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Dear Sir/Madam

European (EP) Patent Application No: 17189595.6
Applicant(s): Bristol-Myers Squibb Company
Mewburn Ref: 007609563

I write in response to the examination report dated 7 October 2019.

To avoid unnecessary duplication of effort I request that amendment of the description be deferred until an allowable claim set is agreed upon with the examiner.

Inventive step (Article 56 EPC)

The Examining Division objects to claims 1-14 for allegedly lacking inventive step over newly introduced document D10 which it uses as starting point in its assessment of inventive step. The Examining Division acknowledges that "D10 does not disclose the exact regimen recited in claim 1" (section 3.4 of the examination report). However, the Examining Division asserts that "the application does not demonstrate that a surprising technical effect has been demonstrated with the regimen of claim 1" (section 3.5).

Based on the afore-mentioned assertion, the Examining Division formulates the objective technical problem as the provision of an alternative combinatorial use of an anti-CTLA4 and an anti-PD-1 antibody in the treatment of cancer.

According to the Examining Division the skilled person would have arrived at the subject matter of claim 1 without inventive skill and with an expectation of success.

We strongly disagree with that assessment.

The characterization of D10 as set forth in the examination report is not correct. It seems as if the Examining Division did not have the time to duly consider the contents of document D10. However, leaving that aside, what determines the result of the inventive step assessment is that the skilled person would have had no reason to arrive at the anti-PD-1 antibody for use of claim 1 in view of document D10 or any other cited document. Though the specification does not provide a direct comparison with the various dosing schedules allegedly disclosed in D10, the specification clearly shows that the dosing regimens recited in claim 1 are associated with a surprising technical effect as they are superior to other dosing regimens that are disclosed in the specification. For example, Table 10 of the specification shows the effects of four different dosing regimens on patients. Cohorts 2 and 2a correspond to the dosing regimens recited in claim 1. Cohorts 1 and 3 are two different regimens that were tested. The data in Table 10 clearly show that the dosing regimens of

Cohorts 2 and 2a had superior effects as compared to those of cohorts 1 and 3. The claimed dosing regimens had the highest 80% tumor reduction at 12 weeks, and the treatment of cohort 2 had the highest objective response rate of 53%. These results clearly show that not all dosing regimens combining an anti-PD-1 antibody with an anti-CTLA-4 antibody will have an equal impact on the efficacy of the therapy. And, the dosing regimens recited in claim 1 are superior to the other regimens tested in the specification.

For at least these reasons, claim 1 is inventive over the alleged disclosure of document D10. Claims 2-14 depend directly or indirectly from claim 1 and thus include every element of claim 1. Therefore, claims 2-14 are also inventive over D10.

Precautionary Statements

I ask the examiner to discuss with me any amendments that the Examining Division intends to make to the claims before issuing the Rule 71(3) EPC communication. I refer to the Guidelines at C-V 1.1, which suggest that the Examining Division should only make amendments which the applicant can reasonably be expected to accept. Amendments that affect the scope of the claims are unlikely to be acceptable.

As a routine precaution, I request oral proceedings under Art 116 EPC, to take place only in the event that the Examining Division forms the intention to refuse this application. For compliance with Art 113(1) EPC I request that, before any summons to oral proceedings is issued, the applicant be given a proper opportunity to reply in writing to any objection raised by the Examining Division, especially any objection based on prior art not previously referred to in the examination.

Amendments made during the prosecution of this application are not to be interpreted as acknowledgement of the validity of any objection, nor as acknowledgement that any citation against the application is material to the patentability of the application.

In this application, unless expressly stated otherwise, the cancellation, abandonment or amendment of any claim or any amendment of the description does not amount to abandonment of any subject matter in the application, and the applicant reserves the right to pursue some or all of such subject matter in this application, or in one or more divisional applications. Additionally, the applicant reserves the right to file divisional applications in respect of any subject matter in the application as filed.

Yours faithfully



Dr Thomas Wolter

AUTHORISED REPRESENTATIVE

For and on behalf of MEWBURN ELLIS LLP (Association No. 929)

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