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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 July 2010 (08.07.2010)

PCT

(10) International Publication Number
WO 2010/077854 A1

(51) **International Patent Classification**:
C07K 16/40 (2006.01) ***A61K 39/395*** (2006.01)
C12N 9/64 (2006.01) ***A61P 3/06*** (2006.01)

(21) **International Application Number**:
PCT/US2009/068013

(22) **International Filing Date**:
15 December 2009 (15.12.2009)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:

61/122,482	15 December 2008 (15.12.2008)	US
61/210,566	18 March 2009 (18.03.2009)	US
61/168,753	13 April 2009 (13.04.2009)	US
61/218,136	18 June 2009 (18.06.2009)	US
61/249,135	6 October 2009 (06.10.2009)	US
61/261,776	17 November 2009 (17.11.2009)	US

(71) **Applicant** *(for all designated States except US)*: **REGENERON PHARAMACEUTICALS, INC.** [US/US]; 777 Old Saw Mill River Road, Tarrytown, NJ 10591 (US).

(72) **Inventors; and**

(75) **Inventors/Applicants** *(for US only)*: **SLEEMAN, Mark, W.** [US/US]; 118 Lake Drive, Mahopac, NY 10541 (US). **MARTIN, Joel, H.** [US/US]; 244 Church Road, Putnam Valley, NY 10579 (US). **HUANG, Tammy, T.** [US/US]; 10 Green Hill Road, Goldens Bridge, NY 10526 (US). **MACDONALD, Douglas** [US/US]; 260 West End Avenue, Apt. 10C, New York, NY 10023 (US).

(74) **Agent**: **GREGG, Valeta**; Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, NY 10591 (US).

(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, 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:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

— *with sequence listing part of description (Rule 5.2(a))*

WO 2010/077854 A1

(54) **Title**: HIGH AFFINITY HUMAN ANTIBODIES TO PCSK9

(57) **Abstract**: An human antibody or antigen-binding fragment of a human antibody that specifically binds and inhibits human proprotein convertase subtilisin/kexin type 9 (hPCSK9) characterized by the ability to reduce serum LDL cholesterol by 40-80% over a 24, 60 or 90 day period relative to predose levels, with little or no reduction in serum HDL cholesterol and/or with little or no measurable effect on liver function, as determined by ALT and AST measurements.