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Baca et al.**(10) Patent No.: US 7,375,193 B2**
(45) Date of Patent: May 20, 2008**(54) ANTI-VEGF ANTIBODIES****(75) Inventors:** Manuel Baca, Black Rock (AU);
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Mateo, CA (US)WO WO 92/18619 10/1992
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WO WO 98/45332 10/1998**(73) Assignee:** Genentech, Inc., South San Francisco,
CA (US)**(*) Notice:** Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.**(21) Appl. No.: 11/537,015****(22) Filed: Sep. 29, 2006****(65) Prior Publication Data**

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C07K 16/00 (2006.01)**(52) U.S. Cl.** 530/387.1; 530/387.3;
530/388.85; 424/130.1; 435/320.1; 536/23.53**(58) Field of Classification Search** 530/387.1,
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See application file for complete search history.

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Primary Examiner—David J. Blanchard*Assistant Examiner*—Parithosh K. Tungaturthi**(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.**22 Claims, 16 Drawing Sheets**

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1 10 20 30 40
A4.6.1 EIQLVQSGPELKQPGETVRISCKASGYTFTNYGMNWVKQA
* * * * *
F(ab)-12 EVQLVESGGGLVQPGGSLRLSCAASGYTFTNYGMNWVRQA
* * * * *
humIII EVQLVESGGGLVQPGGSLRLSCAASGFTFSYAMSWVRQA

50 a 60 70 80
A4.6.1 PGKGLKWMGWINTYTGEPYAADF~~KRR~~FTFSLETSASTAYL
* * * * *
F(ab)-12 PGKGLEWVGWINTYTGEPYAADF~~KRR~~FTFSLDTSKSTAYL
* * * * *
humIII PGKGLEWVSVISGDDGSTYADSVKGRFTISRDN~~SKNT~~LYL

abc 90 110
A4.6.1 QISNLKNDTATYFCAKYPHYYGSSHWYFDVWGAGTTVTVSS (SEQ.ID NO:9)
* * * * *
F(ab)-12 QMNSLRAEDTAVYYCAKYPHYYGSSHWYFDVWGQGT~~LV~~TVSS (SEQ.ID NO:7)
* * * * *
humIII QMNSLRAEDTAVYYCARG-----FDYWGQGT~~LV~~TVSS (SEQ.ID NO:11)

FIG. 1A

1 10 20 30 40
A4.6.1 DIQMTQTSSLSASLGDRVIISCSASQDISNYLNWYQQKP
* * * * *
F(ab)-12 DIQMTQSPSSLSASVGD~~RV~~TITCSASQDISNYLNWYQQKP
* * * * *
humKI DIQMTQSPSSLSASVGD~~RV~~TITCRASQDISNYLAWYQQKP

50 60 70 80
A4.6.1 DGTVKVLIYFTSSLHSGVPSRFGSGSGTDYSLTISNLEP
* * * * *
F(ab)-12 GKAPKVLIIYFTSSLHSGVPSRFGSGSGTDFTLTIS~~SLQ~~P
* * * * *
humKI GKAPKLLIYAASSLES~~GV~~PSRFGSGSGTDFTLTIS~~SLQ~~P

90 100
A4.6.1 EDIATYYCQOYSTVPWTFGGG~~TK~~LEIKR (SEQ.ID NO:10)
* * * * *
F(ab)-12 EDFATYYCQOYSTVPWTFGQGT~~K~~VEIKR (SEQ.ID NO:8)
* * * * *
humKI EDFATYYCQOYNSLPWTFGQGT~~K~~VEIKR (SEQ.ID NO:12)

FIG. 1B

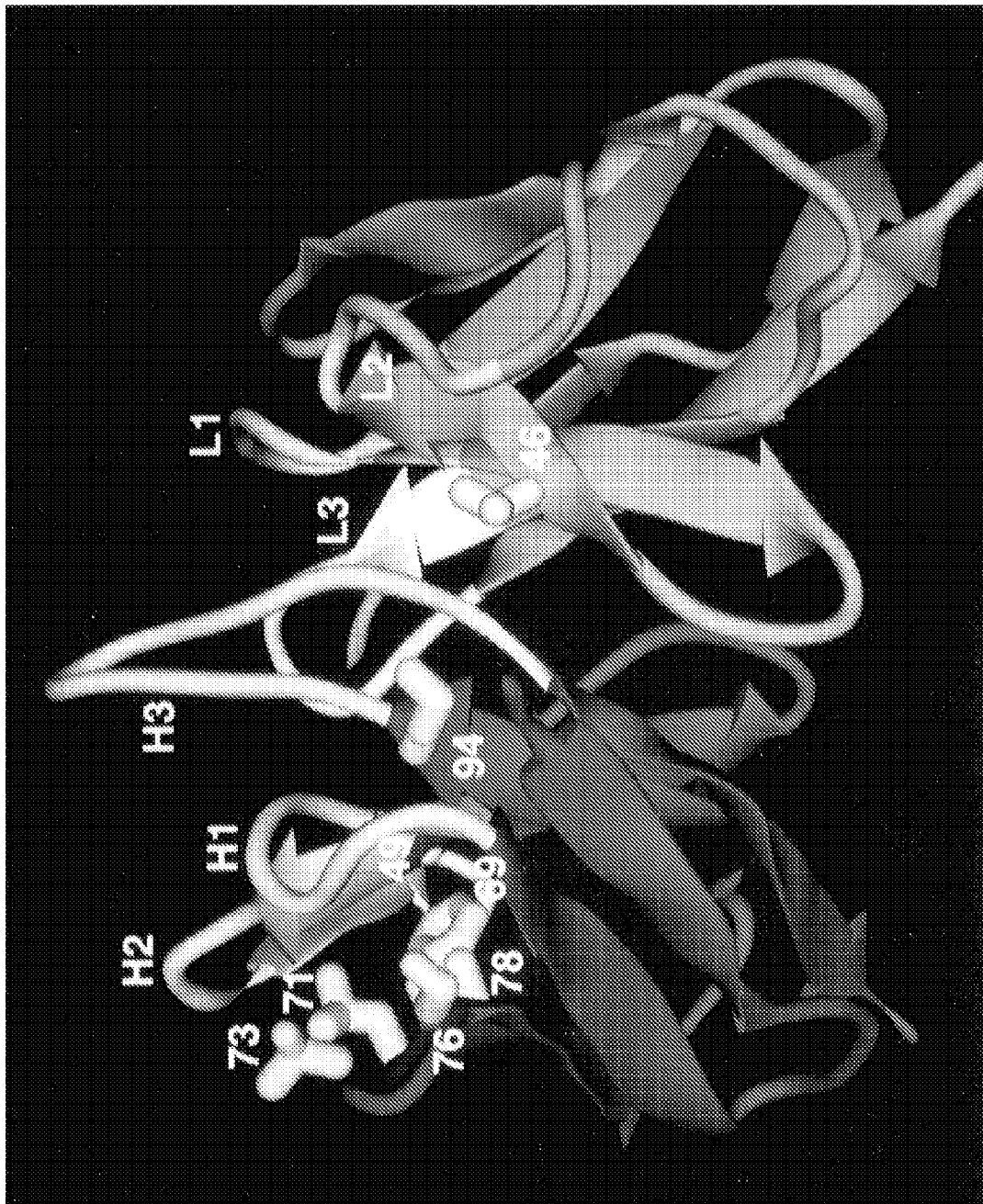


FIG. 2

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