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

\+ CS(COMM) 159/2024

F- HOFFMANN -LA ROCHE AG & ANR. ..... Plaintiffs

Through: Mr. Mukul Rohatgi and Mr. Sandeep Sethi, Senior Advocates with Mr. Pravin Anand, Ms. Archana Shanker, Mr. Shrawan Chopra, Ms. Prachi Agarwal, Mr. Devinder Rawat, Mr. Achyut Tiwari, Ms. Misha Rohatgi, Ms. Shreya Sethi, Mr. Sumer Seth and Ms. Riya Kumar, Advocates.

versus

ZYDUS LIFESCIENCES LIMITED, ... Defendant

Through: Dr. Abhishek Manu Singhvi and Mr. Rajshekhar Rao, Senior Advocates with Ms. Bitika Sharma, Mr. Adarsh Ramanujan, Ms. Vrinda Pathak, Mr. George Vithayathil and Mr. Manjunathan, Advocates.

CORAM:
HON'BLE MR. JUSTICE SANJEEV NARULA

O R D E R

% 23.02.2024

CAV 85/2024

1. Since the counsel for Defendant have appeared, the caveat stands discharged.

I.A. 4199/2024 *(exemption from filing original documents)*

2. Exemption is granted, subject to all just exceptions.

3. Plaintiffs shall file legible and clearer copies of exempted documents, compliant with practice rules, before the next date of hearing.

4. Accordingly, the application stands disposed of.

I.A. 4197/2024 *(seeking leave to file additional documents)*

5. This is an application seeking leave to file additional documents under the Commercial Courts Act, 2015.

6. If Plaintiffs wish to file additional documents at a later stage, they shall do so strictly as per the provisions of the said Act.

7. Accordingly, the application stands disposed of.

I.A. 4198/2024 *(for exemption from pre-institution mediation)*

8. Issue notice. Ms. Bitika Sharma, Advocate, accepts notice on behalf of the Defendant. Reply, if any, be filed in within a period of two weeks from today. Rejoinder thereto, if required, be filed before the next date of hearing.

9. Re-notify on 4th April, 2024.

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10. Issue summons. Ms. Bitika Sharma, Advocate, accepts summons on behalf of the Defendant. She confirms receipt of the suit-paper book and waives the requirement of service of formal summons by the Registry. Written statement be filed by the Defendant within 30 days from today. Along with the written statement, the Defendant shall also file an affidavit of admission/denial of the documents of the Plaintiffs, without which the written statement shall not be taken on record.

11. Liberty is given to the Plaintiffs to file a replication within 15 days of the receipt of the written statement. Along with the replication, if any, filed

by the Plaintiffs, an affidavit of admission/denial of documents of the Defendant, be filed by the Plaintiffs, without which the replication shall not be taken on record. If any of the parties wish to seek inspection of any documents, the same shall be sought and given within the timelines.

12. List before the Joint Registrar for completion of pleadings, filing of joint schedule of documents, marking of exhibits on 29th April, 2024. It is made clear that any party unjustifiably denying documents would be liable to be burdened with costs.

13. List before Court for framing of issues thereafter.

I.A. 4196/2024 *(under Order XXXIX Rules 1 & 2 read with Section 151 of the Code of Civil Procedure, 1908)*

14. Mr. Mukul Rohatgi and Mr. Sandeep Sethi, Senior Counsel, have set out the Plaintiffs' case for urgent interim relief as follows:

14.1. Plaintiffs are among the world's largest pharmaceutical companies, involved in innovation of products and services for detection, prevention, diagnosis and treatment of diseases.

14.2 The present suit is filed for infringement of two patents [*collectively*, ***"Suit Patents"***], both pertaining to 'Pertuzumab', which is a monoclonal antibody (Mab) biologic used to inhibit tumour growth. The details of the patents are as follows:

14.2.1. IN 464646 titled as "PERTUZUMAB VARIANTS AND EVALUATION THEREOF" [***"IN'646"***], registered in the name of Plaintiff No. 1, is a process patent relating to the method for making a composition comprising Pertuzumab and one or more variants. The bibliographic details thereof are set out as under:

Title	*PERTUZUMAB VARIANTS AND EVALUATION THEREOF*
Patentee	*Plaintiff No. 1*
Application No.	*6979/CHENP/2015*
Patent No.	*464646*
Priority Date	*16.04.2013*
PCT International Filing date (Date of patent)	*15.04.2014*
PCT International Application Number	*PCT/US2014/034200*
National Phase entry-filing date in India	*12.11.2015*
Date of Publication u/s 11A	*01.07.2016*
FER Issue Date	*30.12.2019*
FER Response Date	*30.06.2020*
Pre-grant opposition date	*12.10.2020*
Pre-grant order date finding the application in order for grant	*31.10.2023*
Date of Grant	*01.11.2023*
Date of expiry	*15.04.2034*

14.2.2. IN 268632 titled as "PHARMACEUTICAL FORMULATION COMPRISING HER2 ANTIBODY" [***"IN'632"***], registered in the name of Plaintiff No. 2, relates to an aqueous pharmaceutical formulation comprising Pertuzumab and excipients such as sucrose, histidine acetate buffer, polysorbate, such that the pH of the formulation is from 5.5–6.5. The bibliographic details thereof are set out as under:

Title	*PHARMACEUTICAL FORMULATION COMPRISING HER2 ANTIBODY*
Patentee	*Plaintiff No. 2*
Application No.	*1730/DELNP/2007*
Patent No.	*268632*
Priority Date	*20.10.2004*
National Phase entry-filing date in India	*05.03.2007*
Date of Publication u/s 11A	*24.08.2007*
PCT International Application Number	*PCT/US2005/037471*

PCT International Filing date (Date of patent)	*19.10.2005*
FER Issue Date	*26.08.2010*
FER Response Date	*18.05.2011*
Date of Grant	*09.09.2015*
Date of expiry	*19.10.2025*

14.3. Pertuzumab is the first in its class of agents called "HER2 dimerization inhibitors". Overexpression of the HER2 gene is a primary cause for breast cancer, and is also known to cause other cancers. By binding to HER2, Pertuzumab inhibits dimerization of HER2 with other HER receptors and thus inhibits tumour growth.

14.4. Plaintiffs manufacture and sell Pertuzumab under the brand name 'Perjeta ®', which has been approved by regulatory authorities in several countries. The Perjata ® (Pertuzumab) Concentrate for Solution for Infusion 420 mg / 14 ml Vials have been granted approval by the US FDA on 08.06.2012. In India, Perjeta ® (Pertuzumab) Concentrate for Solution for Infusion 420 mg / 14 ml Vials have been granted approval on 29th December, 2014.

14.5. The Suit Patents, granted by the Patent Office after a rigorous examination process, are valid and subsisting. lN'632 has till date not been subjected to any Pre-Grant/ Post-Grant Opposition or revocation proceedings in India, and thus enjoys a strong presumption of validity. As regards IN'646, although a Pre-Grant Opposition was filed on several grounds, the same was rejected by a reasoned order of the Deputy Controller of Patents on 31st October, 2023. Patents corresponding to Suit Patents have also been granted in multiple other countries.

14.6. During the terms of the Suit Patents, the Plaintiffs —being the rightful owners of the Suit Patents and being the exclusive licensees under

Section 109 of the Patents Act, 1970 [***"Patents Act"***]— have the exclusive right by virtue of Section 48 of the Patents Act, to prevent third parties who do not have their consent from making, using, offering for sale, selling, or importing any product(s) which fall within the scope of the claims of either of the Suit Patents.

14.7. In the first week of February 2024, the Plaintiffs came across the recommendations of the Subject Expert Committee (SEC) (Oncology) of the Central Drugs Standard Control Organization (CDSCO). These recommendations disclose that the Defendant has applied for grant of permission to manufacture New Drug Formulation for sale or the distribution of Pertuzumab as per New Drugs and Clinical Trails 2019 in Form CT-21. The Defendant has also applied for permission to conduct clinical trials for their product, under the nomenclature ZRC-3277, as a similar biologic/ biosimilar to that of Plaintiffs' Pertuzumab. Pertinently, the said application categorically mentions the Plaintiffs' product Perjeta®, which is covered within the claims of the Suit Patents, as the reference biologic. A similar mention of Perjeta® as the reference product is made by the Defendant for undertaking clinical trials with the Clinical Trial Registry of India (CTRI). The SEC has recently recommended for grant of permission to the Defendant to manufacture and market Pertuzumab 30 mg/ml concentrate solution for infusion (420 mg/14ml single-dose vial).

14.8. Unlike the case with chemical compounds, a similar biologic can never be an exact copy of the innovator reference biologic, given the intrinsic nature of the biologic product. Nonetheless, a similar biologic is nearly identical to its reference biologic. This is evident from the 'Guidelines on Similar Biologics' issued by the Department of

Biotechnology (Ministry of Science and Technology) and CDSCO (Ministry of Health and Family Welfare), Government of India [***"Guidelines"***]. The said guidelines stipulate that a Similar Biologic product is that which is similar in terms of quality, safety and efficacy to an already approved Reference Biologic product, based on comparability. By claiming their product to be a similar biologic/ biosimilar to that of Plaintiffs' product Perjeta®, the Defendant admits that both products are identical in all important parameters. In light of the above facts, it is apparent that the Defendant's similar biologic closely mirrors the Plaintiffs' patented product in terms of its composition, thus infringing on IN'632. Further, since no methodology for production of the similar biologic has been disclosed, the Plaintiffs also apprehend that the process employed is identical to that of Perjeta®, thereby infringing upon the claims of IN'646.

14.9. The Defendant has also filed applications for registering their patents relating to formulations of Pertuzumab, which are pending consideration. Copies of Defendant's patent applications No. 2020084503 and No. 2021079337 are Document No. 64 and Document No. 65 respectively annexed with the plaint.

14.10. In view of the foregoing circumstances, the present suit is filed as a *quia timet* action as the Plaintiffs strongly apprehend that the threat of launch of the infringing biosimilar product is imminent, and if not injuncted, irreparable harm would be caused to the Plaintiffs. The aforenoted applications of the Defendant clearly indicate that the drug applied for, admittedly being a similar biologic, is identical to the Plaintiff's product and therefore would amount to infringement of the scope, teachings and claims of both Suit Patents (i.e., formulation and process). Moreover, it is submitted

that the Defendant is already aware of the Plaintiffs' rights in the Suit Patents, as they were one of the members of the organisation which had unsuccessfully filed Pre-Grant Opposition to IN'646. Thus, the plaint discloses a strong *prima facie* case of potential infringement and the Plaintiffs are entitled to seek interim protection in respect of their Suit Patents.

15. *Per contra*, Dr. Abhishek Manu Singhvi and Mr. Rajshekhar Rao, Senior Counsel representing the Defendant, strongly argue that the Plaintiffs' apprehension is entirely misconceived. Dr. Singhvi emphasises that no urgency is disclosed in the plaint to warrant grant of an *ex-parte ad interim* injunction, and therefore, considering the nature of the lawsuit having regard to law relating to grant of interim injunctions, the Defendant must be afforded an opportunity to put forth their stand before the Court forms its *prima facie* view.

16. Dr. Singhvi also points out that the Plaintiffs do not have a patent registered for Pertuzumab in India. Rather, the claims of IN'632 pertain to a formulation comprising Pertuzumab which specifically uses a histidine acetate buffer, and it is this formulation that is sold under the brand name Perjeta®. Further, Dr. Singhvi emphasises that the plaint does not disclose any claim mapping in order to demonstrate that the Defendant's product would in fact be infringing upon the Suit Patents. Rather, the Plaintiffs' case rests on a proposition that a similar biologic is identical to its reference biologic product and therefore amounts to infringement, which is entirely untenable as there is sufficient jurisprudence on this issue to the contrary.

17. The Court has deliberated upon the extensive submissions advanced by the Senior Counsel for both sides. In response to a specific inquiry, both

Mr. Rohatgi as well as Mr. Pravin Anand, counsel for Plaintiffs, conceded that although there are international cases on the subject which would be shared with the Court, there is no Indian caselaw directly addressing the specific issue at hand. Notably, the sole precedent[1] cited during the proceedings was found to be tangentially related, failing to squarely address the nuanced matter before us.

18. A short provisional order was dictated in open court with a clarification that the final version would be made accessible subsequently, subject to further deliberations in chamber. In this context, the undersigned has researched on the subject to analyse the complexities we are required to confront. This detailed order is exposition of such endeavours, aiming to crystalize the legal and technical facets of the case.

19. This lawsuit concerns allegations of patent infringement, specifically targeting the 'formulation' and 'process' associated with an innovator 'Reference Biologic Product'. The Plaintiffs contend that their Suit Patents are on the verge of being infringed upon by a competing entity (the Defendant) through development of a 'Similar Biologic product'. Thus, this case delves into the complexities inherent in the intersection of biotechnological innovation and intellectual property law. At issue is the precise determination of whether the Similar Biologic's development encroaches upon the intellectual proprietary rights encapsulated within the patents of its Reference counterpart. Thus, the Court is called upon to not only navigate the intricacies of patent law, but also scientific principles that are foundational for the biologic and its biosimilar contender.

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[1] *Genentech Inc. & Ors. v. Drug Controller General of India & Ors.*, judgment dated 25th April, 2016 in CS(OS) 3284/2015; Neutral Citation No. 2016:DHC:3159

20. A biologic pharmaceutical, often simply called a ‘biologic’, is a type of medication derived from living organisms or their cells. The inherent complexity of biologics stems from their molecular size, structure, and the intricacies of their development process. Unlike traditional pharmaceuticals, which are typically synthesized through chemical processes to create small molecule drugs, biologics are produced using biotechnological methods involving recombinant DNA technology, controlled gene expression, and antibody production. Biologic medicines represent a paradigm shift from traditional small molecule pharmaceuticals, introducing a new spectrum of challenges for the intellectual property architecture designed to safeguard them.

21. The aforementioned Guidelines lay down the regulatory pathway for a Similar Biologic claiming to be similar to an already authorized Reference Biologic. A Reference Biologic is an innovator’s product which has been approved after evaluation of complete dossier and is critical for the development of a Similar Biologic, which is defined as being comparable in quality, safety, and efficacy to an approved product. There are no clinically meaningful differences between a Similar Biologic and an approved reference biological product. Similar Biologics can only be developed against the Reference Biologic that has been approved using a complete data package in India. A product can only be considered as a Similar Biologic if it is proven to be Similar using extensive quality characterization against the Reference Biologic and further product development should only be considered once the Similar Biologic is demonstrated to be similar in quality

to a Reference Biologic[2]. Just as a generic drug undergoes an abbreviated regulatory review upon referencing an already approved drug, a Similar Biologic also goes through an abbreviated review process that references an approved "reference product" or "reference biological drug". This process underscores the fundamental principle that biosimilars, by leveraging the exhaustive data of their reference biologics, can offer similar therapeutic benefits without necessitating a repeat of the extensive clinical trials conducted for the innovator reference product.

22. As per the Plaintiffs, given the fact that the Defendant's product has not yet been commercially launched in the market, it is not possible to map the Suit Patent claims with the potentially infringing product. Plaintiffs are also in the dark about the specific processes used by the Defendant in making their biologic product that is pending drug approval. Nonetheless, they firmly contend that the only feasible process to produce the infringing Similar Biologic is by utilising the method outlined in their process patent, i.e. IN'646.

23. In the above background, and having regard to the regulatory framework for Similar Biologics which has been availed by the Defendant, the Court has raised certain queries, to which Dr. Singhvi, on instructions, has confirmed as follows:

23.1. The Defendant has applied for a drug approval/ license for a similar biologic product, which is a formulation.

23.2. In the drug approval/ licensing application submitted by the Defendant, the referenced biologic is the Plaintiffs' formulation known as

[2] See Pg.10 of 'Guidelines on Similar Biologics: Regulatory Requirements for Marketing Authorisation in India' (2016); available at Pg.1910 of Plaintiffs' Documents filed along with the plaint.

Perjeta ®.

23.3. The formulation of the Similar Biologic that has been submitted for drug approval is related to Claim 1 of the Defendant's patent application No. 2021079337, which is currently under consideration.

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.

25. Thus, in view of the aforenoted responses by Dr. Singhvi, and given the fact that the reference biologic is protected under the Suit Patent IN'632 and the Defendant's similar biologic is encapsulated by Claim 1 in their patent application No. 2021079337, we must begin with the process of claim mapping. The Court will have to discern whether the formulation disclosed in Claim 1 of patent application No. 2021079337 is a variant of Pertuzumab, different from the Plaintiffs' formulation patent which is also "*pharmaceutical formulation comprising Pertuzumab"*. However, the absence of such claim mapping substantially restricts the Court from fully assessing the infringement allegations. In the Court's opinion, the Plaintiffs ought to have carried out this claim mapping, as this procedural step is

essential not only for clarifying the contours of the controversy but also for enabling the Court to make an informed decision on the matter. Accordingly, they must now do so expeditiously and present the same to the Court. The Defendant is also permitted to do the claim mapping, in case they so desire.

26. The Court also acknowledges the dual aspects of intellectual property concerning biologic medicines, which encompass not only the molecular structure of the biologic but also the sophisticated processes required for its reliable, safe, and consistent large-scale manufacturing within living systems. This recognition aligns with the detailed stipulations of the Indian regulatory guidelines for similar biologics, as outlined in Clause 6.2 of the Guidelines, according to which, manufacturers of Similar Biologics are mandated to refine their manufacturing processes to ensure that the resultant product closely matches the Reference Biologic in terms of identity, purity, and potency. Furthermore, the Guidelines stress the importance of process validation as well as the demonstration of a manufacturing procedure that is both highly consistent and robust. In scenarios where the host cell line utilized in the production of the Reference Biologic is publicly disclosed, there is a strong preference for employing the same host cell line in the manufacturing of Similar Biologics. This requirement underscores the balance between innovating within the framework of existing biologics and adhering to the stringent standards set forth to maintain the integrity and efficacy of these therapeutic products.

27. The Plaintiffs have a process patent IN’646, as discussed above. Thus, to determine the allegations of process infringement, the Court intends to invoke Section 104A of the Patents Act. Under this provision, when a patent

covers a process for obtaining a product, the Court is empowered to require the Defendant to demonstrate that their method for creating an identical product diverges from the patented process, subject to certain pre-requisites. This shift in the burden of proof is predicated on the novelty of the product and the patentee's disclosure of the process in the patent document in a sufficiently detailed manner for replication by a person skilled in the art.

28. Given the above-discussed context of similar and reference biologics in this case, the Court, drawing upon the aforementioned provision, deems it appropriate for the Defendant to reveal the process employed by them to develop the formulation for which drug approval/ licensing has been sought. However, as the issue of whether the Defendant's biologic formulation is identical to the Plaintiff's remains to be thoroughly examined, it is directed that the Defendant shall submit the aforementioned information in a sealed envelope with the Court. This measure, in the Court's opinion, would ensure the preservation of sensitive information pending further deliberations. The Court will subsequently also assess the need for establishing a confidentiality club to manage the disclosed information, to ensure that access to such information is appropriately controlled and limited to authorized individuals.

29. Considering the complexities of this case, particularly given the intricate intersection of biologic pharmaceuticals and intellectual property rights, the Court also finds it appropriate to issue directions to both parties to ensure a comprehensive adjudication of the interim application:

29.1. Given the stature of both parties as pharmaceutical industry leaders with access to patent legal expertise, the Court expects exhaustive assistance in the form of presenting all pertinent case law and jurisprudence

related to medical and patent matters concerning biologic medicines. This expectation extends to both domestic and international precedents that may offer insight into the issues at hand.

29.2. Each party is required to disclose the names and credentials of their respective experts in the field of biologic pharmaceuticals and related intellectual property issues. This disclosure should be made in a timely manner, to facilitate an organized examination of expert opinions, if deemed necessary at this interim stage.

29.3. Recognizing the technical complexity of the matters involved, the Court will also consider appointing an independent Scientific Advisor. The role of this Advisor will be to provide neutral expert analysis on the scientific aspects critical to the case, thereby aiding the Court in understanding the nuances of biologic medicine production and patent protection.

29.4. To ensure a thorough exploration of the technical issues, the Court may employ the process of 'hot tubbing' for simultaneous questioning of experts from both sides in an open-court format, allowing for a direct comparison of their insights.

30. Let the reply to the application be filed within three weeks from today. Rejoinder thereto, if any, be filed within one week thereafter.

31. List on 4th April, 2024.

SANJEEV NARULA, J

FEBRUARY 23, 2024
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