

(12) **United States Patent**
Baca et al.(10) **Patent No.:** **US 7,060,269 B1**
(45) **Date of Patent:** **Jun. 13, 2006**(54) **ANTI-VEGF ANTIBODIES**(75) Inventors: **Manuel Baca**, Foster City, CA (US);
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CA (US)(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 697 days.(21) Appl. No.: **09/723,752**(22) Filed: **Nov. 27, 2000****Related U.S. Application Data**(62) Division of application No. 08/908,469, filed on Aug.
6, 1997, now Pat. No. 6,884,879.(51) **Int. Cl.**
A61K 39/395 (2006.01)(52) **U.S. Cl.** **424/133.1**; 424/156.1;
530/387.3; 530/388.85(58) **Field of Classification Search** 424/130.1,
424/133.1, 135.1, 141.1, 155.1, 156.1; 530/387.1,
530/387.3, 388.1, 388.24, 388.8, 388.85
See application file for complete search history.(56) **References Cited**

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Primary Examiner—Larry R. Helms(74) *Attorney, Agent, or Firm*—Steven X. Cui; Genentech,
Inc.(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.

2 Claims, 16 Drawing Sheets

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Variable Heavy

A4.6.1 EIQLVQSGPELKQPGETVRISCASGYTFETNYGMNWVKQAPGKGLKWMG
 * * ** * *** * * * * * * * * * * *
 F(ab)-12 EVQLVESGGGLVQPGGSLRLSCAASGYTFETNYGMNWVRQAPGKGLEWVG
 * * * * * * * * * * * * * * * * * * * * * *
 humIII EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVS
 1 10 20 30 40

A4.6.1 WINTYTGEPTAADFKRRFTFSLETSASTAYLQISNLKNDTATYFCAK
 * * * * * * * * * * * * * * * * * * * * * *
 F(ab)-12 WINTYTGEPTAADFKRRFTSLDTSKSTAYLQMNSLRAEDTAVYYCAK
 * * * * * * * * * * * * * * * * * * * * * *
 humIII VISGDGGSTYYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAR
 50 a 60 70 80 abc 90

Fig. 1A

A4.6.1 YPHYGSSHWYFDVWGAGTTVTVSS (SEQ ID NO: 9)
 * * * * * * * * * * * * * * * * * * * * * *
 F(ab)-12 YPHYGSSHWYFDVWGQGLVTVSS (SEQ ID NO: 7)
 * * * * * * * * * * * * * * * * * * * * * *
 humIII G-----FDYWGQGLVTVSS (SEQ ID NO: 11)
 110

Variable Light

A4.6.1 DIQMTQTTSSLSASLGDRVIISCSASODISNYLNWYQQKPDGTVKVLIIY
 ** * * * * * * * * * * * * * * * * * * * * * *
 F(ab)-12 DIQMTQSPSSLSASVGDRVTITCSASODISNYLNWYQQKPGKAPKVLIIY
 * * * * * * * * * * * * * * * * * * * * * *
 humKI DIQMTQSPSSLSASVGDRVTITCRASQISNYLAWYQQKPGKAPKLLIIY
 1 10 20 30 40

Fig. 1B

A4.6.1 FTSSLHSGVPSRFSGSGSGTDYSLTISNLEPEDIATYYCQOYSTVPWTF
 ** * * * * * * * * * * * * * * * * * * * * * *
 F(ab)-12 FTSSLHSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQOYSTVPWTF
 ** * * * * * * * * * * * * * * * * * * * * * *
 humKI AASSLESGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQOYNSLPWTF
 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

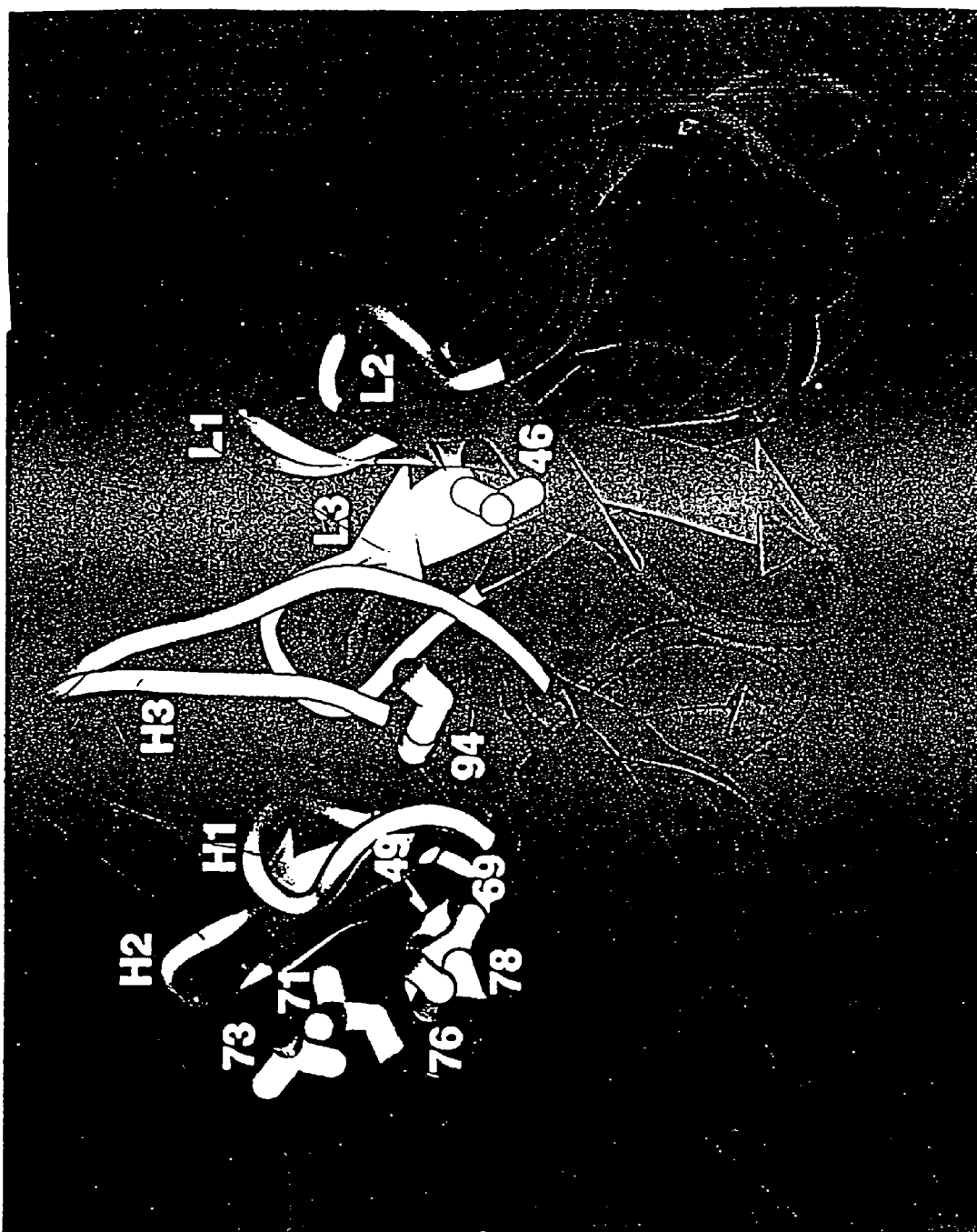


Fig. 2

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