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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
12 April 2018 (12.04.2018)

WIPO | PCT

(10) International Publication Number
WO 2018/068012 A1

(51) International Patent Classification:
A61K 9/00 (2006.01) *A61K 9/19* (2006.01)
A61K 9/08 (2006.01) *A61K 38/00* (2006.01)

(21) International Application Number:
PCT/US2017/055651

(22) International Filing Date:
06 October 2017 (06.10.2017)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/405,610 07 October 2016 (07.10.2016) US

(71) Applicant: **REGENERON PHARMACEUTICALS, INC.** [US/US]; 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US).

(72) Inventors: **TANG, Xiaolin**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US). **LUDWIG, David Brett**; c/o Regeneron Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown, New York 10591 (US).

(74) Agent: **TERMES, Lance A.**; Schwabe, Williamson & Wyatt PC, 1211 SW 5th Ave., Suite 1900, Portland, Oregon 97204 (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, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, 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, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, 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, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

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

WO 2018/068012 A1

(54) Title: ROOM TEMPERATURE STABLE LYOPHILIZED PROTEIN

(57) Abstract: Stable lyophilized therapeutic protein compositions and their methods of manufacture are provided. Specifically, the use of water as a solid cake plasticizer and protein stabilizer is described. Also, the inclusion of a multicomponent stabilizer comprising a larger molecular entity and a smaller molecular entity is described. Also, the inclusion of post-drying annealing under certain conditions improves protein stability. Proteins are predicted to remain stable over 24 months at 25°C.