UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

APOTEX INC., APOTEX CORP., APOTEX PHARMACEUTICALS HOLDINGS INC., and APOTEX HOLDINGS, INC.,
Petitioners,
v.

OSI PHARMACEUTICALS, INC.,
Patent Owner.

U.S. Patent No. 6,900,221
Issue Date: May 31, 2005

Case No. IPR2016-01284

REPLY DECLARATION OF GIUSEPPE GIACCONE, M.D., PH.D.

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I, Giuseppe Giaccone M.D., Ph.D, declare and state as follows:

1. The opinions and conclusions I express in this declaration are based on my education, my extensive experience in the diagnosis and treatment of various lung cancers, and my review of materials related to this matter.

2. For the purposes of my opinions and conclusions, I apply the definition of "treating" and "treatment" as provided by U.S. Patent No. 6,900,221. (*See* "the '221 patent, col. 14, ll. 9-15.)

I. QUALIFICATIONS

3. For a discussion of my qualifications and credentials, I refer to my June 17, 2016 declaration (Ex. 1002) and my curriculum vitae, which is **Appendix A** to Ex. 1002.

II. MATERIALS REVIEWED

4. In forming my opinions, I have relied upon my accumulated knowledge and experience. I have reviewed Patent Owner OSI Pharmaceuticals, LLC's ("OSI") Response (Paper 20) and the materials cited in **Appendix A** attached thereto. I have further reviewed the documents referenced herein.

III. OBJECTIVE INDICIA OF NONOBVIOUSNESS

A. A Person of Ordinary Skill in the Art Cannot Assess if Patent Owner's Alleged Results are Unexpected

5. OSI and Dr. Bunn contend that erlotinib's therapeutic efficacy and ability to provide survival benefits to non-small cell lung cancer (NSCLC) patients was unexpected. (Paper 20 at 61; Ex. 2021 at ¶ 109.) However, logic would dictate that a comparator is necessary to evaluate whether a result is unexpected. Indeed, in the context of patent claims, I understand that the correct comparator for evaluating whether a result is "unexpected" is to compare it with what is identified as being the closest prior art. In this case, the closest prior art is Schnur (U.S. Patent No. 5,747,498 (Ex. 1009)), which discloses the compound erlotinib as being effective to treat a range of conditions that involve inhibition of the EGF receptor, including lung cancer. (*See* Ex. 1009 at col. 14, ll, 1 – 16.) I understand that no such comparison was made. (*See* Paper 20 at 61; Ex. 2021 at ¶¶ 108-109.) Dr. Bunn subsequently testified that he used chemotherapy as the closest prior art for his analysis. (Ex. 1048 at 111:9 – 113:16.) However, Dr. Bunn's declaration provides no analysis of why a survival benefit derived from the challenged claims of the '221 patent would be unexpected in comparison with chemotherapy. (*See* Ex. 2021 at ¶¶ 108-109.) Neither does Patent Owner's Response. (*See* Paper 20 at 61.) Thus, OSI's and Dr. Bunn's statements that erlotinib's therapeutic efficacy

and potential survival benefits for NSCLC patients are unexpected is mere conjecture.

6. OSI refers to a "majority of compounds" failing at some point during preclinical and clinical development. (*See* Paper 20 at 61.) However, that is just a general statement about drug development. If FDA-approval is the benchmark and a failure to pass through various stages of preclinical and clinical development in general is the baseline comparator, this would mean that all FDA-approved drugs provide unexpected results. Moreover, because the compound erlotinib was already patented, I understand the issue here as being whether the use of erlotinib to treat NSCLC was unexpected in view of Schnur, which discloses its use to treat lung cancer generally. As set forth in my earlier Declaration, the use of erlotinib to treat NSCLC was not unexpected, particularly in view of Schnur, as well as the statements in OSI's 10-K and Gibbs.

B. Patent Owner's Alleged Unexpected Results Do Not Apply to All NSCLC Patients

7. I further disagree with OSI's and Dr. Bunn's contentions that erlotinib's efficacy in treating NSCLC was unexpected because erlotinib plainly does not provide a survival to all, or even a majority, of NSCLC patients. Instead, in my experience, and as set forth in more recent articles, only a small subset of NSCLC patients actually respond to erlotinib. (*See* Ex. 1053 at ¶ 10; Ex. 1051 at

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