

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTAS PHARMACEUTICALS LTD.
Petitioner,

v.

ATOSSA THERAPEUTICS, INC.
Patent Owner.

PGR 2023-00043

**PATENT OWNER'S RESPONSE TO PETITIONER'S OBSERVATIONS
ON THE CROSS-EXAMINATION OF DR. STEPHEN G. DAVIES**

Pursuant to the Board's email (EX3002) authorizing Patent Owner to file a Response to Petitioner's Observations on the Cross-Examination of Dr. Stephen G. Davies (Paper 26), Patent Owner provides the following responses to Observations 1 and 4.

Petitioner's Observation 1	Petitioner's Citations
Dr. Davies admits that the alleged modifications Dr. Bihovsky made to Liu's synthesis were not beyond the ordinary skill of a POSA and were either (1) due to the differences in scale; (2) an attempt to avoid introducing water which Liu suggests is necessary; or (3) routine.	22:23-24:20, 25:14-27:24; 28:17-30:6 30:21-32:7; 32:19-25; 40:16-41:6
<u>Patent Owner's Response to Observation 1</u>	
Patent Owner's Response	Patent Owner's Citations
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 22:23-24:20 because Dr. Davies testified that Liu suggests it "is not a good idea" to modify Liu's reaction temperature as done by Dr. Bihovsky to compensate for the scale of the reaction because such modifications would affect the experimental results.	25:11-13.
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 25:14-27:24 because Dr. Davies testified that a person of ordinary skill would not expect to have to make the modifications to Liu's procedure to exclude moisture as did Dr. Bihovsky.	28:4-7.
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 28:17-30:6 because Dr. Davies testified that a person of	29:25-30:11, 30:13-20.

ordinary skill in the art would not routinely purify a reaction at every step as done by Dr. Bihovsky.	
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 30:21-32:7 because Dr. Davies testified that a person of ordinary skill in the art would recognize that a small amount of water may actually catalyze some reactions to achieve better results.	26:21-21; 31:12-20.
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 32:19-25 because Dr. Davies testified that a person of ordinary skill in the art would understand that Liu's reagents would necessarily introduce some water to the reaction and may even catalyze the reaction to achieve better results.	31:12-20, 33:14-21.
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 40:16-41:6 because Dr. Davies testified that the modifications Dr. Bihovsky made to compensate for the scale of the reaction are not routine as they would affect the results of the experiments.	41:13-15.

Petitioner's Observation 4	Petitioner's Citations
Dr. Davies acknowledges that Dr. Bihovsky performed two purification schemes addressed by Liu (sequential recrystallization and isomerization), and Dr. Davies addressed only the sequential recrystallization pathway (Liu Examples 5 and 7), and not the isomerization pathway (Liu Examples 6 and 7)—both of which independently achieved 90% pure (Z)-endoxifen.	54:7-14; 56:24-57:10; 61:4-62:12; 70:2-72:22.
<u>Patent Owner's Response to Observation 4</u>	
Patent Owner's Response	Patent Owner's Citations

Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 54:7-14; 61:4-62:12 because Dr. Davies testified that he has not seen experimental data to confirm Dr. Bihovsky's reported E:Z ratios.	61:11-16; 62:2-19; 76:18-25, 78:1-10.
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 56:24-57:10 because Dr. Davies did not agree that Liu discloses two methods that each independently achieve 90% pure (Z)-endoxifen.	48:24-50:1.
Patent Owner disagrees with Petitioner's characterization of Dr. Davies' testimony at 70:2-72:22 because Dr. Davies testified that the sequential recrystallization pathway starts from a 1:1 ratio of E:Z endoxifen and the isomerization pathway results in a 1:1 ratio of E:Z endoxifen.	72:19-22.

Dated: October 21, 2024

Respectfully Submitted,

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on this 21st day of October 2024, a true copy of the foregoing materials was served on Petitioner INTAS PHARMACEUTICALS LTD. by emailing a copy to counsel of record for Petitioner at the email addresses listed below:

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