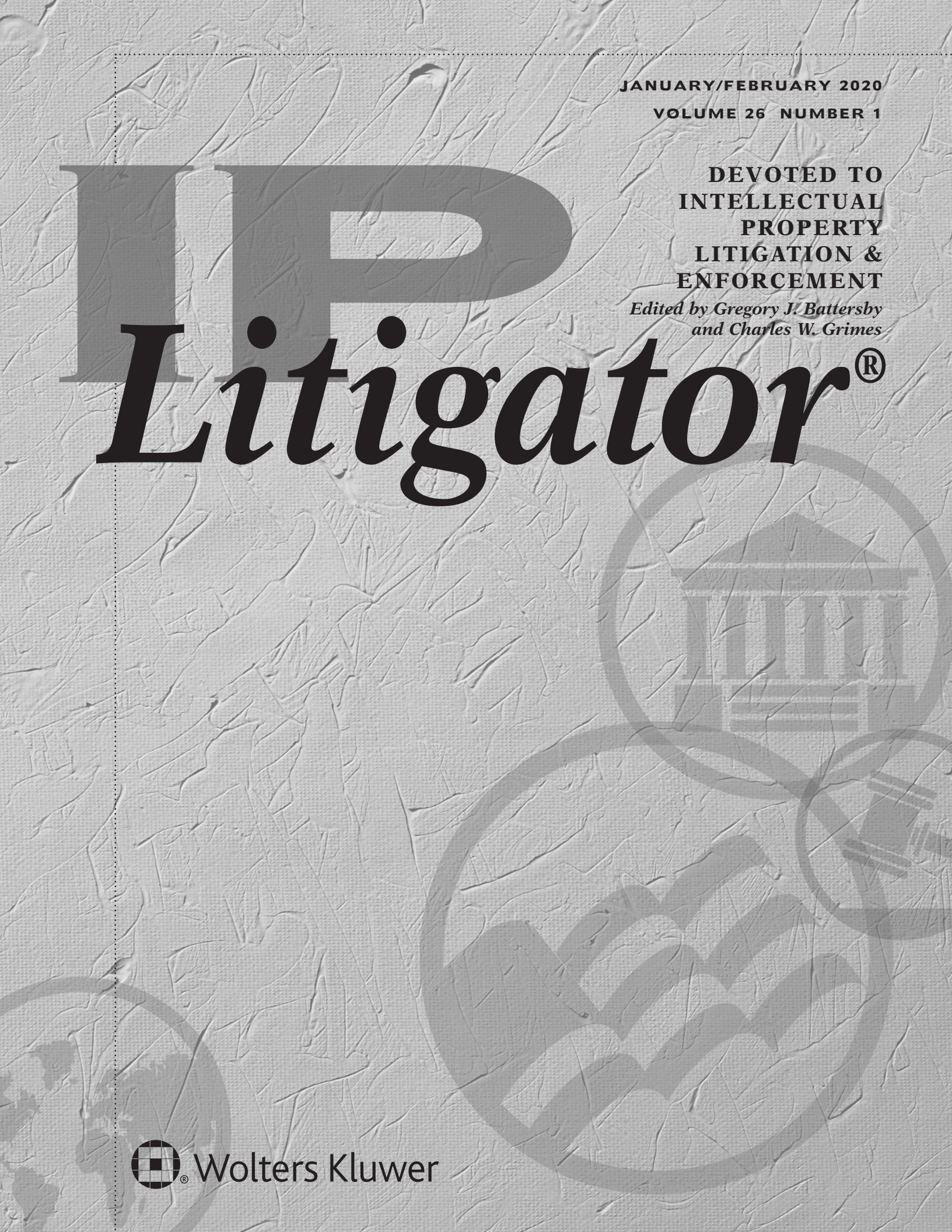
JANUARY/FEBRUARY 2020
VOLUME 26 NUMBER 1

IP Litigator®

DEVOTED TO INTELLECTUAL PROPERTY LITIGATION & ENFORCEMENT

Edited by Gregory J. Battersby and Charles W. Grimes



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Did the Federal Circuit Just Raise the Evidentiary Bar for Establishing Obviousness?

According to the panel in *OSI Pharmaceauticals, LLC v. Apotex, Inc.*, Slip Op. No. 2018-1925 (Fed. Cir. Oct. 4, 2019), the answer to the question posed in this article's title is a solid *no*. Considering the opinion's precedential nature and the facts in the case, the Federal Circuit, however, may have just given patentees extra ammunition to defeat an obviousness challenge on evidentiary grounds. The Federal Circuit analyzed whether certain pharmaceutical method claims related to a treatment for lung cancer were obvious and concluded that the lack of efficacy data in asserted prior art showed a person of ordinary skill would not have a reasonable expectation of success in applying their teachings. This holding reversed an obviousness determination by the PTAB in a preceding IPR of the patent at issue, and shows that for challengers mounting an obviousness challenge, prior art containing data-based evidence may be needed to be successful, particularly if the patent being targeted is in the pharmaceutical or chemical arts.

Technical and Procedural Background

Patentee OSI Pharmaceuticals, LLC (OSI) owns U.S. Patent 6,900,221 (the '221 patent), which it filed in November of 2000. Claims 44-46 and 53 of the '221 patent are directed to methods of treating Non-Small Cell Lung Cancer (NSCLC) with a chemical compound known as "*erlotinib.*"[1] By the end of the late 1990's, NSCLC was the leading cause of cancer deaths in the U.S., and existing therapies, particularly chemotherapy, were inadequate.[2] Throughout this period, investigators pursued numerous studies examining different ways to inhibit the epidermal growth factor receptor (EGFR) in cancers. These studies included examining the efficacy of *erlotinib* to treat a variety of cancers, including NSCLC. After an extended period of prosecution, the '221 patent issued in May of 2005.

In 2015, OSI filed suit against Apotex, alleging infringement of the '221 patent.[3] Apotex responded with an IPR, asserting claims 44-46 and 53 were invalid as being obvious over U.S. Patent 5,747,498 to Schnur in view of either an article by Gibbs printed in early 2000 or an annual SEC-required 10-K Form filed by OSI in 1998. The PTAB instituted the IPR and found that "a person of ordinary skill would have combined Gibbs or [the] OSI 10-K with Schnur and had a reasonable expectation of success in achieving the invention" disclosed in the claims, and that "Schnur disclose[d] all of the limitations of claims 44 and 53 except the treatment of NSCLC."[4] OSI appealed the obviousness decision to the Federal Circuit, and also challenged the constitutionality of the IPR process. The panel disposed of the constitutionality issue by citation to several recent decisions, and that aspect of the opinion will not be discussed here.

The Asserted Prior Art Discloses the Use of *erlotinib* to Treat Lung Cancer

There was no dispute among the parties that the asserted prior art was available to the public before the date of invention of the asserted claims, which was March 30, 2000.[5] Therefore, the main issue for the Federal Circuit to decide was whether the combination of Schnur and Gibbs or Schnur and OSI's 10-K sufficiently disclosed the use of *erlotinib* to treat NSCLC such that a person of ordinary skill would have a reasonable expectation of success.

Schnur disclosed a variety of chemical compounds useful for treatment of diseases "such as cancers, in mammals." The patent listed *erlotinib* as "a preferred compound, and [a] method for synthesizing *erlotinib* is described."[6] It also stated the compounds were "potent inhibitors" of EGFR and that the compounds are "therapeutics 'for the treatment of a variety of *human tumors* (renal, liver, kidney, bladder, breast, gastric, ovarian, colo-rectal, prostate, pancreatic, *lung*, vulval, thyroid, hepatic carcinomas, sarcomas, glioblastomas, various head and neck tumors) . . . .'"[7]

The Gibbs article summarized a series of published research studies,

including a study that referred to *erlotinib* being in clinical trials to treat cancer. In reviewing the status of the clinical trials, Gibbs asserted that "these compounds appear to have good anti-cancer activity in preclinical models . . . particularly in patients with *non-small cell lung cancer*."[8]

Finally, the OSI 10-K plainly stated:

> "[erlotinib] which targets a variety of cancers including ovarian, pancreatic, *non-small cell lung* and head and neck, achieved a significant milestone with the completion of Phase I safety trials and the initiation of Phase II clinical trials in the United States in cancer patients. [Erlotinib] is a potent, selective and orally active inhibitor of the epidermal growth factor receptor, a key oncogene in these cancers."[9]

The Federal Circuit Finds a Lack of Substantial Evidence to Support Obviousness

Despite the foregoing, the Federal Circuit panel determined that "properly read, these combinations do not provide substantial evidence supporting the Board's findings of reasonable expectation of success."[10]

Two facts colored the panel's analysis. First, the opinion emphasized the lengthy process and time frame needed for a drug to proceed from conception to FDA approval.[11] The process includes filing an Investigational New Drug application following preclinical studies, followed by Phase I, Phase II, and finally, Phase III studies that conclude with the filing of a New Drug application to the FDA.[12] Second, the panel observed evidence in the record showing that 95% of therapies to treat NSCLC never made it out of Phase II and on to FDA approval.

Viewing the record through the foregoing lens, the opinion criticized the examination of the Gibbs article by the PTAB. Digging into the substance behind the disclosure that *erlotinib* "appear[s] to have good anti-cancer activity," the panel found that the underlying study cited to support that statement did not test *erlotinib* in treating NSCLC, and they noted that Apotex's expert agreed.[13] Based on these findings, the panel essentially disqualified the relevance of Gibbs in the obviousness analysis.

More critically, the opinion appears to hinge on its view that the asserted prior art references "contain *no data* or *other promising information* regarding *erlotinib's* efficacy in treating NSCLC."[14] In the panel's view, the high failure rate of NSCLC drugs in Phase II coupled with the lack of "efficacy data or any other reliable indicator of success" showed that "the only reasonable expectation at the time of the invention was failure, not success."[15] Thus the Federal Circuit reversed the PTAB and held the claims at issue to be non-obvious.

The Efficacy of the Federal Circuit's Analysis

Close scrutiny of the panel's analysis demonstrates the questionable value of this precedential decision.

The Federal Circuit's central thesis is that, because of the high failure rate of *erlotinib* targeting NSCLC in Phase II trials and the lack of efficacy data, there was no reasonable expectation of success.[16] In addition to dismissing the Gibbs reference, the panel similarly dismisses the *patentee's* very own 10-K because it lacked any data.[17] As a result, the Federal Circuit rejected Apotex's argument that the combination of Schnur, which discloses the use of *erlotinib* as a therapy against lung cancers, with OSI's 10-K supported an obviousness determination.

In doing so, the panel seems to disregard its own precedent. In *Allergan, Inc. v. Sandoz, Inc.*, the Federal Circuit cautioned "that [while] formulation science carries with it a degree of unpredictability, 'obviousness cannot be avoided simply by a showing of some degree of unpredictability in the art so long as there was a reasonable probability of success.'"[18] What qualifies as "a reasonable probability" will be dependent on the field of art, yet the decision is silent on this point. Expert testimony from both parties acknowledged the high failure rate during drug development,[19] establishing that high failure rate in drug development is presumably "reasonable." Furthermore, in its 10-K that is to be relied on by investors, the patentee stated that "[erlotinib,] which targets . . . *non-small cell lung* [cancer], achieved a significant milestone with the completion of Phase I safety trials and the initiation of Phase II clinical trials in the United States in cancer patients."[20] As such, the patentee arguably believed there was a reasonable probability of success that erlotinib would be an effective therapy against NSCLC. Otherwise, it would not have entered Phase II. Thus, it could be argued that a person of ordinary skill at the time of the invention would have recognized that the teachings of Schnur could be applied to treat NSCLC as described in the claimed invention with a reasonable probability of success. Yet, the panel concluded that "a fact finder could not reasonably find that the 10-K

statement combined with Schnur would have been sufficient to create a reasonable expectation of success."

Conclusions

The panel's silence on what qualifies as a "reasonable" expectation or probability of success in this case may leave the reader questioning the result. Despite the panel's express limitation that "we do not hold today that efficacy data is always required for a reasonable expectation of success,"[21] the curious designation of the opinion as precedential means that practitioners should consider keeping this decision on the shelf when litigating obviousness in fields that require extensive data to support product development and commercialization.

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1. Slip op. at 4, 5. Claim 44 is an independent claim with claims 45–46 and 53 being dependent.
2. Slip op. at 2.
3. *OSI Pharm., LLC v. Apotex, Inc.*, No. DED01-15-cv-0772, Complaint (D.Del. Sept. 2, 2015).
4. Slip op. at 9–10.
5. Slip op. at 5.
6. Slip op. at 6.
7. *Id.* (emphasis added).
8. *Id.* at 7 (emphasis added).
9. *Id.* at 8–9 (emphasis added).
10. *Id.* at 15.
11. *Id.* at 3, 16.
12. *Id.* at 3–4.
13. *Id.* at 14–15.
14. *Id.* at 16 (emphasis added).
15. *Id.* at 18.
16. *Id.*
17. *Id.* at 17.
18. *Allergan, Inc. v. Sandoz, Inc.*, 726 F.3d 1286, 1929 (Fed. Cir. 2013) (quoting *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007)).
19. Slip op. at 16, 17.
20. *Id.* at 8–9 (emphasis added).
21. *Id.* at 18.