

Lead Compound Analysis Is Inappropriate for Method of Treatment Claims

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Addressing the obviousness analysis for method of treatment claims, the US Court of Appeals for the Federal Circuit affirmed the district court's finding of non-obviousness but rejected part of its reasoning that applied lead compound analysis to method of treatment claims. *Novartis Pharm. Corp. v. West-Ward Pharm., LTD.*, Case No 18-1434 (Fed. Cir. May 13, 2019) (Stoll, J).

Novartis owns the Orange-Book-listed patent for Afinitor with claims that cover methods of treating "advanced solid excretory system tumors" such as advanced renal cell carcinoma (RCC) by administering the compound everolimus, an mTOR inhibitor. Novartis initiated a Hatch-Waxman lawsuit after West-Ward's predecessor in interest filed an abbreviated new drug application seeking to market a generic version of Afinitor.

At trial, West-Ward cited four pieces of prior art in support of its obviousness defense. Two prior art references discussed different mTOR inhibitors (rapamycin and temsirolimus), their mechanism of action and Phase I clinical trial data. The two prior art references disclosed the compound everolimus, oral formulations and dosing ranges, but did not disclose any pre-clinical or clinical data showing or suggesting that everolimus had anti-tumor activity. According to West-Ward, knowledge in the art about the molecular biology of advanced RCC, the antitumor activity of mTOR inhibitors, phase I temsirolimus clinical trial results and safe dosing ranges for everolimus would have provided a skilled artisan with a reasonable expectation of success in effectively treating advanced RCC with everolimus.

The district court disagreed and found the claims non-obvious. The district court first found that a person of ordinary skill "would have been motivated to pursue everolimus as one of several potential treatment options for advanced solid tumors, including RCC," but that "a [person of skill in the art] would not have been motivated to select everolimus," and therefore West-Ward had not demonstrated a motivation to combine the prior art references. West-Ward appealed.

On appeal, the Federal Circuit explained that the district court's analysis was flawed because it incorrectly applied a "lead compound analysis" to "method of treatment claims." In lead compound cases, a court first determines whether a skilled artisan would have selected the asserted prior art compounds as lead compounds for further development. The Court found that *methods of using* compounds are different, and that this "heightened standard" does not apply. Rather, it is

sufficient that a skilled artisan would have been motivated to pursue everolimus as one of several potential treatment options for advanced solid tumors, including advanced RCC.

The Federal Circuit found no clear error in the district court's finding that West-Ward's asserted prior art combination failed to provide clear and convincing evidence of a reasonable expectation of success. First, Phase 1 data had "diminished weight," because these studies involved small sample sizes and were designed to test safety, not efficacy. Further, the pharmacological properties of the prior art drugs, everolimus and temsirolimus, were different from those of the claimed compound—for example, they had different binding affinities and half-lives than the claimed compound. Finally, the molecular mechanism by which mTOR inhibitors might inhibit tumor growth in RCC was poorly understood. In light of this evidence, the Federal Circuit affirmed the district court's conclusion that the asserted claims had not been proven to be obvious in view of the prior art by clear and convincing evidence.

Practice Note: While the Federal Circuit has suggested that there is a lower standard applied in analyzing whether method of treatment claims are obvious in view of the prior art—rejecting the district court's "lead compound analysis" in this case—the Court has also indicated that something more than Phase I clinical trials, which test safety not efficacy, is required to demonstrate that a skilled artisan would have a reasonable expectation of success in practicing a method of treatment claim. For example, data supporting a drug's mechanism of action and efficacy may be relied on where possible to support an obviousness defense when confronted with method of treatment claims.

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