

**BEFORE CONTROLLER OF PATENTS THE PATENT OFFICE, NEW DELHI
THE PATENTS ACT, 1970 (AS AMENDED)
SECTION 15
IN THE MATTER OF AN APPLICATION FOR PATENT,**

APPLICATION NO: 7124/CHENP/2010

Hearing date scheduled on 15th July 2019

DECISION

Applicant's name & address	IMMUNOGEN INC., 830 Winter Street, Waltham, MA 02451, United States of America.
Date of filing	03/11/2010
Title of invention	" CROSS-LINKERS AND THEIR USES "
Publication date (u/s 11a)	05/08/2011
Request for examination date	30/12/2010, 9819/RQ-CHE/2010
PCT international application number	PCT/US2009/042267
Priority date and country	U.S.A. 61/049,291 30 Apr 2008 U.S.A. 61/147,966 28 Jan 2009
PCT international filing date	WO/2009/134977
First examination report date (FER)	01/02/2017
Reply to FER date	24/07/2017

Important activities in relation to representation by way of opposition to grant of the patent u/s 25(1) of the Act

1st February 2017	Notice issued by the Controller on the pre-grant opposition filed by the Indian Pharmaceutical Alliance, represented by Nayan Rawal & Associates
29th April 2017	Reply Statement was filed along with amended claims
29th April 2017:	Claims were amended and filed in the prescribed Form 13.
(a)	Claims 11, 29, 30, 37, 38, 43 to 45 have been deleted;
(b)	Claims 22 have been merged with claim 21;
(c)	Claims 23, 34 & 40 have been revised.
24th July 2017:	Response to the First Examination Report (FER) was filed by the Applicant
8th July 2019:	Opponent withdrawn the representation in view of the amended claims
15th July 2019:	Hearing in pre-grant opposition u/s 25(1) was conducted
1st August 2019:	Claims were further amended in pursuant to the hearing attended on 15th July 2019
8th August 2019:	Written submission filed by the Applicant.

With reference to the request for examination no., in the instant application for examination of application and Grant of Patent, Examination has been conducted under Section 12 and 13 of the Patents Act 1970, and certain objections were communicated to applicant in the First Examination report on dated as mentioned above.

In response to FER the authorized registered patent agent under section 125 of Patents Act 1970, Rule 108 of the Patents Rules 2003, replied on the objections communicated to them with amended set of claims, however, the reply and amended documents are not found as per requirement of Act. Certain other requirements were also found not met hence applicant has provided an opportunity of being heard u/s 14 of the act and following objections were communicated with hearing letter to the applicant at agent's address for Service.

Objections which are communicated to applicant u/s 14 of the act and

The subject matter of amended Claims prima facie appears to be not inventive over the cited document u/s 2(1) (j) (a) D1: US 3420876 A D2: LEER J ET AL: "DELIVERY OF LIPOSOMES INTO CULTURED KB CELLS VIA FOLATE RECEPTOR-MEDIATED ENDOCYTOSIS", JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, INC, BETHESDA, MD, USA, vol. 269, no. 5, 4 February 1994 (1994-02-04), pages 3198-3204, XP009059971, ISSN: 1 083-351 X D3: MARTIN L ET AL: "Beta-amino-thiols inhibit the zinc metallopeptidase activity of tetanus toxin light chain", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 41, no. 18, 27 August 1998 (1998-08-27), pages 3450-3460, XP002092584, ISSN: 0022-2623, DOI: 10.1021/JM981015Z D1 discloses a compound which relevant compound II of present application further, e.g. glutamic acid would be regarded to be anticipating (Y and R being CO₂H; Q being amino). D2 discloses activate folate (D2, figure 1, "NHS-folate"), in which the folate's glutamic acid may be regarded to be a linker with R=CO₂. Additional D3 (Table 2, compound 37) discloses compound according to the formula of claim 1. In view the documents D1-D2 claim 1-46 lacks inventive step.

Grounds of opposition filed by Mr. Nayan Rawal & Associates on behalf of Indian Pharmaceutical Alliance, represented

- a. **Wrongfully obtaining**
- b. *that the invention so far as claimed in any claim of complete specification has been published before the priority date of the claim-*
- c. *invention so far as claimed in any claim of the complete specification is claimed in a claim of a complete specification published on or after the priority date of the applicant's claim and filed in pursuance of an application for a patent in India, being a claim of which the priority date is earlier than that of the applicant's claim;*
- d. *publicly known or publicly used in India*
- e. *is obvious and clearly does not involve any inventive step*
- f. *subject matter of any claim of the complete specification is not invention*
- g. *information required by section 8*

On dated 08/08/2019, Applicant has filed Combined Written submission to the hearing on the Pre-Grant Opposition under Section 25(1) and Hearing under Section 14 in respect of Indian Patent Application No. 7124/CHENP/2010

The authorized Patent Attorney on behalf of applicant filed detailed submission with respect to various aspects of the invention of instant application. In hearing for section 25(1) and section 14 of the Patents Act, Ld Attorney Dr Archana Sanker and her associate Mr Devinder Rawat were present and represented the case on the objections raised u/s 14 and u/s 25(1) in representation by way of opposition to grant of the patent of instant application.

The main features of the invention of instant application figured out by applicant as under,

ADVANTAGE Further, the Applicant at the hearing, in the written submissions as well as through the affidavit of the inventor clearly demonstrates the advantages of the present invention as being: i. greater water solubility of the final product, ii. ability to operate at a higher concentration in aqueous solutions, iii. ability to link a greater number of drug molecules per molecule of cell-binding agent, resulting in higher potency, iv. potential for the charged conjugate species to be retained inside the target cell, resulting in higher potency, and v. improved sensitivity of multidrug resistant cells, which would be unable to export the charged drug species from the cell.

UNEXPECTED & SURPRISING EFFECT

Also, the unexpected and surprising effects of the claimed linkers lead to increased drug loading, enhanced conjugate potency against tumor cells and enhanced in vivo anti-tumor activity. This is a significant technical contribution to the art. Thus, in terms of the problem and solution approach, the present invention provides a solution to the technical problem of how to provide linkers that improve the potency of immune-conjugates. It is therefore clear from the evidence detailed above that the claimed cross linkers and conjugates increase drug loading, enhance conjugate potency against tumor cells and enhance in vivo anti-tumor activity.

Ld. Attorney to the applicant, further illustrated the differences of the technical features over cited prior art with respect to novelty and non-obviousness.

The applicant has filed affidavit of Dr. Ravi V.J. Chari wherein he maintained "Moreover, the data described in the instant application and Annex B and C submitted herewith show that the charged or pro-charged cross linkers of the present invention leads to several unexpected advantages of the resulting immune-conjugates, such as increased drug loading, enhanced conjugate potency against tumor cells, particularly against multidrug resistant tumor cells, and enhanced in vivo anti-tumor activity. These advantages would not have been expected or predicated based on the teachings of the documents cited by the Opponent."

Applicant has filed new set of amended claims 1-35 with following subject matter,
A cell-binding agent-drug conjugates of formula (II) (claim 1-20)
A cross linker represented by formula (I)(claim 21-28)
A compound of formula (III): (claim 29-31)
A compound of formula (IV) (claim 32-34)
A pharmaceutical composition(claim 35)

On dated 09/07/2019, Mr Nayan Rawal on behalf of opponent (Indian Pharmaceutical Alliance) filed written submission wherein it is mentioned specifically that " since the applicant has amended the claims the opponent wish to submit that the opponent do not have any objection to the amended claims and controller can decide on these claims on the merit"

In view of statement filed by opponent, the subject matter of the amended set of claims 1-35 filed on dated 08/08/2019 considered as unopposed by opponent on the grounds as stated above and disposed of. The subject matter of claims 1-35 consists of A cell-binding agent-drug conjugate of formula (II) (claim 1-20) A cross linker represented by formula (I)(claim 21-28) A compound of formula (III): (claim 29-31) A compound of formula (IV) (claim 32-34), A pharmaceutical composition(claim 35) having technical features of the invention which are non-obvious to person skilled in art because the cited prior arts discloses subject matter of invention different from that of instant invention in terms of technical advance as compared to the existing knowledge.

The submission was found to be satisfactory and convincing, therefore accepted. The amendments as carried out fall within the scope of the specification and no new matter has been added. Having considered all the circumstances, submission made by the agent for the applicant during the hearing including all the documents on record and also in view of my above findings, I, hereby proceed for grant of Patent, in relation to subject matter of instant application.

Dated 03/03/2022

Dr. A P Singh
Assistant Controller of Patents & Designs