

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
24 February 2022 (24.02.2022)



(10) International Publication Number
WO 2022/040447 A2

(51) International Patent Classification:
A61K 41/00 (2020.01)

(21) International Application Number:
PCT/US2021/046742

(22) International Filing Date:
19 August 2021 (19.08.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
63/068,235 20 August 2020 (20.08.2020) US

(71) Applicant: **THE BOARD OF TRUSTEES OF THE LE-
LAND STANFORD JUNIOR UNIVERSITY** [US/US];
P.O. Box 20386, Office of the General Counsel, Build-
ing 170, 3rd Floor, Main Quad, Stanford, California
94305-2038 (US).

(72) Inventors: **MILLA, Carlos**; 415 Broadway Street, 2nd
Floor, MC5884, Redwood City, California 94063 (US).
VLADAR, Eszter; 415 Broadway Street, 2nd Floor,
MC8854, Redwood City, California 94063 (US). **AXEL-
ROD, Jeffrey**; 415 Broadway Street, 2nd Floor, MC5884,
Redwood City, California 94063 (US).

(74) Agent: **FIELD, Bret E.**; 201 Redwood Shores Parkway,
Suite 200, Redwood City, California 94065 (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, IT, 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, ST, SV, SY, TH, 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, 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).

Published:

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

(54) Title: METHODS FOR TREATING RESPIRATORY DISEASES CHARACTERIZED BY MUCUS HYPERSECRETION

(57) Abstract: The invention therefore provides methods of treating a respiratory disease characterized by mucus hyper-secretion comprising administering to a human patient in need of such treatment a gamma secretase inhibitor (GSI), wherein the administration of a GSI is effective in reducing mucus in such patient's lungs or inhibiting mucus accumulation in said patient's lungs. In some embodiments, the methods of the invention are effective in treating a respiratory disease selected from the group consisting of cystic fibrosis, chronic obstructive pulmonary disease, primary ciliary dyskinesia, chronic bronchitis, asthma, idiopathic and secondary bronchiectasis, bronchiolitis obliterans, idiopathic pulmonary fibrosis and other fibrotic lung disorders, respiratory infection including exacerbations in chronic respiratory disorders, and mucus accumulation in response to acute infection. Methods of the invention further include methods of treating cystic fibrosis wherein a GSI is administered to a patient being administered or in need of a CFTR modulator, wherein the mucus in such patient's lungs is reduced or mucus accumulation in such patient's lungs is inhibited.



WO 2022/040447 A2