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(54) **ANTI-VEGF ANTIBODIES**

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Related U.S. Application Data

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(51) **Int. Cl.**[7] **C07H 21/04**

(52) **U.S. Cl.** **536/23.53**; 435/320.1; 530/387.3; 530/388.85

(58) **Field of Search** 435/327, 252, 435/1, 320.1, 252.3, 69.1; 536/23.1, 23.53; 530/382.1, 387.3, 388, 388.85

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(57) **ABSTRACT**

Humanized and variant anti-VEGF antibodies and various uses therefor are disclosed. The anti-VEGF antibodies have strong binding affinities for VEGF; inhibit VEGF-induced proliferation of endothelial cells in vitro; and inhibit tumor growth in vivo.

14 Claims, 16 Drawing Sheets

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Variable Heavy

```
A4.6.1     EIQLVQSGPELKQPGETVRISCKASGYTFTNYGMNWVKQAPGKGLKWMG
F(ab)-12   EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVRQAPGKGLEWVG
humIII     EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS
           1         10        20        30        40

A4.6.1     WINTYTGEPTYAADFKRRFTFSLETSASTAYLQISNLKNDDTATYFCAK
F(ab)-12   WINTYTGEPTYAADFKRRFTFSLDTSKSTAYLQMNSLRAEDTAVYYCAK
humIII     VISGDGGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAR
           50 a      60        70        80 abc    90

A4.6.1     YPHYYGSSHWYFDVWGAGTTVTVSS (SEQ ID NO:9)
F(ab)-12   YPHYYGSSHWYFDVWGQGTLVTVSS (SEQ ID NO:7)
humIII     G----------FDYWGQGTLVTVSS (SEQ ID NO:11)
                      110
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Fig. 1A

Variable Light

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A4.6.1     DIQMTQTTSSLSASLGDRVIISCSASQDISNYLNWYQQKPDGTVKVLIY
F(ab)-12   DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAPKVLIY
humKI      DIQMTQSPSSLSASVGDRVTITCRASQSISNYLAWYQQKPGKAPKLLIY
           1         10        20        30        40

A4.6.1     FTSSLHSGVPSRFSGSGSGTDYSLTISNLEPEDIATYYCQQYSTVPWTF
F(ab)-12   FTSSLYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYSTVPWTF
humKI      AASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSLPWTF
           50        60        70        80        90

A4.6.1     GGGTKLEIKR (SEQ ID NO:10)
F(ab)-12   GQGTKVEIKR (SEQ ID NO:8)
humKI      GQGTKVEIKR (SEQ ID NO:12)
          100
```

Fig. 1B

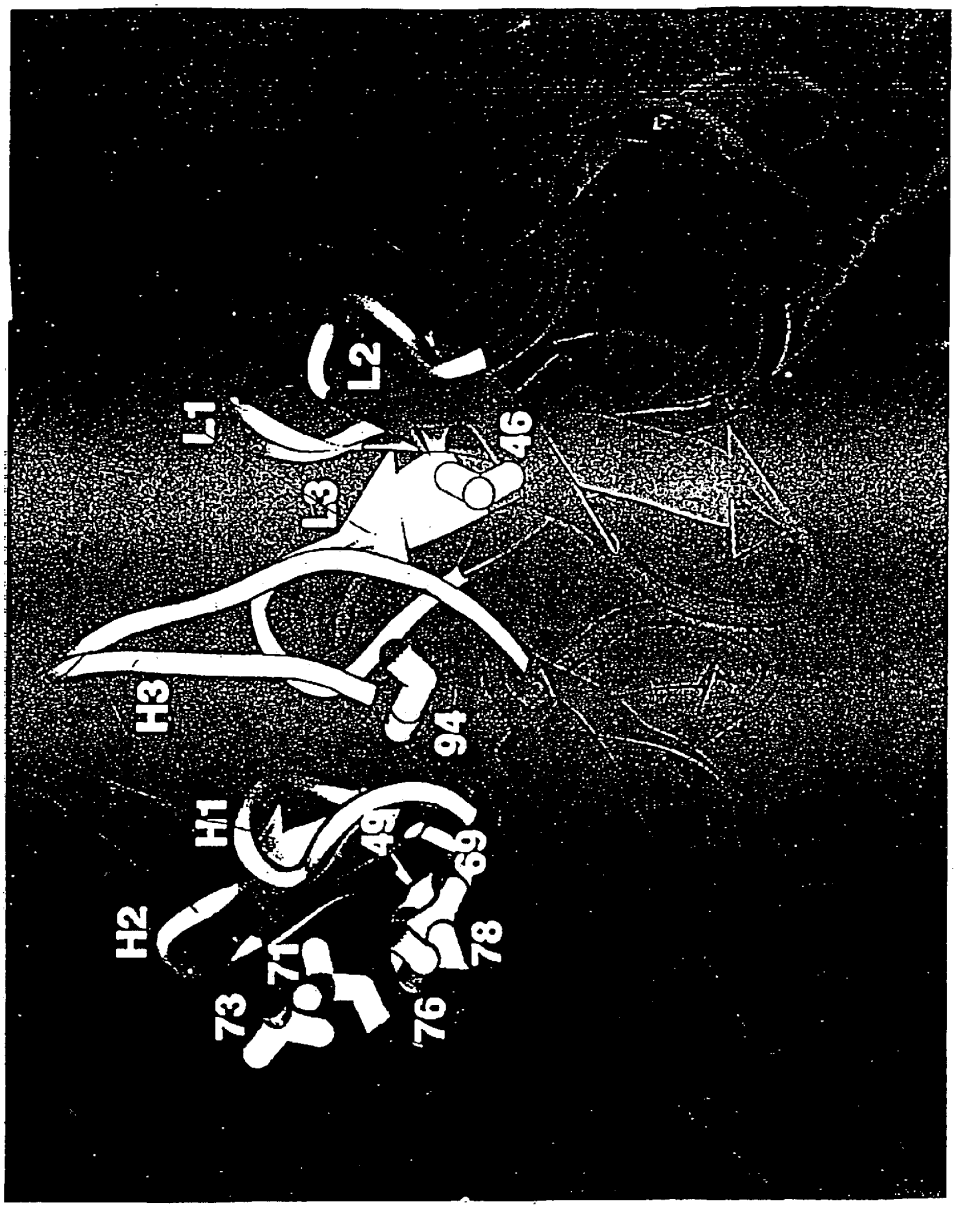

Fig. 2

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