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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/765,515	04/03/2018	Philip E. Brandish	23597-US-PCT	3652
210 MERCK P O BOX 2000 RAHWAY, NJ 07065-0907	7590 07/29/2021		EXAMINER DUFFY, PATRICIA ANN	
			ART UNIT 1645	PAPER NUMBER
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**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):

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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.

**RESPONSE TO AMENDMENT**

The amendment filed 4-8-2021 has been entered into the record. Claims 5-16, 22-50 and 52-65 have been cancelled. Claims 1-4, 17-21, 51 and 66-75 are pending. Claims 1-4, 51, 66 and 68-75 are under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

**Election/Restrictions**

This application contains claims 17-21 and 67 drawn to an invention nonelected without traverse. These claims remain withdrawn from consideration.

**Rejections Withdrawn**

Any objection/rejection not maintained herein is withdrawn based upon the amendment to the claims.

**New Rejections Based on Amendment**

**Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

(a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 66 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The independent claim has been amended to remove the functional property that the conjugate binds CD74. The anti-inflammatory agent is disclosed as specifically delivering the drug to cells expressing CD74 and upregulating genes corresponding to the effects of glucocorticoid agonists. In the absence of binding CD74, the conjugated anti-inflammatory agent has no demonstrated pharmaceutical activity.

The art teaches that anti-inflammatory agents and glucocorticoid receptor agonists in particular bind to the glucocorticoid receptor which is a family of *intracellular receptors* (Timmermans et al, *Frontiers in Immunology*, 10:1545, pages 1-17, 2019; page 1 second full paragraph). Due to their lipophilic nature, free glucocorticoids diffuse through the cell membrane to exert their function (page 2, column 2, third paragraph and paragraph bridging pages 2-3). Other anti-inflammatory agents such as non-steroidal anti-inflammatory agents (NSAIDs) also act in the intracellular environment as the cyclooxygenase enzyme inhibitors. The claimed conjugates would not be expected to diffuse through a cell membrane in order for the agonist to bind the receptor or enzyme to exert the known biological effects of these anti-inflammatory agents. The specification does not demonstrate that the conjugate freely diffused through the plasma membrane of cells and as such, in the absence of further guidance from Applicants, the skilled artisan would not know how to use a conjugate that does not bind CD74. The art fails to teach diffusion across the plasma membrane for these large conjugates and rely upon mechanisms such as endocytosis, pinocytosis and receptor/protein internalization/recycling to deliver the drug intracellularly. In the absence of a specific delivery the specification disclose no mechanism to deliver the anti-inflammatory agent to a cell and the art suggests none.

For the foregoing reasons, the claims are not enabled for a use.

#### ***Status of Claims***

Claims 1-4 and 66 stand rejected. Claims 51 and 68-75 are allowable. Claims 17-21 and 67 remain withdrawn from consideration.

### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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 <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on 7:30 am - 4:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor Gary Nickol can be reached at 571-272-0835.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Patricia Duffy/

Primary Examiner, Art Unit 1645