

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Harrison et al.
Serial No.: Not Assigned Yet Art Unit: Not Assigned Yet
Filed: Herewith Examiner: Not Assigned Yet
For: ANTI-TNF ANTIBODIES, COMPOSITIONS, AND METHODS
FOR THE TREATMENT OF ACTIVE ANKYLOSING
SPONDYLITIS

Preliminary Amendment

Dear Commissioner,

Please enter the following preliminary amendment to the application to revise/add the related applications paragraph of the specification to show Applicants' claim to domestic priority, to correct typographical errors in the specification and make certain claim amendments.

Amendments to the specification begin on page 2 of this paper.

Amendment to the claims begin on page 3 of this paper.

Remarks begin on page 6 of this paper.

Amendments to the Specification

In the Specification:

Please insert the following cross-reference paragraph after the title on page 1 of the specification:

--This application is a continuation application of US Serial No. 15/818,015, filed November 20, 2017, which claims priority to US Serial No. 62/455,651, filed February 7, 2017, the contents of which are hereby incorporated by reference in their entirety.--

Amendments to the Specification

The specification has been amended because it contained embedded hyperlinks and/or other form of browser-executable code. To remove browser-executable code, throughout the specification as currently amended the embedded hyperlinks are disabled by the addition of a space after “www.”. See, e.g., page 28, paragraph [57] and page 60, paragraph [138].

The specification has been amended because it contained the use of registered trademarks that were not capitalized or accompanied by the generic terminology. In the specification as currently amended the registered trademarks are capitalized and generic terminology is included. For terms that were identified as not being registered trademarks, the ® was removed. See, e.g., pages 59-60, paragraph [138], and pages 77-78, paragraph [176].

Applicants submit herewith substituted specification as a Marked-Up Copy and a Clean Copy. No new matter is added with the amendments to the specification. Also submitted herewith is a Verified Statement Under 37 CFR §1.125(c).

Amendments to the Claims:

This listing of claims replaces all prior versions, and listings, of claims in the captioned application.

In the Claims:

1. (Currently amended) A ~~composition comprising method~~ for treating a TNF related condition, wherein the TNF related condition is active Ankylosing Spondylitis, the method comprising: administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising SEQ ID NO:36 and a light chain (LC) comprising SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent ~~for use in the safe and effective treatment of active Ankylosing Spondylitis,~~ wherein said composition is administered via IV infusion, and wherein a patient treated with the composition achieves an Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment.
2. (Currently amended) The ~~composition method~~ according to claim 1, wherein said composition is administered such that said anti-TNF antibody is administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.
3. (Currently amended) The ~~composition method~~ according to any one of claims 1-2, further comprising administering said composition with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ).
4. (Currently amended) A ~~composition comprising method~~ for treating a TNF related condition, wherein the TNF related condition is active Ankylosing Spondylitis, the method comprising: administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising SEQ ID NO:36 and a light chain (LC) comprising SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent ~~for use in the safe and effective treatment of active Ankylosing Spondylitis,~~ wherein said composition is administered via IV infusion, and wherein at week 16 of treatment patients treated with

the anti-TNF antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Bath Ankylosing Spondylitis Functional Index (BASFI) = -2.4 ± 2.1 Standard Deviation (SD), Bath Ankylosing Spondylitis Metrology Index (BASMI) = -0.4 ± 0.6 SD, 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS) = 8.5 ± 7.5 SD, 36-item Short-Form Health Survey Mental Component Summary (SF-36 MCS) = 6.5 ± 9.1 SD, and Ankylosing Spondylitis Qualify of Life questionnaire (ASQoL) = -5.4 ± 5.0 SD.

5. (Currently amended) The ~~composition~~ method according to claim 4, wherein said composition is administered such that said anti-TNF antibody is administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.
6. (Currently amended) The ~~composition~~ method according to any one of claims 4-5, further comprising administering said composition with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ).
7. (Currently amended) A method for treating a TNF related condition, wherein the TNF related condition is active Ankylosing Spondylitis, the method comprising: administering a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising SEQ ID NO:36 and a light chain (LC) comprising SEQ ID NO:37 for use in the safe and effective treatment of active Ankylosing Spondylitis, wherein said anti-TNF antibody is administered via intravenous (IV) infusion, and wherein $\geq 65\%$ of patients receiving the treatment achieve Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment.
8. (Currently amended) The ~~anti-TNF antibody~~ method according to claim 7, wherein said $\geq 65\%$ of patients that achieve ASAS20 at week 16 of treatment ~~with~~ have a treatment difference (improvement compared to placebo) of $\geq 45\%$.
9. (Currently amended) The ~~anti-TNF antibody~~ method according to any one of claims 7-8, wherein said antibody is administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.

10. (Currently amended) The ~~anti-TNF antibody~~ method according to any one of claims 7-8, wherein said antibody is administered with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ).

Remarks

In the specification, a paragraph has been added to include a cross-reference to related applications. The specification has been reviewed and amended to correct errors. Claims 1-10 have been amended. Support for the amendments to the claims can be found throughout the application as originally filed. See, for example, support for claims 1-3 can be found on pages 5-6, paragraphs [21]-[24], support for claims 4-6 can be found on pages 9-10, paragraphs [31]-[34], and support for claims 7-10 can be found on pages 12-13, paragraphs [40]-[43]. No new matter is added with the amendments to the claims.

The specification has been amended because it contained embedded hyperlinks and/or other form of browser-executable code. To remove browser-executable code, throughout the specification as currently amended the embedded hyperlinks are disabled by the addition of a space after “www.”. See, e.g., page 28, paragraph [57] and page 60, paragraph [138].

The specification has been amended because it contained the use of registered trademarks that were not capitalized or accompanied by the generic terminology. In the specification as currently amended the registered trademarks are capitalized and generic terminology is included. For terms that were identified as not being registered trademarks, the ® was removed. See, e.g., pages 59-60, paragraph [138], and pages 77-78, paragraph [176].

Applicants submit herewith substituted specification as a Marked-Up Copy and a Clean Copy. No new matter is added with the amendments to the specification. Also submitted herewith is a Verified Statement Under 37 CFR §1.125(c).

The Examiner is invited to confer with the applicants' undersigned attorney.

No fees are believed due with this paper, but the Commissioner is hereby authorized to charge any deficiency or credit any overpayments necessitated by this Amendment to Deposit Account No. 10-0750.

Respectfully submitted,

/W SIMMONS /

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Dated: July 17, 2019



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/517,592	07/20/2019	Diane D. Harrison	206389-0002-01US	3778
171672	7590	07/22/2020		
Riverside Law LLP/J&J Glenhardie Corporate Center, Glenhardie Two 1285 Drummers Lane, Suite 202 Wayne, PA 19087			EXAMINER CHANDRA, GYAN	
			ART UNIT	PAPER NUMBER
			1646	
			NOTIFICATION DATE	DELIVERY MODE
			07/22/2020	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

LMorozin@ITS.JNJ.COM
dcoccia@riversidelaw.com
dockets@riversidelaw.com

Office Action Summary

Application No.

16/517,592

Applicant(s)

Harrison et al.

Examiner

GYAN CHANDRA

Art Unit

1646

AIA (FITF) Status

Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 7/20/2019.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2a) ☐ This action is **FINAL**.

2b) ☒ This action is non-final.

3) ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

4) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☒ Claim(s) 1-10 is/are pending in the application.

5a) Of the above claim(s) ____ is/are withdrawn from consideration.

6) ☐ Claim(s) ____ is/are allowed.

7) ☒ Claim(s) 1-10 is/are rejected.

8) ☐ Claim(s) ____ is/are objected to.

9) ☐ Claim(s) ____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see

http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

Application Papers

10) ☒ The specification is objected to by the Examiner.

11) ☒ The drawing(s) filed on 7/20/2019 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some** c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. ____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

3) ☐ Interview Summary (PTO-413)

Paper No(s)/Mail Date ____.

2) ☒ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b)

4) ☐ Other: ____.

Paper No(s)/Mail Date 8/8/2019 and 2/4/2020 (2).

DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Claims 1-10 are pending and under examination.

Information Disclosure Statement

The Information Disclosure Statements (IDSs) filed on 8/8/2019 and 2/4/2020 (2) have been considered.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (pg. 26-27, 58 and others of the specification). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code; references to websites should be limited to the top-level domain name without any prefix such as http:// or other browser-executable code. See MPEP § 608.01.

The disclosure is objected to because of the specification use a number of Trademarks (see- pg.58 [138], pg. 76 [176]). It should be capitalized wherever it appears and be accompanied by the generic terminology. MPEP 6.20

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is

requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

Claims 1, 4 and 7 are objected to because of the following informalities: the examiner suggests that syntax of claims 1, 4 and 7 can be improved by replacing the term “Ankylosing Spondylitis” with the term “ankylosing spondylitis” because it a rater arthritis disease. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of 35 U.S.C. 112(b):

(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention.

Claims 1, 4 and 7 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: (i) claims 1, 4, and 7 recite the term “anti-TNF antibody having a heavy chain (HC) comprising SEQ ID NO: 36, however a heavy chain of an antibody comprises a heavy chain that comprises the amino acid sequence as set forth

in SEQ ID NO: 36 (because an antibody is a polypeptide that comprises amino acids and not a SEQ ID); and (ii) claims 1, 4 and 7 recite the term “anti-TNF antibody having a light chain (LC) comprising SEQ ID NO: 37, however a light chain of an antibody comprises the amino acid sequence as set forth in SEQ ID NO: 36 (because an antibody is a polypeptide that comprises amino acids and not a SEQ ID).

Claims 2-3 are rejected for depending from a broad and indefinite claim 1.

Claims 5-6 are rejected for depending from a broad and indefinite claim 4.

Claims 8-10 rejected for depending from a broad and indefinite claim 7.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent for a claimed invention may not be obtained, notwithstanding that the claimed invention is not identically disclosed as set forth in section 102, if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 are rejected under 35 U.S.C. 103 as being unpatentable over Inman et al. (IDS, Arthritis and Rheum. 58: 3402-3412, 2008) in view of Doyle et al. (Rheumatology 52:1214-1219, 2013).

The instantly claimed invention is broadly drawn to a method for treating a TNF related condition, wherein the TNF related condition is active Ankylosing Spondylitis, the method comprising: administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising SEQ ID NO:36 and a light chain (LC) comprising SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via IV infusion, and wherein a patient treated with the composition achieves an Ankylosing Spondylitis Disease Activity Score (ASDASJ inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment, wherein said composition is administered such that said anti-TNF antibody is administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter and the method according to any one of claims 1- 2, further comprising administering said composition with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ).

Inman et al teach a method for treating ankylosing spondylitis using golimumab antibody and a pharmaceutically acceptable carrier by a subcutaneous injection. The specification discloses that golimumab comprises a light chain comprising amino acid sequence of SEQ ID NO:37 and a heavy chain comprising amino acid sequence of SEQ ID NO: 36. Regarding achieving ASDAS score after a treatment of 4 weeks, because the reference teaches treating 2 mg/kg or about 100 mg per subject (methods,

pg. 3402), the result would be the same, unless evidence to contrary. Regarding the limitation of claim 3, 6, 10, the reference teaches that patients were allowed to continue treatment with methotrexate (MTX), sulfasalazine or hydroxychloroquine (pg. 3403, left col.). They used two dosages 50 mg or 100 mgs per subject and the determined the ankylosing spondylitis using a Bath Ankylosing spondylitis disease activity index greater than equal or ≥ 4 and a week treat that improves in the assessment in AS (ASAS20) criteria at week 14 (Methods, pg. 3402). Inman et al do not teach administering golimumab by intravenous route.

Doyle et al teach that the administration of golimumab by subcutaneous as well as intravenous route (see the title). They teach that administration by intravenous route is superior to subcutaneous in reducing anti-TNF α markers (see Fig. 1), pg. 1216. They teach administering 2 mg/kg golimumab iv infusion vs. subcutaneous for 4 weeks and 12 weeks (pg. 1215, Patients and Methods).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of invention to administer the anti-TNF- α antibody golimumab as taught by Doyle et al for treating ankylosing spondylitis as taught by Inman et al. Further, one of ordinary skill of the art would have been motivated to administer golimumab by an intravenous infusion because Doyle et al teach that golimumab when administered through iv it reduces TNF- α markers better than when administered subcutaneously. One would have a reasonable expectation of success in administering golimumab intravenously because Doyle et al. teach administering golimumab intravenously. Therefore, the invention is obvious over the combined teachings of the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on Mon-Friday 8:30AM-5:00P.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vanessa Ford can be reached on 571-272-0857. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <https://ppair-my.uspto.gov/pair/PrivatePair>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GYAN CHANDRA/
Primary Examiner, Art Unit 1646

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application of:
Diane D. Harrison, et al.

Art Unit: 1646
Confirmation No.: 3778

Application No.:
16/517,592

Examiner:
Chandra, Gyan

Filing date:
July 20, 2019

Atty Docket No.:
206389-0002-01US

Title: ANTI-TNF ANTIBODIES, COMPOSITIONS, AND METHODS FOR THE
TREATMENT OF ACTIVE ANKYLOSING SPONDYLITIS

AMENDMENT

This Amendment is responsive to the non-final Office Action mailed on July 22, 2020 in connection with the above-referenced application. This Response is timely filed in view of the deadline for a timely response being to and through October 22, 2020.

No fee is believed due for filing of this response. Please charge any fee that is due, and credit any overpayment, to deposit account no. 50-5366.

In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently Amended) A method for treating a TNF related condition, wherein the TNF related condition is active ankylosing spondylitis ~~Ankylosing Spondylitis~~, the method comprising: administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via IV infusion, and wherein a patient treated with the composition achieves an Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment.
2. (Previously Presented) The method according to claim 1, wherein said composition is administered such that said anti-TNF antibody is administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.
3. (Previously Presented) The method according to any one of claims 1-2, further comprising administering said composition with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ).
4. (Currently Amended) A method for treating a TNF related condition, wherein the TNF related condition is active ankylosing spondylitis ~~Ankylosing Spondylitis~~, the method comprising: administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via IV infusion, and wherein at week 16 of treatment patients treated with the anti-TNF antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Bath Ankylosing Spondylitis

Functional Index (BASFI) = -2.4 ± 2.1 Standard Deviation (SD), Bath Ankylosing Spondylitis Metrology Index (BASMI) = -0.4 ± 0.6 SD, 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS) = 8.5 ± 7.5 SD, 36-item Short-Form Health Survey Mental Component Summary (SF-36 MCS) = 6.5 ± 9.1 SD, and Ankylosing Spondylitis Quality of Life questionnaire (ASQoL) = -5.4 ± 5.0 SD.

5. (Previously Presented) The method according to claim 4, wherein said composition is administered such that said anti-TNF antibody is administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.

6. (Previously Presented) The method according to any one of claims 4-5, further comprising administering said composition with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ).

7. (Currently Amended) A method for treating a TNF related condition, wherein the TNF related condition is active ankylosing spondylitis ~~Ankylosing Spondylitis~~, the method comprising: administering a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37, wherein said anti-TNF antibody is administered via intravenous (IV) infusion, and wherein $\geq 65\%$ of patients receiving the treatment achieve Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment.

8. (Previously Presented) The method according to claim 7, wherein said $\geq 65\%$ of patients that achieve ASAS20 at week 16 of treatment have a treatment difference (improvement compared to placebo) of $\geq 45\%$.

9. (Previously Presented) The method according to any one of claims 7-8, wherein said antibody is administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.

Response to Office Action dated July 22, 2020
U.S. Patent Application No.: 16/517,592

10. (Previously Presented) The method according to any one of claims 7-8, wherein said antibody is administered with or without methotrexate (MTX), sulfasalazine (SSZ) or hydroxychloroquine (HCQ).

REMARKS

Claims 1-10 are pending and under consideration.

Claim Amendments

Claims 1, 4 and 7 have been amended to recite “ankylosing spondylitis” and that the anti-TNF antibody has a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37. Support for this amendment can be found throughout the originally filed Specification. No new matter has been added by way of these amendments.

Objection to the Specification

The Examiner has objected to the Specification for inclusion of hyperlinks and trademarks.

Applicants submit that the Specification was amended to remove browser-executable code and to properly recite registered trademarks with generic terminology in the Preliminary Amendment and Substitute Specification filed on July 20, 2019.

Applicants respectfully request reconsideration and withdrawal of the objection.

Claim Objections

The Examiner has objected to claims 1, 4 and 7 and has suggested that the term “Ankylosing Spondylitis” be replaced with “ankylosing spondylitis.” While not necessarily agreeing with the Examiner, claims 1, 4 and 7 have been amended to recite “ankylosing spondylitis.” Applicants respectfully request reconsideration and withdrawal of the objection.

Rejection of claims 1-10 under 35 U.S.C. 112(b)

The Examiner has rejected claims 1-10 as allegedly being indefinite. Specifically, the Examiner contends that the claims are indefinite because claims 1, 4, and 7 recite a heavy chain comprising SEQ ID NO: 36 and a light chain comprising SEQ ID NO: 37, which allegedly omits essential structural elements.

While not necessarily agreeing with the Examiner, but rather in a good faith effort to advance prosecution, claims 1, 4 and 7 have been amended to recite a heavy chain comprising the amino acid sequence set forth in SEQ ID NO:36; and a light chain comprising the amino acid sequence set forth in SEQ ID NO:37.

Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejection of claims 1-10 under 35 U.S.C. 103

The Examiner has rejected claims 1-10 under 35 U.S.C. 103 as allegedly being unpatentable over Inman et al. (2008, Arthritis and Rheum, 58: 3402-3412; hereinafter “Inman”) in view of Doyle et al. (2013, Rheumatology, 52: 1214-1219; hereinafter “Doyle”). The Examiner contends that Inman teaches a method for treating ankylosing spondylitis using golimumab by subcutaneous injection. The Examiner admits that Inman does not teach administering golimumab by intravenous route. However, the Examiner contends that Doyle teaches administration of golimumab by subcutaneous and intravenous routes. The Examiner contends that it would have been obvious for a skilled artisan to administer golimumab as taught by Doyle for treating ankylosing spondylitis as taught by Inman.

According to the U.S. Supreme Court ruling in *Graham v. John Deere*, 383 U.S. 1 (1960), in making a case for obviousness, the Examiner must 1) determine the scope and content of the prior art; 2) ascertain the differences between the prior art and the claims at issue; 3) resolve the level of ordinary skill in the pertinent art; and 4) evaluate evidence of secondary considerations. These principles have been reconfirmed by the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007).

In *KSR Int’l Co.*, the US Supreme Court restated the requirements for a finding of obviousness. Encouraging the application of common knowledge and common sense, the Court took care to guard against hindsight bias and *ex post* reasoning and to distinguish the predictable from the unpredictable arts (“If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability.” [Emphasis added]). Based on the combination of references set forth by the Examiner, Applicants assert that the rejection of the claims under §103 could only have been made with hindsight bias and *ex post* reasoning.

When applying 35 U.S.C. § 103, the following tenets of patent law must be followed: 1) the claimed invention must be considered as a whole; 2) the references must be considered as a whole; 3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and 4) reasonable expectation of success is the standard with which obviousness is determined (MPEP § 2141 II).

Cited art does not teach or suggest each and every element

Establishing a prima facie case of obviousness of a claimed invention “requires a suggestion of all limitations in a claim” in the prior art. 35 U.S.C. § 103(a); CFMT, Inc. v. Yieldup Intern. Corp., 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing In re Royka, 490 F.2d 981, 985 (CCPA 1974); see also In re Ochiai, 71 F.3d 1565, 1572 (Fed. Cir. 1995). Therefore, in order to render the instant claims obvious under 35 U.S.C. §103(a), the cited prior art must teach or suggest each and every element of the claims.

Applicants submit that Inman and Doyle, alone or in combination with each other, do not teach or suggest administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via IV infusion, as recited in claim 1 (from which claims 2 and 3 depend), claim 4 (from which claims 5 and 6 depend), and claim 7 (from which claims 8-10 depend). Applicants submit that Inman does not teach IV infusion of golimumab for treating ankylosing spondylitis. Further, Applicants submit that Doyle does not make up for the deficiency of Inman, because Doyle does not teach IV infusion of golimumab for treating ankylosing spondylitis.

Claim 1

Applicants submit that Inman and Doyle, alone or in combination with each other, do not teach or suggest administering a safe and effective amount of a composition comprising the recited anti-TNF antibody, wherein said composition is administered via IV infusion such that a patient treated with the composition achieves an Ankylosing Spondylitis Disease

Activity Score (ASDAS) inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment, as recited in claim 1. The Examiner indicates that because Inman teaches administering 2mg/kg or about 100mg per subject, the result would be the same. Applicants submit that subcutaneous administration of 100mg golimumab per subject would not necessarily result in the subject achieving an ASDAS inactive disease (<1.3) at 4 weeks or 2 weeks of treatment. That is, a different route of administration, as taught by Inman, would not necessarily result in an ASDAS inactive disease (<1.3) at 4 weeks or 2 weeks of treatment achieved by IV infusion as presently claimed. Applicants submit that Doyle does not make up for the deficiencies of Inman, because Doyle does not teach or suggest a patient treated with IV infusion of golimumab achieves an ASDAS inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment.

Claim 4

Applicants submit that Inman and Doyle, alone or in combination with each other, do not teach or suggest administering a safe and effective amount of a composition comprising the recited anti-TNF antibody, wherein said composition is administered via IV infusion such that at week 16 of treatment patients treated with the anti-TNF antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Bath Ankylosing Spondylitis Functional Index (BASFI) = -2.4 ± 2.1 Standard Deviation (SD), Bath Ankylosing Spondylitis Metrology Index (BASMI) = -0.4 ± 0.6 SD, 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS) = 8.5 ± 7.5 SD, 36-item Short-Form Health Survey Mental Component Summary (SF-36 MCS) = 6.5 ± 9.1 SD, and Ankylosing Spondylitis Qualify of Life questionnaire (ASQoL) = -5.4 ± 5.0 SD, as recited in claim 4. For example, Applicants submit that Inman reports the clinical efficacy of subcutaneous golimumab at 14 and 24 weeks, using the criteria of BASFI, BASMI, SF 36PCS and SF MCS (see Table 2 of Inman), where the change from baseline of each of these criteria at 14 and 24 weeks post-subcutaneous golimumab, as reported by Inman, is less than the claimed change from baseline at week 16 post-IV golimumab. Applicants submit that Doyle does not make up for the deficiencies of Inman, because Doyle does not teach or

suggest that at week 16 patients treated with the anti-TNF antibody would achieve a mean change from baseline in any of the recited criteria.

Claim 7

Applicants submit that Inman and Doyle, alone or in combination with each other, do not teach or suggest administering a safe and effective amount of the recited anti-TNF antibody, wherein said anti-TNF antibody is administered via IV infusion that $\geq 65\%$ of patients receiving the treatment achieve Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment., as recited in claim 7. For example, Applicants submit that Inman reports the clinical efficacy of subcutaneous golimumab at 14 and 24 weeks, and reports that 60% of subjects achieve ASAS20 at 14 weeks post-subcutaneous golimumab (see page 3405 of Inman) and a similar proportion achieves ASAS20 at 24 weeks post-subcutaneous golimumab (see page 3407 of Inman). Applicants submit that Doyle does not make up for the deficiencies of Inman, because Doyle does not teach or suggest that $\geq 65\%$ of patients receiving the treatment achieve ASAS20 at week 16 of treatment.

Claims 2, 5 and 8

Regarding claims 2, 5 and 8, Applicants submit that Inman and Doyle, alone or in combination with each other, do not teach or suggest a dosing comprising golimumab being administered at a dose of 2 mg/kg, administered over 30 ± 10 minutes, at Weeks 0 and 4, and then every 8 weeks (q8w) thereafter.

Cited art does not provide a reasonable expectation of success

Further, to establish a prima facie case of obviousness, a reference or combination of references must: (1) suggest to those of ordinary skill in the art that they should make the claimed invention, and (2) reveal to those of ordinary skill in the art that they would have a reasonable expectation of success. In re Vaack, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Both the suggestion and the reasonable expectation of success must be found in the prior art and not in the Applicant's disclosure. In re Dow Chemical Company, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). However, there is nothing in any of the cited references that would motivate

one of ordinary skill in the art to combine the teachings of these references to produce the presently claimed invention.

“Reasonable expectation of success” is premised on predictability. In other words, to have a reasonable expectation of success, the ordinarily skilled artisan must be able to predict the likely outcome for an experiment. A direct corollary of this fact is that if one cannot predict the likely outcome for an experiment, one cannot have a reasonable expectation of success in achieving a given outcome. Indeed, the USPTO clearly recognizes the relationship between predictability and reasonable expectation of success. Specifically, MPEP 2143E articulates how to determine if a claim can be rejected on an “obvious-to-try” rationale using the following language:

Office personnel must articulate the following:

- (1) a finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;
- (2) a finding that there had been a finite number of identified, **predictable potential solutions** to the recognized need or problem;
- (3) a finding that one of ordinary skill in the art could have pursued the known potential solutions with **a reasonable expectation of success**; and
- (4) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. (emphasis added)

Thus, it is the ability to predict the outcome of a solution that underlies a reasonable expectation of success for pursuing that solution.

Applicants submit that Inman and Doyle do not prove a reasonable expectation of success at arriving at a method for treating ankylosing spondylitis by administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via IV infusion.

Claim 1

The present invention is based, in part, upon the surprising discovery that IV infusion of golimumab is an effective therapy for ankylosing spondylitis, which can show efficiency as quick as 2 to 4 weeks after treatment. Applicants submit that Inman describes subcutaneous delivery of golimumab. Nothing in Inman provides a skilled artisan with any predictability that golimumab can be delivered by IV infusion to treat ankylosing spondylitis, much less that a patient who is administered golimumab by IV infusion would achieve ASDAS inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment, as recited in claim 1.

Applicants submit that Doyle does not cure any of the deficiencies of Inman. Doyle describes the effect of subcutaneous and intravenous golimumab on inflammatory biomarkers. However, Applicants submit that Doyle does not provide a skilled artisan with any predictability that intravenous golimumab can be used to treat ankylosing spondylitis, much less that a patient who is administered intravenous golimumab would achieve ASDAS inactive disease (<1.3) at 4 weeks of treatment or 2 weeks of treatment. First, Applicants submit that Doyle does not describe the effects of IV golimumab on a subject with ankylosing spondylitis. Second, Doyle does not describe any clinical improvement from IV golimumab on any subject, let alone a subject with ankylosing spondylitis. Third, Doyle describes that inflammatory biomarkers began to increase in subjects where golimumab was administered intravenously. Finally, Doyle describes the limitations of its study – small sample size that is not optimal for assessing pharmacodynamic effects (see Doyle, page 1217; paragraph spanning the 1st and 2nd columns). Applicants submit that skilled artisan reading Doyle would not have any reasonable expectation that administration of IV golimumab could be used to effectively treat ankylosing spondylitis.

Claim 4

Nothing in Inman provides a skilled artisan with any predictability that golimumab can be delivered by IV infusion to treat ankylosing spondylitis, much less that at week 16 of treatment patients treated with the anti-TNF antibody achieve a mean change from baseline in one or more criteria selected from the group consisting of: Bath Ankylosing Spondylitis

Functional Index (BASFI) = -2.4 ± 2.1 Standard Deviation (SD), Bath Ankylosing Spondylitis Metrology Index (BASMI) = -0.4 ± 0.6 SD, 36-item Short-Form Health Survey Physical Component Summary (SF-36 PCS) = 8.5 ± 7.5 SD, 36-item Short-Form Health Survey Mental Component Summary (SF-36 MCS) = 6.5 ± 9.1 SD, and Ankylosing Spondylitis Quality of Life questionnaire (ASQoL) = -5.4 ± 5.0 SD, as recited in claim 4. As described above, Inman reports changes from baseline of such criteria at 14 and 24 weeks post-subcutaneous golimumab, which are less than the claimed changes from baseline at week 16 as recited in claim 4. Applicants submit that a skilled artisan would not have any reasonable expectation from Inman that at week 16 of treatment patients receiving IV golimumab would achieve a mean change from baseline in any of the recited criteria.

Claim 7

Nothing in Inman provides a skilled artisan with any predictability that golimumab can be delivered by IV infusion to treat ankylosing spondylitis, much less that $\geq 65\%$ of patients receiving the treatment achieve Assessment in Ankylosing Spondylitis 20 (ASAS20) at week 16 of treatment, as recited in claim 7. As described above, Inman reports that about $\sim 60\%$ of patients achieve ASAS20 at 14 weeks post-subcutaneous golimumab with a similar proportion of patients achieving ASAS20 at 24 weeks post-subcutaneous golimumab. Given the data of Inman, Applicants submit that a skilled artisan would not reasonably expect that greater than 65% of patients receiving IV golimumab would achieve ASAS20 at week 16.

Secondary Considerations

Importantly, “secondary considerations” may include evidence of commercial success, long-felt but unsolved needs, failure of others, and unexpected results. Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. Rebuttal evidence may also include evidence that the claimed invention yields unexpectedly improved properties or properties not present in the prior art. See MPEP § 2145.

In *Crocs, Inc. v. U.S. Int’l Trade Commission*, 598 F.3d 1294 (Fed. Cir. 2010), the Federal Circuit reaffirmed the requirements for a finding of non-obviousness in view of

“unexpected results.” Rejecting the proposition that a combination of prior art elements is per se obvious, the Federal Circuit held that a claimed combination of prior art elements is non-obvious when the combination yields “more than predictable results.” In *Crocs*, testimony on record indicated that the combined elements in the shoe reduced wearer discomfort in ways that were not suggested or contemplated by the prior art. The Federal Circuit pointed out that this combination “yielded more than predictable results” and was thus patentable. *Id.* at 1310. This ruling affirmed prior holdings that inventions that have new and unexpected properties are patentable (*In re Papesch*, 315 F.2d. 381, 387 (C.C.P.A. 1963)). The determination that the result is “unexpected” depends upon what a person of ordinary skill in the art would have predicted based upon the prior art (*Procter & Gamble Co. v. Teva Pharms. USA, Inc.*, 566 F.3d 989, 997-98 (Fed. Cir. 2009); *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1367 (Fed. Cir. 2007)). Consistently, under MPEP § 2143 A(3), merely pointing to the presence of all claim elements in the prior art is not a complete statement of a rejection for obviousness. In accordance with MPEP § 2143 A(3), a rejection based on the rationale that the claimed invention is a combination of prior art elements is improper if it does not include a finding that results flowing from the combination would have been predictable to a person of ordinary skill in the art. MPEP § 2143 A(3). If results from the invention would not have been predictable, an obviousness rejection using the combination of prior art elements rationale is improper.

Applicants submit that the presently claimed methods of administering a composition comprising a safe and effective amount of at least one isolated mammalian anti-TNF antibody having a heavy chain (HC) comprising the amino acid sequence set forth in SEQ ID NO:36 and a light chain (LC) comprising the amino acid sequence set forth in SEQ ID NO:37, and at least one pharmaceutically acceptable carrier or diluent, wherein said composition is administered via IV infusion, produces surprising and unexpected results that could not have been predicted by the combination of Inman and Doyle.

Smolen et al., *Ann Rheum Dis* 2014; 73:6–16 (hereinafter “Smolen”; and provided herein as Exhibit A), is a publication of recommendations of an international task force related to treatment targets for spondyloarthritis, including ankylosing spondylitis. See, for example, Smolen, page 9, 2nd column, 2nd to last paragraph, where it states, “Common

recommendations 1. A major treatment target should be clinical remission/inactive disease...”. Also, note that in the preceding paragraph, page 9, 1st column, last paragraph, the authors in Smolen indicated that the sequence of the recommendations reflects the level of importance considered by the committee for each individual bullet point. It follows, therefore, that the number 1 recommendation related to the treatment target of remission/inactive disease was considered the most important consideration of the international task force. It is demonstrated herein that IV golimumab surprisingly was able to induce inactive disease, the most important metric of ankylosing spondylitis treatment efficacy, in only 2 weeks after treatment.

As described in the present application, intravenous administration of golimumab resulted in inactive disease, as measured by ASDAS score of < 1.3 , as early as 4 weeks and 2 weeks after treatment. As noted above, none of the cited references teach or suggest that an ASDAS inactive disease score could be achieved in such a short time, after only 4 weeks or 2 weeks of IV golimumab treatment. Thus, the teaching of Inman and Doyle, alone or in combination, could not have led a skilled artisan to expect such surprising and unpredictable results.

Achieving an ASDAS inactive disease score (i.e. < 1.3) after only 2 weeks or 4 weeks of IV golimumab treatment is a very surprising and unpredictable result that would not be obvious to a person skilled in the art. For example, Van der heijde et al. J Rheumatol, 2014, 41(6): 1095-103 (hereinafter “Van der heijde”; and provided herein as Exhibit B) describes the 2-year results of a clinical trial of subcutaneous golimumab treatment and only reports proportion of patients with ADAS inactive score (< 1.3) at week 14 and week 24 after subcutaneous injections of golimumab. Applicants submit that a skilled artisan, at the time of filing, could not have reasonably predicted or expected the surprising and unexpected results demonstrated herein, that patients could achieve an ASDAS inactive disease score (< 1.3) in such a short time, after only 4 weeks or 2 weeks of IV golimumab treatment.

Similarly, Applicants submit that the application demonstrates that IV golimumab exhibited surprising and unexpected results in showing improved efficacy, as measured by the change from baseline in the criteria listed in claim 4 and by the proportion of subjects achieving ASAS20. Each of the clinical measures at 16 weeks post-IV golimumab was

surprisingly and unexpectedly improved over the same clinical measures at 14 and 24 weeks post-subcutaneous golimumab as reported by Inman. Applicants submit that such improved clinical efficacy of IV golimumab demonstrated by the present application would not be expected by a skilled artisan reading Inman and Doyle.

For at least these reasons, Applicants submit that claims 1-10 are not rendered obvious by the combination of Inman and Doyle. Applicants respectfully request reconsideration and withdrawal of the rejection.

Response to Office Action dated July 22, 2020
U.S. Patent Application No.: 16/517,592

Summary

Early consideration and allowance of the claims in the present application is requested at the earliest possible time.

Respectfully submitted,

Diane D. Harrison, ET AL.

October 21, 2020

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NOTICE OF ALLOWANCE AND FEE(S) DUE

171672 7590 01/25/2021
Riverside Law LLP/J&J
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1285 Drummers Lane, Suite 202
Wayne, PA 19087

EXAMINER

CHANDRA, GYAN

ART UNIT

PAPER NUMBER

1646

DATE MAILED: 01/25/2021

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/517,592	07/20/2019	Diane D. Harrison	206389-0002-01US	3778

TITLE OF INVENTION: ANTI-TNF ANTIBODIES, COMPOSITIONS, AND METHODS FOR THE TREATMENT OF ACTIVE ANKYLOSING SPONDYLITIS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	04/26/2021

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 1/2 the amount of undiscounted fees, and micro entity fees are 1/2 the amount of small entity fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

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IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

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Complete and send this form, together with applicable fee(s), by mail or fax, or via EFS-Web.

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CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

171672 7590 01/25/2021
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Glenhardie Corporate Center, Glenhardie Two
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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

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I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via EFS-Web or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/517,592	07/20/2019	Diane D. Harrison	206389-0002-01US	3778

TITLE OF INVENTION: ANTI-TNF ANTIBODIES, COMPOSITIONS, AND METHODS FOR THE TREATMENT OF ACTIVE ANKYLOSING SPONDYLITIS

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	UNDISCOUNTED	\$1200	\$0.00	\$0.00	\$1200	04/26/2021

EXAMINER	ART UNIT	CLASS-SUBCLASS
CHANDRA, GYAN	1646	424-142100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-09 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required) ☐ Advance Order - # of Copies _____

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☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. **Change in Entity Status** (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment. **NOTE:** If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/517,592	07/20/2019	Diane D. Harrison	206389-0002-01US	3778
171672	7590	01/25/2021	EXAMINER	
Riverside Law LLP/J&J			CHANDRA, GYAN	
Glenhardie Corporate Center, Glenhardie Two			ART UNIT	
1285 Drummers Lane, Suite 202			PAPER NUMBER	
Wayne, PA 19087			1646	

DATE MAILED: 01/25/2021

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b) (2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether disclosure of these records is required by the Freedom of Information Act.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspection or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

Notice of Allowability	Application No. 16/517,592	Applicant(s) Harrison et al.	
	Examiner GYAN CHANDRA	Art Unit 1646	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 10/21/2020.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are 1-10. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☐ All b) ☐ Some *c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.

☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892) 2. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date <u>10/23/2020</u> . 3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material _____. 4. ☒ Interview Summary (PTO-413), Paper No./Mail Date. <u>1/8/2020</u> .	5. ☒ Examiner's Amendment/Comment 6. ☐ Examiner's Statement of Reasons for Allowance 7. ☐ Other _____.
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/ GYAN CHANDRA/ Primary Examiner, Art Unit 1646	
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DETAILED ACTION

Notice of Pre-AIA or AIA Status

The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Applicant's response filed on 10/21/2020 is acknowledged and fully considered.

Status of Application, Amendments, And/Or Claims

The amendments of claims 1, 4 and 7 have been made of record.

Claims 1-10 are pending and under examination.

Information Disclosure Statement

The Information Disclosure Statement filed on 10/23/2020 has been considered.

EXAMINER'S COMMENT

Claim Rejections - 35 USC § 112-withdrawn

The rejection of claims 1-10 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor, or for pre-AIA the applicant regards as the invention is withdrawn in view of applicants' amendments to claims 1, 4 and 7 by inserting the term "the amino acid sequence set forth in" before SEQ ID NO: 36 and 37.

Claim Rejections - 35 USC § 103-withdrawn

The rejection of claims 1-10 under 35 U.S.C. 103 as being unpatentable over Inman et al. (IDS, Arthritis and Rheum. 58: 3402-3412, 2008) in view of Doyle et al. (Rheumatology 52:1214-1219, 2013) is withdrawn in view of applicants' arguments of surprising result that the combination of references Inaman and Doyle would be obvious

to administer a mammalian antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO: 36 and a light chain comprising the amino acid sequence of SEQ ID NO: 37, however, the combination of references would not have predicted a surprising results in treating ankylosing spondylitis in a subject in need thereof to achieve an ASDAS inactive disease (<1.3) at 4 weeks or at 2 weeks. The instantly claimed invention requires that the administration of the composition achieves an ASDAS inactive disease (<1.3) at 4 weeks of treatment or at 2 weeks of treatment, and applicants cite the reference Van der Heijde et al (Exhibit B, J. Rheumatology 41: 1095-1103, 2014). The reference Van der Heijde et al, or the references applied towards instant rejection (Inman et al. in view of Doyle et al) do not suggest if the ASDAS inactive disease can be achieved after 2 or 4 weeks of treatment. Therefore, the rejection is withdrawn.

Conclusion

Claims 1-10 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on Mon-Friday 8:30AM-5:00P.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vanessa Ford can be reached on 571-272-0857. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <https://ppair-my.uspto.gov/pair/PrivatePair>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/GYAN CHANDRA/
Primary Examiner, Art Unit 1646

<i>Examiner-Initiated Interview Summary</i>	Application No. 16/517,592	Applicant(s) Harrison et al.		
	Examiner GYAN CHANDRA	Art Unit 1646	AIA (First Inventor to File) Status Yes	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
GYAN CHANDRA	Primary Examiner	Telephonic
PALLAB SINGH	Attorney of Record	

Date of Interview: 08 January 2021

Issues Discussed:

35 U.S.C. 103

Applicant's attorney argued in response filed on 10/21/2020 that the instant invention of administering the antibody comprising a heavy chain comprising the amino acid sequence of SEQ ID NO:36 and a light chain comprising the amino acid sequence of SEQ ID NO: 37 to a person in need thereof by intravenous injection and achieves at 2 weeks or 4 weeks time point, however, the administration of the same antibody by subcutaneous injection achieves a response at week 14 or 24 weeks and cites the reference Van der heijde (Exhibit B) in support. The examiner discussed the reference with applicant's attorney and found to be persuasive.

/GYAN CHANDRA/ Primary Examiner, Art Unit 1646	
Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04 Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing	

Applicant recordation instructions: It is not necessary for applicant to provide a separate record of the substance of interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.