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* **IN THE HIGH COURT OF DELHI AT NEW DELHI**

\+ CS(COMM) 376/2024 & I.A. 10533/2024

E. R. SQUIBB AND SONS, LLC & ORS. .....Plaintiffs

Through: Mr. Sandeep Sethi, Sr. Advocate, Mr. P.S. Raman, Sr. Advocate, Mr. Amit Sibal, Sr. Advocate with Mr. Pravin Anand, Ms. Archana Shanker, Ms. Prachi Agarwal, Mr. Devinder Rawat, Ms. Elisha Sinha and Mr. Manan Mondal, Advocates

versus

ZYDUS LIFESCIENCES LIMITED .....Defendant

Through: Mr. Harish Salve, Sr. Advocate, Mr. Dushyant Dave, Sr. Advocate, Mr. Rajiv Nayar, Sr. Advocate, Mr. Dayan Krishnan, Sr. Advocate with Mr. Adarsh Ramanujan, Ms. Bitika Sharma, Ms. Vrinda Pathak, Ms. Sandhya Kukreti, Mr. Rajnish Kumar, Ms. S.L. Soujanya, Mr. Parth Singh and Mr. Manjunathan P.S., Advocates

CORAM:
HON'BLE MS. JUSTICE MINI PUSHKARNA

JUDGMENT

% 18.07.2025

MINI PUSHKARNA, J:

I.A. 10533/2024 (Application under Order XXXIX Rules 1 and 2, read with Section 151 of the Code of Civil Procedure, 1908 for injunction)

Introduction:

1. By way of the present judgment, this Court shall decide the

application of the plaintiffs for injunction, being *I.A. 10533/2024*.

2. The present suit has been filed seeking permanent injunction for restraining infringement of *Indian Patent No. IN 340060* ("IN '060"), which is titled as, *"Human Monoclonal Antibodies to Programmed Death 1 (PD-1) for use in treating Cancer"* ("suit patent"). The suit patent is registered in the name of the plaintiffs and is currently valid and subsisting.

3. The suit patent covers and claims a monoclonal antibody, also known as 'Nivolumab' or '5C4', in the complete specification of IN '060. Nivolumab is a therapeutic antibody used in the treatment of various forms of cancer. PD-1 is a protein found on T-cells, which are a type of immune cell, that help to keep the body's immune responses in check. Monoclonal antibodies are laboratory-produced engineered bio-molecules that can restore, enhance, modify or mimic the immune system's attack on cells that are not wanted, such as cancer cells.

4. The suit patent has a term of 20 years, starting from 02nd May, 2006, which expires on 02nd May, 2026. The suit patent was granted after adjudication of four pre-grant oppositions, contested under Section 25(1) of the Patents Act, 1970 ("Patents Act"). Furthermore, a post-grant opposition under Section 25(2) of the Patents Act, filed by Zydus Healthcare Limited, a sister concern of the defendant, challenging the grant of the suit patent, is currently pending.

Factual Matrix:

5. An Application no. 5057/CHENP/2007 was filed as a National Phase Entry of International (PCT) Application no. PCT/JP2006/309606, filed on 02nd May, 2006, and published as International Publication no. WO2006/121168 A1 on 16th November, 2006. This application claims

priority to U.S. Provisional Application nos. 60/679,466 filed on 09th May, 2005; 60/738,434 filed on 21st November, 2005 and 60/748,919 filed on 08th December, 2005.

6. The pharmaceutical product, Nivolumab is sold under the brand name Opdivo® outside India, whereas, in India, Nivolumab is imported and marketed by plaintiff no. 3 as Opdyta®.

7. As noted above, four pre-grant oppositions were filed during the suit patent's prosecution history, which were rejected by the Controller of Patents *vide* order dated 30th June, 2020, subsequent to which, the suit patent was granted on 01st July, 2020. The four pre-grant oppositions were filed by Indian Pharmaceutical Alliance ("IPA"), Mumbai; Pankaj Kumar Singh, Delhi; Restech Pharmaceuticals, Ahmedabad and Dr. Reddy's Laboratories, Hyderabad, respectively.

8. Subsequent to the grant of the suit patent on 01st July, 2020, a post-grant opposition under Section 25(2) of the Patents Act was filed against it by Zydus Healthcare Limited, a sister concern of the defendant, on 01st July, 2021, which is currently pending before the Controller of Patents. The Opposition Board Recommendation ("OBR") dated 31st January, 2023, opining that IN '060 is invalid and liable to be revoked, was set aside by the High Court of Madras *vide* its order dated 15th March, 2024 in *W.P. No. 8451/2023*, filed by plaintiff nos. 1 and 2 herein. Thereafter, an appeal, i.e., *W.A. No. 1697/2024* was preferred by the defendant herein against the order dated 15th March, 2024, wherein, *vide* order dated 13th June, 2024, the Division Bench of High Court of Madras held that the order dated 15th March, 2024, passed by the Single Judge, shall be kept in abeyance.

9. Subsequently, *vide* order dated 10th January, 2025, the appeal, *W.A.*

No. 1697/2024, was disposed of by way of a consent order, wherein, the order dated 15th March, 2024, passed by the Single Judge was quashed and set aside and the matter was remanded back to the Single Judge for disposing of the writ petition expeditiously.

10. Plaintiffs, sometime in April, 2022, became aware that the defendant (former name, Cadila Healthcare Ltd.), had applied for clinical trial approval of Nivolumab before the Central Drugs Standard Control Organisation ("CDSCO"). Thereafter, a letter was issued on behalf of the plaintiffs to the defendant on 06th May, 2022, calling upon the defendant to cease-and-desist from making or using Nivolumab, until the expiry of the term of IN '060. The defendant issued a response dated 17th May, 2022, stating that seeking approvals from the Directorate General of Commercial Intelligence and Statistics ("DCGI") for conducting clinical trials was within the scope of the Patents Act and did not amount to infringement of the suit patent. As per the plaintiffs' case, pursuant to the defendant's reply indicating that no unauthorized activities were being carried out, the plaintiffs did not apprehend any immediate threat at that stage, since clinical trials were under progress.

11. However, further investigation by the plaintiffs revealed that the defendant had registered a clinical trial for its bio-similar ZRC-3276 with the Clinical Trial Registry of India ("CTRI"). In the said registration before the CTRI, the defendant had mentioned plaintiffs' product Nivolumab, identifying Opdivo®, as the reference product. The plaintiffs also came across the permission granted by the CDSCO in September, 2022 to the defendant to manufacture and import new drugs for clinical trials under the provisions of New Drugs and Clinical Trials Rules, 2019 for its similar

biologic/bio-similar, ZRC-3276, with the reference drug being Nivolumab, i.e., Opdivo®.

12. Thereafter, in April, 2024, the plaintiffs, through plaintiff no. 3's healthcare professional and later from their distribution network discovered that the defendant might be planning to launch a bio-similar version of Nivolumab, during the term of the suit patent, since several inquiries were received regarding the defendant's product by the plaintiffs. It was also revealed that the defendant had applied for regulatory approval from the CDSCO/DCGI, for marketing the said bio-similar version of Nivolumab.

13. As per the plaintiffs, there existed a real, credible and reasonable apprehension that the defendant intended to manufacture, launch and otherwise deal in Nivolumab during the term of the suit patent without the plaintiffs' authorisation, and thus, the present suit came to be filed as a *quia timet* action. *I.A. No. 10533/2024* has been filed along with the present suit seeking interim relief, which is subject matter of adjudication herein.

14. It is noted that this Court, *vide* order dated 08th May, 2024, restrained the defendant from placing its products in the market without prior permission of the Court. The said order is continuing till date.

Submissions on Behalf of the Plaintiffs:

15. On behalf of the plaintiffs, it is submitted as follows:

15.1 A *prima facie* case of infringement has clearly been established by the plaintiffs in view of the fact that the suit patent is valid and subsisting. Further, the defendant has clearly admitted that only their activities of carrying out research are exempt from patent infringement under Section 107A of the Patents Act, and commercial use. Moreover, if an *ad interim* injunction is not granted, irreparable loss and harm will be caused to the

plaintiffs, which cannot be compensated in monetary terms, particularly in the present *quia timet* action.

15.2 There has been no delay in filing the present suit. The plaintiffs, around April, 2022 became aware that the defendant had applied for a clinical trial approval of Nivolumab before the CDSCO. Moreover, since April, 2022, the plaintiffs continued to receive credible information in relation to defendant's proposed launch of infringing products till 04th May, 2024, at which stage the plaintiff no.3's representative received emails enquiring about the defendant's launch of a bio-similar Opdivo® without the authorization of the plaintiffs. Thus, on account of apprehension of commercial launch of product by the defendant, the present suit came to be filed.

15.3 The defendant never made any official request from the plaintiffs seeking to procure Nivolumab (Opdivo®) vials, nor have the plaintiffs supplied any Nivolumab to the defendant. The affidavit of the independent investigator has the records of imports of Nivolumab by the defendant, as per which, the defendant had on multiple occasions, imported Nivolumab (Opdivo®) in the years 2018 (4 instances), 2019 (6 instances), 2020 (2 instances), 2022 (6 instances), 2023 (2 instances), 2024 (1 instances) and some of these imports were allegedly for test/research purposes. Further, the defendant had also exported 1 glass bottle containing Nivolumab (bulk) in the year 2024.

15.4 The plaintiffs, on account of the reply dated 17th May, 2022 by the defendant, to the cease-and-desist letter issued by the plaintiffs on 06th May, 2022, did not apprehend any immediate threat at that stage. Since clinical trials were in progress, the outcome of which was uncertain, the plaintiffs

did not take any action.

15.5 The defendant is well aware of the rights of the plaintiffs in the suit patent as its sister concern, Zydus Healthcare Limited, filed a post-grant opposition against the grant of the suit patent, and was also served with a cease-and-desist letter in May, 2022, to which they had categorically responded. The defendant's disregard towards the plaintiffs' statutory rights in the suit patent, is wilful. Additionally, one of the pre-grant oppositions was filed by an organisation, IPA, of which the defendant is a member.

15.6 Furthermore, on 12th May, 2020, the Defendant has also filed a Patent Application no. 202021019976 before the Indian Patent Office in respect of *"PROCESS OF PURIFYING ANTI-PD-1 ANTIBODY"*, wherein, the preferred anti-PD-1 is Nivolumab, and the application is still pending.

15.7 Nivolumab is covered and claimed by the suit patent through Claims 1 and 3 of the suit patent, as Nivolumab contains the six Complementary Determining Regions ("CDRs") as claimed in granted Claim 1 and the Heavy Chain Variable (VH) domain and Light Chain Variable (VL) domain sequences as claimed in granted Claim 3. Further, the Claim 7 of the suit patent also claims Nivolumab as a composition with a pharmaceutically acceptable carrier.

15.8 IN '060 is a valid and subsisting patent in India, and the term of IN '060 expires on 02nd May, 2026. Since the plaintiffs are the rightful owners of IN '060 under Section 48 of the Patents Act, the plaintiffs have the exclusive right to prevent third parties, who, without the plaintiffs' authorization, cannot perform in India, the act of making, using, offering for sale, selling, exporting or importing the product(s) that fall within the scope of the claims of the suit patent till 02nd May, 2026.

15.9 The suit patent has been granted after thorough scrutiny and it is in its 20th year, and despite the four pre-grant oppositions and one post-grant opposition, the suit patent has not been revoked. Moreover, the plaintiffs' patent has been granted in more than 50 countries, without being revoked in any of the jurisdictions.

15.10 The challenge in post-grant opposition by the defendant's sister concern has not attained finality. Therefore, the defendant should have waited for the outcome of the said opposition.

15.11 The prior art document, i.e., EP1537878 B1 ("EP '878") (corresponding patent WO 2004/004771) on the basis of which the OBR recommended that the suit patent is not novel and valid, has already been dealt with by the plaintiffs in the pre-grant opposition proceedings, wherein, it has been noted that the said prior art document does not disclose the isolated monoclonal antibody or antigen binding portion that specifically binds to human Programmed Death.

15.12 The OBR is not binding upon the Controller of Patents in deciding the post-grant opposition, and has only a recommendary value, therefore, the reliance of the defendant on the OBR is misplaced. Moreover, the validity of the OBR is under challenge before the High Court of Madras, wherein, *vide* order dated 10th January, 2025 in *W.A. No. 1697/*2024, the matter in relation thereof, was remanded back to the Single Judge, which is currently pending adjudication.

15.13 The defendant, at the interlocutory stage, is required to place on record scientific material supported by expert evidence to discharge the burden of proving invalidity of the suit patent, in relation to the foreign patents.

15.14 The plaintiffs have mapped Sequence Identifier ID ("SEQ ID") defined by Opdivo®/Opdyta® (Nivolumab), including the six CDR sequences in figure 4A and figure 4B of suit patent and SEQ 4 and SEQ 11 with that of the International Non-Proprietary Name ("INN"), clearly in the plaint. Therefore, the defendant claiming its product to be bio-similar to Nivolumab can only do so, if the said bio-similar version has six CDR sequences of Claim 1, or the VH/VL region amino acid sequence of Claim 3.

15.15 There existed no commercial product of the defendant against which claim mapping could be done. Therefore, the plaintiffs have mapped with the Nivolumab INN, which is used as a reference product by the defendant for development of its bio-similar product, ZRC-3276. By virtue of the said claim mapping, Nivolumab INN is equivalent to Claims 1 and 3 of the suit patent. Therefore, any reference to Nivolumab by the defendant would constitute infringement of the suit patent.

15.16 The submission of the defendant that Nivolumab is not an anti-PD-1 antibody, as it binds to other cell surface receptors of the CD-28 family and therefore is not covered by the suit patent, is incorrect. Further, the plaintiffs have placed reliance on paragraphs 8 and 9 of the affidavit dated 15th August, 2022 of Dr. Brian T. Fife, wherein at page 18 of the said affidavit, he has confirmed that the claims of the suit patent are for Nivolumab.

15.17 The defendant has evaluated the binding specificity of the plaintiffs' product titled "*Evaluation of the binding specificity of Opdivo® with human PD1 and other proteins of CD28 family, i.e. ICOS, CTLA-4, and CD28 by using ELISA method"*, through conducting the tests done by its own research centre and through Sardar Patel University. Additionally, the defendant has also evaluated the binding specificity of the defendant's product, i.e. ZRC-

3276. The results of the said experiments of the defendant further demonstrate infringement, as they establish the following:

> *"(i) Opdivo® is an anti-PD-1 antibody and is Nivolumab;*
> *(ii) ZRC-3276 is also an anti-PD-1 antibody having the same claimed sequences of the suit patent which is admittedly Nivolumab;*
> *(iii) The difference in the binding affinity is common and is known as "standard variations" in the art."*

15.18 Therefore, it is evident that the defendant's product is admittedly Nivolumab. Additionally, since Nivolumab is claimed and covered under the suit patent, the defendant's product is also covered within the scope of the claims of the suit patent. Thus, both products fall under the claims of the suit patent, and therefore, on basis of the admissions by the defendant, it has admitted to infringement.

15.19 The word, 'specifically' in the claims of the suit patent does not mean 'exclusively' or 'only'. The suit patent nowhere mentions that it only binds to PD-1 nor does it state that there is no binding to other CD-28 receptors. Further, the reliance on the usage of the term 'isolated' is misplaced, as the same is defined in the complete specification, wherein, it is noted that the isolated antibody may have cross-reactivity with other antigens.

15.20 None of the prior art documents cited by the defendant from any jurisdiction disclose any amino acid sequence, let alone the sequence of Nivolumab as claimed in the suit patent. Further, if any sequence from a prior art does not exactly match with the claimed sequence, the subject matter of such claims cannot be said to be anticipated by the prior art sequence, in terms of the Guidelines for Examination of Biotechnology Applications for Patent, 2013.

15.21 At the stage of interim injunction, it is the onus of the defendant to show a credible challenge to the validity of the suit patent, and the same is

raised only based on the report from experts of Opposition Board, analysis of independent expert and independent analysis of prior art by the defendant.

15.22 The defendant already has the requisites for manufacturing the drug substance and drug product, i.e., Active Pharmaceutical Ingredient ("API") and finished formulation of Nivolumab. Additionally, the defendant also has the requisite approval to import new drugs or an investigational new drug for the purpose of clinical trials. Therefore, the plaintiffs have approached this Court before the commercial sale/launch of the drug by the defendant. Moreover, the defendant will not suffer any prejudice by the grant of an interim injunction. However, the plaintiffs will suffer an irreparable injury.

15.23 The defendant's acts would cause huge damage to the plaintiffs' business/public interest and reputation, which cannot be accounted for in monetary terms. The plaintiffs would also lose substantial sales if the defendant is permitted to manufacture a similar biologic/bio-similar version of Nivolumab or a generic product in India in contravention of plaintiff nos. 1 and 2's patent rights. The balance of convenience lies in favour of the plaintiffs as the patent term expires within a year and thereafter the defendant would be free to launch its product.

Submissions on Behalf of the Defendant:

16. On behalf of the defendant, it is submitted as follows:

16.1 The inventive feature in the suit patent is claimed to have specific binding affinity to PD-1, while the defendant's product also binds to other members of the CD-28 family, which shows that the defendant's product is outside the purview of the suit patent. Moreover, the plaintiffs' Nivolumab also falls outside the scope of suit patent as even plaintiffs' Nivolumab targets and binds to other members of the CD-28 family. Therefore, the

plaintiffs cannot seek protection of a product which itself is not protected within the claims of the suit patent.

16.2 The defendant's product, ZRC-3276 is bio-similar to plaintiffs' Nivolumab. However, bio-similarity by itself does not substantiate infringement as it is based upon product-to-product comparison, whereas, infringement requires claim to product mapping. However, the exercise of mapping undertaken by the plaintiffs is incorrect and incomplete, as the plaintiff's focus is the reference to Nivolumab. However, the term 'Nivolumab' is assigned by World Health Organisation ("WHO"), and the term cannot be exclusive to any one person. Further, as per WHO description for Nivolumab, even non-isolated antibodies that do not bind specifically to PD-1 can be termed as 'Nivolumab', as long as they have the sequences as mentioned in the WHO drug information document.

16.3 It is the plaintiffs' case that the claim scope of the suit patent is limited to only those antibodies which bind to PD-1 with no binding or statistically insignificant binding with other receptors in the CD-28 family. The defendant's product does not fulfil this limitation and thus, is not infringing the suit patent. Further, in the defendant's product there is statistically significant binding, therefore, the defendant is following the prior art.

16.4 The Subject Expert Committee under the 'Guidelines on Similar Biologics, 2016' ("Similar Biologics Guidelines"), found that the defendant's product is similar to plaintiffs' Nivolumab, in terms of efficacy, safety and quality. Thus, the lack of infringement does not affect the status of the plaintiffs' product as bio-similar.

16.5 The defendant has raised the grounds *inter alia*, that the suit patent

lacks novelty (Section 64(1)(e)), lacks inventive step (Section 64(1)(f)) and is non-patentable (Section 64(1)(k)). Further, the suit patent is invalid on the grounds, that, Nivolumab was already claimed in the patent WO 2004/004771; that the process for making Nivolumab is known in the art before the priority date of the patent. Further, the monoclonal antibody used in the suit patent is a natural phenomenon which is produced from transgenic mice and does not involve any substantive human intervention. The inventors of the current Indian patent have used hybridoma technology, which is a well-known art. The suit patent is ostensibly drafted as a product patent of Nivolumab and the claims are merely directed to the identification of SEQ IDs, without providing any corresponding disclosure as to how the present patent is different from the patent WO 2004/004771, which is also the plaintiffs' patent.

16.6 The factors of balance of convenience and irreparable injury both are in favour of the defendant, as the defendant's application for approval for a similar biologic/bio-similar product was in the knowledge of the plaintiffs since April 2022. Further, the plaintiffs, to plead a fresh cause of action and overcome the arguments of delay, have relied on a self-serving email sent by an unknown party.

16.7 The plaintiffs are attempting to increase the monopoly of Nivolumab, and thus, the suit patent is *prima facie* vulnerable to challenge. Further, the contention of invalidity of the suit patent, and vulnerability at the interim stage, raised by the defendant is based *inter alia* on the basis of prior arts D1-D3, wherein, the prior art D3 belongs to the plaintiffs themselves.

16.8 The plaintiffs, in a suit patent of D3 patent family, in the U.S., have admitted that they have developed Nivolumab antibody by practising the

invention mentioned in the U.S. patents (US 8728474, US 9073994 and US 9067999), with a priority of year 2002, which also are from the same patent family of D3, having the same priority particulars as the Japanese patents, i.e., JP 2002194491 dated 03rd July, 2002 and JP 2003029846 dated 06th February, 2003.

16.9 The Patent Term Extension ("PTE") for Opdivo® (Nivolumab) product has been approved to plaintiff no. 2 and Mr. Tasuku Honjo in Japan for the Japanese patent JP4409430 in 2015. The Japanese patent is a member of the patent family of D3 which has a priority of 2002. Therefore, the plaintiffs have sought extension of member D3 patent for Opdivo® (Nivolumab), which evidences the admission that patent D3 is for Nivolumab.

16.10 The plaintiffs, in submissions before the European Patent Office ("EPO") dated 28th August, 2008, have submitted 'example 18' of pending WO2006/121168 A1 that is corresponding to the suit patent, IN '060, as additional data during examination to demonstrate the inventiveness of the invention claimed in prior patent application D3, during the prosecution of D3. Therefore, it is clear that the product Opdivo® (Nivolumab) which is claimed in suit to be the subject matter of IN '060, was already a subject matter of D3.

16.11 It is plaintiffs' own admission that Opdivo®/Nivolumab is part of prior patent D3 and not a product arising from the suit patent IN '060. The plaintiffs' only case of infringement is premised on the fact that the defendant was developing a bio-similar Opdivo® containing Nivolumab, thus, by plaintiffs' own admission, Opdivo/Nivolumab is part of the prior art D3 and not a product of the suit patent.

16.12 The defendants undertook a study of Opdivo® for which tests were conducted both by the defendant at Zydus Research Centre and by an independent entity, i.e., Sardar Patel University, which follow the protocol disclosed in Example 3 of the complete specification of IN '060. The defendant submits that both tests conclude that the binding of Opdivo® is to human PD-1 as well as other CD-28 family proteins (ICOS, CD-28 and CTLA4). Therefore, it is evident that Opdivo®, the product of the plaintiffs, arises out of prior art D3 and not from the suit patent IN '060.

16.13 The in-house experiment reports conducted by the defendant and the report of an independent university, i.e., Sardar Patel University, show the binding affinity of the defendant's product to other members of the CD-28 family. Therefore, defendant's product does not infringe the suit patent.

16.14 The Similar Biologics Guidelines, assess 'similarity' in terms of 'safety, efficacy and quality', and does not make reference to patent infringement. Additionally, the said Guidelines provide a caveat stating that they are not meant to substitute/rephrase the Drugs and Cosmetics Act, 1940 or Rules made thereunder.

16.15 Preparation of anti-PD1 antibody by using transgenic mice is already known and in the public domain, and the present invention is merely preparing an antibody and therefore, is not new.

16.16 Process steps were already known from the prior art. There were several techniques for the preparation of human anti-PD1 antibodies, which were well-known on the priority date of the suit patent.

16.17 The post-grant opposition that was filed by Zydus Healthcare Limited, led to the recommendation for revocation of the suit patent by the Opposition Board, and the said recommendation clearly shows that such a

method is commonly employed to produce antibodies.

Findings and Analysis:

17. Before adverting to the discussion in relation to the merits of the case, this Court deems it appropriate to address the contention on behalf of the defendant that there is a delay in filing of the present suit. This Court notes that it is the submission of the plaintiffs that around April, 2022 they became aware that the defendant had applied for a clinical trial approval of a drug, with the suit patent, Nivolumab, as the reference drug, before the CDSCO. Consequently, on 06th May, 2022, plaintiff nos. 1 and 2 issued a cease-and-desist letter to the defendant with regard to using Nivolumab until the expiry of the suit patent. However, the defendant, in its response dated 17th May, 2022, had stated that the defendant was only conducting clinical trials and took up the defence of Bolar Exemption under Section 107A of the Patents Act. On account of the same, the plaintiffs took no further action. Subsequently, upon receipt of certain information in April/May, 2024 by the plaintiffs, with regard to the defendant's proposed commercial launch of bio-similar of Nivolumab, the plaintiffs filed the present suit.

18. It is noted that in May, 2022, on account of the Bolar Exemption under Section 107A of the Patents Act being invoked by the defendant, the plaintiffs did not initiate any action, as the said exemption is an exception to patent infringement. Furthermore, receipt of information by the plaintiffs in April/May, 2024 regarding possibility of the defendant launching an infringing product commercially, gives rise to a cause of action in favour of the plaintiffs to initiate legal proceedings, as the present one, against the defendant. Further, nothing has been brought before this Court by the defendant to show that the plaintiffs had any knowledge of the proposed

commercial launch of defendant's product, ZRC-3276, prior to the timeline averred by the plaintiffs before this Court.

19. Thus, this Court agrees with the submission of the plaintiffs that cause of action for initiating legal proceedings against the defendant arose only in the year 2024, when the knowledge with regards to the commercial launch of defendant's product was received by the plaintiffs in April/May, 2024. Therefore, this Court rejects the contention on behalf of the defendant that there is a delay in filing of the present suit.

20. The present suit concerns the infringement of Indian Patent No. IN 340060, i.e., IN '060, which is titled as, *"Human Monoclonal Antibodies to Programmed Death 1 (PD-1) for use in treating Cancer"*. The bibliographic details of the suit patent are as under:

Indian Patent Number	340060
Patent Application Number	5057/CHENP/2007
Applicants/Patentees	Plaintiff No.1 Plaintiff No. 2
Title	Human Monoclonal Antibodies to Programmed Death I (PD-1) for use in treating Cancer
International Application No.	PCT/JP06/309606
India Application No.	5057/CHENP/2007
International Filing Date (Date of Patent)	May 02, 2006
National Phase entry-filing date of Indian Application	November 09, 2007
Date of Priority	May 09, 2005 November 21, 2005 December 8, 2005
WO Publication No.	WO2006/121168
International Publication date	November 16, 2006
Publication Date (u/S 11A)	May 30, 2008
Date of Grant	July 01, 2020
Publication Date (u/S 43(2))	July 03, 2020
Date of Expiry	May 02, 2026
Pre-Grant Oppositions (u/S 25(1))	4 i. July 13, 2015 - filed by Indian Pharmaceutical Alliance (IPA), Mumbai ii. November 02, 2016 – filed by Pankaj Kumar Singh, Delhi

	iii. July 13, 2017 – filed by Restech Pharmaceuticals, Ahmedabad iv. February 23, 2018 – filed by Dr. Reddy's Laboratories Ltd., Hyderabad
Pre-Grant Opposition Decision dismissing the 4 pre grant oppositions and granting the suit patent	June 30, 2020
Post-Grant Opposition (u/S 25(2))	July 01, 2021 – filed by Zydus Healthcare Limited (subsidiary of the Defendant)
Post-Grant Opposition Decision	Pending

21. The suit patent, i.e., IN '060 is a therapeutic antibody used in treatment of various forms of cancer, such as non-small cell lung cancer, kidney cancer, head and neck cancer, melanoma and Hodgkin lymphoma. The antibody in the suit patent is defined by Claims 1 and 3 of IN '060 and is called Nivolumab (5C4) monoclonal anti-PD-1 antibody, which is used in treatment of cancer. Nivolumab is the INN originally assigned by the WHO in the year 2013.

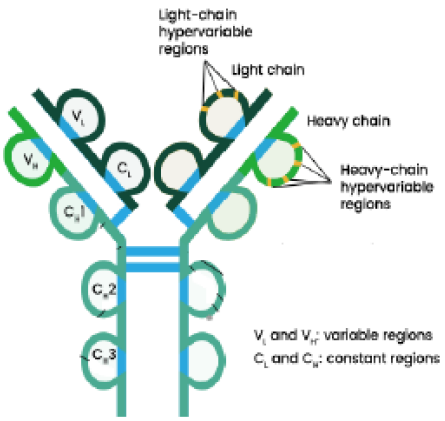
22. For the purposes of better understanding the present matter, this Court finds it apposite to bring forth the technical/scientific discipline involved in the suit patent.

23. The white blood cells ("WBCs") in our blood are divided into five types, one of them being, lymphocytes. Lymphocytes are immune cells which are prepared in our bone marrow, and are found in the blood and lymph tissue. Lymphocytes further consist of B-lymphocytes (B-cells) and T-lymphocytes (T-cells).

24. B-cells are the ones responsible for producing antibodies. Antibodies are Y-shaped proteins that protect us when an unwanted foreign substance enters our body. They are produced by our immune systems to neutralise pathogens such as bacteria, virus, etc. In the event that such a pathogen enters our body, it stimulates our immune system to produce antibodies that

bind with a unique molecule of the pathogen, called an antigen.

25. The 'Y'-shaped structure of an antibody contains two 'Heavy' and two 'Light' chains. The variable region in each heavy and light chain, responsible for generating antigen-binding site of the antibody, are termed Complementarity Determining Regions - CDRs, which are immunoglobulin (Ig) hypervariable domains. Thus, the CDRs are responsible for binding to the target antigen. The variable regions of both the heavy chain and the light chain have three CDRs each and these CDRs are specific to an antibody for binding to an antigen. General structure of an antibody, is represented in the following manner:



26. The antibodies present in our body are basically proteins. Proteins in turn are made up of amino acids which are small molecules that are the building blocks of proteins. There are 20 amino acids commonly found in the protein present in our body. The amino acids present in our body are represented by standard codes. The unique arrangement of amino acids is called an amino acid sequence.

27. Further, the T-cells in our WBCs are responsible for the identification and destruction of abnormal/infected cells. They have CD-28 proteins, which signal the immune system if a cell is normal or abnormal. When T-

cells receive this signal, the immune system attacks the abnormal cells. One important CD-28 protein on T-cells is called Programmed Death 1, i.e., PD-1, which helps in identification of abnormal cells.

28. PD-1 has two ligands, i.e., PD-L1 (Programmed Death-Ligand 1) and PD-L2 (Programmed Death-Ligand 2). PD-L1 and PD-L2 are proteins which are located on the surface of normal cells. In a healthy human body, once PD-1 binds with either of its ligands, it essentially signals to the T-cell to tolerate those normal cells, and not attack them. Thus, engagement of PD-1 with either of its two ligands suppresses immune system responses in case of healthy normal cells.

29. However, cancer cells also have PD-L1 on their surface and have the potential to impair PD-1's ability to send signals to the T-cell. Therefore, when PD-1 on our T-cell binds to the PD-L1 ligand on a cancerous cell, it deactivates the PD-1 on the T-cell. When PD-1 is inactive, T-cells do not attack the cancer cells.

30. Thus, to prevent this binding between PD-1 and PD-L1 on a cancer cell, monoclonal antibodies have been developed in order to allow the immune system to recognise and destroy cancer cells. Monoclonal antibodies are man-made antibodies which are created artificially in laboratories and are designed to act like human antibodies for specific purposes. As the name suggests, they are a single kind of antibody that bind to a single target receptor/antigen or ligand.

31. The suit patent, i.e., Nivolumab, is one such monoclonal antibody, which is an anti-PD-1 antibody, also called '5C4' antibody. In other words, Nivolumab binds with the PD-1 protein on our T-cell, which prevents PD-1 from binding itself with PD-L1 ligand on a cancer cell. This ensures that our

T-cells are not rendered inactive and the immune system is able to identify the cancer cell and act accordingly.

32. For the purpose of adjudicating the various issues raised before this Court pertaining to infringement of the suit patent, it would be imperative to construct the Claims 1, 3 and 7 of the suit patent, which are material to the issues at hand. Emphasizing that claim construction is generally the first and foremost exercise carried out in adjudicating patent infringement, this Court in the case of ***Jay Switches India Pvt. Ltd. Versus Sandhar Technologies Ltd. and Others***, ***2024 SCC OnLine Del 8434***, noted as follows:

> *"xxx xxx xxx*
>
> *23. One of the most significant issues that arise for consideration while deciding a patent infringement suit relates to the construction of the claims. According to section 10(4)(c) of the Patents Act 1970, the claims define the scope of the invention. However, claims have to be read along with the Complete Specification. In this regard, a reference may be made to the observations made by the coordinate bench in the recent judgment Guala Closures SPA v. Agi Greenpac Ltd., which are set out below:*
>
> > ***"40. Claim construction is generally the first and foremost exercise carried out in adjudicating patent infringement suits, especially when confronted with products like tamper-evident closures which are based on mechanical features. The same has also been highlighted in 'Chapter 9: Construction of the Specification and Claims', in Terrell on the Law of Patents, Eighteenth Edition. As per Terrell, determination of the actual scope of the Claims of a complete specification, is one of the most significant issues, in litigation involving patents. Once the scope of the claims is clarified, questions regarding infringement and invalidity often find swift resolution.*** *Therefore, it has been highlighted that patentees must navigate a delicate balance, as they have to assert their claim in such a way that the Claim is broad enough to cover infringement while not excessively broad to avoid coverage by prior art. On the contrary, it has been highlighted that Defendants, employ a 'squeeze' argument, often claiming that if a claim encompasses their activities, it must also encompass prior art.* ***This highlights the pivotal role of claim construction in patent litigation, shaping the foundation for determining***

infringement and assessing patent validity. The relevant extract from Terrell is set out below:

> *"**Determination of the true construction of the claims of a patent specification, which are to be read in the context of the specification, is commonly one of the most significant issues, if not the single most significant issue, in litigation involving patents**.""*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

33. The Supreme Court in the case of ***Bishwanath Prasad Radhey Shyam Versus Hindustan Metal Industries, (1979) 2 SCC 511***, emphasised that in order to understand the scope of an invention, it would be imperative to refer to the description of the invention before referring to the claims. The relevant portion of the said judgement is as follows:

> *"xxx xxx xxx*
>
> ***43. As pointed out in Arnold v. Bradbury the proper way to construe a specification is not to read the claims first and then see what the full description of the invention is, but first to read the description of the invention, in order that the mind may be prepared for what it is, that the invention is to be claimed, for the patentee cannot claim more than he desires to patent.*** *In Parkinson v. Simon Lord Esher M. R. enunciated that as far as possible the claims must be so construed as to give an effective meaning to each of them, but the* ***specification and the claims must be looked at and construed together****.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

34. Therefore, to understand the actual scope of the claims, reference to the specifications of the suit patent is imperative.

35. To better understand the purpose and scope of the patented invention, reference may be made to the *'Technical Field'* of invention given in the Complete Specification of the suit patent. The Technical Field of the invention, as given in the suit patent, is reproduced as follows:

Technical Field

The present invention relates generally to immunotherapy in the treatment of human disease and reduction of adverse events related thereto. More specifically, the present invention relates to the use of anti-PD-1 antibodies and the use of combination immunotherapy, including the combination of anti-CTLA-4 and anti-PD-1 antibodies, to treat cancer and/or to decrease the incidence or magnitude of adverse events related to treatment with such antibodies individually.

36. Apart from the use of anti-PD-1 antibodies, the present invention is also related to the use of combination immunotherapy, including, the anti-PD-1 combination with CTLA-4 to treat cancer, as well as to address the severity of adverse events associated with the treatment with these antibodies individually. In this regard, the *'Disclosure of the Invention'*, which is part of the Complete Specification of suit patent, is reproduced as under:

Disclosure of the Invention

The present invention provides isolated monoclonal antibodies, in particular human monoclonal antibodies, that bind to PD-1 and that exhibit numerous desirable properties. These properties include, for example, high affinity binding to human PD-1, but lacking substantial cross-reactivity with either human CD28, CTLA-4 or ICOS. Still further, antibodies of the invention have been shown to modulate immune responses. Accordingly, another aspect of the invention pertains to methods of modulating immune responses using anti-PD-1 antibodies. In particular, the invention provides a method of inhibiting growth of tumor cells *in vivo* using anti-PD-1 antibodies.

37. Thus, this Court notes that the *'Disclosure of the Invention'* in the Complete Specification describes that the claimed isolated monoclonal antibody exhibits numerous properties, such as high binding affinity to human PD-1, but lacks substantial cross-reactivity with human CD-28, CTLA-4 or ICOS. However, the binding affinity with other proteins, such as human CD-28, is not completely absent.

38. Thus, from reading of the specification of the suit patent it is manifest that PD-1 is a protein found on T-cells that assists in maintaining the body's

immune responses. These monoclonal antibodies are laboratory-produced engineered bio-molecules that can restore, enhance, modify, mimic or behave like the immune system's attack on unwanted cells, such as cancer cells. In the suit patent, Nivolumab is claimed under Claims 1, 3 and 7.

39. The Claims 1, 3 and 7 of the suit patent, which are relevant for the present case, are reproduced as under:

> *"1. An isolated monoclonal antibody or an antigen-binding portion thereof that binds specifically to human Programmed Death (PD-1), comprising:*
>
> *a) a heavy chain CDR1 consisting of the amino acid sequence set forth in SEQ ID NO: 18;*
>
> *b) a heavy chain CDR2 consisting of the amino acid sequence set forth in SEQ ID NO: 25;*
>
> *c) a heavy chain CDR3 consisting of the amino acid sequence set forth in SEQ ID NO: 32;*
>
> *d) a light chain CDR1 consisting of the amino acid sequence set forth in SEQ ID NO: 39;*
>
> *e) a light chain CDR2 consisting of the amino acid sequence set forth in SEQ ID NO: 46; and*
>
> *f) a light chain CDR3 consisting of the amino acid sequence set forth in SEQ ID NO: 53.*
>
> *xxx xxx xxx*
>
> *3. The monoclonal antibody or antigen-binding portion thereof, as claimed in claim 1, which comprises:*
>
> *a) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 4; and*
>
> *b) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 11.*
>
> *xxx xxx xxx*
>
> *7. A composition comprising the monoclonal antibody or antigen-binding portion thereof as claimed in any one claims 1-6 and a pharmaceutically acceptable carrier.*
>
> *xxx xxx xxx"*

40. The sequence of 5C4 antibody, i.e., Nivolumab, showing the same as artificially created antibody, is reproduced as under:

<210> 18
<211> 5
<212> PRT
<213> Artificial

<220>
<223> VH CDR1 of 5C4 Antibody

<400> 18

Asn Ser Gly Met His
1 5

xxx xxx xxx

<210> 25
<211> 17
<212> PRT
<213> Artificial

<220>

G_3338_018IN03_SeqListing
<223> VH CDR2 of 5C4 Antibody

<400> 25

Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15

Gly

41. As noted by this Court hereinabove, amino acids are organic compounds that are the building blocks of proteins. Every protein has a unique amino acid arrangement which is called an amino acid sequence. In the present case, the plaintiffs have made changes in the sequencing of amino acids.

42. As noted above, antibodies are proteins that protect us when an unwanted substance enters the body. All antibodies are constructed in the same way. As per the suit patent, Nivolumab is a PD-1 blocking antibody for treatment of cancer. It has specific amino acid sequences of heavy and light chains of an antibody termed as the '5C4 antibody', which contains six

CDRs. Changes have been made in the amino acid sequencing, which has resulted in creation of the suit patent, Nivolumab, i.e., monoclonal anti-PD-1 antibody for treatment of cancer. Three changes have been made in the sequencing of amino acid in the heavy chain variable and three changes have been made in the sequencing of amino acid in the light chain variable, totalling to six changes.

43. The changes, as made by the plaintiffs, in the amino acid sequencing in the heavy chain variable region and light chain variable region, which is reflected in red colour, is reproduced as under:

Amino acid	Gln	Val	Gln	Leu	Val	Glu	Ser	Gly	Gly	Gly	Val	Val	Gln	Pro	Gly	Arg
Amino acid code	Q	V	Q	L	V	E	S	G	G	G	V	V	Q	P	G	R
Amino acid	Ser	Leu	Arg	Leu	Asp	Cys	Lys	Ala	Ser	Gly	Ile	Thr	Phe	Ser	Asn	Ser

Amino acid code	S	L	R	L	D	C	K	A	S	G	I	T	F	S	N	S
Amino acid	Gly	Met	His	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys	Gly	Leu	Glu	Trp	Val
Amino acid code	G	M	H	W	V	R	Q	A	P	G	K	G	L	E	W	V
Amino acid	Ala	Val	Ile	Trp	Tyr	Asp	Gly	Ser	Lys	Arg	Tyr	Tyr	Ala	Asp	Ser	Val
Amino acid code	A	V	I	W	Y	D	G	S	K	R	Y	Y	A	D	S	V
Amino acid	Lys	Gly	Arg	Phe	Thr	Ile	Ser	Arg	Asp	Asn	Ser	Lys	Asn	Thr	Leu	Phe
Amino acid code	K	G	R	F	T	I	S	R	D	N	S	K	N	T	L	F
Amino acid	Leu	Gln	Met	Asn	Ser	Leu	Arg	Ala	Glu	Asp	Thr	Ala	Val	Tyr	Tyr	Cys
Amino acid code	L	Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C
Amino acid	Ala	Thr	Asn	Asp	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Leu	Val	Thr	Val	Ser
Amino acid code	A	T	N	D	D	Y	W	G	Q	G	T	L	V	T	V	S
Amino acid	Ser															
Amino acid code	S															

b. SEQ ID No. 11 (light chain variable region)

Amino acid	Glu	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Thr	Leu	Ser	Leu	Ser	Pro	Gly
Amino acid code	E	I	V	L	T	Q	S	P	A	T	L	S	L	S	P	G
Amino acid	Glu	Arg	Ala	Thr	Leu	Ser	Cys	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Tyr
Amino acid code	E	R	A	T	L	S	C	R	A	S	Q	S	V	S	S	Y
Amino acid	Leu	Ala	Trp	Tyr	Gln	Gln	Lys	Pro	Gly	Gln	Ala	Pro	Arg	Leu	Leu	Ile
Amino acid code	L	A	W	Y	Q	Q	K	P	G	Q	A	P	R	L	L	I
Amino acid	Tyr	Asp	Ala	Ser	Asn	Arg	Ala	Thr	Gly	Ile	Pro	Ala	Arg	Phe	Ser	Gly

Amino acid code	Y	D	A	S	N	R	A	T	G	I	P	A	R	F	S	G
Amino acid	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Ser	Ser	Leu	Glu	Pro
Amino acid code	S	G	S	G	T	D	F	T	L	T	I	S	S	L	E	P
Amino acid	Glu	Asp	Phe	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	Ser	Ser	Asn	Trp	Pro	Arg
Amino acid code	E	D	F	A	V	Y	Y	C	Q	Q	S	S	N	W	P	R
Amino acid	Thr	Phe	Gly	Gln	Gly	Thr	Lys	Val	Glu	Ile	Lys					
Amino acid code	T	F	G	Q	G	T	K	V	E	I	K					

44. The six separate changes in the amino acid sequencing, as done by the plaintiffs, are reproduced as under:

"27. ... ...

a. SEQ ID No. 18 (heavy chain CDR1)

Amino acid	Asn	Ser	Gly	Met	His
Amino acid code	N	S	G	M	H

b. SEQ ID No. 25 (heavy chain CDR2)

Amino acid	Val	Ile	Trp	Tyr	Asp	Gly	Ser	Lys	Arg	Tyr	Tyr	Ala	Asp	Ser	Val	Lys	Gly
Amino acid code	V	I	W	Y	D	G	S	K	R	Y	Y	A	D	S	V	K	G

c. SEQ ID No. 32 (heavy chain CDR3)

Amino acid	Asn	Asp	Asp	Tyr
Amino acid code	N	D	D	Y

d. SEQ ID No. 39 (light chain CDR1)

Amino Acid	Arg	Ala	Ser	Gln	Ser	Val	Ser	Ser	Tyr	Leu	Ala
Amino acid code	R	A	S	Q	S	V	S	S	Y	L	A

e. SEQ ID No. 46 (light chain CDR2)

Amino Acid	Asp	Ala	Ser	Asn	Arg	Ala	Thr
Amino acid code	D	A	S	N	R	A	T

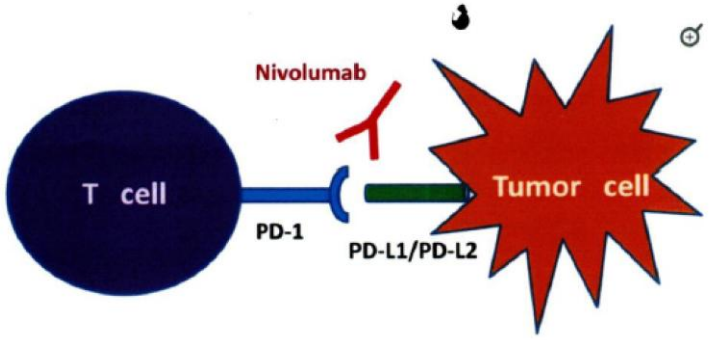
f. SEQ ID No. 53 (light chain CDR3)

Amino Acid	Gln	Gln	Ser	Ser	Asn	Trp	Pro	Arg	Thr
Amino acid code	Q	Q	S	S	N	W	P	R	T

45. On account of the aforesaid changes made by the plaintiffs in the amino acid sequencing, a new protein, i.e., suit patent antibody 5C4 has been created by the plaintiffs, which has the assigned INN Nivolumab.

46. When cancer cells develop in human body, they attach/lock with the immunity cells present in our body, on account of which the body immunity is suppressed. The suit patent, Nivolumab, provides a solution to this situation, by preventing attachment/locking of the immunity cell (T-cell) in

the blood to the cancer cell ligand (PD-L1/PD-L2). The graphic representation of the working of Nivolumab, in preventing the locking/attachment of the T-cell, is reproduced as under:



47. The two issues that arise for consideration before this Court are as to whether the defendant is infringing the suit patent in developing a bio-similar version of Nivolumab; and the issue as regards the invalidity of the suit patent, as raised by the defendant. The defence taken by the defendant in the present case is two folds, firstly, invalidity of the suit patent, and secondly, non-infringement by defendant's bio-similar product.

48. This Court takes note of the contentions of the defendant that the suit patent is invalid on the grounds that there are already existing prior arts to the suit patent, which envisage the claims in the suit patent, and therefore, the process for making 'Nivolumab' is a known art. Furthermore, it is the defendant's case that the monoclonal antibody used in the suit patent is a natural phenomenon, which on the face of it, is non-patentable. It is also the ground of the defendant that the OBR which has been issued by an expert body constituted in relation to the suit patent in the post-grant opposition, has made recommendations to the effect that the suit patent is invalid. These contentions raised by the defendant are dealt with hereinafter.

49. The defendant has challenged the validity of the suit patent on the

ground that Nivolumab was already claimed by plaintiffs' own International corresponding patent WO 2004/004771, D3, in the present case. It is the case of the defendant that the process for making Nivolumab is known in the art before the priority date of the suit patent. For this purpose, the defendant has relied upon prior arts, D1-D3, i.e., WO 2001/014557, WO 2002/079499 and EP '878 (corresponding WO 2004/004771), respectively, to substantiate the aspect of prior disclosure and in effect, the invalidity of the suit patent.

50. The defendant has specifically relied upon D3, which belongs to the plaintiffs themselves. The prior art D3 is a European Patent Specification, with International Publication No. WO 2004/004771. The description of Technical Field in the said patent's specification, as per the record, is extracted as below:

> *"xxx xxx xxx*
>
> *TECHNICAL FIELD*
>
> ***[0001]** The present invention relates to immunopotentiation characterized by inhibiting immunosuppressive signals induced by PD-1, PD-L1 or PD-L2, compositions for cancer or infection treatment, and therapies that use them.*
>
> ***[0002] More specifically, the present invention relates to a use of an anti-PD-1-antibody for the manufacture of a medicament for cancer treatment.***
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

51. The disclosure of the invention of the aforesaid prior art D3, is extracted as below:

> *"xxx xxx xxx*
>
> ***[0011] A problem of the present invention is to provide compositions to activate immunity by inhibiting the Inhibitory signals of PD-1, PD-L1 or PD-L2 and compositions for cancer or infection treatment through this mechanism.***
>
> ***[0012] The present inventors paid attention to PD-1, PD-L1, or PD-L2 as a new target in cancer or infection treatment and found that***

substances that inhibit the inhibitory signals of PD-1, PD-L1 or PD-L2 inhibit cancer proliferation through the mechanism of the recovery and activation of immune function*. Further, they found that PD-1 signal, concretely, an interaction of PD-1 and PD-L1 or PD-1 and PD-L2 took part in the exclusion of infectious virus. According to those facts, they found the substances that could inhibit the inhibitory signals of PD-1, PD-L1 or PD-L2 having therapeutic potential for cancer or infection and completed the present invention.*

That is, the present invention relates to

1. ***Use of an anti-PD-1 antibody which inhibits the immunosuppressive signal of PD-1 for the manufacture of a medicament for cancer treatment.***

2. The use according to item 1, wherein the anti-PD-1 antibody is a human anti-PD-1 antibody*.*

xxx xxx xxx"

(Emphasis Supplied)

52. Reference may also be made to the claims of the said prior art D3, i.e., EP '878, which are reproduced as under:

"xxx xxx xxx

Claims

1. ***Use of an anti-PD-1 antibody which inhibits the immunosuppressive signal of PD-1 for the manufacture of a medi- cament for cancer treatment.***

2. ***The use according to claim 1, wherein the anti-PD-1 antibody is a human anti-PD-1 antibody.***

3. ***Anti-PD-1 antibody which inhibits the immunosuppressive signal of PD-1 for the use in cancer treatment****.*

4. ***Anti-PD-1 antibody for the use according to claim 3, wherein the anti-PD-1 antibody is a human anti-PD-1 antibody****.*

xxx xxx xxx"

(Emphasis Supplied)

53. Perusal of the aforesaid disclosure and claims of the D3 prior art document reveals that the said prior art document as cited by the defendant, dealt with anti-PD-1 antibody for use in cancer treatment. However, the suit patent on the other hand, invents the monoclonal antibody, i.e., Nivolumab. Thus, while the prior art as cited, provided the target, the suit patent provides the actual product.

54. As noted above, the contention of invalidity of the suit patent and vulnerability has been raised by the defendant *inter alia* on prior arts, D1-D3, details of which, as given in the reply of the defendant, are as follows:

Document	**Publication date**	**Disclosure**
WO 2001/014557 (D1) **Annexed as DOCUMENT B**	01.03.2001	Discloses the manufacture of human antibody against human PD-1 using transgenic mice and hybridoma technology which inhibits the interaction between PD-L1 (called B7-4 therein) and PD-1 and also discusses that PD-1 is involved in immunoevasion by tumours (Examples 9, 10, 17 and figure 26)
WO 2002/079499 (D2) **Annexed as DOCUMENT C**	10.10.2002	Discloses the manufacture of human antibody against human PD-1 using transgenic mice and hybridoma technology which inhibits the interaction between PD-L1 (called B7-4 therein) and PD-1 and also discusses that PD-1 is involved in immunoevasion by tumours (Examples 9, 10, 21 and figure 26)
EP1537878B1 (Corresponding WO 2004/004771) (D3) **Annexed as DOCUMENT D**	15.01.2004	Discloses manufacturing process of human antibody against human anti-PD-1 using transgenic mice and use of said antibodies for the

		treatment of cancer (Paragraphs [0018] and [0030] of D3). It also discloses that anti-PD-1 antibodies significantly reinforced activity of PD-1 expressing cytotoxic T lymphocytes (CTL) (Example 12, paragraph [0127] and Figure 17 of D3) and suppressed metastasis of carcinoma cells to liver in a mouse model of melanoma (Paragraph [0044], example 13 of D3).

55. In this regard, this Court notes that document B (D1) and C (D2) do not provide sequence of any anti-PD-1 antibody. Furthermore, though D3 talks about anti-PD-1 antibody, however, *prima facie*, the same does not disclose Nivolumab in any manner. It is apparent that while the prior art documents pertain to process patents, the suit patent is a product patent.

56. Thus, the defendant has not been able to show that Nivolumab was disclosed in the prior arts cited by the defendant. Nothing has been brought before this Court to indicate that the documents WO2001/014557 (D1), WO2002/079499 (D2) and EP '878 (D3) disclose the specific sequences of the antibody, as claimed in the suit patent. The defendant has failed to show that any feature of the plaintiffs' claimed invention is present in any of the cited references.

57. Further, it is to be noted that D3, i.e., EP '878, is not directed to a product like the suit patent, rather it is directed to the use of an anti-PD-1 antibody in the treatment of cancer. As noted by this Court, the defendant has not pointed that D3 discloses the specific sequence of the antibodies as

claimed in the suit patent.

58. In this regard, it would be fruitful to refer to the submissions of the plaintiffs, in respect of the referred documents D1, D2 and D3 which have been filed by the defendant. The said submissions are reproduced as below:

> *"xxx xxx xxx*
>
> *51.* ***The suit patent claims new and improved anti-PD-1 antibodies, particularly monoclonal antibodies that specifically bind to human PD-1 with higher affinity and increased specificity relative to anti-PD-1 antibodies. The anti-PD- 1 antibodies disclosed in the suit patent can modulate an immune response in a subject and can be used to treat tumors. Anti-PD-1 antibodies comprising CDRs of the antibody referred to as 5C4 in the specification of suit patent have exceptional properties of treating tumors****. The detailed submissions in respect of referred documents WO2001/014557 (D1), WO2002/079499 (D2) & EP1537878 B1 (D3) filed by the Defendant as Document B, Document C and Document D are as below:*
>
> > *a) WO 2001/014557 (D1):* ***The referred document D1 does not disclose the claimed sequence of the suit patent****. WO '557 is directed to the identification of B7-4 as a PD-L1. Further, it is disclosed on page no. 56 of the documents filed by the Defendant that anti-B7-4 or anti- PD-1 antibodies are obtainable by techniques like hybridoma.* ***D1 does not provide the sequence of any anti-PD-1 antibody, and it does not provide any guidance that would have led to the particular CDRs claimed in the suit patent. Thus, WO2001/014557 (D1) does not disclose or suggest creating an anti- PD-1 antibody comprising the six CDRs of the 5C4 antibody, as claimed in the suit patent****.*
> >
> > *b) WO2002/079499 (D2): D2 WO' 499 discloses generation of antibodies including humanized antibody, murine antibody, human antibody, antigen-binding portions, and scFv, or any compound which can bind to B7-4 or PD-1 to modulate signaling. Further, WO' 499 (D2) is a patent application that relates to "[a]ssays for identifying compounds which modulate signaling via PD-1." One of a wide range of possible methods in WO' 499 (D2) discloses to modulate PD-1 activity is using "a blocking antibody that recognizes PD-1.* ***However, WO' 499 (D2) does not provide the sequence of any anti-PD-1 antibody and does not provide any guidance that would have led to the particular CDRs claimed in the current application****.*
> >
> > *c) WO2004/004771 and its US/EP and JP family (D3): The reliance on D3 by the Defendant is erroneous in view of the*

following:

> *(i) WO2004/004771 (WO '771 (D3) relates to immunopotentiation characterized by inhibition of immunosuppressive signals induced by PD-1, PD-L1, or PDL2.*
>
> *(ii)* ***WO '771 claims use of an anti-PD-1 antibody for manufacture of a medicament for treatment of cancer****.*
>
> *(iii)* ***WO '771 discloses use of an anti-PD-1 antibody which inhibits immunosuppressive signal of PD-1 for the manufacture of a medicament for cancer treatment. It is not directed to an anti-PD-1 antibody (i.e., is not directed to a product), but is directed to the use of an anti-PD-1 antibody in the treatment of cancer****.*
>
> *(iv)* ***On the other hand, the suit patent provides new and improved anti-PD-1 antibodies (product), particularly human monoclonal antibodies that specifically bind to human PD-1 with higher affinity and increased specificity relative to anti- PD-1 antibodies. The anti-PD-1 antibodies disclosed in the suit patent can modulate an immune response in a subject and can be used to treat tumors****.*
>
> *(v)* ***Further, WO '771 does not disclose the specific sequence of the antibodies as presently claimed comprising the CDRs of the 5C4 antibody.*** *Anti-PD-1 antibodies comprising CDRs of the 5C4 antibody are claimed in the present patent and it has been demonstrated that the said antibodies have exceptional properties for treating tumors. Example 2 of WO '771 discloses mouse antibody J110 (International trust number: FERM BP-8392). Examples 12 and 13 also disclose J43, a hamster antibody that binds to mouse PD-1 and another antimouse antibody. There is no sequence for any antibody let alone against human PD-1 disclosed in WO '771. As stated above, J110 is a mouse monoclonal antibody and therefore has low similarity to a human monoclonal antibody. Similarly, J43 is a hamster antibody that binds to mouse PD- 1 and has different CDRs with very low alignment to the claimed antibodies. Each of the six CDRs of J43 has 0% to 50% homology to the corresponding CDR of 5C4.* ***Thus, D3 does not disclose or teach or suggest an anti-PD-1 antibody or an antigen-binding portion thereof comprising the six CDRs of the 5C4 antibody. Due to the absolute lack of teaching or suggestion of the 5C4 CDR sequences in the cited references, a person skilled in the art would not have been motivated to start from the***

antibodies disclosed in the references and modify the CDRs to arrive at the exact six CDRs of the 5C4 antibody.

xxx xxx xxx"

(Emphasis Supplied)

59. Apart from prior arts D1-D3, the defendant has placed reliance on other prior art documents as well which, as per the defendant, disclose key aspects of the suit patent. Submissions of the defendant in this regard, in their reply to the present application, are as under:

> *"xxx xxx xxx*
>
> *a. WO 2004/056875 (D4 published on 08.07.2004, annexed as **DOCUMENT N)** which describes manufacture of human anti-PD-1 antibodies PD-1-17, PD-1-28, PD-1-33, PD-1-35 and PD-1-F2 and their characteristics;*
>
> *b. Document D5, annexed as **DOCUMENT O** describes human anti-PD- 1 antibodies PD-1-17 and PD-1-35 disclosed in D4 with their KD values. (Page 713, left column, and 2nd paragraph);*
>
> *c. Document D6, annexed as **DOCUMENT P,** describes generation of mAbs against human PD-1 and provides experimental details of the preparation of several anti-human PD-1 mAbs including J105, J108, J110, J116 and J121 (Page 216, left-hand column, section 2.2);*
>
> *d. Document D7, annexed as **DOCUMENT Q,** describes a rat anti-mouse PD-1 mAb and related in vivo studies.*
>
> *xxx xxx xxx"*

60. Perusal of the aforesaid description of the prior arts, D4 to D7, relied upon by the defendant, has not been shown to include the same sequencing as Nivolumab, i.e., the subject matter of the present suit. The defendant has not *prima facie* brought before this Court that the prior arts D4-D7, disclose in any manner, the specific amino acid sequencing of the '5C4' monoclonal antibody of the plaintiffs.

61. Thus, it is evident that the prior arts cited by the defendant do not disclose the specific sequences of the antibodies comprising the CDRs of the 5C4 antibody ("Nivolumab"), as claimed in the suit patent. There is no enabling disclosure of the claimed 5C4 CDRs or an antibody comprising the

same in any of the prior art documents cited.

62. Reference at this stage may also be made to the Guidelines for Examination of Biotechnology Applications for Patent, 2013, issued by the Office of the Controller General of Patents, Designs and Trade Marks, wherein, it has been stated that if any sequence from a prior art does not exactly match with the claimed sequence, then, the subject matter of such claims cannot be said to be anticipated by the prior art sequence. The relevant portion of the aforesaid Guidelines are extracted as under:

> *"xxx xxx xxx*
>
> ***7.2. SEQUENCE CLAIMS***
>
> *A claim to a polynucleotide sequence that was available, e.g. as part of a library before the priority date, lacks novelty, even if activity or function of the said sequence of the polynucleotide has not been previously determined. A claim to a specific fragment of polynucleotide may be considered to be novel, but subject to fulfilment of the inventive step and non-patentability under relevant clauses of Section 3 of the Act.*
>
> *A prior disclosure of the same sequence as the claimed sequence, even without any indication of its activity, would prima facie constitute anticipation to the novelty of the claimed sequence. The reasoning is that the earlier sequence inherently possesses the activity of the claimed sequence.* ***If any sequence of a polynucleotide/polypeptide from a prior art does not exactly match with the claimed sequence of polynucleotide/polypeptide, then the subject-matter of such claims cannot be said to be anticipated by the prior art sequence.*** *However, such sequence of polynucleotide/polypeptide of the prior art would be relevant for deciding inventive step or non-patentability under relevant clauses of Section 3 of the Act.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

63. Thus, the defendant, *prima facie*, has not been able to raise a credible challenge with respect to the assertions made in relation to the prior arts, nor have they been able to show, that the anti-PD-1 antibody, as disclosed in the said prior arts, have the same amino acid sequence, as Nivolumab. Therefore, the said issues as regards the averment of the defendant regarding

cited prior arts disclosing anti-PD-1 antibody similar to plaintiffs' Nivolumab, would be subject matter of trial. Hence, all such factors would be the subject matter of trial in order to arrive at any definite finding and would not be delved into at this interim stage, in the absence of any *prima facie* credible challenge being raised by the defendant.

64. Further, this Court takes note of the fact that the post-grant Opposition proceedings, initiated by a sister concern of the defendant, are still pending. Though the OBR contains a recommendation to the Controller of Patents that the suit patent is invalid due to lack of novelty, inventive step, etc., however, proceedings pertaining thereto are pending before the learned Single Judge of the High Court of Madras.

65. This Court notes that the said OBR was challenged by way of a writ petition being *W.P. No. 8451/2023,* whereby, the OBR was set aside. However, the matter travelled to the Division Bench, by way of an appeal being *W.A. No. 1697/2024*, wherein, upon the consent of the parties, the order of the learned Single Judge in *W.P. No. 8451/2023* was quashed and set aside and the question of validity of the OBR was remanded back to the Single Bench.

66. Even otherwise, the OBR, as the name suggests, is a recommendation given by the Opposition Board to the Controller which only has a persuasive value and is not binding in nature. Reference in this regard may be made to the judgment of this Court in the case of ***Novonordiskas Versus Union of India and Others, 2022 SCC OnLine Del 1944***, wherein, it has been held as follows:

> *"xxx xxx xxx*
>
> *24.* ***It is also the settled legal position that the Opposition Board is to merely give a recommendation to the Controller under Sections***

25(3) and 25(4) of the Act. The said recommendation has a persuasive value but the ultimate decision is that of the Controller. The recommendations of the Opposition Board are not binding on the Controller. *However, the recommendation of the Opposition Board forms a crucial part of the material to be considered by the Controller. The Supreme Court in Cipla (supra) has held as under:*

> *"The aforesaid provisions indicate that the Opposition Board has to conduct an examination of notice of opposition along with the documents filed under Rules 57 to 60 and then to submit a report with reasons on each ground taken in the notice of opposition. The Opposition Board has, therefore, to make recommendation with reasons after examining documents produced by the parties as per Rules.*
>
> *Section 25(4) of the Act says that on receipt of the recommendation of the Opposition Board and after giving the patentee and the opponent an opportunity of being heard, the Controller shall order either to maintain or to amend or to revoke the patent. The procedure to be followed by the Controller is provided in Rule 62 of the Rules, which reads as follows:"*

xxx xxx xxx"

(Emphasis Supplied)

67. This Court further notes that the prior art document, on the basis of which the OBR has been made, is EP '878. The said prior art document has been dealt with in pre-grant oppositions filed against the suit patent, wherein, the Controller of Patents passed the decision dated 30th June, 2020 while dealing with the prior art document cited by the OBR, in the following manner:

> *"xxx xxx xxx*
>
> *The cited prior art document for lack of novelty in both the oppositions PGO-3 and 4 is EP1537878 B1 [WO 2004004771] [referred as _878 herein after].* ***The prior art document cited _878 does not disclose the isolated monoclonal antibody or antigen binding portion thereof that specifically binds to human Programmed Death (PD-1), comprising SEQ ID No. 18, 25, 32, 39, 46 and 53 as claimed in claim 1 of the present invention, hence the product claimed in claim 1 of the present invention is held new or novel over the cited prior art _878****. The opponents arguments based on the submissions of the applicant during the EP prosecution and also the submissions made by applicant in obtaining*

regulatory approval for Nivolumab from the US FDA are not tenable as the opponent relied mainly on the prior document _878 and which never discloses the monoclonal antibody as claimed in claim 1 with six CDR sequences. The inherent anticipation by cited document _878 as argued by the opponent along with the applicants' assertion in complaints filed before US courts is also cannot be forming basis for the lack of novelty in the absence of disclosure of the monoclonal antibody as claimed in claim 1 with six CDR sequences in cited document _878. ***Therefore, the antibody claimed in amended claim 1 is new or novel over the disclosures of cited prior art „878. The amended claims 2 to 6 are dependent claims on claim 1 and hence these claims are also said to be new or novel over the disclosures of cited prior art _878****.*

xxx xxx xxx"

(Emphasis Supplied)

68. Perusal of the aforesaid shows that in the said pre-grant opposition, a categorical finding has been given that the prior art document, EP '878, does not disclose the isolated monoclonal antibody that specifically binds to human programmed death PD-1 comprising SEQ ID Nos. 18, 25, 32, 39, 46 and 53, as claimed in Claim 1 of the suit patent. Thus, the Controller held that the product claimed in Claim 1 of the suit patent is new or novel over the cited prior art.

69. Further, dealing with the various cited documents, the Assistant Controller of Patents, in the aforenoted decision dated 30th June, 2020, while rejecting all four pre-grant oppositions, has held as follows:

"xxx xxx xxx

On perusal of the disclosures and teachings in cited documents CD1 to CD22 with the submissions by all the Opponents and applicant along with all the affidavits submitted as expert evidences, case laws submitted and also considering the arguments during the hearing by all the parties attended hearing, ***it is clear that none of the cited documents CD1 to CD22 either alone or in combination with each other make the isolated monoclonal antibody or an antigen-binding portion thereof that binds specifically to human Programmed Death (PD-1) claimed in amended claim 1 of the _5057 is obvious to a person skilled in the art. The cited prior art documents though they are disclosing the antibody against the human PD-1 protein but there is no disclosure or teaching to achieve for the human antibody having SIX specific CDR sequences of 5C4 as***

claimed in amended claim 1.

The opponents argument that the generation of monoclonal antibody against PD-1 protein is known in the art by hybridoma technology in transgenic mice and hence the monoclonal antibody claimed in claim 1 of the present invention is obvious to a person skilled in the art is not tenable as ***there are no specific disclosures or teachings in any of the cited documents CD1 to CD22 for obtaining the specific monoclonal antibody as claimed in amended claim 1 with SIX CDR sequences***.

The opponents arguments for obviousness of the claimed antibody based on the comparative data given by applicant and KD value are also not proving the antibody claimed in amended claim 1 with SIX CDR sequences is obvious to a person skilled in the art in view of the disclosures in any of the cited documents CD1 to CD22.

xxx xxx xxx"

(Emphasis Supplied)

70. Therefore, on the basis of aforenoted pendency of the proceedings in relation to the OBR, the same being *sub-judice* before the High Court of Madras, and in view of the pendency of the post-grant opposition proceedings, and further, keeping in mind the categorical findings of the Controller of Patents in its decision dated 30th June, 2020, while rejecting the pre-grant oppositions, it cannot be said that a credible challenge has been made by the defendant to the validity of the suit patent with regard to its reliance on the OBR.

71. The defendant further seeks to highlight the lack of inventive step involved in making of the suit patent by submitting that the use of transgenic mice to produce monoclonal antibodies, including, against human PD-1, has already been disclosed in the prior arts D1-D3. Though the prior arts cited by the defendant disclose the use of transgenic mice to prepare monoclonal antibodies, they do not disclose the claimed sequence of the suit patent.

72. It is evident from the analysis as aforesaid, the defendant has not been able to show that in the cited prior arts, there is disclosure or teaching to achieve the sequence for Nivolumab, as per the suit patent. Based on the

documents on record, the averments made before this Court and the discussion hereinabove, this Court is of the *prima facie* view that no specific disclosures or teachings in the cited documents have been pointed out by the defendant, wherein, the prior arts provide the sequence of any anti-PD-1 antibody, or any guidance that would have led to the particular CDRs claim in the suit patent. As noted above, though the prior arts cited by the defendant disclose the use of transgenic mice to prepare monoclonal antibodies, they do not disclose the claimed sequence of the suit patent. Therefore, the defendant has been unable to show as to how the prior arts, as cited by it, disclose or suggest creating an anti-PD-1 antibody comprising the six CDRs of the 5C4 antibody (Nivolumab), as claimed in the suit patent.

73. The onus to show that the suit patent is invalid, or that there is credible challenge to the validity of the patent, is on the person alleging the same. To discharge this burden, the defendant is required to place on record credible scientific material indicating that the plaintiffs' patent is *prima facie* vulnerable to revocation. However, the same is not the position in the present case. Reference in this regard may be made to the judgment in the case of ***Strix Limited Versus Maharaja Appliances Limited, 2009 SCC Online Del 2825***, wherein, it has been held as follows:

> *"xxx xxx xxx*
>
> *22.* ***It was contended by learned counsel for the Defendant that at an interlocutory stage, the Defendant should be held to have discharged its burden of raising a 'credible challenge' to the validity of the Plaintiff's patent by merely pointing out the existence of the European Patent. This court is unable to agree. In order to raise a credible challenge to the validity of a patent, even at an interlocutory stage, the Defendant will have to place on record some acceptable scientific material, supported or explained by the evidence of an expert, that the Plaintiff's patent is prima facie vulnerable to***

> ***revocation.*** *The burden on the Defendant here is greater on account of the fact that there was no opposition, pre-grant or post-grant, to the Plaintiff's patent.* ***In Beecham Group Ltd. v. Bristol Laboratories Pty Ltd., (1967-68) 118 CLR 618 and Australian Broadcasting Corporation v. O'Neill, (2006) 229 ALR 457 it was held that the defendant alleging invalidity bears the onus of establishing that there is "a serious question" to be tried. In Hexal Australia Pty Ltd. v. Roche Therapeutics Inc., 66 IPR 325 it was held that where the validity of a patent is raised in interlocutory proceedings, "the onus lies on the party asserting invalidity to show that want of validity is a triable question****."*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

74. It is pertinent to note that patents corresponding to IN '060 for Nivolumab have been granted in more than fifty countries and the same have not been revoked or invalidated in any jurisdiction. In fact, in the European Union, the corresponding patent was granted after several oppositions. This Court further notes that Nivolumab has also been granted approvals by health regulatory authorities worldwide in over fifty countries, including in India, the United States, Japan and countries in the European Union.

75. This Court notes that the suit patent was filed in India in the year 2007, claiming priority since the year 2005, and was granted in the year 2020. Further, the grant of the suit patent was subject to four pre-grant oppositions under Section 25(1) of the Patents Act, which were rejected by the Controller of Patents, upholding the novelty of the suit patent.

76. As noted above, the suit patent is a product patent, while the other cited prior arts, D1 to D3 are apparently process patents. The defendant has failed to show that the amino acid sequencing in the suit patent was disclosed in any prior art. It is *prima facie* apparent that the suit patent is a monoclonal antibody, which is artificial and does not exist naturally.

Accordingly, when the suit patent apparently pertains to an artificial monoclonal antibody, with no prior existence, creation of the artificial monoclonal antibody, i.e., Nivolumab, involves inventive step. Any invention cannot be said to be patentable without an inventive step. Therefore, the challenge of the defendant to the suit patent on the basis of lack of inventive step, is not acceptable and accordingly, rejected.

77. Further, this Court notes that while rejecting the pre-grant oppositions, the Controller of Patents, in the order dated 30th June, 2020, has held that the suit patent meets the criteria of inventive step. The relevant portion of the said order, is noted as follows:

> *"xxx xxx xxx*
>
> ***Therefore, in my opinion, the disclosures in these documents CD1 to CD22 either alone or in combination do not make the claimed antibody 5C4 in amended claim 1 in the _5057obvious to a person skilled in the art and hence meets the criteria of the inventive step as per the provisions of the section 2 (1) (ja) of the Patents Act, 1970. The amended claims 2 to 6 are dependent claims on amended claim 1 and hence they also involve inventive step as required under section 2 (1) (ja) of the Patents Act, 1970.***
>
> ***The amended claim 7 is claiming for a composition comprising the monoclonal antibody or antigen-binding portion thereof as claimed in any one claims 1-6 and a pharmaceutically acceptable carrier. As the composition is claimed with the novel and inventive antibody 5C4 of claim 1 and hence this claim also involve inventive step as required under section 2 (1) (ja) of the Patents Act, 1970****.*
>
> *The amended claim 8 is claiming for an isolated nucleic acid encoding the monoclonal antibody or antigen-binding portion thereof as claimed in any one claims 1- 7, wherein the nucleic acid sequence encoding the heavy chain comprises sequence defined in Figure 4A and that encoding the light chain comprises sequence defined in figure 4B. The isolated nucleic acid claimed in claim 8 is encoding the novel and inventive antibody 5C4 of claim 1 and hence this claim also involve inventive step as required under section 2 (1) (ja) of the Patents Act, 1970.*
>
> ***Hence, the amended claims 1 to 8 are involving the inventive step as required under section 2(1)(ja) of the Patents Act, 1970.Therefore, all***

the opponents clearly failed to establish this ground of opposition u/s 25 (1) (e) of the Patents Act, 1970.”

(Emphasis Supplied)

78. Considering the detailed discussion hereinabove, *prima facie*, validity of the suit patent is established. Thus, no credible challenge to the validity of the suit patent can be said to have been raised by the defendant.

79. At this stage, this Court notes that the defendant has asserted the claim of non-infringement on the grounds that despite their product being bio-similar, regardless, the same does not constitute infringement of the plaintiffs' drug, as firstly, it is essential to do product claim mapping in cases of patent infringement. However, the defendant's product has not been launched in the market, therefore, it is the defendant's case that the manner in which claim mapping has been done by the plaintiffs, is incorrect. Further, the defendant contends that the plaintiffs' scope of the suit patent and claims thereof, themselves do not cover the claims as asserted by the plaintiffs, and limits the patent to 'specific' binding with only PD-1, and not with other members of the CD-28 family. Lastly, it is asserted that the balance of convenience lies in favour of the defendant and against the plaintiffs. The aforenoted contentions of the defendant are dealt hereinafter.

80. Bio-similarity refers to the similarity of a biological medicine (bio-similar) with its reference product, i.e., previously approved biological medicine (biologic) in terms of safety, efficacy and quality. Essentially, biological medicines are complex drugs which are produced using a living system/organic life, such as a micro-organism, plant cell, or animal cell by removing organic proteins or genetic materials from said cellular lifeforms and reproducing or growing them in laboratories. Bio-similars are not exact replicas of the reference biologics, however, they must demonstrate that

there are no meaningful clinical differences in their purity, molecular structure and bioactivity. The process of preparation of a biologic and bio-similar may differ, however, the end result, i.e., the effect of the drugs must be the same.

81. It is to be noted that all the studies for regulatory approvals are being carried out by the defendant with respect to Opdivo®, i.e., Nivolumab, the suit patent, which is the reference product for the bio-similar of the defendant, i.e., ZRC-3276. As per the Similar Biologics Guidelines, issued by the Department of Biotechnology, Government of India, 'Similar Biologic product' has been defined as follows:

> *"xxx xxx xxx*
>
> ***A Similar Biologic product is that which is similar in terms of quality, safety and efficacy to an approved Reference Biological product based on comparability**.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

82. As per the aforesaid Similar Biologics Guidelines, the following attributes are to be established to show bio-similarity:

i. Bio-similarity is a concept that entitles subsequent companies to apply for an abridged and shortened regulatory approval process based on demonstration of similarity in the comparative assessment. This includes ensuring comparable safety, efficacy and quality of a Similar Biologic to the Reference Biologic.

ii. The demonstration of similarity depends upon detailed and comprehensive product characterization, preclinical and clinical studies in comparison with Reference Biologic.

iii. Any product can be considered as a Similar Biologic, only if it is proven to be similar using extensive quality characterisation against the

Reference Biologic.

iv. Similar Biologics are developed through a sequential process to demonstrate the similarity by extensive characterization studies revealing the molecular and quality attributes with regard to the Reference Biologic.

v. The dosage form, strength and route of administration of the Similar Biologic should be the same as that of the Reference Biologic.

vi. The active drug substance (active ingredient) of the Reference Biologic and that of the Similar Biologic must be shown to be similar.

vii. Similar Biologics manufacturers should develop the manufacturing process to yield a comparable quality product in terms of identity, purity, and potency to the Reference Biologic.

viii. The target amino acid sequence of the Similar Biologic should be confirmed and is expected to be the same as for the Reference Biologic.

ix. The quality comparison between Similar Biologic and Reference Biologic is essential for an abridged study.

83. Thus, it is clear that as per the aforesaid Similar Biologics Guidelines, the target amino acid sequence of the similar biologic should be confirmed and is expected to be the same for the reference biologic. The relevant extract from the Similar Biologics Guidelines, is reproduced as under:

> *"xxx xxx xxx*
>
> ***6.3.2 Product Characterization***
>
> *.....*
>
> ***i. Structural and Physicochemical Properties: <u>The analysis of physicochemical characteristic should include determination of primary and higher order structure of the drug substance and the product along with other significant physicochemical properties. The target amino acid sequence of the Similar Biologic should be confirmed and is expected to be the same as for the Reference Biologic.</u> <u>Analytical methods that are used (including Biological and functional assays) should have acceptable precision and accuracy.</u>*** *In cases, where post translational modifications are taking place, these modifications need to be identified*

and quantified. In case any significant differences are found, these should be scientifically justified and critically examined in preclinical studies and clinical trials.

xxx xxx xxx"

(Emphasis Supplied)

84. Thus, in bio-similar drugs, the efficacy and amino acid sequencing, is also similar, however, chemically, the said drugs would be different.

85. In the present case, the defendant has specifically admitted that their similar biologic product has the plaintiffs' product, Nivolumab, as the reference biologic. Thus, the aforesaid attributes as per the Similar Biologic Guidelines issued by the Government of India, would be available in the product of the defendant, including, the sequence ID of the amino acid, otherwise, the defendant could not have claimed their product as bio-similar of Opdivo®. Further, this Court notes that it is not the case of the defendant that the sequencing of their product is different from the suit patent.

86. On its claim of its product being bio-similar of Nivolumab, the defendant in its note dated 17th February, 2025, has stated as follows:

"xxx xxx xxx

*12. **The Defendant's product can certainly be called a bio-similar of "Nivolumab". A product can be called "Nivolumab" so long as it comprises the specific sequence of amino acids mentioned in the "WHO Drug Information" document**. However, claim 1 of the suit patent has an added limitation over and above such sequences, i.e., the product having such sequences must be isolated and bind specifically to PD-1. Defendant's product does not fulfill this additional requirement of claim 1 of the suit patent.*

xxx xxx xxx"

(Emphasis Supplied)

87. Further, in the same note dated 17th February, 2025, the defendant has asserted as follows:

"xxx xxx xxx

18. .....

.....

c. ***Under the "WHO Drug Information" document, any product can be called "Nivolumab" if it includes the sequences mentioned in that document [Pg. 308, Document PF]. This list of sequences includes the Complementarity-Defining Regions (CDRs)****.*

Note: *In simple terms, CDRs are the part of the monoclonal antibody that binds with the target. It is the target binding site.*

xxx xxx xxx"

(Emphasis Supplied)

88. Perusal of the aforesaid, establishes the defendant's assertion that its product is bio-similar of Nivolumab and that any product can be called Nivolumab, if it includes the sequences mentioned in the WHO information document. Thus, *prima facie*, similarity in the amino acid sequencing of Nivolumab and the bio-similar product of the defendant, is established.

89. Reference may also be made to the clinical trial application filed by the defendant before the CTRI, wherein, the defendant has categorically named the comparator agent as Opdivo®, i.e., Nivolumab of the plaintiffs. The comparator agent, as given in the clinical trial application of the defendant, is reproduced as under:

Regulatory Clearance Status from DCGI	**Status**	**Date**	
	Approved/Obtained	30/09/2022	
Health Condition / Problems Studied	**Health Type**	**Condition**	
	Patients	Malignant neoplasm of unspecifiedpart of bronchus or lung	
Intervention / Comparator Agent	**Type**	**Name**	**Details**
	Intervention	ZRC-3276 (Cadila Healthcare Ltd.)	Dose :- 3 mg/kg Route :- IV infusion Frequency :- every 14 day Duration :- 6 month
	Comparator Agent	Opdivo (Bristol-Myers Squibb)	Dose :- 3 mg/kg Route :- IV infusion Frequency :- every 14 day Duration :- 6 month

Inclusion Criteria

Inclusion Criteria	
Age From	18.00 Year(s)
Age To	75.00 Year(s)
Gender	Both
Details	1.Male or female with? 18 years of age 2.Subjects with histologically or cytologically-documented locally advanced or metastatic NSCLC who present with Stage IIIB/IIIC/Stage IV or recurrent or progressive disease following multi-modality therapy (radiation therapy, surgical resection or definitive chemo radiation therapy for locally advanced disease). Note: Subjects eligible for study therapy after acceptable prior therapy are as specified below: o Subjects must have experienced disease recurrence or progression during or after one first line therapy for advanced or metastatic disease. o A switch of an agent within a regimen in order to manage toxicity does not define the start of a new line of therapy. Subjects must have received at least 2 cycles of platinum doublet based chemotherapy before discontinuation for toxicity. o Maintenance therapy following first line chemotherapy is not considered as a separate regimen of therapy and could comprise continuation of one or more of the agents used in the first-line therapy regimen or switch to another non cross-resistant agent. The initiation of maintenance therapy requires the lack of progressive disease with front-line therapy. Subjects who showed disease progression during or after maintenance therapy will be eligible. o Treatment given for locally advanced disease is not considered as a line of therapy for advanced disease. Participants with recurrent disease >6 months after platinum containing adjuvant, neoadjuvant or definitive chemo-radiation therapy given for locally advanced disease, who also subsequently progressed during or after a platinum doublet-based regimen given to treat the recurrence, are eligible. o Experimental therapies when given as separate regimen are considered as separate line of therapy. Subject who received experimental therapies for disease progression after fist line therapy will not be eligible. - Participants who received adjuvant, neoadjuvant chemotherapy or definitive chemo-radiation therapy given for locally advanced disease, and developed recurrent disease within 6 months of completing therapy are eligible. o Adjuvant or neoadjuvant platinum-doublet chemotherapy (after surgery and/or radiation therapy) followed by recurrent or metastatic disease within 6 months of completing therapy is considered as first line therapy for advanced disease. 3.With at least one measurable target lesion (based on response evaluation criteria in solid tumors [RECIST] criteria, version 1.1) performed within 28 days of randomization a. Target Lesions may be located in a

	previously irradiated field if there is documented (radiographic) disease progression in that site 4.Eastern Co-operative Oncology Group (ECOG) performance status of 0 or 1. 5. Subjects who meets following laboratory values (assessed within 28 days prior to randomization): a. WBCs ?2000/?L b. Neutrophils ?1500/?L c. Platelets ?100 X 10^3/?L d. Hemoglobin ?9.0 g/dL e. Serum creatinine of ?1.5 X ULN or creatinine clearance >40 mL/minute (using Cockcroft/Gault formula) f. AST & ALT ?1.5 X ULN g. Total bilirubin ? 1.5 X ULN 6. Female subjects who are not pregnant or breastfeeding and at least one of the following conditions applies: -Are postmenopausal for at least 24 months before the screening visit, OR -Are surgically sterile by bilateral tubal ligation, hysterectomy, or bilateral oophorectomy, OR -If they are of childbearing potential, agree to practice highly effective methodsof contraception (failure rate of less than 1% per year) with low user dependency when used consistently and correctly, from at least 28 days before starting study drug through 5 months after the last dose of study treatment, OR agree to completely abstain from heterosexual intercourse - A woman of child bearing potential must have a negative highly sensitive serum beta-human chorionic gonadotropin (beta-hCG) test at Screening and urine beta-hCG test at Baseline 7.Male subjects, even if surgically sterilized (i.e., status post vasectomy), who: -Agree to completely abstain from heterosexual intercourse, OR -Agree to practice effective barrier contraception during the entire study treatment period and through 5 months after the last dose of study treatment if their partner is of childbearing potential, even if they have had a successful vasectomy. 8.No clinically significant findings on clinical and/or physical examination, 12 lead ECG, or laboratory tests after signing the ICF but before receiving the first dose study drug. The Investigator will determine if a particular finding is clinically significant. 9. Subjects must have signed and dated an Institutional Review Board (IRB)/ Independent Ethics committee (IEC) approved written informed consent form in accordance with regulatory and institutional guidelines. This must be obtained before the performance of any protocol related procedures that are not part of normal subject care. 10. Subjects must be willing and able to comply with scheduled visits, treatment schedule, laboratory tests and other requirements of the study

90. Further, as regards Nivolumab, the defendant in the brief summary of the clinical trial application, has stated as follows:

Brief Summary	Lung cancer is the most common cancer and the leading cause of cancer-related deaths globally. Non–small-cell lung cancer accounts for 85% to 90% of lung cancers . Based on the national cancer registry data, incidence of lung cancer is highest amongst all approved indication of Nivolumab in India. Therefore, the selection of target patient population for current study was based on data in Indian population. Nivolumab is a fully human IgG4 programmed death-1 (PD-1) immune checkpoint inhibitor antibody, that binds with high affinity to PD-1 receptors expressed on T cells and disrupts negative signaling induced by PD-ligand 1 (PD-L1) and PD-ligand 2 to restore T-cell effector function. In one of the Phase I study in patients with advanced NSCLC, Nivolumab monotherapy demonstrated a mean ORR of 17% and 18% in pateints with squamous and nonsquamous histologies, respectiely. The survival rates were 42% (95% CI, 33 to 50) at 1 year, 24% (95% CI, 17 to 33) at 2 year, and 18% (95% CI, 11 to 25) at 3 year in the total population across all dose levels. [13]. These initial signals of efficacy and tolerability prompted two phase III trials that demonstrated a survival benefit for salvage Nivolumab over docetaxel in patients with advanced pretreated NSCLC leading to its approval in the United States for treatment of patients with metastatic NSCLC whose disease has progressed on or after platinum based chemotherapy and after an approved TKI therapy (if expressing EGFR or ALK genomic tumor aberrations). Also, Nivolumab is approved in the European Union for locally advanced or metastatic NSCLC after prior chemotherapy.

91. Thus, there is a categorical reference to Nivolumab, the plaintiffs' product, by the defendant in its clinical trial application, which is the reference product for the bio-similar product of the defendant.

92. The defendant has further recognised Nivolumab being anti-PD-1 antibody with high affinity to PD-1 receptors. Figure from the Complete Specification of the suit patent showing the binding specificity of Nivolumab to PD-1 and other antibodies, is reproduced as under:

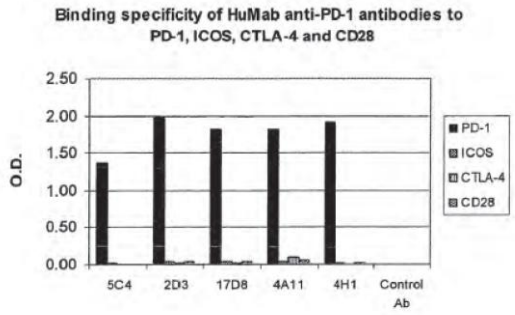


Figure 14

93. Further, the plaintiffs have done complete mapping of the suit patent with Nivolumab as given in INN, which is reproduced as under:

Claims 1 and 3 of IN '060	Sequence ID	Nivolumab INN
Claim 1 1. An isolated monoclonal antibody or an antigen-binding portion thereof that binds specifically to human Programmed Death (PD-1), comprising: a) a heavy chain CDR1 consisting of the amino acid sequence set forth in SEQ ID NO: 18; b) a heavy chain CDR2 consisting of the amino acid sequence set forth in SEQ ID NO: 25; c) a heavy chain CDR3 consisting of the amino acid sequence set forth in SEQ ID NO: 32;	SEQ ID NO:18 as per sequence listing and read with fig 8 Asn Ser Gly Met His N S G M H SEQ ID NO:25 as per sequence listing and read with fig 8 Val Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr Ala Asp Ser Val Lys Gly V I W Y D G S K R Y Y A D S V K G SEQ ID NO:32 as per sequence listing and read fig 8 Asn Asp Asp Tyr N D D Y	**Heavy chain** QVQLVESGGG VVQPGRSLRL DCKASGITFS NSGMHWVRQA PGKGLEWVAV 50 IWYDGSKRYY ADSVKGRFTI SRDNSKNTLF LQMNSLRAED TAVYYCATND 100 DYWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC LVKDYFPEPV 150 TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG TKTYTCNVDH 200 KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPPKP KDTLMISRTP 250 EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN STYRVVSVLT 300 VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ VYTLPPSQEE 350 MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY 400

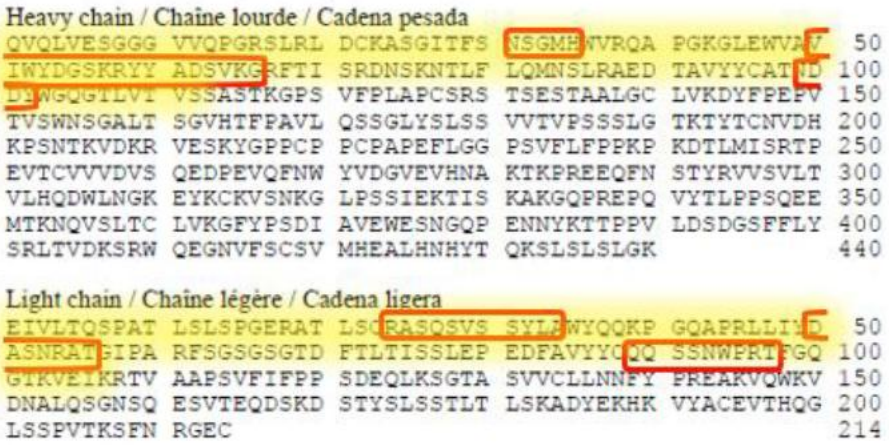
d) a light chain CDR1 consisting of the amino acid sequence set forth in SEQ ID NO: 39; e) a light chain CDR2 consisting of the amino acid sequence set forth in SEQ ID NO: 46; and f) a light chain CDR3 consisting of the amino acid sequence set forth in SEQ ID NO: 53.	SEQ ID NO:39 as per sequence listing and read with fig 9 Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala R A S Q S V S S Y L A SEQ ID NO:46 as per sequence listing and read fig 9 Asp Ala Ser Asn Arg Ala Thr D A S N R A T SEQ ID NO:53 as per sequence listing and read with fig 9 Gln Gln Ser Ser Asn Trp Pro Arg Thr Q Q S S N W P R T	SRLTVDKSRW QEGNVFSCSV MHEALHNHYT QKSLSLSLGK 440 **Light chain** EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD 50 ASNRATGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQSSNWPRTFGQ 100 GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150 DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200 LSSPVTKSFN RGEC 214
Claim 3 3. The monoclonal antibody or antigen-binding portion thereof, as claimed in claim 1, which comprises: a) a heavy chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 4; and	SEQ ID NO:4 as per sequence listing Gln Val Gln Leu Val Glu Ser Gly Gly Gly Q V Q L V E S G G G Val Val Gln Pro Gly Arg Ser Leu Arg Leu	**Heavy chain** QVQLVESGGG VVQPGRSLRL DCKASGITFS NSGMHWVRQA PGKGLEWVAV 50 IWYDGSKRYY ADSVKGRFTI SRDNSKNTLF LQMNSLRAED TAVYYCATND 100

	V V Q P G R S L R L Asp Cys Lys Ala Ser Gly Ile Thr Phe Ser D C K A S G I T F S Asn Ser Gly Met His Trp Val Arg Gln Ala N S G M H W V R Q A Pro Gly Lys Gly Leu Glu Trp Val Ala Val P G K G L E W V A V Ile Trp Tyr Asp Gly Ser Lys Arg Tyr Tyr I W Y D G S K R Y Y Ala Asp Ser Val Lys Gly Arg Phe Thr Ile A D S V K G R F T I Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe S R D N S K N T L F Leu Gln Met Asn Ser Leu Arg Ala Glu Asp L Q M N S L R A E D Thr Ala Val Tyr Tyr Cys Ala Thr Asn Asp	DYWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC LVKDYFPEPV 150 TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG TKTYTCNVDH 200 KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPPKP KDTLMISRTP 250 EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN STYRVVSVLT 300 VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ VYTLPPSQEE 350 MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY 400 SRLTVDKSRW QEGNVFSCSV MHEALHNHYT QKSLSLSLGK 440

b) a light chain variable region comprising the amino acid sequence set forth in SEQ ID NO: 11.	T A V Y Y C A T N D Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr D Y W G Q G T L V T Val Ser Ser V S S SEQ ID NO:11 as per sequence listing and fig 9 Glu Ile Val Leu Thr Gln Ser Pro Ala Thr E I V L T Q S P A T Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr L S L S P G E R A T Leu Ser Cys Arg Ala Ser Gln Ser Val Ser L S C R A S Q S V S Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro S Y L A W Y Q Q K P Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp G Q A P R L L I Y D	**Light chain** EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD 50 ASNRATGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ SSNWPRTFGQ 100 GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150 DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200 LSSPVTKSFN RGEC 214
	Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala A S N R A T G I P A Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp R F S G S G S G T D Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro F T L T I S S L E P Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln E D F A V Y Y C Q Q Ser Ser Asn Trp Pro Arg Thr Phe Gly Gln S S N W P R T F G Q Gly Thr Lys Val Glu Ile Lys G T K V E I K	

94. The aforesaid claim mapping with respect to Claims 1 and 3 of the suit patent, IN '060 are shown to map to the International Non-Proprietary Name -INN.

95. The claim chart mapping the amino acid sequences as per Claims 1 and 3 of IN '060, *vis-a-vis* the Nivolumab INN, is as follows:



96. The structure/sequence of Nivolumab, the originally assigned INN by the WHO in the year 2013, with an amendment in the description later in the year 2014, as mentioned in the WHO recommended INN list, is reproduced as under:

> *"immunoglobulin G4-kappa, anti-[Homo sapiens PDCD1 (programmed cell death 1, PD-1, PD1, CD279)], Homo sapiens monoclonal antibody; gamma4 heavy chain (1-440) [Homo sapiens VH (IGHV3-33*01 (91.80%) (IGHD)-IGHJ4*01) [8.8.6] (1-113) -IGHG4*01 hinge S10>P (221) (114-440)], (127-214')-disulfide with kappa light chain (1'-214') [Homo sapiens V-KAPPA (IGKV3-11*01 (98.90%) -IGKJ1*01) [6.3.9] (1'-107') -IGKC*01 (108'-214')]; (219-219":222-222")-bisdisulfide dimer.*
>
> **Heavy chain / Chaîne lourde / Cadena pesada**
> QVQLVESGGG VVQPGRSLRL DCKASGITFS NSGMHWVRQA PGKGLEWVAV 50
> IWYDGSKRYY ADSVKGRFTI SRDNSKNTLF LQMNSLRAED TAVYYCATND 100
> DYWGQGTLVT VSSASTKGPS VFPLAPCSRS TSESTAALGC LVKDYFPEPV 150
> TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG TKTYTCNVDH 200
> KPSNTKVDKR VESKYGPPCP PCPAPEFLGG PSVFLFPPKP KDTLMISRTP 250
> EVTCVVVDVS QEDPEVQFNW YVDGVEVHNA KTKPREEQFN STYRVVSVLT 300
> VLHQDWLNGK EYKCKVSNKG LPSSIEKTIS KAKGQPREPQ VYTLPPSQEE 350
> MTKNQVSLTC LVKGFYPSDI AVEWESNGQP ENNYKTTPPV LDSDGSFFLY 400
> SRLTVDKSRW QEGNVFSCSV MHEALHNHYT QKSLSLSLGK 440
>
> **Light chain / Chaîne légère / Cadena ligera**
> EIVLTQSPAT LSLSPGERAT LSCRASQSVS SYLAWYQQKP GQAPRLLIYD 50
> ASNRATGIPA RFSGSGSGTD FTLTISSLEP EDFAVYYCQQ SSNWPRTFGQ 100
> GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV 150
> DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG 200
> LSSPVTKSFN RGEC 214
>
> **Disulfide bridges location / Position des ponts disulfure / Posiciones de los puentes disulfuro**
> Intra-H 22-96 140-196 254-314 360-418
> 22"-96" 140"-196" 254"-314" 360"-418"
> Intra-L 23'-88' 134'-194'
> 23'"-88'" 134'"-194'"
> Inter-H-L 127-214' 127"-214'"
> Inter-H-H 219-219" 222-222"
>
> **N-glycosylation sites / Sites de N-glycosylation / Posiciones de N-glicosilación**
> H CH2 84.4:
> 290, 290"

97. Thus, it is evident that the amino acid sequencing is same in the suit patent as well as Nivolumab INN. Therefore, Nivolumab INN is disclosed in the suit patent.

98. The discussion as aforesaid discloses that Nivolumab is covered and claimed in the suit patent by Claims 1, 3 and 7. The submission of the plaintiffs in this regard, as encapsulated in their rejoinder, is reproduced as under:

> *"xxx xxx xxx*
>
> *16.* ***Thus, IN '060 claims an isolated monoclonal antibody or an antigen-binding portion thereof that binds specifically to human Programmed Death (PD-1) comprising a heavy chain CDR1*** *consisting of the amino acids sequence set forth in SEQ ID NO: 18, a heavy chain CDR2 consisting of the amino acids sequence set forth in SEQ ID NO: 25, and a heavy chain CDR3 consisting of the amino acids sequence set forth in SEQ ID NO: 32, and a light chain CDR1 consisting of the amino acids sequence set forth in SEQ ID NO: 39, a light chain CDR2 consisting of the amino acids sequence set forth in SEQ ID NO: 46, and a light chain CDR3 consisting of the amino acids sequence set forth in SEQ ID NO: 53 (Claim 1).*
>
> *17.* ***The six CDRs recited in claim 1 are the CDRs of an antibody termed as the "5C4 antibody" embodied in the complete specification of IN '060. Other than 5C4 antibody, IN '060 also discloses 6 other antibodies, namely 17D8, 2D3, 4H1, 4A11, 7D3, 5F4. All these antibodies, including 5C4, are not naturally occurring and are artificially produced****.*
>
> *18. The 5C4 antibody contains a heavy chain variable domain (VH) of amino acid sequence set forth as SEQ ID NO: 4 (Claim 3), which contains CDR's of SEQ ID NOs: 18, 25, and 32, and a light chain variable domain (VL) of amino acid sequence set forth as SEQ ID NO: 11 (Claim 3), which contains CDR's of SEQ ID NOs: 39, 46, and 53.* ***The CDR's, heavy chain, light chain sequences, and corresponding sequences of nucleic acids are provided in the sequence listing which is part of the complete specification of IN '060.*** *The nucleic acid sequence encoding the VH and VL domains are defined in Figure 4A and 4B, respectively of the complete specification of IN '060 and the same are reproduced hereinbelow:*

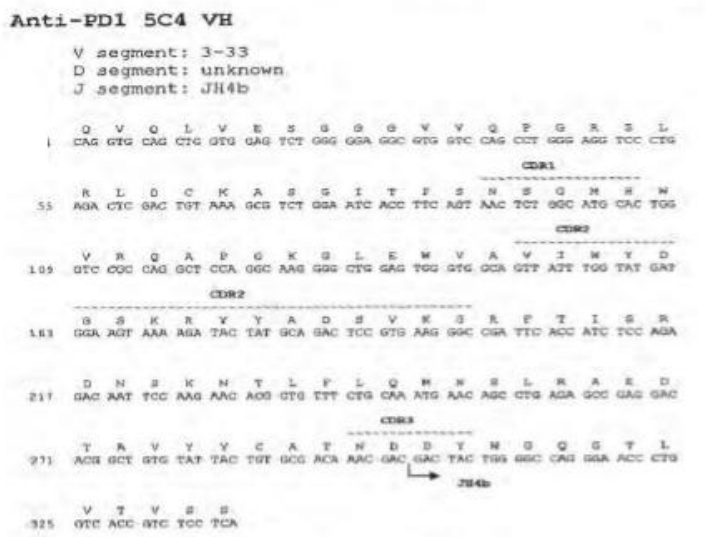


Figure 4A

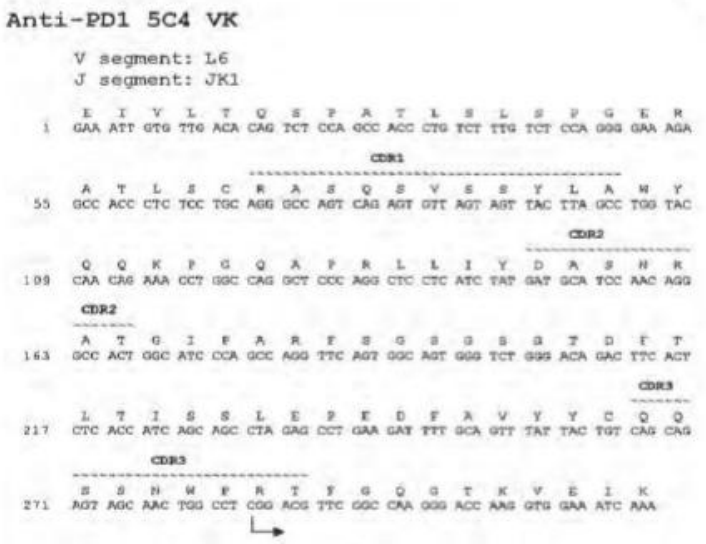


Figure 4B

xxx xxx xxx"

(Emphasis Supplied)

99. In order to support their claim that the suit patent is for Nivolumab and that Nivolumab is disclosed in the patent specification IN '060, the plaintiffs have relied upon the affidavit of Dr. Brian T. Fife dated 15th August, 2022, filed with the Patent Office, wherein, it has been stated as follows:

"xxx xxx xxx

8. ***As I explained in a previous Affidavit, nivolumab is disclosed by the current specification. (See Annexure III). The entirety of SEQ ID NO: 4 aligns perfectly with the first 113 amino acids of nivolumab's heavy chain sequence.*** *(See Opposition, 112.5.3.)* ***Because SEQ ID NO: 4 contains all of 5C4's heavy chain CDRs, a person of ordinary skill in the art would have understood that all of the antigen-binding regions of the disclosed 5C4 heavy chain are the same as those in nivolumab.*** *(See Specification, pp. 10, 22 and Fig. 4A.)* ***Similarly, a person of ordinary skill in the art would have understood that all of the antigen-binding regions of the disclosed 5C4 light chain variable region (i.e., SEQ IN NO: 11) are the same as those in nivolumab.*** *(See Specification, pp. 10, 22 and Fig. 48.)* ***These disclosures are the critical aspects of disclosing nivolumab, as the CDRs (i.e., complementarity determining regions) have long been known as the regions that determine an antibody's specificity, with the surrounding variable region providing the framework for presenting the CDRs****.*

xxx xxx xxx"

(Emphasis Supplied)

100. The defendant claims to conform to the INN, Nivolumab. The plaintiffs have mapped their suit patent, 5C4 antibody (Nivolumab) in order to show that the suit patent conforms to INN, Nivolumab. Thus, it is clear that when the suit patent of the plaintiffs conforms to INN Nivolumab and the defendant has shown its product, ZRC-3276 to be conforming to INN Nivolumab, the product of the defendant would have to have the same sequencing as that of the plaintiffs' Nivolumab.

101. Defendant has nowhere stated that the sequencing of amino acids of their product is different from the sequencing of amino acids of anti-PD-1 antibody of the suit patent. The defendant has conducted tests on both Opdivo®, i.e., the product of the plaintiffs under which Nivolumab is sold, and their own product, i.e., ZRC-3276. The drug of the defendant, i.e., ZRC-3276, also has a high binding specificity to PD-1, as evidenced by the said test results, as shown in the charts below. The relevant extract from the test

report by Zydus as filed by the defendant with regard to evaluation of binding specificity of defendant's product, i.e., ZRC-3276 with PD-1 and other proteins of CD-28 family, is reproduced as under:

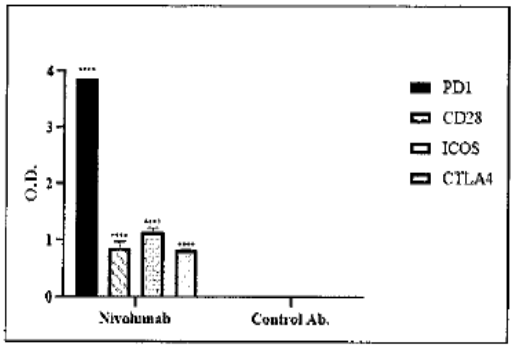


Figure 1: Experiment 1 result showing binding of Nivolumab (ZRC-3276) and control antibody to CD28 family members. Statistics performed by three-way ANOVA with sidak's multiple comparison test, ** indicate p<0.0001**

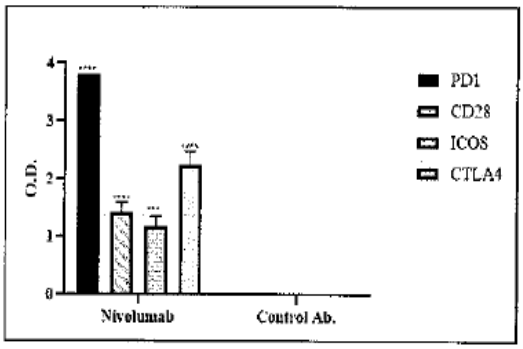


Figure 2: Experiment 2 result showing binding of Nivolumab (ZRC-3276) and control antibody to CD28 family members. Statistics performed by three-way ANOVA with sidak's multiple comparison test, ** indicate p<0.0001, ***indicates p=0.0001**

102. The defendant also tested the product of the plaintiffs, i.e., Opdivo® in its in-house laboratory, the test results of which, as filed by the defendant, are reproduced as under:

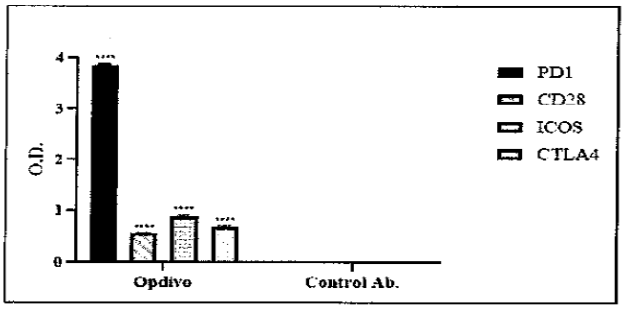


Figure 1: Experiment 1 result showing binding of Opdivo® and control antibody to CD28 family members. Statistics performed by three-way ANOVA with sidak's multiple comparison test, ** indicate p<0.0001**

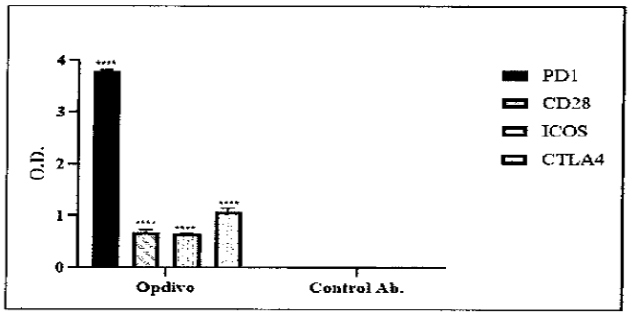
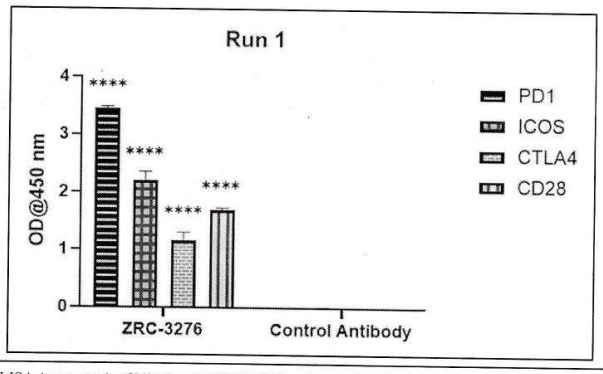


Figure 2: Experiment 2 result showing binding of Opdivo® and control antibody to CD28 family members. Statistics performed by three-way ANOVA with sidak's multiple comparison test, ** indicate p<0.0001**

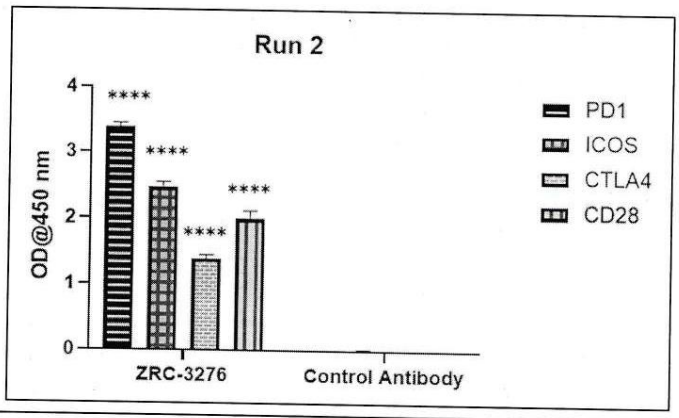
103. The defendant also got its own product, ZRC-3276, tested from Sardar Patel University, which showed the results as follows:

6.2. Run 1



Run 1: ELISA Assay result of Nivolumab (ZRC-3276) and control antibody binding to CD28 family receptors CD28, PD1, CTLA4, and ICOS. Statistical analysis was done using Three-way ANOVA with Bonferroni's multiple comparisons test. **** indicates p-value<0.0001

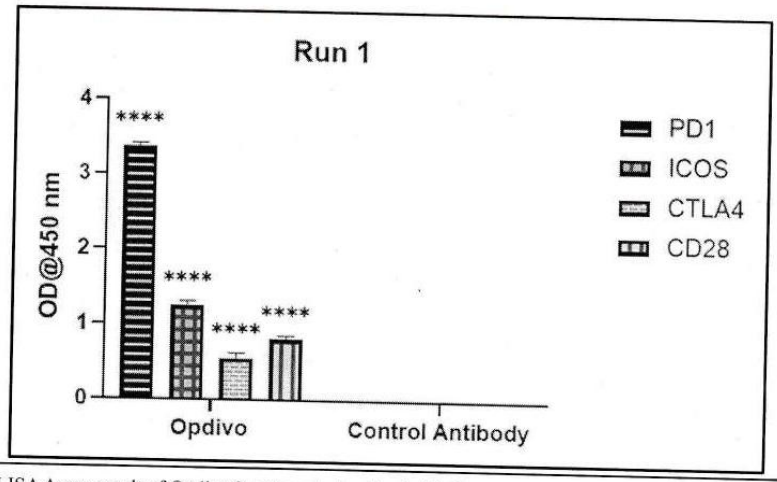
6.3. Run 2



Run 2: ELISA Assay result of Nivolumab (ZRC-3276) and control antibody binding to CD28 family receptors CD28, PD1, CTLA4, and ICOS. Statistical analysis was done using Three-way ANOVA with Bonferroni's multiple comparisons test. **** indicates p-value < 0.0001

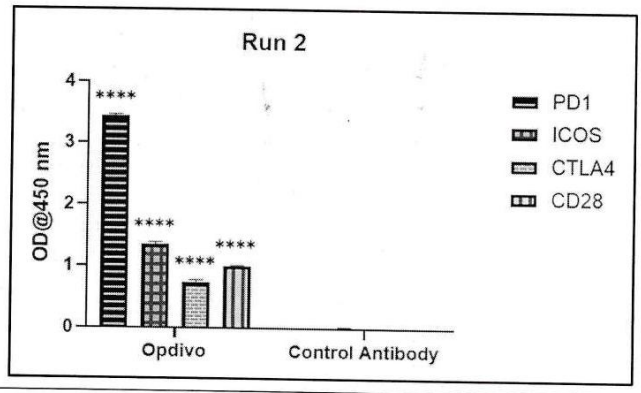
104. The defendant also got the product of the plaintiff, i.e., Opdivo® tested from Sardar Patel University, test results of which, as filed by the defendant, are reproduced as under:

6.2. Run 1



Run 1: ELISA Assay result of Opdivo® and control antibody binding to CD28 family receptors CD28, PD1, CTLA4, and ICOS. Statistical analysis was done using Three-way ANOVA with Bonferroni's multiple comparisons test. **** indicates p-value<0.0001

6.3. Run 2



Run 2: ELISA Assay result of Opdivo® and control antibody binding to CD28 family receptors CD28, PD1, CTLA4, and ICOS. Statistical analysis was done using Three-way ANOVA with Bonferroni 's multiple comparisons test. **** indicates p-value<0.0001

105. Based on the results of the tests carried out by the defendant and by Sardar Patel University with the product of the plaintiffs, the defendant submits that both tests conclude that the binding of Opdivo® is to human PD-1, as well as other CD-28 family proteins (ICOS, CD-28 and CTLA4) and therefore, it is not Nivolumab. On the contrary, the results clearly show that Opdivo® has higher binding affinity to human PD-1 receptor as compared to other CD-28 family receptors, and therefore, it is an anti-PD-1 antibody, i.e., Nivolumab, as claimed in the suit patent. The *"Disclosure of the Invention"* is further evident by describing that the claimed isolated monoclonal antibody binds to the PD-1 and exhibits numerous properties, such as high affinity binding to human PD-1, but lacks substantial cross-reactivity with either human CD-28, or CTLA-4 or ICOS.

106. The aforesaid test results to determine the binding specificity of Opdivo®, the product of the plaintiffs, and ZRC-3276, the product of the defendant, clearly demonstrate that both Opdivo® and ZRC-3276, are anti-PD-1 antibodies, that bind with PD-1 with high specificity than the other CD-28 family receptors, and do not bind substantially with human CD-

28/CTLA4 or ICOS receptors. The table summarising the test results of the tests carried out at the behest of the defendant of the product of the plaintiffs and defendant, is reproduced as under:

Receptor	ZYDUS				SARDAR PATEL UNIVERSITY			
	OPDIVO®		ZRC-3276		OPDIVO®		ZRC-3276	
	FIG 1	FIG 2	FIG. 1	FIG 2	RUN 1	RUN 2	RUN 1	RUN 2
PD1	3.8	3.7	3.9	3.9	3.4	3.5	3.5	3.5
CD28	0.5	0.7	0.9	1.3	0.8	1.0	1.7	2.0
ICOS	0.8	0.7	1.1	1.0	1.3	1.3	2.25	2.5
CTLA4	0.6	1.0	0.9	2.2	0.5	0.8	1.1	1.4

107. Considering the aforesaid test results filed by the defendant, it is apparent that both the products, i.e., Opdivo® of the plaintiffs and ZRC-3276 of the defendant, fall within the scope of the claims of the suit patent. The experiments and the technical reports of the defendant clearly demonstrate that the product of the defendant, ZRC-3276, is a bio-similar of the plaintiffs' product, i.e., Opdivo® and thus, ZRC-3276, the product of the defendant, on account of being bio-similar, has the same claimed sequences of the suit patent, which is admittedly Nivolumab.

108. As regards the difference in the binding affinity of Opdivo® and ZRC-3276, which is demonstrated from the aforesaid test results filed by the defendant, it is to be noted that the difference in the binding affinity is common and is known as 'Standard Variations in the Art'. Thus, the contention of the defendant that the product of the defendant is not an 'isolated monoclonal antibody that binds specifically to PD-1', as required under Claim 1 of the suit patent, cannot be accepted. Therefore, the test reports demonstrate that both Opdivo® and ZRC-3276 are anti-PD-1 antibodies as they both bind with PD-1 antibody with higher specificity than the other CD-28 family receptors. This shows that both products fall within the scope of the claims of the suit patent.

109. It is undisputed that it is not possible to produce a biologic product, i.e., protein, that has identical characteristics/properties as the original drug, as similarity in properties is not dependent on the manufacturing process, the conditions of manufacture, the cell system used to manufacture, etc. However, what remains identical is the sequence of the claimed amino acid. Reference in this regard may be made to the judgment in the case of ***Roche Products (India) Pvt. Ltd. & Ors. Versus Drugs Controller General of India and Ors., 2016 SCC OnLine Del 2358***, wherein, it has been held as follows:

> *"xxx xxx xxx*
>
> *180.* ***It is undisputed fact that biological drugs are synthesised by cells of living organisms, as opposed to chemical drugs which are produced by chemical synthesis. 'Biosimilars' are biological drugs that are similar to the innovator biological drug. Due to Owing to the complexity in the molecular arrangement and manufacturing process of a biological drug, it is not possible to replicate the structure and steps involved in the manufacture of the innovator biological drug and to produce an identical follow-on biological drug. Biosimilars, therefore, cannot be generic equivalents of the innovator biological drug. The generic drugs are characterised by their chemical and therapeutic equivalence to the original, low molecular weight chemical drugs. These are identical to the original product and are sold under the same chemical name****.*
>
> *xxx xxx xxx*
>
> *184. In order to avoid any confusion, it is mentioned (as admitted by the parties also) that* ***the approval process for generic drugs is not the same as the approval process for biosimilars. Biological drugs are synthesised by cells of living organisms, as opposed to chemical drugs which are produced by chemical synthesis. The 'Biosimilars' are biological drugs that are similar to the innovator biological drug. It is admitted by all parties that it is not possible to replicate the structure and steps involved in the manufacture of the innovator biological drug and to produce an identical follow-on biological drug. Thus, biosimilars cannot be generic equivalents of the innovator biological drug****.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

110. This Court also notes that the defendant has filed a patent application

no. 202021019976 ("IN '976") before the Indian Patent Office on 12th May, 2020, in respect of *'Process of Purifying anti-PD-1 Antibody'*, wherein, the preferred anti-PD-1 antibody, is Nivolumab and the same is pending. The subject matter of IN '976 application of the defendant, is in relation to purification of the anti-PD-1 antibody, in particular Nivolumab, for a finished formulation. Thus, it is evident that the defendant is dealing in Nivolumab, which is claimed in the suit patent, IN '060.

111. As per the defendant, patent infringement requires claim-to-product mapping, which has not been done by the plaintiffs. However, it is to be noted that the present suit is a *quia timet* action. By order dated 08th May, 2024, this Court had restrained the defendant from placing its product in the market, without prior permission of the Court. Thus, there was no commercial product of the defendant against which claim mapping could be done.

112. The plaintiffs have done claim mapping with the Nivolumab INN assigned by WHO, which is used as the reference product by the defendant for the development of its bio-similar. The document pertaining to the claim mapping of suit patent with the Nivolumab INN and documents of the defendant, wherein, reference has been made to plaintiffs' product Opdivo®, i.e., Nivolumab, as a reference biologic, are on record before this Court.

113. Reference at this stage may be made to the judgment of this Court in the case of ***Novartis AG and Another Versus Zydus Healthcare Limited and Another, 2022 SCC OnLine Del 4373***, wherein, it has been held that the High Court of Delhi Rules Governing Patent Suits, 2022, dealing with claim mapping use the word 'to the extent possible' and questions the applicability of the said Rules pertaining to claim mapping to a *quia timet*

action. The relevant portions of the aforesaid judgment, are extracted as below:

> *"xxx xxx xxx*
>
> *59.* ***All that Rule 3(A)(ix) and (x) of the Delhi High Court Patent Rules require is that a plaint in a patent infringement action shall, to the extent possible, include "precise claims v. product (or process) chart mapping" and "infringement analysis explained with respect to the granted claims in this specification". The applicability of these provisions, in the case of a quia timet action where the patent of the defendant has yet to be granted, is itself questionable****. That apart, the Delhi High Court Patent Rules do not, at any point, indicate that, if these formalities are not contained in a plaint alleging infringement of patent, the plaint can be rejected. The various contents which a plaint in a patent suit is required to contain, as envisaged by Rule 3(A) thereof are merely in the nature of guidelines, intended at facilitating an expeditious resolution of the dispute. Even if the plaint in a patent infringement suit does not, stricto sensu, contain all the details envisaged in the various clauses of Rule 3(A), in the manner as contemplated therein, the plaint would not be liable to be rejected on that score.*
>
> *60.* ***The fact that the various clauses in the Rule 3(A) of the Delhi High Court Patent Rules are not cast in iron is apparent even from the use of the word "to the extent possible"****".*
>
> *xxx xxx xxx*
>
> *67.* ***The use of the expression "to the extent possible" in Rule 3(A) of the Delhi High Court Patent Rules, therefore, indicates that strict compliance with the rigour of the various clauses of the said rule is not mandatory and that a plaintiff is expected to comply therewith only to the extent it is possible to do so. This reasoning would apply, mutatis mutandis, to Rule 4(A) of the Delhi High Court Patent Rules as well, which, too, requires the documents enumerated in the Rule to be filed with the plaint "to the extent possible"****.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

114. In the present case, the drug under the suit patent is being sold under the name Opdyta® (Nivolumab) in India. Since the product of the defendant is not available commercially in the market, the plaintiffs have mapped their suit patent to the Nivolumab INN. The defendant has already stated its product to be bio-similar to Nivolumab. Such indirect method has been

accepted by the Courts on various occasions. Thus, in the case of ***Intex Technologies (India) Ltd. Versus Telefonaktiebolaget L.M. Ericsson (Publ), 2023 SCC OnLine Del 1845***, it has been held as follows:

> *"xxx xxx xxx*
>
> *93.* ***There is the direct test of infringement which is applied in all standard patent cases. The other is the indirect method which involves proving the following steps:***
>
> *(i)* ***Mapping patentee's patent to the standard to show that the patent is a Standard Essential Patent****.*
>
> *(ii)* ***Showing that the implementer's device also maps to the standard****.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

115. The mapping done by the plaintiffs with that of Nivolumab sequence clearly shows that the sequence ID of Nivolumab and the suit patent 5C4 antibody, is identical. Thus, any person who wishes to call their product as bio-similar of Nivolumab, necessarily will have to have identical CDR sequences and sequences of variable heavy chain and light chain. The plaintiffs' product, Opdivo® is an anti-PD-1 antibody and is Nivolumab (INN as declared by WHO) having the claimed sequences as that of the suit patent. Furthermore, the product of the defendant, ZRC-3276 is also an anti-PD-1 antibody like Opdivo®. Since the defendant claims its product as bio-similar to Nivolumab, its product will essentially have the same claim sequences of the suit patent, which is Nivolumab.

116. Thus, by virtue of the claim mapping done by the plaintiffs and the discussion hereinabove, it is evident that Nivolumab INN is equivalent to Claims 1 and 3 of the suit patent. Further, it is to be noted that defendant has admitted that its product is a bio-similar of Nivolumab.

117. It is the contention of the defendant that there is no infringement

because the suit patent only protects *'Isolated'* monoclonal antibodies that *'Specifically'* binds to human Programmed Death 1 (PD-1), whereas, the defendant's product is not within the scope of the claims of the plaintiffs, as the antibody of the defendant interacts with other proteins in the CD-28 family as well. In this regard, it is to be noted that Claim 1 of the suit patent states that the suit patent is an isolated monoclonal antibody or an antigen binding portion thereof, that binds specifically to PD-1. This Court takes into account the submission made by the plaintiffs that 'Specifically' does not mean 'exclusively' or 'only'. Furthermore, the claims of the suit patent nowhere state that there is exclusive or only binding to PD-1.

118. As regards the rules of claim interpretation, a Division Bench of this Court, in the case of ***F. Hoffman-La Roche Ltd. & Anr. Versus Cipla Ltd., 2015 SCC OnLine Del 13619***, has held as follows:

> *"xxx xxx xxx*
>
> *66. Before we apply the aforenoted legal position to the facts of the instant case we need to discuss the legal position concerning construction of claims. In the decision reported as AIR 1969 BOMBAY 255 FH & B v. Unichem Laboratories it was held that specifications end with claims, delimiting the monopoly granted by the patent and that the main function of a Court is to construe the claims without reference to the specification; a reference to the specification being as an exception if there was an ambiguity in the claim.* ***Claims must be read as ordinary English sentences without incorporating into them extracts from body of specification or changing their meaning by reference to the language used in the body of the specification. In a recent decision in FAO (OS) No. 190/2013 Merck v. Glenmark the Division Bench held that claim construction to determine the coverage in the suit patent has to be determined objectively on its own terms with regard to the words used by the inventor and the context of the invention in terms of the knowledge existing in the industry.*** *Abandonment of an application cannot remove what is patented earlier nor can it include something that was excluded earlier and that a patent is construed by the terms used by the inventor and not the inventors subjective intent as to what was meant to be covered. Merely because an inventor applies for a latter patent that is already objectively included in a prior patent, but which inventor subjectively feels needs a separate patent application, doesn't mean it is to be taken at face*

value and therefore neither Section 3(d) or abandonment of subsequent patent application can be used to read into terms of prior application, which has to be construed on its own terms. ***In the decision reported as 415 F. 3d 1303 Edward H. Phillips v. AWH Corporation it was held that claims have to be given their ordinary and general meaning and it would be unjust to the public, as well as would be an evasion of the law, to construe a claim in a manner different from plain import of the terms and thus ordinary and customary meaning of the claim term is the meaning of the term to a Person of Ordinary Skill in the Art as of effective date of filing of the patent application. In case of any doubt as to what a claim means, resort can be had to the specification which will aid in solving or ascertaining the true intent and meaning of the language employed in the claims and for which the court can consider patent prosecution history in order to understand as to how the inventor or the patent examiner understood the invention.*** *The Court recognized that since prosecution is an ongoing process, it often lacks clarity of the specification and thus is less useful for claim construction. The Court also recognizes that having regard to extrinsic evidence such as inventor testimony, dictionaries and treaties would be permissible but has to be resorted to with caution because essentially extrinsic evidence is always treated as of lesser significance in comparison with intrinsic evidence. In the decision reported as 457 F.3. 1284 (United States) Pfizer v. Ranbaxy the Court held that the statements made during prosecution of foreign applications are irrelevant as they are in response to unique patentability requirements overseas. The Court also held that the statement made in later unrelated applications cannot be used to interpret claims of prior patent. In the decision reported as 1995 RPC 255 (UK) Glaverbel SA v. British Coal Corp the Court held that a patent is construed objectively, through the eyes of a skilled addressee.* ***The Court also held that the whole document must be read together, the body of specification with the claims. But if claim is clear then monopoly sought by patentee cannot be extended or cut down by reference to the rest of the specification and the subsequent conduct is not available to aid the interpretation of a written document.***

67. For the above conspectus, pithily put, principles of claim construction could be summarized as under:-

(i) Claims define the territory or scope of protection (Section 10(4) (c) of the Patents Act, 1970.

(ii) There is no limit to the number of claims except that after ten claims there is an additional fee per claim (1st Schedule of the Act).

(iii) Claims can be independent or dependent.

(iv) The broad structure of set of claims is an inverted pyramid with the broadest at the top and the narrowest at the bottom (Manual of Patents

Office - Practice and procedure).

(v) Patent laws of various countries lay down rules for drafting of claims and these rules are used by Courts while interpreting claims.

(vi) One rule is that claims are a single sentence defining an invention or an inventive concept.

(vii) Different claims define different embodiments of same inventive concept.

(viii) The first claim is a parent or mother claim while remaining claims are referred to as subsidiary claims.

(ix) If subsidiary claims contain an independent inventive concept different from the main claim then the Patent office will insist on the filing of a divisional application.

(x) Subject matter of claims can be product, substances, apparatus or articles; alternatively methods or process for producing said products etc. They may be formulations, mixtures of various substance including recipes. Dosage regimes or in some countries methods of use or treatment may also be claimed.

(xi) Where claims are 'dependent' it incorporates by reference 'everything in the parent claim, and adds some further statement, limitations or restrictions'. (Landis on Mechanics of Patent Claim Drafting).

(xii) Where claims are 'independent' although relating to the same inventive concept this implies that the 'independent claim stands alone, includes all its necessary limitations, and is not dependent upon and does not include limitations from any other claim to make it complete .... An independent Claim can be the broadest scope claim. It has fewer limitations than any dependent claim which is dependent upon it'. (Landis on Mechanics of Patent Claim Drafting)

(xiii) For someone wishing to invalidate a patent the said person must invalidate each claim separately and independently as it is quite likely that some claims may be valid even while some are invalid.

(xiv) At the beginning of an infringement action the Courts in the United States conduct what is known as a 'Markman hearing' to define the scope of the claims or to throw light on certain ambiguous terms used in the claims. Although this is not technically done in India but functionally most Judges will resort to a similar exercise in trying to understand the scope and meaning of the claims including its terms.

xxx xxx xxx"

(Emphasis Supplied)

119. Thus, it is evident upon perusal of the aforenoted judgment that

claims have to be given their ordinary and general meaning, which is the meaning of the term to a Person of Ordinary Skill in the Art. However, in case of doubt as to the meaning and import of a term, resort can be made to the specifications of a patent. Therefore, while the claims of the plaintiffs nowhere state 'exclusive' or 'only binding' to PD-1, reliance can be placed on the specification of the suit patent. The relevant extracts from the complete specification of the claims of the suit patent, read as under:

> *"xxx xxx xxx*
>
> ***Disclosure of the Invention***
>
> *xxx xxx xxx*
>
> ***In one aspect, the invention pertains to an isolated monoclonal antibody, or an antigen- binding portion thereof, wherein the antibody exhibits at least one of the following properties****:*
> *(a)* ***binds to human PD-1 with a K_D of 1 x 10^{-7} M or less;***
> *(b)* ***does not substantially bind to human CD28, CTLA-4 or ICOS****;*
> *(c) increases T-cell proliferation in an Mixed Lymphocyte Reaction (MLR) assay;*
> *(d) increases interferon-gamma production in an MLR assay;*
> *(e) increases IL-2 secretion in an MLR assay;*
> *(f) binds to human PD-1 and cynomolgus monkey PD-*
> *(g) inhibits the binding of PD-L1 and/or PD-L2 to PD-1;*
> *(h) stimulates antigen-specific memory responses;*
> *(i) stimulates antibody responses;*
> *(j) inhibits tumor cell growth in vivo*
>
> *xxx xxx xxx*
>
> *An "isolated antibody", as used herein, is intended to refer to an antibody that is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds PD-1 is substantially free of antibodies that specifically bind antigens other than PD-1).* ***An isolated antibody that specifically binds PD-1 may, however, have cross-reactivity to other antigens, such as PD-1 molecules from other species****. Moreover, an isolated antibody may be substantially free of other cellular material and/or chemicals.*
>
> *xxx xxx xxx*
>
> *Anti-PD-1 Antibodies*

The antibodies of the invention are characterized by particular functional features or properties of the antibodies. For example, the antibodies bind specifically to PD-1 (e.g., bind to human PD-1 and may cross-react with PD-1 from other species, such as cynomolgus monkey). ***Preferably, an antibody of the invention binds to PD-1 with high affinity****, for example with a* K_D *of* $1x10^{-7}$ *M or less. The anti-PD-1 antibodies of the invention preferably exhibit one or more of the following characteristics:*
(a) ***binds to human PD-1 with a*** K_D ***of*** $1x10^{-7}$ ***M or less****;*
(b) ***does not substantially bind to human CD28, CTLA-4 or ICOS****;*
(c) increases T-cell proliferation in an Mixed Lymphocyte Reaction (MLR) assay;
(d) increases interferon-gamma production in an MLR assay;
(e) increases IL-2 secretion in an MLR assay;
(f) binds to human PD-1 and cynomolgus monkey PD-1;
(g) inhibits the binding of PD-L1 and/or PD-L2 to PD-1;
(h) stimulates antigen-specific memory responses;
(i) stimulates antibody responses;
(j) inhibits tumor cell growth in vivo.
Preferably, the antibody binds to human PD-1 with a K_D ***of*** $5x10^{-8}$ ***M or less, binds to human PD-1 with a*** K_D ***of*** $1x10^{-8}$ ***M or less, binds to human PD-1 with a*** K_D ***of*** $5x10^{-9}$ ***M or less, or binds to human PD-1 with a*** K_D ***of between*** $1x10^{-8}$ ***M and*** $1x10^{-10}$ ***M or less****.*

An antibody of the invention may exhibit any combination of the above-listed features, such as two, three, four, five or more of the above-listed features.

Standard assays to evaluate the binding ability of the antibodies toward PD-1 are known in the art, including for example, ELISAS, Western blots and RIAS. The binding kinetics (e.g., binding affinity) of the antibodies also can be assessed by standard assays known in the art, such as by Biacore analysis. Suitable assays for evaluating any of the above-described characteristics are described in detail in the Examples.

xxx xxx xxx"

(Emphasis Supplied)

120. The defendant has further relied upon example 3, figure 14 of Complete Specification to argue that there is high binding affinity to PD-1, but no binding affinity to other CD-28 receptors. However, perusal of the specification, in particular to example 3, with reference to figure 14 shows that it has nowhere been mentioned that the product of the plaintiffs has exclusive binding with PD-1. It states regarding 'High Specificity to PD-1'.

Relevant extract from example 3 of the Complete Specification, is reproduced as under:

> *"xxx xxx xxx*
>
> *Binding specificity by ELISA against other CD28 family members*
>
> *A comparison of the binding of anti-PD-1 antibodies to CD28 family members was performed by standard ELISA using four different CD28 family members to examine the specificity of binding for PD-1.*
>
> *Fusion proteins of CD28 family members, ICOS, CTLA-4 and CD28 (R&D Biosystems) were tested for binding against the anti-PD-1 human monoclonal antibodies 17D8, 2D3, 4H1, 5C4, and 4A11. Standard ELISA procedures were performed. The anti-PD-1 human monoclonal antibodies were added at a concentration of 20 ug/ml. Goat-anti-human IgG (kappa chain-specific) polyclonal antibody conjugated with horseradish peroxidase (HRP) was used as secondary antibody. The results are shown in Figure 14.* ***Each of the anti-PD-1 human monoclonal antibodies 17D8, 2D3, 4H1, 5C4, 4A11, 7D3 and 5F4 bound with high specificity to PD-1, but not to the other CD28 family members****.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

121. Upon perusal of the above, it comes to the fore that Nivolumab has been shown as an anti-PD-1 antibody, with high/substantial affinity to bind to PD-1 receptors. Moreover, there is a clear mention that there is no substantial binding to CD-28 receptors, which cannot be construed to mean that there is no binding with the CD-28 receptors. The specification nowhere states that there is no binding to other CD-28 receptors, thus, negating the argument of the defendant.

122. Reference may also be made to the order dated 30th June, 2020 passed by the Controller of Patents in the pre-grant opposition proceedings, wherein, with regard to high binding specificity of the antibody in the suit patent to PD-1, it has been stated as follows:

> *"xxx xxx xxx*
>
> *60.* ***The 5C4 antibody also has a high binding specificity to PD-1. Example 3 of the PCT specification (figure 14) teaches that the 5C4***

antibody bound to PD-1 with high specificity, but not to other CD28 family members (ICOS, CTLA-4, CD28).

61. ***In contrast, the PDI-17, PDI-28, PDI-33 and PDI-35 antibodies bind to human PD- 1, but also bind to at least one of CTLAA. CD28 and I COS. Sec fife Affidavit at Figure I and 10-17. As shown by Dr. Fife's af1idavit, the superior specificity of the 5C4 antibody to the reference antibodies "would not have been expected***.*"*

xxx xxx xxx

64. The 5C4 antibody (nivolumab) is shown to have unexpectedly superior therapeutic efficacy to standard chemotherapy. Dr. Feltquate has explained the details in his evidence, a summary of which is also enclosed herewith. In particular:

a. Nivolumab has repeatedly shown "unprecedented" responses in comparison to standard-of-care treatments and in various tumor types. As evidence of the unprecedented response, Dr. Feltquate cites multiple reports and scientific articles showing "the transformative nature that nivolumab [the 5C4 antibody] is expected to have on cancer treatments."

b. Dr. Feltquate quotes a statement of Professor Weber who conducted the first phase Ill clinical trial of the 5C4 antibody indicating that "the impressive data on duration or response suggest that there will be significant prolongation of progression-free and overall survival when the analysis of those data is mature."

c. Nivolumab has been investigated in more than l 00 human clinical trials both as a monotherapy and in combination with other therapies.

xxx xxx xxx"

(Emphasis Supplied)

123. It is also to be noted that examples do not limit the scope of the claims. While working examples are essential for demonstrating the feasibility and workability of the invention, they do not define the patent's scope. Thus, in the judgment dated 13th March, 2024, in the case of ***Bayer Pharm Aktiengescllschaft Versus Controller General of Patents and Designs, 2024 SCC OnLine Del 2044***, it has been held as follows:

"xxx xxx xxx

9. Therefore, the Court finds merit in the contention of Mr. Banerjee that mere recitations of the unit numbers of the components in claim 1 cannot render it ineligible for patent protection under Section 3(i) of the Act. Notably, in the said claim, as defined, there is neither any reference to a

particular disease/ treatment, nor any reference regarding the modes/ manner of administration of the composition. In patent law, the claims of a patent define the boundaries of the patent protection. That is, they set out the legal limits of what the patent covers. The claims must be clear, specific, and supported by the description within the patent application. They are the most critical part of a patent application because they determine the extent of protection granted by the patent. ***Working examples, on the other hand, are provided in the subject application to demonstrate the practical implementation of the invention. These examples are intended to show that the invention is feasible and workable and how it can be carried out in practice. They provide support and understanding for the claimed invention, showing that it is not just a theoretical concept, but has practical applicability. Thus, while working examples are essential for demonstrating the feasibility and workability of an invention, they do not define the patent's scope. The scope is determined by the claims, which must be interpreted in light of the description and any examples provided.*** *The reasoning for applying Section 3(i) of the Act to the subject application is therefore, misplaced. Mr Banerjee also relies on the decision of this Court in* ***Societe Des Produits Nestle SA v. The Controller of Patents and Design and Anr.****, where, in a similar situation, the Court referenced the Manual of Patent Office, Practice and Procedure, which gives the guidance for examination with respect to exclusion of medical, surgical, curative, prophylactic, diagnostic, therapeutic or other treatment, and held that the claims in respect of the composition are patentable, and not hit by Section 3(i) of the Act. In the present case as well, the claim 1, as defined, in the opinion of the Court, does not render the application to be non-patentable.*

xxx xxx xxx"

(Emphasis Supplied)

124. Even otherwise, the test results filed by the defendant themselves show high binding specificity of the product of the plaintiffs with PD-1. Further, the test results of the defendant do not in any manner show that the antibody, i.e., 5C4 (Nivolumab), does not bind to other CD-28 receptors.

125. This Court has already noted above that non-substantial binding cannot be equated to no binding at all, therefore, even the test results of the defendant which show that the product of the plaintiffs substantially does not bind to CD-28, cannot be construed so as to mean that there exists no binding with the CD-28 receptors. Therefore, to say that the suit patent

exclusively binds to PD-1, is *prima facie* incorrect.

126. Further, it is to be noted that the defendant in its own application before the CTRI has stated that Nivolumab is an anti-PD-1 antibody with high binding affinity to PD-1 receptors. Therefore, even as per the defendant, the suit patent discloses high affinity of Nivolumab with PD-1 receptors, in comparison to other receptors, such as that of CD-28 protein family. Even the defendant does not state that Nivolumab exclusively and only binds to PD-1. Further, high affinity of Nivolumab with PD-1 does not, in any manner, exclude its binding with other receptors of CD-28, though it does not have high specificity towards other CD-28 family members. However, the same cannot be interpreted as claim of exclusive specificity to PD-1.

127. As regards the expert evidence of Professor Ipshita Roy, filed on behalf of the defendant, the same is a matter of trial and cannot be taken into consideration at this interim stage, as the same would be subject to examination and counter on part of the plaintiffs, who have the right to ascertain the veracity of the claims made by the defendant's expert. Moreover, the plaintiffs have placed on record the report of their own expert, which is in contrast to the findings of the defendant's expert. Thus, it is imperative that questions which are in dispute be a subject matter of trial.

128. Further, with regard to the defendant's claims that its product is bio-similar to the product of the plaintiff, this Court agrees with the submission of the plaintiffs that infringement may arise even where each and every element of the patented claim is not identically found in the infringing product, so long as the pith and marrow of the invention is taken under the concept of Doctrine of Equivalence. Non-literal infringement is recognized

where the substituted element performs substantially the same function in substantially the same way to achieve substantially the same result. Thus, in the case of ***SNPC Machines Private Limited and Others Versus Vishal Choudhary***, ***2024 SCC OnLine Del 1681***, it has been held as follows:

> *"xxx xxx xxx*
>
> *35. The three decisions of this Court cited by plaintiffs and defendant, of which relevant extracts have been reproduced above, are Sotefin (supra) a decision of Single Judge of this Court of February, 2022, FMC Corporation (supra) a decision of Division Bench of December, 2022 and RxPrism (supra) a decision of Single Judge of July, 2023. All these decisions have extensively relied upon earlier decisions of the Indian Courts as well as Courts of foreign jurisdictions. Our analysis is contoured on the test which needs to be used for assessing a prima facie infringement of the suit patent. The following principles can be culled out collectively from the aforenoted decisions, since all of them rely upon the same previous sources while articulating them from different perspectives:*
>
> *A)* ***Infringement is to be adjudged objectively and defendant's intention may not be material to determine this question; the emphasis however has to be on mapping of 'essential elements'***.
>
> *B)* ***Whether elements which are missing in the defendant's products are so essential or substantial that the absence would entitle the plaintiff to an injunction***.
>
> *C)* ***Patent infringement analysis, comparison of elements of the suit patent's claims is to be done with the elements/claims of the infringing products***.
>
> *D)* ***There can be a case of non-literal infringement where each and every component of patent specification is not found in the infringing products i.e. all elements of a claim may not entirely correspond with the infringing product, but it still can be a case of infringement***.
>
> *E)* ***It is the pith and marrow of the invention claimed that is required to be looked into. This test had been referred to in Clark v. Adie, [L.R.] 2 App. Cas. 315 [House of Lords].***
>
> *F) Non-essential or trifling variations or additions in the product would not be germane, so long as substance of the invention is found to be copied.*
>
> *G) Pure literal construction is not to be adopted, rather* ***doctrine of purposive construction*** *should be applied.*

*H) **Doctrine of equivalents is to be examined and applied if the substituted element in the infringing product does the same work, in substantially the same way, to accomplish substantially the same result.** The source of this doctrine traces its origin to an old decision in Winans v. Denmead, 15 How. 330, 14 L.Ed. 717 which was cited with approval in Graver Tank and Manufacturing Co. v. Linde Air Products Co., 339 US 605 (1950) (Supreme Court of United States).*

I) The essential feature in an infringing article or process are of no account. If the infringing goods are made with the same object in view, which is attained by the patented product, then a minor variation does not mean that there is no piracy. Some trifling or unessential variation has to be ignored. This principle was cited by the Division Bench of this Court in Raj Prakash v. Mangat Ram, ILR (1977) 2 Del 412.

J) While product v. product comparison shall not to be determinative of infringement as opposed to the granted claim v. product comparison, an essential comparison between the products of the plaintiffs and the defendants may be necessary.

K) The triple identity test is important - focusing on function, way the elements serve the function and the result obtained is suitable for analyzing mechanical device (cited in Warner-Jenkinson Co. Inc. v. Hilton Davis Chemical Co., 520 US 17 (1997) (Supreme Court of United States).

xxx xxx xxx"

(Emphasis Supplied)

129. This Court also notes the judgment in the case of ***F-Hoffmann-La Roche AG and Another Versus Zydus Lifesciences Limited, 2024 SCC OnLine Del 7663***, wherein, the Court held that if the bio-similar utilizes any aspect which is patented by the reference biologic, then, there will be a case of patent infringement. Thus, it was held as follows:

"xxx xxx xxx

***24.** Biosimilars are designed to be highly similar to the reference product, but not identical. As discussed above, the Guidelines lay out the pathway for approval of biosimilar, however, these focus on the approval process and do not directly address patent issues. The determination of infringement must begin with understanding the scope of the patent(s) held by the reference biologic. We know that Patents can cover a wide range of protectable subject matter,*

including the biologic's molecular structure, the process by which it is manufactured, formulations, methods of use, and more. ***If the biosimilar or similar biologic utilizes or embodies any aspect that is patented by the reference biologic, only then there could be a case for patent infringement.***

xxx xxx xxx"

(Emphasis Supplied)

130. In view of the aforesaid detailed discussion, this Court is *prima facie* of the view that in case the defendant launches its product commercially, the same shall amount to infringement of the suit patent.

131. Further, the defendant has averred that there has been evergreening and double patenting by the plaintiffs in view of the stand taken by the plaintiffs in the prosecution history of other patents. However, the said averment is found without any merit, in view of the discussion made hereinafter.

132. It is the defendant's case that the plaintiffs have admitted in their complaints against one Merck and Co. Inc. that they have developed Nivolumab antibody by practising the US patents, US 87828474, US 9073994 and US 9067999. In this regard, it would be useful to refer to the said patents.

133. The invention claimed in US 87828474, is as follows:

"xxx xxx xxx

The invention claimed is:

1. A method for treatment of a tumor in a patient, comprising administering to the patient a pharmaceutically effective amount of an anti-PD-I monoclonal antibody.

xxx xxx xxx"

134. The invention claimed in US 9073994, is as follows:

"xxx xxx xxx

The invention claimed is:

1. A method of treating a metastatic melanoma comprising intravenously

administering an effective amount of a composition comprising a human or humanized anti-PD-I monoclonal antibody and a solubilizer in a solution to a human with the metastatic melanoma, wherein the administration of the composition treats the metastatic melanoma in the human.

xxx xxx xxx"

135. The invention claimed in US 9067999, is as follows:

"xxx xxx xxx

The invention claimed is:

1. A method of treating a lung cancer comprising administering a composition comprising a human or humanized anti-PD-I monoclonal antibody to a human with the lung cancer, wherein the administration of the composition treats the lung cancer in the human.

xxx xxx xxx"

136. Perusal of the aforesaid makes it apparent that the aforesaid patents are method claims and none of them disclose the sequence of Nivolumab, as claimed in the suit patent.

137. Even otherwise, it is to be noted that the subject matter of the US patent cases was in relation to the first step of drug discovery, i.e., the discovery that PD-1 receptor is a useful target in our body for treatment of cancer. The entire document, i.e., the complaint filed by the plaintiffs against Merck and Co. Inc. before the United States District Court, only demonstrates that an antibody that is developed for PD-1 receptor will be useful for treatment of cancer. Thus, it was the case of the plaintiffs that any third party, who makes an anti-PD-1 antibody for treatment of cancer, will infringe the US patents. The subject matter of the US complaints was the use/method for treatment of cancer using an anti-PD-1 antibody Pembrolizumab, which was developed by said Merck and Co., and has a different sequence from that of Nivolumab, as per the case put forth by the plaintiffs.

138. Thus, as per the plaintiffs, the plaintiffs filed the US complaints in the context that a third party who uses any anti-PD-1 human antibody for treatment of cancer, will infringe D3's US equivalent. It is to be noted that Merck was planning to make, use, sell, etc., an anti-PD-1 antibody, Pembrolizumab for treatment of cancer, and not Nivolumab.

139. Relevant extract from the complaint filed by the plaintiffs against Merck before the United States District Court, is reproduced as under:

> *"xxx xxx xxx*
>
> *4. The invention at issue here covers using antibodies that bind to PD-1 ("anti-PD-1 antibodies") in a method for treating cancer. By binding to PD-1 and blocking the PD-1 checkpoint pathway, the anti-PD-1 antibodies allow a patient's immune system to resume its ability to recognize, attack, and destroy cancer cells.*
>
> *xxx xxx xxx*
>
> *6.* ***Merck is threatening to exploit that invention with a later-developed anti-PD-1 antibody. As described below, Merck is preparing to infringe plaintiffs' patent for methods of treating cancer with anti-PD-1 antibodies****.*
>
> *xxx xxx xxx*
>
> *13. On May 20, 2014, the United States Patent & Trademark Office ("USPTO") duly and legally issued United States Patent No. 8,728,474 (the "474 patent" (Exhibit 1)) titled "Immunopotentiative Composition." The inventors of the 474 patent showed for the first time that anti-PD-1 antibodies were useful in methods to treat cancer. Ono is an assignee of the 474 patent. BMS is an exclusive licensee of the 474 patent. The 474 patent claims methods for treating cancer with an antibody against PD-1.*
>
> *14.* ***Plaintiffs have put the invention of the 474 patent into practice by developing the breakthrough biologic drug nivolumab. Nivolumab is a monoclonal antibody that recognizes and binds to the PD-1 protein. When nivolumab binds to the PD-1 protein, that PD-1 protein cannot interact with its natural binding partners. Using nivolumab to block the interaction between PD-1 and its binding partners allows a more robust T cell response by the patient's own immune system****.*
>
> *xxx xxx xxx*
>
> *18.* ***Merck is planning to exploit the invention of the 474 patent with an anti-PD-1 antibody called pembrolizumab. On information and belief,***

Merck started developing pembrolizumab after Plaintiffs had made and started testing nivolumab, and Merck has since been engaged in efforts to meet the FDA regulatory requirements for marketing, distributing, offering for sale, and selling pembrolizumab for the treatment of cancer. According to Merck, pembrolizumab is a PD-1 antibody that works by blocking the PD-1 checkpoint to treat cancer*.*

19. On information and belief, Merck has known about the 474 patent and has known that the use of pembrolizumab will infringe claims of the 474 patent since at least approximately May 20, 2014, when the 474 patent was issued by the USPTO. In its August 7, 2014, 10-Q filing with the U.S. Securities and Exchange Commission ("SEC"), Merck acknowledged that the USPTO had granted the 474 patent (Merck & Co., Inc. U.S. Securities & Exchange Commission Form 10-Q at 22 (filed August 7, 2014)). In that same SEC filing, Merck admits that the use of pembrolizumab to treat cancer is covered by the European counterpart to the 474 patent (id. ("As previously disclosed, Ono Pharmaceutical Co. ("Ono") has a European patent (EP 1 537 878) ("'878") that broadly claims the use of an anti-PD-1 antibody, such as the Company's immunotherapy, pembrolizumab (MK-3475), for the treatment of cancer.")).

xxx xxx xxx"

(Emphasis Supplied)

140. Reading of the aforesaid clearly shows that the US patents are method patents, while the suit patent is a product patent. As noted above, none of the US patents disclose the sequence of Nivolumab. Furthermore, the complaint filed in the US is a post published document, subsequent to the priority date of the suit patent and does not assist the defendant in establishing that D3 discloses specific anti-PD-1 antibodies.

141. It is further to be noted that the plaintiffs had filed a suit against Merck for infringement. This Court notes the submission made on behalf of the plaintiffs that the said suit has since been settled between the plaintiffs and Merck, and Merck is paying royalty to the plaintiffs.

142. Further, the defendant has relied upon Patent Term Extension-PTE by plaintiffs for Japanese Patent being JP4409430. This Court notes the submission of the plaintiffs that the Japanese Patent belongs to the same

family as US 87828474, which claims the use of anti-PD-1 antibodies for treatment of cancer. Further, the Japanese Patent is equivalent of EP '878. The PTE was for the use of an anti-PD-1 antibody, i.e., Nivolumab for treatment of cancer. Further, nothing has been brought before this Court that there was disclosure of any sequence relating to Nivolumab in the Japanese Patent. The Japanese Patent, which has been relied upon by the defendant, covers the use of PD-1 antibodies for treatment. However, the sequence of Nivolumab has not been disclosed in the Japanese Patent. The English translation of the claims of the Japanese Patent, as filed by the plaintiffs, is reproduced as under:

Claims

1. PD-1 AntibodyAs an active ingredient;Melanoma having an effect of suppressing melanoma growth or metastasis in vivoTherapeutic Agents.

2. The antibody of claim 1, wherein the PD-1 antibody comprises:Fully Human Anti-Human PD-1MonoclonalThe antibody according to claim 1, wherein the antibody is1What is describedMelanomaTherapeutic Agents.

Other claims

1. PD-1抗体を有効成分として含み、インビボにおいてメラノーマの増殖または転移を抑制する作用を有するメラノーマ治療剤。

2. PD-1抗体が、完全ヒト型抗ヒトPD-1モノクローナル抗体である請求項1記載のメラノーマ治療剤。

143. Similarly, the submissions made by the plaintiffs during the prosecution of EP '878, again do not *prima facie* show the vulnerability of the suit patent. The submissions of the plaintiffs were in response to the post-grant opposition filed by Merck to D3. D3 showed that the inhibition of PD-1 is effective in the treatment of cancer, to further show that any human anti-PD-1 antibody, has been successful in the treatment of cancer. The plaintiffs relied upon the data in the specification of the suit patent. However, obviousness of the suit patent has not *prima facie* been established by the defendant, and the same would be subject matter of trial.

144. Likewise, the supplementary patent protection sought in Europe does not show that Nivolumab is the subject matter of EP '878. As noted earlier,

EP '878 relied upon by the defendant, merely claims the use of an anti-PD-1 antibody and does not disclose the sequences of Nivolumab. Thus, reliance on EP '878 is misplaced and does not raise a credible challenge to the validity of the suit patent or come in aid to the defendant's defence with respect to non-infringement of the suit patent.

145. This Court further takes note of the submission of the plaintiffs that the monoclonal antibody of Nivolumab is a man-made antibody and is not merely a discovery, i.e., human intervention is present in preparation of Nivolumab. Therefore, Nivolumab cannot be said to be non-patentable under Section 64(1)(k) of the Patents Act. The said submission, as encapsulated in the plaintiffs' rejoinder, is reproduced as under:

> *"xxx xxx xxx*
>
> *62. That the contents of paragraph nos. 21 & 22 under reply are denied for being false and frivolous. It is submitted that the contents of paragraph 21 are generic statements wherein the Defendant attempts to suggest that anti PD-1 antibody is known in the art and that the suit patent is a mere preparation of an antibody against an alternate antigen.* ***It is submitted that for the first time PD-1 receptor was identified in 2002 as a target for treatment of cancer as is evident from document WO2004/004771 (EP1537878)****. Further submissions are as below:*
>
> *a)* ***In response to the paragraph nos. 21 (a)-(e), it is submitted that the suit patent is in relation to specific antibody which have been clearly defined by the sequence ID. The process for preparing anti PD-1 antibody using hybridoma clones is well known technique to prepare antibodies. By simply knowing the process, does not result in the generation of novel and unknown antibodies. Recombinant human antibodies can be generated in the laboratory by using two most common method for antibody generation i.e. library-based method and transgenic mouse-based methods. Notwithstanding the above, the Plaintiffs' suit patent does not claim the process for preparing a known antibody.*** *The claims of the Defendant are completely flawed in as much that each of the three documents referred i.e. WO2002/12500 (D23) and WO2002/12502 (D24) have been granted patents in India as Indian Patent No. 236195 and 225434 respectively. WO2001/014424D25 is directed to novel human sequence antibodies against human CTLA-4 and methods of treating human diseases, infections and other conditions using these antibodies.* ***None of the said documents referred to by the Defendant***

disclose 5C4 antibody. It is further denied that once the antigen is injected, the antibody is automatically generated and therefore is an essential biological process. This is also incorrect as each of the mAb production requires human intervention and has to be generated through recombinant and hybridoma technology*.*

b) Further, in response to the paragraph no, 21 (f), it is submitted that ***the monoclonal antibody of Nivolumab is a manmade antibody and therefore neither Section 3(j) nor Section 3(c) is attracted. An anti- PD-1 monoclonal antibody or an antigen-binding portion thereof in claim 1 or any of the claims dependent thereon of the suit patent is not a discovery or a product of nature for the reasons as follows:***

- ***Not a discovery: Oxford dictionary defines "discovery" as "the action or an act of finding or becoming aware of for the first time, esp., the first bringing to light of a "scientific phenomenon". The claimed antibodies are novel because the claimed CDR sequences are not disclosed in any of the prior art documents and were not known before the priority date of the present invention, and are different from the human germline sequences. Therefore, the claimed antibody of suit patent cannot be considered, at the outset, as merely a discovery of a natural or scientific phenomenon****.*
- ***Not occurring in nature/not "product of nature"/made by human intervention: The antibodies recited in the claims of suit patent are not occurring in nature/not merely isolated from nature****.*
- *It is submitted that in the GUIDELINES FOR EXAMINATION OF BIOTECHNOLOGY APPLICATIONS FOR PATENT issued by Office of the Controller General of the Patents and Designs, issued in March 2013, at page 11 for Section 3(c) it is mentioned that, "products such as microorganisms, nucleic acid sequences, proteins, enzymes, compounds, etc., which are directly isolated from nature, are not patentable subject-matter".*
- ***The Defendant has failed to point out any naturally occurring anti- PD-1 antibody containing the six CDR sequences recited in the suit patent's claims. No reference cited by the Defendant shows an antibody or antigen-binding portion thereof that comprises the six CDRs recited in the suit patent's claims****.*
- ***Human PD-1 is a naturally occurring protein in the human body. The claimed antibodies specifically bind human PD-1. A skilled artisan would have known that a human would not naturally produce an antibody against a self-antigen, PD-1. Said antibodies can only be created in artificially with human intervention****.*

xxx xxx xxx"

(Emphasis Supplied)

146. Thus, the statements of the plaintiffs made during the prosecution of

foreign patent applications, as relied by the defendant, do not assist the defendant in any manner, in the facts and circumstances of the present case.

147. This Court notes the submission of the plaintiffs that Nivolumab is a blockbuster drug, since it has generated revenue of around 9.01 billion USD in the year 2023 itself. In this regard, reference may be made to the *'Statement Regarding the Working of Patented Invention(s) on a Commercial Scale in India'* in Form 27, as submitted by the plaintiff no.1, which is reproduced as under:

220

FORM 27
THE PATENTS ACT, 1970
(39 of 1970)
AND
THE PATENTS RULES, 2003

No Fee

STATEMENT REGARDING THE WORKING OF PATENTED INVENTION(S) ON A COMMERCIAL SCALE IN INDIA
[*See* section 146(2) and rule 131(1)]

1. Insert name, address, nationality, patent number(s).	I/ We, the Patentee(s)/ ~~Licensee~~ **NAME: E.R. SQUIBB & SONS, L.L.C,** **Nationality: USA** **Address: Route 206 & Province Line Road, Princeton, New Jersey 08540 USA,** **NAME: ONO PHARMACEUTICAL CO., LTD.,** **Nationality: Japan** **Address: 1-5, Doshomachi 2-chome, Chuo-ku, Osaka-shi, Osaka 541-8526 Japan.** in respect of patent number(s) **340060**, furnish this statement,
2. State the financial year to which the statement relates.	in respect of the financial year 2021-2022

3. Worked / not worked. Please state whether each patent in respect of which this form is being filed is worked or not worked.

Patent Number(s)	Worked [Tick (√) if applicable]	Not worked [Tick (√) if applicable]
340060	√	

4. If worked.

(a) Approximate revenue / value accrued in India to the patentee(s)/ licensee furnishing the statement from patent number(s) where the working is through:

(1) Manufacturing in India (in INR) Please refer to para 4(b)	(2) Importing into India (in INR) Please refer to para 4(b)

(b) Brief in respect of (a) above (maximum 500 words)
The sales details of the Patented Invention are as follows:

01 April 2021 to 31 March 2022	Net sales (INR)	Remarks
Opdyta	2,81,45,65,063	Sales return

~~5. If not worked.~~ ~~Reasons for not working the patented invention(s) and steps being taken for working of the invention(s). (maximum 500 words)~~

The facts and matters stated above are true to the best of my/ our knowledge, information and belief.

Dated this 30th day of September 2022

6. To be signed by ~~Patentee(s) / Licensee~~ / Authorised Agent furnishing the statement.

Archana Shanker
of ANAND & ANAND, Advocates
Patent Agent No. IN/PA-149

To
The Controller of Patents
The Patent Office,
At Mumbai/ Delhi/ Kolkata/Chennai

148. Further, as noted hereinabove, Nivolumab has been granted approvals in more than fifty countries, for more than twenty indications *(Indication – a specific use or application of an invention)* worldwide and ninety indications in India. It is also to be noted that the suit patent has been granted after thorough scrutiny and after four pre-grant oppositions in India. Even otherwise, the post-grant opposition filed by the defendant's sister concern is still pending. Merely filing the challenge is not enough. The defendant was aware of the litigation that would ensue if they sought for launch of their product, indicative of the said knowledge are the multiple notices and the post-grant opposition itself, as filed by defendant's sister concern. In this regard reference may be made to the judgment in the case of ***Eisai Co. Ltd. and Another Versus Satish Reddy and Another***, ***2019 SCC OnLine Del 8496***, wherein, it has been held as follows:

> *"xxx xxx xxx*
>
> *66.* ***The balance of convenience for the grant of interim injunction lies in favour of the plaintiffs as the defendants have evidently not "cleared the way" before going ahead with obtaining a marketing approval for launch of the infringing drug. The defendants were aware that there may be a possible challenge to its product, but they chose to go ahead to seek the marketing approvals without first invoking revocation proceedings or attempting to obtain a license. Where litigation is bound to ensue if the defendants introduce their product, the defendants could have avoided the interlocutory injunction if they had cleared the way first****. Reference be made to Merck v. Glenmark; (2015) 63 PTC 257 [Del] [DB].*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

149. Delving on the issue of 'clearing the way', this Court in the case of ***Novartis AG and Another Versus NATCO Pharma Limited, 2019 SCC OnLine Del 12436***, has held as follows:

> *"xxx xxx xxx*
>
> *15. The Court has heard both sides on the grant of ad-interim relief. It is*

the admitted position that the post grant opposition is now pending decision with the Patent Office and the question as to whether the patent is to be maintained or not will be decided therein. Thus, in so far as the validity of the patent itself is concerned, this court would not like to make any observation at this stage, so as to ensure that the post grant opposition is decided without being affected by any observation which may be made by this court.

xxx xxx xxx

17. The actual commercial launch has also admittedly been done only on 20th March, 2019. ***Thus, during the period when the post-grant opposition decision was yet to come, the Defendant has chosen to commercially launch the product. While the Supreme Court in Aloys Wobben (supra) held that the rights would be crystallized once the post grant opposition is decided, launch of an allegedly infringing product, prior to the said decision in the opposition by the entity opposing the Patent, did not arise in the facts of the said case****. Section 48 of the Patents Act grants rights in favour of a patentee, which are not affected during the pendency of a post-grant opposition. Section 48 provides as under:*

> *"48.* ***Rights of patentees*** *- Subject to other provisions contained in this Act and the conditions specified in section 47, a patent granted under this Act shall confer upon the patentee-*
>
> *(a) where the subject matter of the patent is a product, the exclusive right to prevent third parties, who do not have his consent, from the act of making, using, offering for sale, selling or importing for those purposes that product in India*
>
> *(b) where the subject matter of the patent is a process, the exclusive right to prevent third parties, who do not have his consent, from the act of using that process, and from the act of using, offering for sale, selling or importing for those purposes the product obtained directly by that process in India"*

18. ***During the pendency of the post-grant opposition, the rights of a patentee subsist - though they may be crystallized once the opposition is actually decided. The Defendant ought to have awaited the decision in the post grant opposition before launching its product.*** *However, since it chose to launch earlier, the Plaintiff has filed the present suit.*

xxx xxx xxx"

(Emphasis Supplied)

150. In the case of ***Smithkline Beecham Plc Versus Generics (UK) Ltd,***

2001 WL 1346930, the High Court of Justice Chancery Division discussed the concept of 'clearing the way' while granting an injunction, in the following manner:

> *"xxx xxx xxx*
>
> *As between the two, I will put it this way, the claimant's damage is more unquantifiable than that of the defendant's but both are unquantifiable. There are degrees (sic) of unquantifiability, just as there are degrees of infinity.* ***I turn to another factor which, to my mind, indicates that the injunction should be granted. It is this. The defendants have known for a long time about this patent. You would have to be very naive in the pharmaceutical industry to think that the patentee, with a product as important as this, would not, if it had anything other than a frivolous chance of success, take action. So the defendants knew, when they set out upon this project in 1997 that if the patentees would cause trouble they would.***
>
> ***The defendants could, so soon as they settled upon the product they were intending to sell, have caused the litigation to start. They could have done a number of things: First, they could have launched a petition for the revocation of the patent and started a claim for a declaration of non-infringement. Or, since there are certain difficulties with the latter (for example onus of proof goes the other way round), they could simply have said to the patentees, "We intend (we are not saying when but it is a settled intention) to launch our product within the next five years. If you intend to sue us, sue us now". If they had taken such a course, having settled upon the product they intended to sell, the whole of this dispute would have been got out of the way before their date of intended launch.*** *Mr. Arnold says, "That is quite unfair. It puts the burden upon the defendant. Why should there be any such burden to start litigation when they are firmly of the opinion they do not infringe and" — as a back-up opinion — "the patent is no good?" The answer, to my mind, is self-evident.* ***They knew perfectly well the issue of infringement was likely to arise. If they wanted to be sure of their position they could and would have made sure that all their experimental data was properly in place and vouched for by an independent scientist. And they would have presented the evidence to the patentees.***
>
> *xxx xxx xxx*
>
> ***I see no question of principle involved here of any sort. It is purely commercial common sense. If there may be an obstacle in your way, clear it out. To my mind, this is a case where the retention of the status quo is a rational thing to do. It was something that could have been avoided by the defendants; they chose not to do it.***

> *Other matters are prayed in aid by the defendants which I will mention just briefly. They say they have taken a lot of orders. They did so in the full knowledge of this patent action. I doubt, as they suggest, that they will lose much face with their customers — they can and will blame the patentees or this Court. Whether they do lose face or not, it was a course which they invited.*
>
> ***Accordingly, I grant the injunction sought. I will hear submissions as to directions for trial.***
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

151. Thus, the defendant has failed to 'clear the way' despite being aware of the suit patent.

152. This Court also takes note of the submission made on behalf of the plaintiffs that the plaintiffs run an affordable scheme for patients in India, being Patient Assistant Programme ("PAP"). Under the PAP, patients have to pay for upto first five paid doses that will be alternated with upto five free doses. For the rest of the year, the patient will get the balance doses free of cost. Further, the plaintiffs have categorically stated before this Court that pricing in India is at a low end for the patented product of the plaintiffs.

153. The present suit was occasioned since the plaintiffs became aware that the defendant, under its former name, Cadila Healthcare Ltd., had applied for clinical trial approval of Nivolumab. Further, permissions were granted to the defendant on 29th September, 2022 for the purposes of clinical trial for its bio-similar drug, ZRC-3276.

154. Thus, as per the case put forward by the plaintiffs, the act of applying for such approval reflects careful planning, intent and investment, which points towards imminent infringement. In this regard, reference may be made to the judgment in the case of ***Bristol Myers Squibb Company and Anr. Versus V.C. Bhutada & Ors., 2013 SCC OnLine 4129***, wherein, it has been held as follows:

"xxx xxx xxx

*29. The above decisions are in line with the **position in common law as regards quia timet actions**. Illustratively reference may be made to the recent decision in Merck Sharp Dohme v. Teva Pharma B. V. (2012) EWHC 627 (Pat). In the said case, the Defendant, Teva Pharma, obtained the market authorization for a drug. **It was held that while the obtaining of such market authorization could not itself be constituted an infringement, "application for a market authorization is not a trivial matter and is the product of careful planning and work." It was held that such obtaining of market authorization provided "a concrete basis for inference that TEVA threaten and intend to sell efavirenz sometime**."*

xxx xxx xxx

*31. It is not necessary at this stage, for the Plaintiff to name the particular customers of Defendants 1 and 2 to whom the product is to be sold since what is expressed is only an apprehension of "offer for sale". At this stage, the Plaintiff can at best refer to the fact that Defendant 2 supplies oncology APIs to various generic companies and that the said APIs are sold in Delhi. **The apprehension that such oncology APIs may in the near future include the infringing product which is also an oncology API cannot, in the circumstances, be characterised as lacking credibility and having been asserted merely to attract the jurisdiction of the Court. The above averments in the present plaint, which is in a quia timet action, are prima facie sufficient to show that Defendant No. 2 "carries on business" in Delhi and that the prima facie the cause of action arises within the jurisdiction of this Court**.*

xxx xxx xxx"

(Emphasis Supplied)

155. At this stage, reference may be made to Section 107A of the Patents Act, which is also known as the Bolar Exemption that outlines specific acts that are not considered patent infringement. Primarily, the said Section allows the use of a patented product for research and development purposes, as well as for submitting data to regulatory bodies for product approval, without infringing the patent. Said Section 107A of the Patents Act, reads as under:

"xxx xxx xxx

107A. Certain acts not to be considered as infringement.—For the

purposes of this Act —

(a) any act of making, constructing, using, selling or importing a patented invention solely for uses reasonably related to the development and submission of information required under any law for the time being in force, in India, or in a country other than India, that regulates the manufacture, construction, use, sale or import of any product;

(b) importation of patented products by any person from a person who is duly authorised under the law to produce and sell or distribute the product,

shall not be considered as a infringement of patent rights.

xxx xxx xxx"

156. Thus, Section 107A of the Patents Act provides a mechanism for certain activities related to patented products, to be exempt from infringement. However, manufacturing under the same is allowed only for clinical trials, but not for commercial sale. Thus, Division Bench of this Court, in the case of ***Bayer Corporation Versus Union of India and Others***, ***2019 SCC OnLine Del 8209***, with regard to guidelines under Section 107A of the Patents Act, has held as under:

"xxx xxx xxx

112. The approach of the learned single judge in permitting export, without any inquiry and holding that export of 1000 or 2000 tablets constituted reasonable use, in this case, cannot be countenanced. In such case, upon the patent proprietor alleging the infringement was to institute legal proceedings to injunct the alleged exporter or seller, it is equally possible for the seller or exporter to seek a declaration or appropriate relief (including in a suit for groundless threat, if such action lies) that its overseas sales are for research and purposes covered by Section 107A. ***This Court is of the opinion that the inquiry and adjudication in such cases would be in regard to the following:***

(1) The patent granted;

(2) The nature of the product or elements sought to be exported;

(3) The details of the party or party importing the product,

(4) The quantity sought to be exported

(5) Other particulars with respect to the end use of the product, to establish that it is solely for research and development of information to regulatory authorities in the other country;

(6) All particulars regarding the relevant regulations, covering the kind and scope of inquiry, including the quantities of the product (i.e. the patented product or compound, API or fine chemical needed). These details must be supplied by the exporter/seller of the product to the overseas buyer. In case the defendant is not the seller, it should disclose who had purchased the product in the relevant quantities, to facilitate its impleadment in the proceedings. In the event it cannot do so, the consequences of such result ought to be considered by the court.

(7) If the regulations are in the language of that country, an authentic English translation to facilitate a speedy resolution;

(8) Appropriate interim order, including undertaking by way of affidavit to compensate the plaintiff, in the event the suit were to be decreed and the extent of such monetary compensation. The affidavit should be of an authorized personnel, and kept alive during the pendency of litigation, duly authenticated by the board of director or other controlling body of the defendant-and whenever the company or entity undergoes amalgamation or transfer, suitable undertaking from the successor organization;

(9) If necessary, verification through the Indian mission (and its trade division) abroad regarding the authentication of the third party and/or its facilities abroad.

(10) If it is held by the court that the exporter is not involved in sale or export of any patented product, but a generic article, unprotected by patent law, when denying relief, suitable restitutionary relief should be awarded to the defendants in monetary terms, to preclude litigation that prevents trade or competition.

113. ***The above aspects are only indicative of the matters that need examination, they are in no way exhaustive and the court may consider any other matter relevant to the subject.***

xxx xxx xxx"

(Emphasis Supplied)

157. At this stage, reference may also be made to the reply dated 17th May, 2022 issued on behalf of the defendant to the legal notice of the plaintiffs, wherein, the defendant has categorically affirmed that it has only applied for

clinical trial. The relevant portion of the said reply of the defendant, is extracted as under:

> *"xxx xxx xxx*
>
> *2.* ***Your notice appears to be premised on the ground that our client has applied for clinical trial approval for Nivolumab before the Drug Controller General of India, Central Drugs Standard Control Organization. In this regard, you would note that merely applying for a clinical trial approval does not infract the rights of the patentee, under Section 48. As you are aware, the Patents Act is a self-contained statute, which contains the rights of the patentee, as well as those of the public. Section 107A clearly stipulates that any act of making, constructing, using, selling or importing a patented invention for uses related to the development and submission of information required by law, is permitted****. It has also been clarified through judicial precedents that through Section 107A, it was deemed necessary by the legislature to allow the non-patentee to undertake experimentation and ready a product for its availability for the general public and such preparation/experimentation does not amount to infringement. In view of the same, seeking approvals from the DCGI for conducting clinical trials is well within the purview of the Patents Act, 1970, and does not amount to infringement of any patent in any manner whatsoever.*
>
> *xxx xxx xxx"*
>
> *(Emphasis Supplied)*

158. Reference may also be made to the E-mail dated 04th May, 2024, relied upon by the plaintiffs, wherein, a third party wrote to the plaintiffs regarding the defendant launching the patented product of the plaintiffs, in the following manner:

Elisha Sinha

From: [redacted]
Sent: 04 May 2024 17:46
To: Narang, Akanksha
Subject: Regarding launch of Nivolumab by Zydus

[Use CAUTION when opening links/attachments]

Hi Akansha

I have received the information that Zydus is going to launch Nivolumab in few months. In last conversation you said that BMS have patent till 2026 so will they launch BMS Nivolumab in India Or they are coming with their own Nivolumab?

Please update
Sent from Yahoo Mail for iPhone

159. This Court further notes that in an another suit, i.e., *CS(COMM) 74/2024*, titled as ***E R Squibb and Sons LLC and Ors. Versus Beacon Pharmaceuticals Limited and Ors.***, *vide* order dated 25th January, 2024, an *ex-parte* injunction has been granted in favour of the plaintiffs with regard to the suit patent, wherein, the defendants therein have been restrained, in the following manner:

> *"xxx xxx xxx*
>
> *18. Accordingly, till the next date of hearing, the following directions are issued:*
>
> *(i) Defendant Nos. 1 and 2 or any other entity/person acting for and on their behalf are restrained from using, making, manufacturing, selling, distributing, advertising, exporting, offering for sale, importing in India or in any other manner, directly or indirectly, dealing with generic Nivolumab, under the brand Nivolunix or any other brand that infringes the subject matter of the Suit Patent.*
>
> *xxx xxx xxx"*

160. The aforesaid injunction in favour of the plaintiffs in the other suit is still subsisting, as of date.

161. It is settled that in a *quia timet* action, where there is a reasonable apprehension of imminent infringement likely to cause irreparable harm, Courts are empowered to grant interim relief even before actual infringement occurs, if a strong *prima facie* case is established. Thus, in the case of ***Bristol-Myers Squibb Company and Ors. Versus Mr. J.D. Joshi and Anr.***, ***2015 SCC OnLine Del 10109***, it was held as follows:

> *"xxx xxx xxx*
>
> *85.* ***As far as law with regard to Quia Timet Action is concerned, it is settled law that such action is maintainable. If a party fears or apprehends, who may obtain injunction to prevent some threatened act being done which if done, would cause him substantial damage and which money would not be an adequate or sufficient remedy. In a quia timet action, in the absence of evidence if a strong case is made out against the defendants, after valid justification, the interim order may be passed by the Court.*** *Reliance is placed on the following decisions: -*

i) ***Kuldip Singh v. Subhash Chander Jain, AIR 2000 SC 1410***

> *"**A qui timet action is a bill in equity. It is an action preventive in nature and a specie of precautionary justice intended to prevent apprehended wrong or anticipated mischief and not to undo a wrong or mischief when it has already been done. In such an action the Court, if convinced, may interfere by appointment of receiver or by directing security to be furnished or by issuing an injunction or any other remedial process**" (Para 7)*

ii) ***Rohtas Industries Limited v. IHP. Co. Ltd., AIR 1954 PATNA 492***

> *"**Even proof of an intention to infringe, apart from actual infringement, may justify an injunction to restrain the infringement provided it is established to the satisfaction of the court that the alleged infringer, dealing with what he is doing as a matter of substance, is taking the invention claimed by the patent.**" (Para 16)*

xxx xxx xxx"

(Emphasis Supplied)

162. In the present case, the defendant has not been able to lay a credible challenge to the validity of the suit patent. Further, the incidence of infringement of the suit patent by the defendant also stands established in view of the discussion hereinabove. Thus, holding that where a strong case of infringement exists, Courts must be mindful of the interest in enforcing patent rights, this Court, in the case of ***Merck Sharp and Dohme Corporation and Anr. Versus Glenmark Pharmaceuticals, 2015 SCC OnLine Del 8227***, has held as follows:

> *"xxx xxx xxx*
>
> *85. This leads us to the second principle, which is whether the Court can overlook the public interest in maintaining the integrity of the patent system itself, so that a legitimate monopoly is not distorted. As this Court noted in Bayer Corporation v. Cipla, Union of India (UOI), 162 (2009) DLT 371*
>
> > *"[i]f, after a patentee, rewarded for his toil - in the form of protection against infringement - were to be informed that someone, not holding a patent, would be reaping the fruits*

of his efforts and investment, such a result would be destructive of the objectives underlying the Patents Act.".

The Court must be mindful - especially in a case where a strong case of infringement is established, as here - there is an interest in enforcing the Act. *It may be argued that despite this no injunction should be granted since all damages from loss of sales can be compensated monetarily ultimately if the patentee prevails. This argument though appealing, is to be rejected because a closer look at the market forces reveal that the damage can in some cases be irreparable. This in turn leads to the third principle, which is* ***where an infringer is allowed to operate in the interim during the trial, it may result in a reduction in price by that infringer since it has no research and development expenses to recoup - most revenue becomes profit.*** *The patentee however can only do so at its peril. Importantly, prices may not recover after the patentee ultimately prevails, even if it is able to survive the financial setback (or "hit") during the interim, which may take some time. The victory for the patentee therefore should not be pyrrhic but real. This irreparable market effect in cases of a sole supplier of a product has also triggered the decisions in Smith Kline Beecham v. Generics, (2002) 25(1) IPD 25005 and Smithkline Beecham Plc (2) Glaxosmithkline UK Ltd. v. Apotex, [2003] EWCA Civ L37, where in granting an interim injunction, it was held that damages would not be an adequate remedy for the plaintiff since it was the sole supplier of the product. New entrants to the market would be likely to cause its prices to go into a downward spiral, and Smith Kline's prices may not recover even if it wins eventually. Equally, granting the injunction would not prejudice Glenmark to an equal extent since - if the suit is dismissed - it may return to a market that is largely variable.*

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87. A related concern that this Court heeds - the fourth principle operative in this case - is that of the chronology of events and Glenmark's decision to release Zita without first challenging Januvia or Janumet. Undoubtedly, the Act creates a right to oppose patents even after grant. There is no obligation to only utilize the pre or post grant opposition mechanisms. Neither does a patent benefit from a presumption of validity if it is challenged in the course of an infringement suit. However, ***if a defendant is aware that there may be a possible challenge to its product, but still chooses to release the drug without first invoking revocation proceedings or attempting to negotiate, that is surely a relevant factor. The defendant's legal right to challenge the patent at any point in time is intact, but that does not mean that this factor cannot determine the interim arrangement.*** *This is more so where Glenmark today argues that MSD ought to have disclosed international patent applications for SPM and Sitagliptin plus Metformin since they were the "same or substantially the same" as the suit patent under Section 8. That is Glenmark's stated*

position. Such being the state of things, it is surely reasonable for Glenmark to detect the possibility to challenge, when a US patent application for SPM filed by it was opposed by MSD. Despite this, Glenmark released the drug without initiating revocation proceedings under the Act, which is also a right vested in Glenmark that would have obviated the need for the interim arrangement we are today considering. This does not mean that Glenmark's right to question the validity of the patent in an infringement is affected, but the manner of challenge is a relevant factor against it at the interim stage. As Justice Jacob noted in both Smithkline Beecham cases (supra):

> *"I remain of the same opinion that I was in the Generics case. Where litigation is bound to ensue if the defendant introduces his product he can avoid all the problems of an interlocutory injunction if he clears the way first. That is what the procedures for revocation and declaration of non-infringement are for."*

Similarly, in the Australian decision of Pharmacia Italia S.p.A v. Interpharma Pty Ltd., [2005] FCA 1675, the Court noted the fact that Inter-pharma had acted in full knowledge of Pharmacia's patent and the possible consequences flowing from that. This consideration that the patentee is already in the market and has been operating the patent has found favour in Indian Courts as well*. In K. Ramu v. Adayar Ananda Bhavan and Muthulakshmi Bhavan, 2007 (34) PTC 689 (Mad), Bajaj Auto Ltd. v. TVS Motor Company Ltd., 2008 (36) PTC 417 (Mad) and National Research Development Corporation of India v.* ***The Delhi Cloth and General Mills Co. Ltd., AIR 1980 Del 132, the fact that the patentee was already dealing in the market on the basis of the patent weighed in as a factor in granting the interim injunction****.*

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(Emphasis Supplied)

163. It is further to be noted that when patent is *prima facie* found to be infringed and is being exploited without license, the balance of convenience tilts in favour of restraining such infringement. Thus, in the case of ***Pharmacyclics LLC and Another Versus Hetero Labs Limited and Others, 2023 SCC OnLine Del 8162***, it has been held as follows:

> *"xxx xxx xxx*
>
> *107.* ***Where a granted patent is prima facie found to be infringed, and is being exploited without a license from the patent holder, the balance of convenience is always in favour of restraining further infringement. I am aware that the drug in question is needed for***

treating various serious ailments, including cancer. That said, the law sternly prohibits patent infringement, and it may not be possible to argue that considerations of public interest should be allowed to justify infringing drugs to circulate in the market*.*

xxx xxx xxx"

(Emphasis Supplied)

164. This Court is further of the view that any infringing products manufactured, offered for sale or sold, etc., during the life/term of the patent, do not gain credibility. Thus, manufacture of infringing goods and stockpiling them during the said period, so as to release it/flood the market, would also amount to infringement. Hence, any use and sale of any products manufactured during the said period, in violation of a patent, is also liable to be restrained. Delving on this aspect, in the case of ***Sotefin SA Versus Indraprastha Cancer Society and Research Centre and Others, 2022 SCC OnLine Del 516***, it has been held as follows:

"xxx xxx xxx

49. ***In the opinion of the court, if infringement has occurred during the lifetime of the patent, the infringing goods would not become kosher on expiry of the patent.*** *Plaintiff would be entitled to seek restrain on Smart Dollies which were made or imported at a time when the suit patent was valid and subsisting.* ***Therefore, irrespective of the fact that the patent is to expire the next month, since the Smart Dollies are prima facie infringing the suit patent as on the date of infringement, plaintiff can insist on protection under Section 48 of the Act.*** *On this aspect no case law has been cited and Mr Lall has contended that there is no precedent of an Indian court on this issue.* ***In these circumstances, he has placed reliance on judgments of USA and UK to argue that infringing articles made during the term of patent would continue to be restrained, even after expiry of the patent term****.*

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54. ***Therefore, on a prima facie basis, this Court is in agreement with the views expressed by the foreign courts, which suggest that any product which is infringing, during the term of the patent, would continue to be tainted. The infringement cannot get dissolved with the lapse of the patent. Undoubtedly, the monopoly of the patentee would stand extinguished with the expiry of the term, but the infringement that has***

occurred during the lifetime of the patent would not fade away*. Hence the use of the Smart Dollies, imported during the term of a subsisting patent, in violation of the patentee's exclusive rights, have to be restrained:*

Whether defendants are entitled to protection under Section 107-A(b) of the Act?

xxx xxx xxx"

(Emphasis Supplied)

165. It is to be seen that the patent expires in May, 2026. The defendant will be free to launch its product thereafter. The patent in question is valid in fifty countries across the world. The validity of the patent was challenged in thirty countries and has successfully been sustained. Further, the plaintiffs were granted the suit patent after fourteen years, thereby, shortening the limited monopoly of the plaintiffs.

166. Furthermore, the defendant has already been suffering an injunction since more than a year and did not get a manufacturing license till December, 2024. It is also to be noted that one of the pre-grant oppositions was filed by IPA, of which defendant is also a member. The said pre-grant opposition filed by IPA was rejected along with other pre-grant oppositions, leading to grant of the suit patent.

Conclusion

167. Thus, considering the detailed discussion hereinabove, the plaintiffs have established a *prima facie* case in their favour. The balance of convenience also lies in favour of the plaintiffs. The plaintiffs shall suffer irreparable loss, in case interim relief as prayed for, is not granted. Accordingly, the defendants, and all others acting on its behalf, are restrained from manufacturing, using, selling, offering for sale, importing, exporting, advertising or dealing in any bio-similar/similar biologic of Nivolumab, the suit patent, during the pendency of the present suit.

168. Further, the defendant is also restrained from launching any manufactured product, if any, manufactured during the pendency of the patent of the plaintiffs, even upon expiry of the patent. The defendant is accordingly directed to file an affidavit disclosing the quantity of its manufactured bio-similar product of Nivolumab, within a period of four weeks, from today.

169. It is clarified that the observations made hereinabove, are only *prima facie* in nature for the purposes of deciding the application for interim injunction. Nothing contained herein shall be construed as an expression on the merits of the case, which shall be decided after trial, independent of any observations made herein.

170. The present application being *I.A. 10533/2024* is accordingly, disposed of, with the aforesaid directions.

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171. List before the Roster Bench on 08th August, 2025.

(MINI PUSHKARNA)
JUDGE

JULY 18, 2025/AU/KR