THE PATENTS ACT, 1970

The Patents Rules, 2003

(SECTION 25(1) and RULE 55)

In the matter of the Indian Patent Application No. 201617025251 filed dated 22/07/2016

AND

In the matter of opposition under section 25(1) to the grant of patent

1.PFIZER INC. 2. MERCK SHARP & DOHME LLC**……The Applicant**

1. Mr. Rahul Laxman Gajbniye ,Nagpur,Maharashtra ….....The Opponent

2. Dr. Priyank Purohit ,Uttarakhand ……..The Opponent

Decision

1. An application for a patent bearing number 201617025251 was filed in Patent Office, Delhi on 22/07/2016. A request for examination under Section 11-B was filed on 02/02/2018.The said application was examined under Section 12 and 13 of Patents Act and first examination report containing a statement of objections was forwarded on 15/02/2021 and the applicant's agent filed response to first examination report on 02/08/2021.

2 As per the provisions under Section 13(3) of Patents Act, the said amended case after reply to first examination report was examined and investigated in like manner as the original specification and the applicant was offered a hearing on 28/06/2024 containing statement of objections in the issued hearing letter uploaded in the application documents of the instant case as **201617025251-PreGrant-ExtendedHearingNotice-(HearingDate-28-06-2024).pdf** with the following outstanding objections.:

Claims [u/s 10(5) & 10(4) (c)] 1. Claims 1-14 directs to the composition for use in various cancers and it directs to the use of axitinib salt and its derivatives in the claimed composition, however support is not found for al such features in the

specification. Thus the claims are not fairly based on the disclosure of the specification and do not meet the requirement under section 10(5) of the Patents Act, 1970.

Formal Requirement(s) 1. The inventors MARTINI Jean francois Andre and TARAZI Jamal Christo have assigned the rights only in favor of PFIZER INC similarly the inventors PERINI Rodolfo Fleury and MAURO David J. have assigned the rights only to MERCK SHARP & DOHME CORP. and to PFIZER INC, hence assignment copy submitted on 18-01-2017 is incomplete. Therefore proof of right to file this application has not been furnished as per requirement u/s 7(2) of the Act.

Invention u/s 2(1)(j) 1. The submissions in your letter dated 02-08-2021 have been considered carefuly, however the requirements of the objection raised in FER have not been met, hence they have been maintained as folows: (i) Regarding inventive step, your reply is not satisfactory, hence the inventive step objection is maintained for claims 1-14 in view of documents cited in FER along with further addityonal documents as folows: D5:van Geel et al., "Concise drug review: Pazopanib and axitinib". Oncologist, 25 June 2012, Vol. 17, pages 1081-1089. D6: Approval label of Axitinib by the FDA from January, 2012. The present claims direct to a medicament comprising an antagonist of a Programmed Death 1 protein (PD-1) for use in combination with a vascular endothelial growth factor receptor (VEGFR) inhibitor for treating a cancer in an individual, wherein the PD-1 antagonist is an anti-PD-1 monoclonal antibody which comprises a heavy chain and a light chain, wherein the heavy and light chains comprise SEQ ID NO:21 and SEQ ID NO:22, respectively, and further wherein the VEGFR inhibitor is N-methyl-2-[3-((E)-2-pyridin-2-yl-vinyl)-1H-indazol-6-ylsulfanyl]- benzamide or a pharmaceutica ly acceptable salt thereof. That is, PD-1 antagonist is pembrolizumab and the VEGFR inhibitor is axitinib. D1 describes treatment of advanced renal cel carcinomas with MK-3475 (pembrolizumab), a PD-1 antagonistic antibody and pazopanib, a VEGFR inhibitor (whole document). Your reply states that Document D1 doesn’t even mention VEGFR or PD-1 and pazopanib as disclosed in D1 is a tyrosine kinase inhibitor and selectively inhibits

VEGFR 1, 2, 3 However, the pembrolizumab –MK3465 is an anti PD-1 antibody and Pazopnib is a VEGF inhibitor. This combination is disclosed in D1 for its use in Advanced renal cel carcinoma. The combination of VEGFR inhibitor and PD-1 antibody is also widely known (SeeD2, D3)

D4 discloses the importance of axitinib and it is also a potent multitargeted tyrosine kinase receptor inhibitor, which selectively inhibits vascular endothelial growth factor receptors (VEGFR)-1, -2, and -3. D4 compares the IC50 concentration of other VEGF inbitiors such as sunitinib, sorafenib, pazopanib, but axitinib is found to have less IC50 concentration than others and found to be effective than others. The same is evident from D5 and D6, wherein D5 provides a side-by-side comparison of the second generation potent inhibitors pazopanib and axitinib for the treatment of renal ce l cancer (RCC). D5 moreover highlights important advantages that axitinib achieves compared to pazopanib in that axitinib is more selective and more potent than pazopanib. Additionaly, D5 teaches that the high selectivity of axitinib might contribute to less off-target adverse effects and a better therapeutic window. The VEGFR-TKI axitinib approved in 2012 for the treatment of advanced renal cel cancer (RCC) (see, document D6). Further the specification does not provide any experimental data to provide the efficacy of the claimed composition. The example does not provide any results which demonstrate the efficacy of the claimed combination. Thus the claimed composition is a mere admixture of the two components perolizumab and axitinib which are wel known for its use in advanced renal cel carcinoma. Thus the amended claims 1-14 lack inventive step in view of D1 along with D4 or D1 along with D5.

Non-Patentability u/s 3 1.

(i) The claimed composition is objected under section 3(e) of the Patents Act, 1970. You reply in this regard is not satisfactory. However no data is provided in the specification based on this regard. Even a therapeutic efficacy is not provided. Since the components are known before for RCC it is considered to be an admixture of know components (pembrolizumab and axitinib) and the present application do not provide any data related to synergistic effect and therapeutic

efficacy. Thus the claimed combination as in claims 1-7 and 14 are objected under section 3(e) of the patents Act, 1970.

(ii) (ii) D1 discloses a combination of pembrolizumab and pazopnib and the present claims directs to the combination of pembrolizumab and axitinib. Thus the claimed composition is considered a mere derivative of the known compound and it is not found to have any improved therapeutic effect than the known product of D1. Thus the claims 1-7,14 are objected under section 3(d) of the Patents Act, 1970.

(iii) (iii)The kit as claimed in claims 8-13 also directs to composition, which is a mere admixture and hence objected under section 3(e) of the Patents Act, 1970.

(iv)The claims 8-9 directs to package insert comprise instructions, this feature represents a mere representation of information and hence objected under section 3(n) of the Patents Act, 1970.

(v)The claims 8-14 although they direct to kit or a medicament, they are intended to claim for the dosage regimen used for treating cancer in human, hence disguisedly directs to method of treatment, therefore claims 11 and 14 are objected under section 3(i) of the Patents Act, 1970. The use of the of kit or the medicament as claimed in claims 12-13 is objected as use claims are not considered as an invention under section 2(1)(j) of the Patents Act, 1970. 2. With the introduction of new Rule 55(5A), if the applicant or opponent desires to be heard in the matter of pre-grant opposition, he shal inform the Controler by paying the prescribed fee.

Sufficiency of Disclosure u/s 10 (4) 1. The specification does not provide exemplification for the working of the claimed composition and it does not provide support for the use of the axitinib salt and its derivatives in the claimed composition. No data related to the results has been provided. No exemplification has been provided to shown the synergistic effect and therapeutic efficacy of the claimed composition. The specification does not provide examples of practical implementation of the claimed therapy. Example 1 is a prophetic example disclosing a study protocol for a clinical trial to be implemented, but there is no evidence in the patent that it has been carried out nor any results derived from it. In this regard, al that the example provides is an

expectation: Thus the specification do not meet the requirement of section 10(4)(a) of the Patents Act, 1970.

3**. Pre grant oppositions**: Two Pregrant Oppositions have been filed against the Grant of the Patent on this application.

(i) First pregrant opposition : A representation by way of opposition u/s 25(1) of the Patents Act, 1970 has been filed by Dr. Priyank Purohit ,Uttarakhand through their Agents from Khurana and Khurana Advocates and IP Attorneys on 15/09/2021 under section 25 (1) read with rule 55 of The Patents Act, 1970 (as amended) . The pre grant opposition documents are uploaded as link 201617025251-PRE GRANT OPPOSITION DOCUMENT [15-09-2021(online)].pdf and 201617025251-PRE GRANT OPPOSITION FORM [15-09-2021(online)].pdf in the view application details of the above said application No.

Notice with respect to the pregrant oppositions was sent to the applicant on 28/03/2023 but applicant has not filed any reply statement and evidence u/r 55 of the Patent Rules, 2003 within three months.

ii) Second opposition : A representation by way of opposition u/s 25(1) of the Patents Act,1970 has been filed by Mr. Rahul Laxman Gajbniye ,Nagpur,Maharashtra through their Agents from RAJESHWARI & ASSOCIATES on 19/09/2023 under section 25 (1) read with rule 55 of The Patents Act, 1970 (as amended) and documents are uploaded as 201617025251-PRE GRANT OPPOSITION DOCUMENT [19-09-2023(online)].pdf and 201617025251-PRE GRANT OPPOSITION FORM [19-09-2023(online)].pdf in the view application details of the above said application No.

Notice with respect to the pregrant oppositions was sent to the applicant on 11/01/2024 but applicant has not filed any reply statement and evidence u/r 55 of the Patent Rules, 2003 within three months.

4.In view of the outstanding objections and nature of the objection the Applicant was given an opportunity of being heard and to submit their arguments in favour of their application. Pre grant hearing along with the section 14 hearing was scheduled on

28/06/2024. However, the agent for the Applicant did not appear for hearing to justify their stand and informed on 27/06/2024 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” and the said document is uploaded as **201617025251-Correspondence to notify the Controller [27-06-2024(online)].pdf**

Therefore the Applicants agent has not attended the scheduled hearing .Thus the objections raised in para 1- 5 in the above said hearing notice dated 27/05/2024 are still outstanding and hence the case is not in order for grant.

In view of the above said existing objections, the instant Patent Application does not meet the requirement of the Patent Act hence cannot be allowed. Accordingly the instant Patent Application is refused u/s 15 of the Patents Act, 1970. Consequently, the above said oppositions filed u/s 25(1) stands disposed off.

Dated 5th July, 2024

(Anita Jatav)

Deputy Controller of Patents & Designs