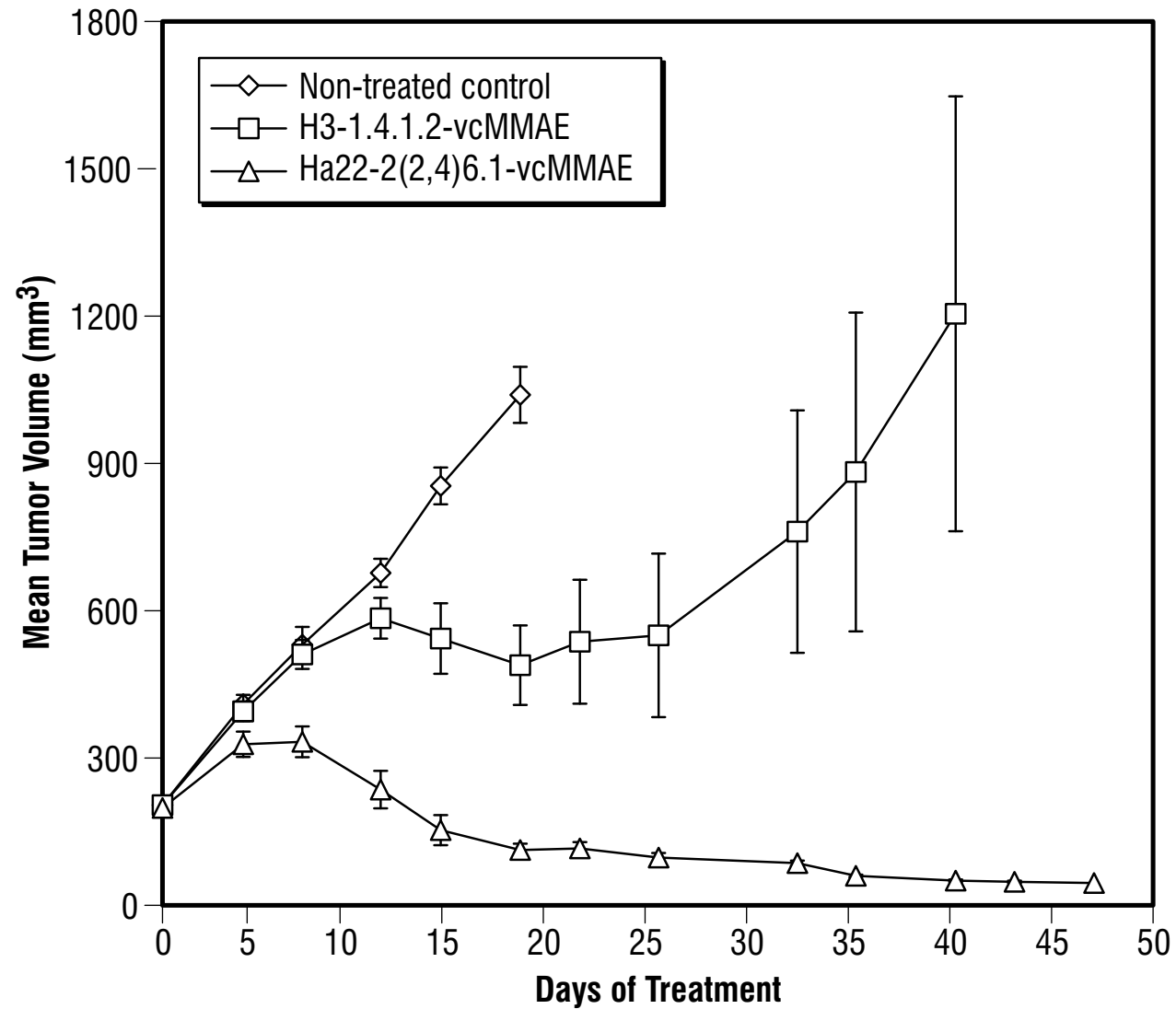
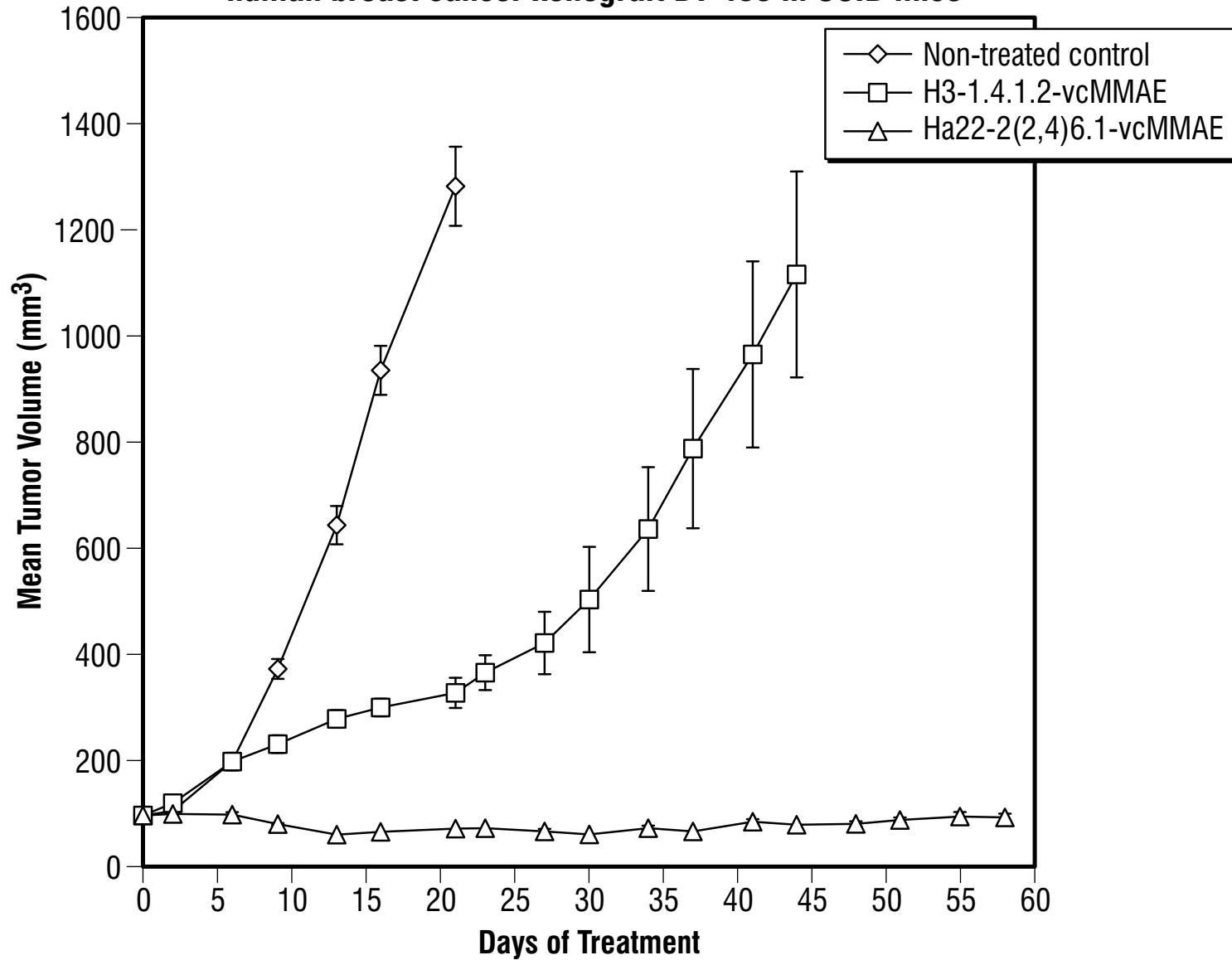


FIG. 3: Efficacy of Ha22-2(2,4)6.1-vcMMAE in subcutaneous established human breast cancer xenograft BT-483 in SCID mice



Breast cancer specimen

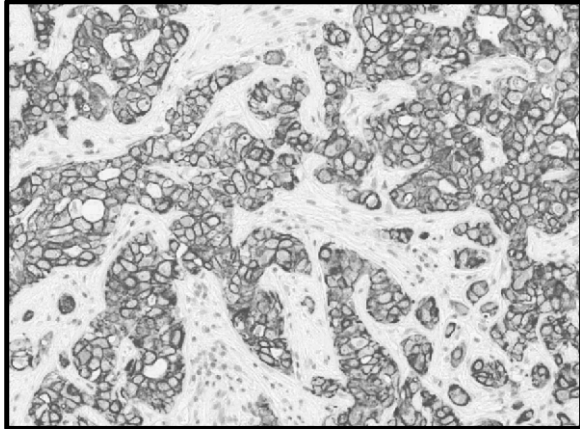


FIG. 4A

Breast cancer specimen

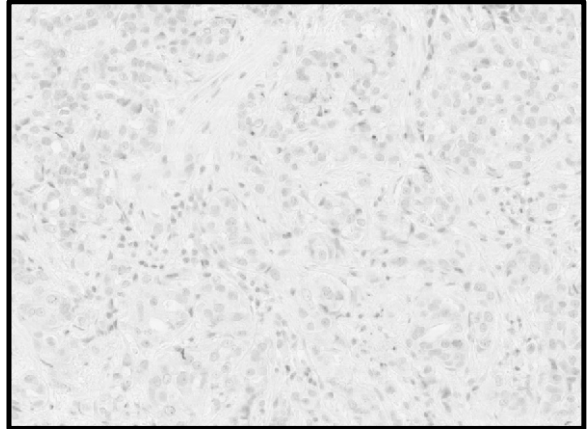


FIG. 4B

Lung cancer specimen

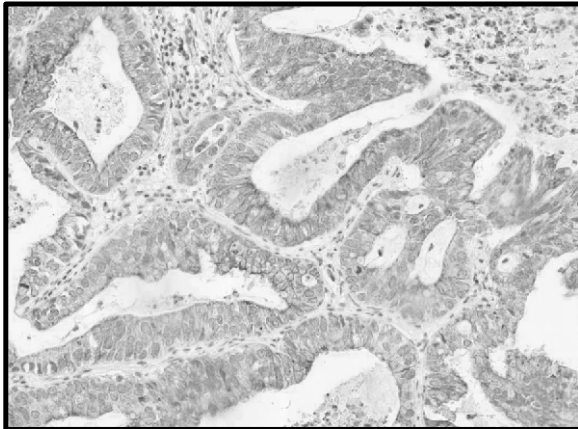


FIG. 4C

Lung cancer specimen

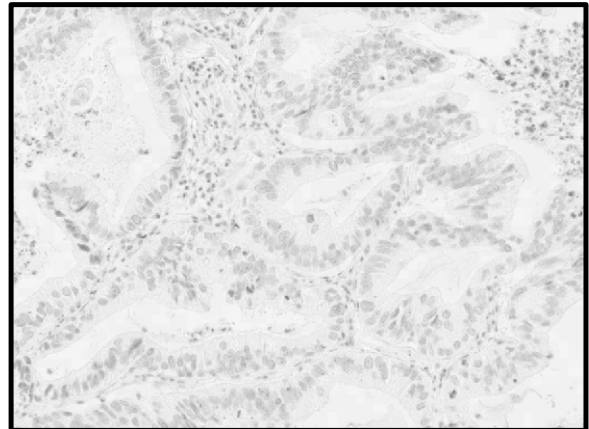


FIG. 4D

Esophageal cancer specimens

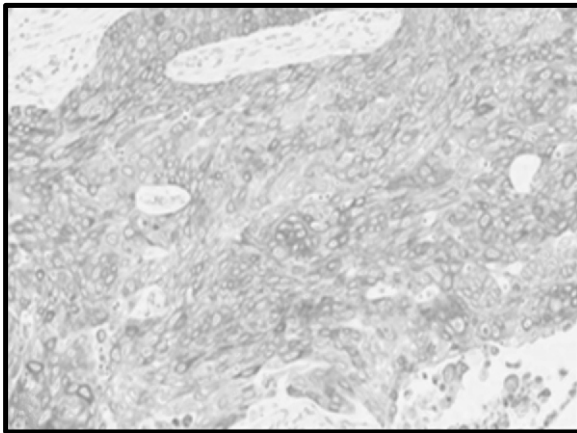


FIG. 4E

Esophageal cancer specimens

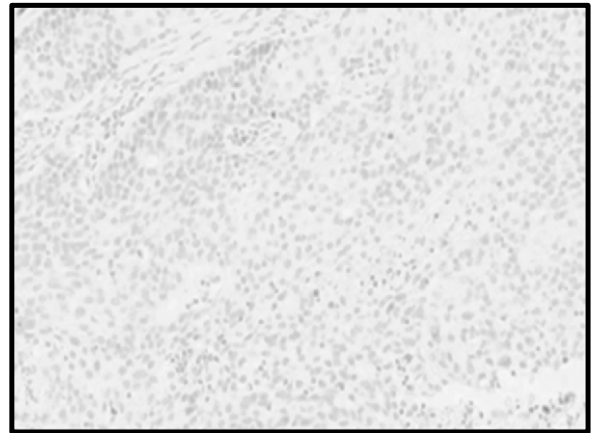


FIG. 4F

Head and neck cancer specimens

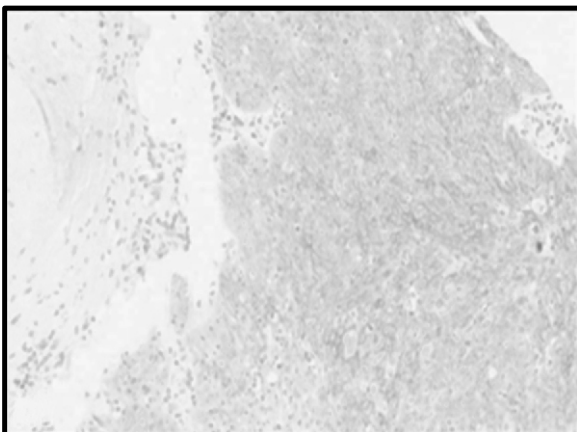


FIG. 4G

Head and neck cancer specimens

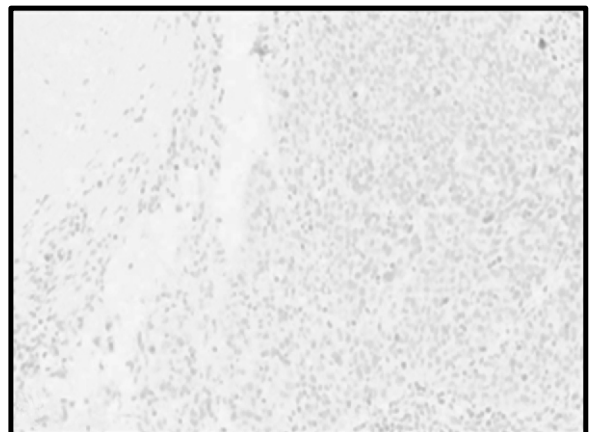


FIG. 4H

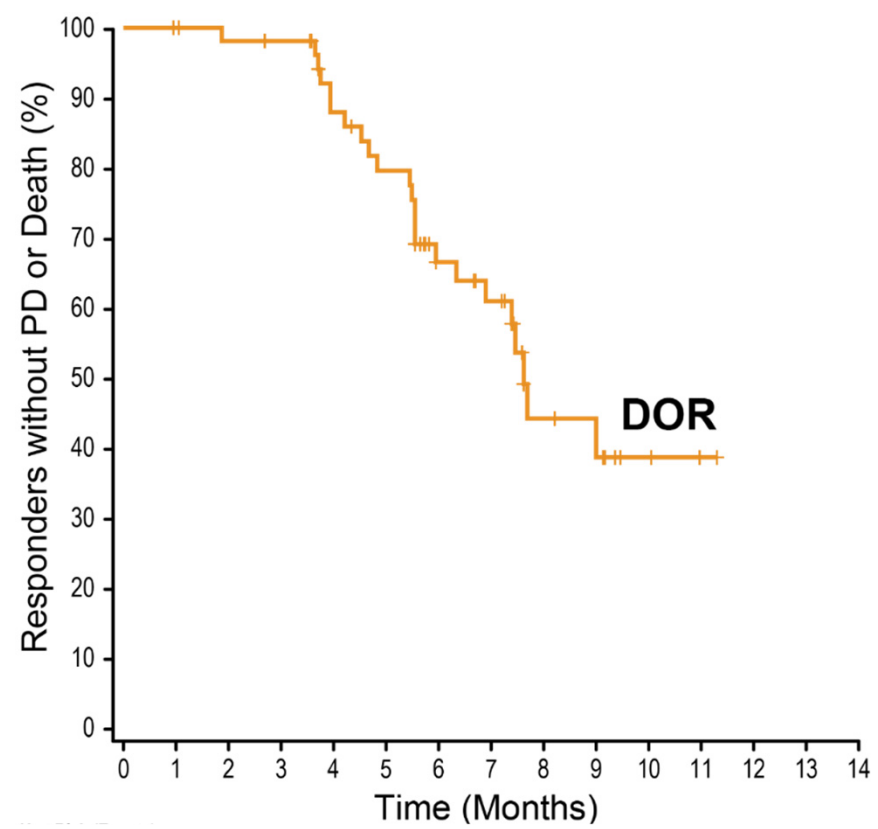


FIG. 5