(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 September 2010 (30.09.2010)

PCT

(10) International Publication Number
WO 2010/109165 A2

(51) **International Patent Classification**:
C07K 16/00 (2006.01)

(21) **International Application Number**:
PCT/GB2010/000500

(22) **International Filing Date**:
22 March 2010 (22.03.2010)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
0905023.8 24 March 2009 (24.03.2009) GB

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(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

WO 2010/109165 A2

(54) **Title**: BINDING MOLECULES

(57) **Abstract**: The present invention provides a high affinity, antigen-specific, soluble heavy chain-only antibody which: lacks hallmark camelid-related amino acid substitutions and has FR2 substitutions which are not found in antibodies which comprise heavy and light chain; shows increased net hydrophobicity within CDR1 and an increased number of charged amino acids present in CDR3; and comprises one or more amino acid substitutions within the framework β-pleated sheet leading to increased net hydrophobicity within FR1 and an increased number of charged amino acids present in FR3. Also provided are VH domains having the same properties, gene segments for their production, methods for their production, transgenic animals and uses of the antibody of the VH domains in therapy.