

Lead Compound Analysis Not Applicable to Certain Method-of-Treatment Claims

IN SHORT

The Situation: In a Hatch-Waxman litigation, a district court determined that the claims covering a method of using the drug everolimus to treat kidney cancers were not obvious. The court found a motivation to "pursue" everolimus, but the defendant failed to show a motivation to "select" everolimus over other treatment options.

The Result: On appeal, the Federal Circuit faulted the district court for applying the "lead compound" analysis and requiring a motivation to select everolimus over other treatment options as a prerequisite for obviousness. The Federal Circuit distinguished method-of-treatment claims from compound claims to which the lead compound analysis applies.

The Impact: In *Novartis*, the district court found a motivation to pursue, and the Federal Circuit faulted it for additionally requiring a motivation to select and for applying the lead compound analysis to method-of-treatment claims. It remains to be seen the effect of this holding on other types of claims and in cases without a finding of motivation to pursue.

In a recent case, the Federal Circuit held that the heightened requirement of preferring the claimed invention over other known alternatives found in the lead compound analysis does not apply to method-of-treatment claims. *Novartis Pharm. Corp. v. W.-Ward Pharm. Int'l Ltd.*, 923 F.3d 1051, 1059 (Fed. Cir. 2019). The Federal Circuit distinguished method-of-treatment claims from other types of claims to which the lead compound analysis applies under its precedent, finding that the district court erred in applying the lead compound analysis to determine whether a skilled artisan would have had a motivation to combine the prior art. But ultimately, the Federal Circuit affirmed the district court's non-obviousness determination because the district court did not clearly err in finding no reasonable expectation of success.

AFINITOR® (everolimus) is approved for treating advanced renal cell carcinoma ("RCC"). Novartis owns U.S. Patent No. 8,410,131 ("131 patent"), which claims a method of using everolimus to treat advanced kidney cancers, including advanced RCC. In a Hatch-Waxman litigation, generic defendant West-Ward sought to invalidate the '131 patent as obvious.



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As of the priority date of the '131 patent, everolimus was known to inhibit mTOR, a protein that regulates cellular processes relating to cancer. Another mTOR inhibitor, temsirolimus, had been tested in Phase I clinical trials in which a small number of RCC patients showed partial or minor responses. Two Phase II clinical trials on temsirolimus were underway, one of which was designed specifically for RCC. However, there was no clinical data on everolimus for treating any cancer, much less RCC, which was known to be difficult to treat.

After a bench trial, the district court found that a skilled artisan "would have been motivated to pursue everolimus as one of several potential treatment options" for advanced RCC. *Novartis*, 923 F. 3d at 1057 (emphasis added). But the district court noted that there were a variety of

other treatments in development at the time, beyond mTOR inhibitors. The district court found that West-Ward failed to show that a skilled artisan "would have been motivated to *select* everolimus." *Id.* at 1058 (emphasis added).

On appeal, the Federal Circuit faulted the district court for applying a heightened standard in requiring a motivation to select everolimus over other treatments. *Id.* at 1059. Noting that the district court found a motivation to pursue everolimus, the Federal Circuit explained that "[t]his finding should have affirmatively answered whether there would have been a motivation to combine" the prior art. *Id.*

The Federal Circuit distinguished the method-of-treatment claims from compound claims. *Id.* at 1060. To those claims, a court applies the lead compound analysis to determine whether there would have been a motivation to select a prior-art compound for further modification to achieve the claimed compound. *Id.* (citing *Otsuka Pharm. Co. v. Sandoz Inc.*, 678 F.3d 1280, 1291–92 (Fed. Cir. 2012); *Daiichi Sankyo Co. v. Matrix Labs., Ltd.*, 619 F.3d 1346, 1354 (Fed. Cir. 2010); *Takeda Chemical Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007)). As to the method-of-treatment claims at issue here, the Federal Circuit explained that "[t]he proper inquiry is whether a person of ordinary skill would have been motivated to modify the prior art disclosing use of temsirolimus to treat advanced RCC with the prior art disclosing everolimus." *Id.*

The district court also found that West-Ward failed to show that a skilled artisan would have reasonably expected everolimus to successfully treat advanced RCC. *Id.* at 1058. The Federal Circuit agreed with that finding and affirmed the district court's conclusion of non-obviousness. *Id.* at 1059. The Federal Circuit specifically noted that (1) the temsirolimus Phase I data had diminished weight because the Phase I studies were designed to test safety, not efficacy, in a small number of patients; (2) Phase II data on temsirolimus were not yet available; (3) more than 70% of cancer drugs failed in Phase II development; (4) everolimus and temsirolimus had different pharmacological properties; and (5) the molecular biology of advanced RCC was not well understood. *Id.* at 1061-62. The Federal Circuit therefore concluded that the district court did not clearly err in finding that a skilled artisan would not have had a reasonable expectation for everolimus to effectively treat advanced RCC.

THREE KEY TAKEAWAYS

1. In *Novartis*, the Federal Circuit distinguished the method-of-treatment claims at issue from compound claims to which the lead compound analysis applies under the court's precedent.
2. The Federal Circuit explained that the district court's finding of motivation to pursue the claimed method of treatment is sufficient to answer the question whether there was a motivation to combine the prior art.
3. In circumstances like this, the district court erred in applying a heightened standard to require a showing of a motivation to select the claimed method over other treatment options.



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