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(54) **RATIONALLY DESIGNED ANTIBODIES**

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(58) **Field of Classification Search**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,642,334	A	2/1987	Moore et al.
4,783,330	A	11/1988	Furie et al.
4,816,397	A	3/1989	Boss et al.
5,116,964	A	5/1992	Capon et al.
5,219,996	A	6/1993	Bodmer et al.
5,223,409	A	6/1993	Ladner et al.
5,260,417	A	11/1993	Grant et al.
5,428,130	A	6/1995	Capon et al.
5,571,698	A	11/1996	Ladner et al.
5,593,666	A	1/1997	McDonald
5,698,435	A	12/1997	Robinson et al.
5,750,373	A	5/1998	Garrard et al.
5,773,569	A	6/1998	Wrighton et al.
5,837,500	A	11/1998	Ladner et al.
5,869,451	A	2/1999	Dower et al.
5,874,253	A	2/1999	Tsujimoto et al.
5,876,961	A	3/1999	Crowe et al.

(Continued)

FOREIGN PATENT DOCUMENTS

EP	1642910	B1	4/2006
WO	94/18221	A1	8/1994
WO	95/11317	A1	4/1995
WO	95/29690	A1	11/1995
WO	96/40189	A1	12/1996
WO	96/40750	A1	12/1996
WO	99/10494	A2	3/1999
WO	99/25378	A1	5/1999
WO	99/25379	A1	5/1999
WO	99/45110	A1	9/1999

(Continued)

OTHER PUBLICATIONS

Kortt, Alexander A. et al., "Recombinant anti-sialidase single-chain variable fragment antibody. Characterization, formation of dimer and higher-molecular-mass multimers and the solution of the crystal structure of the single-chain variable fragment/sialidase complex," Eur. J. Biochem., vol. 221(1):151-157 (1994).

(Continued)

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(57) **ABSTRACT**

Antibodies or fragments thereof having CDR regions replaced or fused with biologically active peptides are described. Flanking sequences may optionally be attached at one or both the carboxy-terminal and amino-terminal ends of the peptide in covalent association with adjacent framework regions. Compositions containing such antibodies or fragments thereof are useful in therapeutic and diagnostic modalities.

13 Claims, 33 Drawing Sheets