

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

(19) World Intellectual Property
Organization
International Bureau

(43) International Publication Date
17 June 2021 (17.06.2021)



(10) International Publication Number
WO 2021/119534 A2

(51) International Patent Classification:
A61K 38/20 (2006.01)

(21) International Application Number:
PCT/US2020/064677

(22) International Filing Date:
11 December 2020 (11.12.2020)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/948,066 13 December 2019 (13.12.2019) US

(71) Applicant: **SYNTHETIKINE, INC.** [US/US]; 1505 O'Brien Drive, Suite D, Menlo Park, California 94025 (US).

(72) Inventors: **PENAFLOP ASPURIA, Paul-Joseph**; c/o Synthetkine, Inc., 1505 O'Brien Drive, Suite D, Menlo Park,

California 94025 (US). **MCCAULEY, Scott Alan**; c/o Synthetkine, Inc., 1505 O'Brien Drive, Suite D, Menlo Park, California 94025 (US). **OFT, Martin**; c/o Synthetkine, Inc., 1505 O'Brien Drive, Suite D, Menlo Park, California 94025 (US). **KAUDER, Steve**; c/o Synthetkine, Inc., 1505 O'Brien Drive, Suite D, Menlo Park, California 94025 (US).

(74) Agent: **HINSCH, Matthew E.** et al.; Kilpatrick Townsend & Stockton LLP, Mailstop: IP Docketing - 22, 1100 Peachtree Street, Suite 2800, Atlanta, GA 30309 (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,

(54) Title: **IL-2 ORTHOLOGS AND METHODS OF USE**

Dilution	cRPM	Vector	wt IL2	Ortho S-QVUKA	-QVUKA	S-VUKA
1:2	4587	5502	7377	8334	59986	19395
1:4	4714	4316	3044	3668	12746	13468
1:8	4516	4175	5790	6734	28444	9692
1:16	4504	4334	4975	8212	6472	7176
1:32	4272	4142	7118	8280	5482	5882
1:64	4346	4804	5720	8360	4798	5088
1:128	4108	3988	5602	5622	5056	4622
1:256	3866	3672	4192	4934	3836	4076

Dilution	SQ-LKA	SQV-KA	SQV-LA	SQV-LK	SQV-L	SQV-L
1:2	10764	13306	47696	46348	51424	49952
1:4	9400	8222	46432	45610	59212	49580
1:8	7054	6612	43264	47642	58170	78172
1:16	6204	6436	55630	57530	49876	50880
1:32	6256	6150	55312	55912	69280	78256
1:64	5184	5834	52060	49596	46482	67102
1:128	5006	5564	48420	45432	45584	48968
1:256	4582	4898	34646	35200	36750	38390

Dilution	E155	H16Q	L19V	D20L	Q22K	M23A
1:2	55892	47518	47334	46676	47674	81520
1:4	58318	69066	62922	76272	53946	82220
1:8	52790	53136	65906	53744	54926	53008
1:16	52778	51802	61672	52938	69172	53090
1:32	53860	52056	53886	53486	55092	54306
1:64	74250	52570	53740	52760	53490	53484
1:128	49874	51610	59880	51668	52860	51362
1:256	49050	46764	49806	49412	45868	44574

FIGURE 1

(57) Abstract: The present disclosure relates to hIL2 orthogonal ligands (IL2 orthologs) that specifically and selectively bind to the extracellular domain (ECD) a transmembrane polypeptide comprising of a modified hCD122 polypeptide. The binding of the hIL2 ortholog to the modified hCD122 polypeptide participates in the transduction pathway of intracellular signaling resulting in a biological activity of the native intracellular signaling patterns associated with hIL2 binding to either the intermediate or high affinity hIL2 receptor but which exhibits selectivity to an engineered cell expressing an hCD122 orthogonal receptor. The hIL2 orthologs of the present invention exhibit significantly reduced binding relative to their binding to the extracellular domain of wild type hCD122, either alone or when hCD122 is present in the form of an endogenous high or intermediate affinity hIL2 receptors.

[Continued on next page]

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).

Declarations under Rule 4.17:

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
- *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

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