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(71) Applicant: **BOEHRINGER INGELHEIM INTERNATIONAL GMBH** [DE/DE]; Binger Strasse 173, 55216 Ingelheim am Rhein (DE).

(72) Inventor; and

(71) Applicant: **FARAG, Ahmed Karim** [US/DE]; Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 Ingelheim am Rhein (DE).

(72) Inventors: **BAUM, Patrick**; Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 Ingelheim am Rhein (DE). **VISVANATHAN, Sudha**; c/o VP, IP Legal, Boehringer Ingelheim USA Corp., 900 Ridgebury Rd., P.O. Box 368, Ridgefield, Ridgefield 06877-0368 (US).

(74) Agent: **LOCKENOUR, Andrea** et al.; BOEHRINGER INGELHEIM CORPORATION, 900 Ridgebury Road, P.O. Box 368, Ridgefield, Connecticut 06877 (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, JM, 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.

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(54) Title: BIOMARKERS ASSOCIATED WITH ANTI-IL-36R ANTIBODY TREATMENT IN GENERALIZED PUSTULAR PSORIASIS

(57) Abstract: This invention generally relates to biomarkers associated with anti-IL-36R antibody treatment in generalized pustular psoriasis (GPP). The invention also relates to methods of using the biomarkers disclosed.

WO 2022/192531 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2022/019742

A. CLASSIFICATION OF SUBJECT MATTER INV. C12Q1/6883 G01N33/53 ADD.		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) C12Q G01N		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) EPO-Internal, BIOSIS, EMBASE, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2019/177888 A1 (BOEHRINGER INGELHEIM INT [DE]) 19 September 2019 (2019-09-19) claims 1-38; example 1 ----- -/--	1-20
☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents : "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance;; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance;; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 13 October 2022		Date of mailing of the international search report 21/10/2022
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Bradbrook, Derek

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2022/019742

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Baum P ET AL: "Treatment with spesolimab, an anti-interleukin-36 receptor antibody, in patients with generalized pustular psoriasis, is associated with the downregulation of biomarkers linked to innate, Th1/17 and neutrophilic pathways", Journal of Investigative Dermatology - ESDR 2019 Annual Meeting, 1 September 2019 (2019-09-01), pages S281-S281, XP055934782, DOI: doi:10.1016/j.jid.2019.07.390 Retrieved from the Internet: URL:https://www.sciencedirect.com/science/article/pii/S0022202X19322444/pdf?md5=ac8118b8e3be16ad1a9cb99391731ea&pid=1-s2.0-S0022202X19322444-main.pdf [retrieved on 2022-06-23] abstract -----	1-20
A	BAUM P. ET AL: "049 Generalized pustular psoriasis (GPP) and palmoplantar pustulosis (PPP) both show upregulation of the IL-36, neutrophil chemokine, and innate pathways that are modulated by spesolimab, an anti-IL-36 receptor antibody, treatment", JOURNAL OF INVESTIGATIVE DERMATOLOGY, vol. 140, no. 7, 1 July 2020 (2020-07-01), page S5, XP055876016, NL ISSN: 0022-202X, DOI: 10.1016/j.jid.2020.03.051 Retrieved from the Internet: URL:http://dx.doi.org/10.1016/j.jid.2020.03.051> abstract -----	1-20
X,P	BAUM PATRICK ET AL: "Pustular psoriasis: Molecular pathways and effects of spesolimab in generalized pustular psoriasis", JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, ELSEVIER, AMSTERDAM, NL, vol. 149, no. 4, 20 October 2021 (2021-10-20), pages 1402-1412, XP087013232, ISSN: 0091-6749, DOI: 10.1016/J.JACI.2021.09.035 [retrieved on 2021-10-20] the whole document ----- -/--	1-20

International application No
PCT/US2022/019742

2

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2022/019742

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ALEXANDER M. FOSTER ET AL: "IL-36 Promotes Myeloid Cell Infiltration, Activation, and Inflammatory Activity in Skin", THE JOURNAL OF IMMUNOLOGY, vol. 192, no. 12, 14 May 2014 (2014-05-14) , pages 6053-6061, XP055701616, US ISSN: 0022-1767, DOI: 10.4049/jimmunol.1301481 the whole document -----	1-20
X	SWINDELL ET AL: "7th International Congress of Psoriasis: from Gene to Clinic The Queen Elizabeth II Conference Centre, London, U.K. 11th-13th December 2014", BRITISH JOURNAL OF DERMATOLOGY, JOHN WILEY, HOBOKEN, USA, vol. 171, no. 6, 09, 18 December 2014 (2014-12-18), XP071095985, ISSN: 0007-0963, DOI: 10.1111/BJD.13488 page 5, column 1, paragraph 2 - column 2, paragraph 1 -----	1-20

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2022/019742

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
1-20 (partially)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims;; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20 (partially)

Method for detecting the presence or absence of a beneficial response in a patient after administration of an anti-interleukin-36 receptor antibody (anti-IL-36R antibody); method of determining whether a potential therapeutic agent is efficacious in the treatment of GPP; method of monitoring patient response to a GPP treatment; method for monitoring patient compliance with a drug treatment protocol for GPP; wherein the method comprises measuring the level of one or more biomarkers comprising at least TNF.

2. claims: 1-20 (partially)

Method for detecting the presence or absence of a beneficial response in a patient after administration of an anti-interleukin-36 receptor antibody (anti-IL-36R antibody); method of determining whether a potential therapeutic agent is efficacious in the treatment of GPP; method of monitoring patient response to a GPP treatment; method for monitoring patient compliance with a drug treatment protocol for GPP; wherein the method comprises measuring the level of one or more biomarkers comprising at least IL1B.

3-71. claims: 1-20 (partially)

Method for detecting the presence or absence of a beneficial response in a patient after administration of an anti-interleukin-36 receptor antibody (anti-IL-36R antibody); method of determining whether a potential therapeutic agent is efficacious in the treatment of GPP; method of monitoring patient response to a GPP treatment; method for monitoring patient compliance with a drug treatment protocol for GPP; wherein the method comprises measuring the level of one or more biomarkers comprising at least one of the further biomarkers specified in the claims.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2022/019742

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2019177888 A1	19-09-2019	AU 2019236105 A1	27-08-2020
		BR 112020016738 A2	15-12-2020
		CA 3093692 A1	19-09-2019
		CL 2020002342 A1	18-12-2020
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		IL 277215 A	29-10-2020
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		KR 20200131871 A	24-11-2020
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		US 2021087285 A1	25-03-2021
		WO 2019177888 A1	19-09-2019
