UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FLATWING PHARMACEUTICALS, LLC and
MYLAN PHARMACEUTICALS, INC.,
Petitioners,

v.

ANACOR PHARMACEUTICALS, INC.,
Patent Owner.

Case Nos. IPR2018-00168, -00169, -00170, and -00171[1]

U.S. Patent Nos. 9,549,938, 9,566,289, 9,566,290, and 9,572,823

DECLARATION OF STEPHEN KAHL, PH.D IN SUPPORT OF PETITIONER'S REPLY TO PATENT OWNER'S RESPONSE

[1] Case Nos. IPR2018-01358, -01359, -01360, and -01361 have been joined with these proceedings.

1. I, Stephen Kahl, Ph.D., hereby declare that the following is true and correct. I previously provided a declaration filed as Ex. 1003 in support of Paper #1, Petition for Inter Partes Review, and my testimony from that first Declaration remains the same. I am competent to make this Declaration based upon my personal knowledge and technical expertise, which I addressed in my first declaration.

2. Dr. Reider bases much of his testimony on what he calls the "promiscuous" nature of boron. (IPR2018-00168, Ex. 2013, ¶¶ 24–30; IPR2018-00169, Ex. 2013, ¶¶ 27–33; IPR2018-00170, Ex. 2013, ¶¶ 28–34; IPR2018-00171, Ex. 2013, ¶¶ 22–28.) I am informed that the Board rejected this same line of reasoning in its previous decision in rejecting Patent Owner's arguments about supposed toxicity concerns:

> Moreover, boron's allegedly "promiscuous" behavior does not dissuade a person of ordinary skill in the art from considering boron-containing compounds generally, or tavaborole in particular.

(Ex. 1014 at 27.) I agree with the Board, that a POSA would not have been dissuaded from considering boron-containing compounds generally, or tavaborole in particular. Instead, a POSA would have considered a boron-containing compound like tavaborole a suitable candidate for development, using routine procedures such as dose ranging studies as discussed by Dr. Murthy.

3. Dr. Reider bases much of his testimony on the supposed degradation of boron, through hydrolysis or oxidation. (IPR2018-000168, Ex. 2013, ¶ 37; IPR2018-00169, Ex. 2013, ¶ 40; IPR2018-00170, Ex. 2013, ¶ 41; IPR2018-00171, Ex. 2013, ¶ 35.) However, Dr. Reider admits he did not consider the kinetics of the reaction, which concern how long any such degradation would take. (Ex. 1045, Reider Dep. at 84:7–85:5 ("I have not seriously thought about the rate . . . .").)

4. In fact, concerning the degradation of boronic acids and esters, the kinetics of the reaction (i.e., the degradation of boronic acids and esters) are usually extremely slow. Thermodynamically, the degradation of boronic acids and esters is a favorable reaction and, given enough time, it will occur. But in many cases, the rate of the reaction is slow enough that noticeable degradation could take years or decades. The rate of reaction is sufficiently slow that these compounds can be formulated into products having a commercially useful shelf life.

5. For tavaborole in particular, the rate of decay is extremely slow, orders of magnitude longer than the treatment period in which tavaborole penetrates the nail, and sufficiently slow to permit formulation of a product having a useful shelf life. As such, it would have no bearing on the use of tavaborole as a pharmaceutical generally. It would also have no bearing on the concentration of tavaborole that a person of ordinary skill in the art would choose to include in a pharmaceutical formulation.

6. Building on his failure to consider the reaction kinetics, Dr. Reider also testifies that tavaborole in *Brehove* would not penetrate the nail plate but would instead undergo hydrolysis to boric acid before doing so. (IPR2018-00168, Ex. 2013 ¶¶ 66–67, 69; IPR2018-00169, Ex. 2013 ¶¶ 69–70, 72; IPR2018-00170, Ex. 2013 ¶¶ 70–71, 73; IPR2018-00171, Ex. 2013 ¶¶ 64–65, 67.) I am informed that the Board has previously determined to the contrary, that a POSA "would have had a reasonable expectation that ***administering tavaborole topically would penetrate the nail***." (Ex. 1014 at 24 (emphasis added).) I agree with the Board that a POSA would have had a reasonable expectation that administering tavaborole topically would penetrate the nail and would not instead undergo hydrolysis to boric acid so, in part because, as explained *supra*, the kinetics of the reaction are sufficiently slow that tavaborole would have more than enough time to penetrate the nail before any such hydrolysis would occur.

7. Moreover, *Austin* expressly discloses using tavaborole as an antifungal on an "aqueous medium":

> If the medium to be protected is an aqueous medium, the carrier is preferably water or a water-miscible organic solvent or mixture thereof. Examples of suitable water-miscible organic solvents are acetic acid, N,N-dimethylformamide, dimethylsulphoxide, N-methyl-2-pyrrolidine, alcohols such as ethanol or glycols such as ethylene glycol, propylene glycol and dipropylene glycol and lower C1-4-alkyl carbitols such as methyl carbitol.

(Ex. 1007, *Austin* at 8:32–38.) Dr. Reider's description of the nail as having "relatively high level of water content" (IPR2018-00168, Ex. 2013, ¶ 41; IPR2018-00169, Ex. 2013, ¶ 44; IPR2018-00170, Ex. 2013, ¶ 45; IPR2018-00171, Ex. 2013, ¶ 39) suggests that a POSA would read *Austin*, in combination with the other references cited, as providing a reasonable expectation of success that tavaborole could indeed be formulated for use in on the nail, including at a percentage solution such as 5% which could be determined by a routine dose ranging study as described by Dr. Murthy.

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As provided in 28 U.S.C. § 1760, I declare under penalty of perjury that the foregoing is true and correct.

Executed on: December __6___, 2018 By:____Stephen B. Kahl_____