THE PATENTS ACT, 1970
(AS AMENDED)

SECTION 15

IN THE MATTER OF A PATENT FOR AN PATENT APPLICATION NO. **201748044868**

D E C I S I O N

The hearing was offered on 25th **November, 2024** intimating the following outstanding objections:

Clarity and Conciseness

1. Amended claim 1 does not comply with the requirements of section 10(4)(c) for the following reasons:

   Claim 1 lacks clarity regarding the term "antibody fragment." It is unclear whether the term includes all types of fragments (e.g., Fab, scFv, F(ab')2, or others), or if it is limited to specific types. Without further specification, the term "antibody fragment" is broad and open to multiple interpretations, which impacts the clarity and scope of the claim.

   The phrase "blocks binding of human PD-L1 and human PD-L2 to human PD-1" is ambiguous. It is unclear what threshold or extent of blocking is required for the claimed antibody to meet this limitation. This phrase could cover any antibody that partially interferes with PD-L1 or PD-L2 binding, leading to an overly broad scope.

   The term "isolated antibody" lacks clarity. It is not clear whether this term includes antibodies in partially purified form, in specific environments, or under particular conditions.

   Claim 1 is vague concerning the specific epitope on PD-1 to which the claimed

antibody or antibody fragment binds. Without specifying which part of PD-1 the antibody binds, the scope of the claim is unclear and potentially overbroad, as it could be interpreted to cover any antibody fragment binding to any region of PD-1.

The use of the term "comprising" in Claim 1 implies the inclusion of additional CDRs, sequences, or structural modifications that are not specified. This language could lead to an overly broad interpretation, allowing for variations that go beyond the intended scope of the invention, potentially encompassing embodiments that do not meet the invention's objective.

2. Claim 2 is not defining any product technical feature and the funtional feature alone cannot qualify as product claim/its dependent claim. It is unclear with the terms “About 1 nM or Lower”: The phrase "about 1 nM or lower" for IC50 values lacks clarity as "about" can imply a range that is not defined. This ambiguity can lead to interpretational issues as to the precise binding strength required, resulting in an unduly broad scope.

   Claim 8 and 9 relates to an “isolated polynucleotide encoding the antibody or antibody fragment” without specifying any polynucleotide sequence features. The claim cannot qualify as product claim unless the strutcural features of the claimed product defined in it. The claim must be definitive with its structural features and hence define the SEQ of polynucleotide claimed. The Claim 9 which define SEQ Ids that are not of polynucleotide sequences.

   Claim 12 host cell is not defined with its deposition number.

   Claim 13 relates a method for producing the antibody but lacks detail regarding “conditions wherein the nucleic acid sequence is expressed.” The absence of specific

culture conditions or parameters makes the claim broad, potentially covering a wide array of unrelated production methods.

Claim 15 includes a composition with a “pharmaceutically acceptable carrier or diluent” without any details on carrier characteristics, leading to broad interpretation. This claim could include any carrier without confirming compatibility or efficacy with the antibody.

Invention u/s 2(1)(ja)

1. The submissions in your letter dated 08-02-2021, have been considered carefully. The original claims 1-17 are replaced with newly filed amended claims 1-16. The submissions/observations in the reply letter do not meet the requirements as detailed below: The amended claims 1, 2, 4-10, 11-14 still lack inventive step in view of the documents cited in FER: D1: WO2006121168 D2: US2006210567 D3: US6808710 D1 discloses isolated monoclonal antibodies, particularly human monoclonal antibodies that specifically bind to PD-1 with high affinity. Nucleic acid molecules encoding the antibodies of the invention, expression vectors, host cells and methods for expressing the antibodies. D1 also discloses methods for detecting PD-1, as well as methods for treating various diseases, including cancer and infectious diseases, using anti-PD-1 antibodies. D2 discloses antibodies and antigen-binding fragments that can act as agonists and/or antagonists of PD-1 (Programmed Death 1), thereby modulating immune responses in general, and those mediated by TcR and CD28, in particular. It also discloses compositions and methods in treating autoimmune diseases, inflammatory disorders, allergies, transplant rejection, cancer, and other immune system disorders. D3 discloses PD-1 is a receptor for B7-4 molecules

expressed on antigen presenting cells. PD-1 transmits a negative signal to immune cells, similar to CTLA4. B7-4 molecules are expressed on the surface of antigen presenting cells and provide a costimulatory signal to immune cells and can transmit down modulatorysignals to immune cells, depending upon the molecule to which they bind. D1, D2, and D3 collectively disclose monoclonal antibodies targeting PD-1 with high binding affinities and discuss anti-PD1 antibodies designed for therapeutic intervention in immune modulation, such as cancer treatment. D1 particularly addresses high-affinity monoclonal antibodies specific to PD-1, alongside nucleic acid encoding methods, vector constructions, and clinical applications. D2 further demonstrates antibodies that act as PD-1 antagonists and are intended for immune response modulation across various diseases, including cancer. D3 emphasizes the interaction between PD-1 and its ligands (PD-L1, PD-L2) to modulate immune responses, underscoring the common mechanism in the current claims. The applicant's claim of "surprisingly better PD-1 binding affinity" due to specific CDR sequences does not sufficiently substantiate an inventive step. Although binding affinity data is presented in the application, this enhancement is part of routine antibody optimization—an expected outcome for a person skilled in the art focusing on PD-1. Further, achieving higher affinity antibodies by manipulating CDR sequences is a predictable technique in antibody engineering, particularly in light of D1's disclosure, which describes high-affinity PD-1 targeting antibodies. While the applicant highlights the selection of CDRs SEQ ID NOs: 9-14 as unique, both D1 and D2 describe processes for developing PD-1 binding antibodies, encompassing sequence variations to enhance binding efficacy. The person skilled in the art, with

established antibody-engineering methods, would likely employ these well-known techniques to produce high affinity PD-1 antibodies with desired therapeutic attributes. D1's and D2's disclosures provide a foundation for similar modifications, thus rendering the claimed CDR sequences a result of routine optimization rather than inventive selection. The applicant contends that their B-cell selection approach is superior to traditional hybridoma techniques and leads to antibodies with unique binding characteristics. However, the application of B-cell technology for antibody selection is wellknown in the field and does not confer an inventive step, as routine antibody discovery and screening processes commonly involve B-cell selection for binding affinity and specificity enhancement. This approach does not produce an unexpected result but instead represents a standard practice that would naturally be utilized by a person skilled to improve binding properties. The applicant argues that hPD-1.08 demonstrates an advantageous binding profile, claiming it as a technical advancement. However, mere improvements in binding kinetics (on-rate/off-rate) or specificity to PD-L1 and PD-L2, as outlined, are a known consequence of antibody engineering efforts. The person skilled in the art, familiar with antibody optimization techniques, would anticipate such outcomes through iterative selection and sequence variation within CDR regions. The prior art collectively suggests that anti-PD-1 antibodies with improved therapeutic efficacy can be developed without necessitating the specific sequences claimed. Based on the teachings of D1, D2, and D3, the development of PD-1-targeting antibodies with enhanced affinity, involving specific CDR modifications, is obvious. The prior art provides adequate guidance for a person skilled in the art to achieve the claimed functional characteristics, including blocking

PD-L1 and PD-L2 binding, through routine optimization methods. The selection of CDRs SEQ ID NOs: 9-14 and the resultant binding improvement are within the expected scope of antibody development and do not reflect a non-obvious technical advance over known anti-PD-1 antibody compositions. The choice of the selecting other sequences does not involve an inventive step as it is obvious to a person skilled in the art to look for further sequences in view of documents cited. Hence, amended claims 1-16 lack inventive step under section 2(1)(j)(a) of The Patents Act, 1970.

Non-Patentability u/s 3

1. Section 3(d):

The applicant has failed to provide concrete evidence demonstrating that the claimed antibody or antibody fragment shows enhanced therapeutic efficacy compared to known antibodies. While the applicant refers to increased binding affinity and a faster on-rate, these characteristics alone do not constitute therapeutic efficacy, as the ultimate clinical benefit must be demonstrated. The comparison with other anti-PD-1 antibodies must include relevant in vivo or clinical efficacy data to substantiate the claims of enhanced efficacy. The applicant argues that the objection is vague by not specifying which known antibodies are relied upon. However, it is critical to recognize that the term “known antibodies” typically refers to well-characterized antibodies in the public domain, such as those described in prior art (D1-D3). The applicant should provide detailed comparisons with these known antibodies to clarify the differences and establish the non-obviousness of the claimed invention. The applicant’s claim of novelty is based primarily on structural features. However,

Section 3(d) prohibits the patenting of mere new forms or structures of known substances without showing that these forms possess significantly different properties, especially concerning efficacy. The applicant must clearly demonstrate that the claimed antibodies possess properties or effects that are significantly different from those of previously known antibodies to overcome this objection. Therefore, amended claims 11 are not patentable u/s 3(d) of the Act.

Section 3(e):

The applicant contends that their claims are outside the scope of Section 3(e) due to the inclusion of a novel antibody. However, the objections were raised concerning claims 15 and 16, which describe the composition as an admixture of an antibody and a pharmaceutical carrier. If the composition lacks a demonstrated synergistic effect, it falls under Section 3(e). The applicant must provide experimental evidence demonstrating that the combination of the antibody and carrier provides unexpected results or enhanced efficacy that would not be anticipated from their individual components.The applicant's assertions of novelty do not address the core issue regarding the lack of demonstrated synergistic effects in the composition. Without empirical data supporting claims of enhanced therapeutic effects from the admixture, the claims remain non-patentable under Section 3(e).

Section 3(c):

Claim 8 relates to an isolated polynucleotide encoding the antibody or antibody fragment of any one of claims 1 to 7. There is no specific sequence claimed. The applicant claims the Controller's objection lacks basis due to the absence of specific references. However, the burden is on the applicant to demonstrate how their

polynucleotides and the resulting antibodies do not fall within the scope of Section 3(c). Without a thorough disclosure of the genetic engineering processes and an explanation of how the resultant polynucleotides differ from naturally occurring sequences, the claims may still be perceived as mere discoveries of substances occurring in nature.

Section 3(j):

The host cell claimed in claim 12 is not patentable u/s 3(j) of the Patents Act, 1970 as it covers the animal/plant cell which are other than microorganisms.

In reply to the notice, the applicant's agent submitted correspondence letter on 21st November 2024, with the following:

"This is in reference to the above identified Indian Patent Application for which a hearing has been scheduled on 25 November 2024. We would like to inform the Ld. Controller that the Applicant has not provided us with the instructions to attend the hearing for the instant case. For this reason, we, the Agent for the Applicant, will not be attending the hearing."

The applicant or his agent has not attended the scheduled hearing as the Applicant did not provide any instructions to the agent for attending the hearing of the instant case, and the merit of the application is that, the requirements (objections as above) which are communicated in the hearing notice are still outstanding, therefore it is hereby decided that the application, **201748044868 is** refused for grant of a patent.

Dated this **25th November, 2024**