

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

(19) World Intellectual Property
Organization

International Bureau

(43) International Publication Date
09 November 2023 (09.11.2023)



(10) International Publication Number
WO 2023/215750 A2

(51) International Patent Classification:

A61K 9/00 (2006.01) *A61K 47/14* (2017.01)
A61K 39/00 (2006.01) *C07K 1/18* (2006.01)
A61K 47/10 (2017.01) *C07K 1/20* (2006.01)
A61K 47/34 (2017.01) *C07K 1/36* (2006.01)
A61K 39/395 (2006.01) *C07K 16/28* (2006.01)

TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS,
ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, CV,
GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, 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, ME, 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).

(21) International Application Number:

PCT/US2023/066500

(22) International Filing Date:

02 May 2023 (02.05.2023)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/337,532	02 May 2022 (02.05.2022)	US
63/436,850	03 January 2023 (03.01.2023)	US
63/499,441	01 May 2023 (01.05.2023)	US

Published:

- without international search report and to be republished
upon receipt of that report (Rule 48.2(g))
- with sequence listing part of description (Rule 5.2(a))

(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 Pharmaceuti-
cals, Inc., 777 Old Saw Mill River Road, Tarrytown, New
York 10591 (US). **BREYDO, Leonid**; c/o Regeneron Phar-
maceuticals, Inc., 777 Old Saw Mill River Road, Tarrytown,
New York 10591 (US). **MATTILA, John**; c/o Regeneron
Pharmaceuticals, Inc., 777 Old Saw Mill River Road, Tar-
rytown, New York 10591 (US).

(74) Agent: **CAPLAN, Jonathan S.**; Kramer Levin Naftalis &
Frankel LLP, 1177 Avenue of the Americas, New York,
New York 10036 (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, CV, CZ, DE, DJ, DK, DM,
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,
HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG,
KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY,
MA, MD, MG, MK, MN, MU, 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, ST, SV, SY, TH,

(54) Title: METHODS FOR REDUCING LIPASE ACTIVITY

(57) Abstract: Pharmaceutical formulations comprising an antibody that specifically binds to human interleukin-4 receptor alpha (hIL-4R α) are provided. The formulations may contain, in addition to an anti-IL-4R α antibody, one or more buffers, at least one amino acid, at least one sugar, and a surfactant comprising a polysorbate, polyethylene glycol or a poloxamer. Methods for producing pharmaceutical formulations with reduced lipase activity are also provided, which may include subjecting a drug substance to anion exchange chromatography in acidic conditions, agitation stress, heat stress, and additional ion exchange or size exclusion chromatography. In one aspect, the pharmaceutical formulations do not have appreciable subvisible particle formation in the presence of lipase, and exhibit a substantial degree of antibody stability during storage and after being subjected to thermal and other physical stresses.