

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ARGENTUM PHARMACEUTICALS LLC, MYLAN PHARMACEUTICALS
INC., BRECKENRIDGE PHARMACEUTICAL, INC., AND ALEMBIC
PHARMACEUTICALS, LTD.,
Petitioners,

v.

RESEARCH CORPORATION TECHNOLOGIES, INC.,
Patent Owner.

IPR2016-00204¹
Patent RE 38,551

**PETITIONERS' RESPONSE TO MOTION FOR OBSERVATIONS
REGARDING THE CROSS-EXAMINATION OF DR. BINGHE WANG**

¹ Case IPR2016-01101, Case IPR2016-01242, and Case IPR2016-01245 have been
joined with this proceeding.

Petitioners file this Response to Patent Owner's Motion for Observations on Cross-examination of Dr. Binghe Wang (Paper 65) by Due Date 5 (Papers 20, 50). Petitioners respectfully disagree that Patent Owner's Observations are relevant or demonstrate inconsistency. Several of Observations are argumentative. Petitioners respectfully reserve their right to respond during oral hearing.

Observation 1: Patent Owner's Observation omits relevant testimony.

Ex.2194, 237:14-247:1. Dr. Wang testified: "So based on what Dr. Roush has in there and then he had a pKa value of minus .068, and *then he had a pKa value of minus .068 for [compound] 3l* and pKa of 6.14 for 3a, which is an amino compound. So if you take those two numbers as a reference point, then the separation is about 7. And separation of 7 is, of course, a very large number and that will certainly take it into the territory under normal physiologic conditions, *one would not consider that basic.*" *Id.* at 241:12-22 (emphasis added). At 192:9-19, he testified that "in *some* cases, having a basic functional group at [the] alpha position indeed helped to improve activity. *However, that's not to say that's the only thing that would improve activity.* And there is other modification there that also helped to improve activity." Dr. Wang continued: "the key question right now here is that is it a reasonable thing to go from NH to a CH at alpha position . . . *[T]here is enough evidence to suggest that that position having an amino group is beneficial and having a methyl group there is beneficial* and maybe wouldn't

tolerate anything else.” *Id.* at 197:2-17 (emphasis added).

Observation 2: Patent Owner’s counsel did not ask Dr. Wang to review his entire declaration during cross-examination. Ex.2194, 152:9-16 (“Q: And you have reviewed your first declaration, Exhibit 1002, correct? . . . THE WITNESS: ***By looking through the table of contents and my memory*** as to how they’re cross-referenced.” (emphasis added)). When asked if a citation to ¶¶ 44-49, 123 indicated those were “the only paragraphs in your first declaration discussing the ’301 patent,” he replied “[t]hat’s not what it means”; he would “have to look into detail” to identify other areas of the declaration in which the ’301 patent was discussed. *Id.* at 149:9-150:11. Dr. Wang then “look[ed] through the table of contents,” cross-referencing to review pages 24-26, and responded, “From what I can see here, that’s true.” *Id.* at 149:15-150:11, 151:22-152:22.

Observation 3: Asked if the methoxyamino group has “a basic nitrogen,” Dr. Wang stated “the strength of that [nitrogen] in terms of it being a base of the amino group is different from the strength of ... an amino group itself... [A] basic nitrogen in the alpha position could contribute to good anticonvulsant activities but other functional groups could also do the same. However, the [basicity of a] methoxyamino group is different from an amino itself.” Ex.2194, 193:9-22.

Observation 4: Dr. Wang did not testify that a methoxyimino group (with an “i”) and a methoxyamino group (with an “a”) “have minor structural

differences.” He testified: “I would say in this particular case, if you look at the structure itself and then when it has a double bunt [*sic*, double bond] or not, it does affect the property tremendously and as well the stability. So these two functional groups in this kind of comparison can be very different.” Ex.2194, 115:22-116:20. Dr. Wang affirmed that “[i]n this particular case” of the methoxyimino group with the double bond in cefuroxime, “looking at the differences between functional groups is important.” *Id.* at 117:6-118:12, Dr. Wang continued “[i]f we extrapolate that to isosteric replacement, I would refer to the Silverman book as to how that should be guided,” but “in this particular case” (referring to ¶42 of his second declaration), the methoxyimino in cefuroxime is “indeed different” from the methoxyamino in compound 31.

Observation 5: Dr. Wang testified: “It would be proper to predict this in such a way to say that if they have a prediction number that could range from 6 to 19 and then calculate a how-many-fold increase use in that range and then use in the range that one would see with 107. And so that would be the calculation one would want to do. That’s what I wanted to do.” Ex.2194, 180:7-13. He further testified: “The range actually would be larger with the calculation based on 107d and the predicted racemic lacosamide ED50.” *Id.* at 180:19-21. Dr. Wang testified:

I did not intend to use that number. . . . So if I look at paragraph 141, so the predicted activity would be 7.6. So I use 7.6 to do the calculations. And then -- so that gives you a range of 13 to 39. So

that's what it is. I did double-check this and I double-checked this and I said these numbers are slightly off. However, they're predicting numbers that doesn't make a whole lot of difference in terms of what the specific numbers are based on approximation. *So in that particular case, and then as it says, it's an approximate number where you're using predicted numbers to predict the outcome. And then it's an approximation and that's in the same general range.*

Id. at 181:8-22 (emphasis added).

Observation 6: Patent Owner's Observation omits relevant testimony.

Regarding *estimated* ED50 values of 6.2 and 7.6, Dr. Wang testified “short of very extensive statistical analysis and significance, one would consider them to be essentially the same in terms of meanings.” Ex.2194, 157:17-158:14. When asked whether “the ED50 for compound 2g is essentially the same as the ED50 of compound 3c based upon the same logic” used in ¶109 of Ex.1002, Dr. Wang responded: “I will look at them somewhat differently in the sense that the first one, we were doing estimations as to what they mean because they have calculated numbers to discuss. In this case, they're experimental numbers. . . . When you try to estimate things by doing calculations, then you don't hold the same standard as if you do experimental studies. And with that said, I do not know specifically what kind of statistical analysis they did[.]” *Id.* at 162:10-163-14.

Observation 7: Dr. Wang testified: “If you look at the specifics, so even if you consider the small, and then there is not much of a difference and then they

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.