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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IDENIX PHARMACEUTICALS LLC and UNIVERSITA DEGLI STUDI DI CAGLIARI, Plaintiffs, v. GILEAD SCIENCES, INC., Defendant.	C.A. No. 14-846-LPS

PLAINTIFFS' NOTICE OF SUPPLEMENTAL AUTHORITY REGARDING *UROPEP v. ELI LILLY*

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Dear Chief Judge Stark,

On August 25, 2017, Federal Circuit Judge Bryson, sitting by designation in the Eastern District of Texas, issued the attached decision in *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.* ("*UroPep*"), which addresses, *inter alia*, challenges to enablement and written description that had been submitted to, and rejected by, a jury. On Lilly's JMOL/new trial motion, Judge Bryson upheld the jury's verdict. A copy of patent at issue in *UroPep* is also attached.

Idenix respectfully submits that Judge Bryson's *UroPep* decision is pertinent authority on the enablement and written description inquiries post-trial and, particularly with respect to enablement, is even more instructive here than the summary-judgment decisions in *Wyeth* and *Enzo*. *See UroPep* at 38-45. *First*, much like Judge Robinson's recent decision denying JMOL and a new trial in *Amgen Inc. v. Sanofi*, 227 F. Supp. 3d 333 (D. Del. 2017) (*see* D.I. 554 at 7, 13), *UroPep* makes clear the intensely factual nature of enablement (and written description) and that disputes of fact are for the jury's resolution not to be second-guessed after trial. *Second*, the record of this case is closely aligned with the record in *UroPep*; indeed, the facts on enablement here are even more favorable to Idenix than the *UroPep* facts were to the patent holder there. *Third*, *UroPep* dispels Gilead's attempt to utilize *Wyeth* as a legal rule to upset the jury's well-supported resolution of the disputed facts. Notably, Judge Bryson joined the *Wyeth* decision at the Federal Circuit, and in *UroPep* he rejected the legal rule that Gilead posits.[1]

I. In *UroPep*, Competing Evidence Was Submitted By Both Sides, And The Jury Was Entitled To Credit The Patentee's Evidence—So Too Here

As Judge Bryson observed in *UroPep*, a post-trial motion is not the time to "reargue[] the disputed case that was tried to the jury" or ask the Court to substitute its own judgment and credibility determinations for that of the jury, as Gilead attempts to do here. *UroPep* at 39. The *UroPep* decision thus underscores the intensely factual nature of enablement (and written description), and sets forth the governing principle for Gilead's pending motions. Where the material facts are hotly contested and competing evidence is submitted by both sides (as was the case here), those factual issues are for a jury to resolve, and the jury's decision to credit the evidence of the prevailing party should not be disturbed.

As an initial matter, *UroPep* makes clear that Gilead's focus on the amount of time it would take to practice the '597 patent claims is the wrong factual inquiry for enablement. In *UroPep*, Lilly similarly argued "that undue experimentation would be required for one artisan to synthesize all members of the genus of selective PDE5 inhibitors." *UroPep* at 42. Judge Bryson rejected that argument as "fundamental error[]": "That is not the correct inquiry. A patent must enable a skilled artisan to practice the full scope of the invention; it does not need to ensure that a skilled artisan can practice the entire scope of the invention within a short period of time." *Id.*

[1] While this letter focuses on *UroPep*'s enablement ruling, it is important to note that Judge Bryson also rejected Lilly's arguments with respect to written description, which are similar to what Gilead urges here—*e.g.*, an insistence that written-description support must be found within the "four corners" of the specification. (*E.g.*, D.I. 565 at 7.) As Judge Bryson explained, such a contention "proceeds from the wrong premise"; "the possession inquiry is not limited to what is expressly described within the 'four corners' of the specification" but instead is "an objective one that is viewed from the perspective of a person of ordinary skill in the art." *UroPep* at 12.

Beyond the legal error of Gilead's focus, *UroPep* also made clear that, after trial, a party may not ask the Court to "assume[] facts that the jury was not required to find," as Gilead does here. *Id.* at 45. As a principal example, Gilead asks this Court to assume, in the face of disputed record evidence, that: (1) "a lot of compounds" are implicated by the claims' structural limitations; (2) each and every one of those compounds would need to be screened; and (3) screening "a lot" of compounds would require undue experimentation. (D.I. 536 at 3, 6.)

Gilead's assumptions suffer from a selective and one-sided recitation of the disputed factual record that was presented to the jury. Idenix submitted substantial evidence refuting each of Gilead's assumptions. (*See generally* D.I. 554 at 3-10; D.I. 582 at 2-4.) For instance, as Dr. Meier explained, because the claims recite the key 2'-methyl modification to a ribonucleoside, and the specification recites the target enzyme, formulas with preferred structures, data, working examples, and so much more, the number of compounds at issue is "significantly" narrowed. (Tr. 1854:8-17, 1866:22-1868:11, 1918:11-19.) Similarly, Gilead's Dr. Secrist testified that, in this art, POSAs are used to working with large classes of compounds and do not "check their common sense at the door." (Tr. 1723:5-20.) In addition, the evidence showed that, with Idenix's '597 patent disclosure in hand, Mr. Clark was able to practice the claimed invention without undue experimentation. (Tr. 696:11-18, 977:14-979:5, 979:18-980:1, 992:3-995:25.) Pharmasset itself read the '597 patent disclosure as teaching a class of "potent" 2'-methyl ribonucleoside inhibitors. (PX0764.0023.) And even if "a lot" of compounds needed to be tested, Dr. DeFrancesco provided detailed testimony that tens of thousands of compounds could be routinely screened in a short period of time. (Tr. 1984:25-1985:13, 1988:23-1989:13.)

As in *UroPep*, it was the jury's role to assess the evidence before it, weigh credibility, and resolve fact disputes. The jury here was entitled to credit Idenix's evidence and conclude not only that Gilead failed to prove the factual assumptions on which its motion rests, but that it failed to present clear and convincing evidence of lack of enablement as a whole.

II. The Facts Of This Case Present An Even More Compelling Case For Enablement Than *UroPep*, Taking It Far Afield From *Wyeth* And *Enzo*

This Court's *Enzo* decisions used *Wyeth*'s non-enablement decision as a yardstick—the Court reasoned that the *Enzo* cases involved less-enabling disclosures than *Wyeth*, so they, too, must have been non-enabling. When the Court compares the facts of *UroPep* to this case using the four factors it considered in *Enzo*, it will find that the '597 patent disclosure and Idenix's other evidence present an even stronger case of enablement than the disclosure upheld as enabling in *UroPep*. Those four factors also encompass the *Wands* inquiry, as noted below.

(1) UroPep's claims were far broader than the '597 claims (*Wands* factor 8). UroPep's claims were "broad" and purely functional. *UroPep* at 44. Although limited to PDE5 inhibitors, UroPep's claims recited no structural limitations common to the functionally defined class of "selective" PDE5 inhibitors used to treat BPH (Judge Bryson construed "selective" in relative terms as 20 times more selective for PDE5, than for PDE1 through PDE4, inhibitors). *Id.* at 6.

Here, by contrast, the '597 patent claims recite several structural limitations in addition to their functional features, and those structural limitations clearly define and limit the claims: 2'-methyl up, the various features of the ribo structure, and a non-hydrogen substituent at 2' down.

(2) Although the level of skill in the art was similarly high, UroPep's patent provided far less guidance than the '597 patent, and did not include any working examples (*Wands* factors 2, 3, and 6). UroPep's patent—under eight columns long—lacked much of the type of guidance set forth in the '597 patent. UroPep's patent supplied no structural limitations common to the covered class. *See UroPep* at 27 ("the disclosure does not expressly discuss the common structural features of PDE5 inhibitors," much less features common to "selective PDE5 inhibitors"). UroPep's patent also did not disclose a single selective inhibitor of PDE5 (much less any working examples of such compounds); none of its working examples fell within the scope of the claims. In fact, the claims excluded all preferred embodiments disclosed in the specification. UroPep's patent also did not disclose any synthetic routes for making PDE5 inhibitors. *See id.* at 3-4, 6, 26-27, 34.

Here, by contrast, the '597 patent provides the POSA with far more abundant guidance. That guidance includes formulas (*e.g.*, Formula XI), several working examples of the claims, specific species (*e.g.*, Fig. 1), repeated emphasis on the NS5B polymerase enzyme as the target (PX1525 at col.ll. 13:43-56, 36:42-60), synthetic routes for modifying nucleosides (*id.* at 52:44-54:3), screening methods (*id.* at 13:50-56, 36:50-60), and biological data (*e.g.*, Figs. 2-3 & Examples 4-7). The evidence also showed that one of *less than* ordinary skill in the art (Mr. Clark) was easily guided by the '597 specification to practice the claimed invention. (D.I. 554 at 3-7; D.I. 582 at 2.) Gilead contends that the '597 patent "does not provide any" information about 2'-methyl up ribonucleosides that fall within the claims other than "a single prior art sugar from the 1960s" with different bases. (D.I. 554 at 6-7; D.I. 581 at 2.) But, like Judge Bryson repeatedly held in *UroPep* with respect to the contested facts in that case, the jury here was entitled to credit Idenix's evidence showing otherwise. *UroPep* at 40 ("The jury was entitled to credit [Dr. Bell's] opinion over that of Lilly's expert"); *id.* at 42 (same).

(3) Contested evidence was submitted in *UroPep* about how developed the field was; here, salient evidence on this factor in favor of Idenix was *undisputed* (*Wands* factors 4, 5, and 7). In *UroPep*, UroPep presented evidence showing that the field for determining whether a PDE5 inhibitor would be more selective than other inhibitors was "mature." *UroPep* at 16, 40. There was also testimony in UroPep's favor that a skilled artisan could "screen half a million compounds" within weeks. *Id.* at 40. Lilly presented contrary evidence, arguing that "PDE inhibitor research was 'an unpredictable and poorly understood field." *Id.* at 45.

Here, by contrast, *both sides* presented testimony that the field of modifying nucleosides for use as viral treatments was well known and routine. (Meier, Tr. 1921:3-19; 1922:2-6; 1936:18-20; Secrist, Tr. 1727:18-22.) Indeed, Mr. Meier discussed at length the long history of successfully using nucleosides to treat viruses as well as the well-understood and predictable field of nucleoside synthesis. (D.I. 554 at 5; D.I. 582 at 3.)

(4) The extensive amount of screening in *UroPep* was undisputed, unlike here, but nevertheless the jury's enablement verdict in *UroPep* was supported (*Wands* factor 1). In *UroPep*, it was undisputed that one preferred embodiment alone counted in the "billions of compounds," and it was also undisputed that "far fewer compounds" within that embodiment would be "selective" to "fall within the claimed genus," requiring extensive screening. *UroPep* at 16. Nonetheless, substantial evidence supported the enablement verdict.

Here, by contrast, Idenix's evidence showed that no extensive amount of screening would be required, such as Pharmasset's contemporaneous recognition of the novel aspect of the '597 patent claims and Mr. Clark's easy identification and routine synthesis of a compound within the class. (D.I. 554 at 3-7; D.I. 582 at 4.) Gilead argues that making and testing compounds "would take longer than in *Wyeth*," based on testimony it reads in its favor. (D.I. 581 at 2.) As discussed above, that testimony was not provided "without contradiction," as Gilead contends. (*Id.*) Moreover, as Judge Bryson noted in rejecting Lilly's similar reliance on testimony supporting it, "the jury was not required to credit that testimony." *UroPep* at 44. Instead, the jury here, like the jury in *UroPep*, credited the patentee's evidence, as it was entitled to do.

III. Judge Bryson's Understanding Of The *Wyeth* Decision Is Consistent With Idenix's And Contradicts Gilead's

Finally, Judge Bryson's discussion of *Wyeth* is also relevant here. Lilly invoked *Wyeth* as "controll[ing]." *UroPep* at 44. Judge Bryson rejected the contention. As Idenix has discussed (D.I. 554 at 7-10; D.I. 582 at 1-4), Gilead's reliance on *Wyeth* suffers from the same infirmities underlying Lilly's argument. Not only does Gilead "assume[] facts that the jury was not required to find" (*UroPep* at 45), *see supra*, but it similarly attributes an incorrect legal principle to *Wyeth*.

Gilead says that *Wyeth* stands for the principle that, if extensive screening is required, a patent claim "lacks enablement as a matter of law." (D.I. 536 at 6.) As Judge Bryson explained, that is an incorrect understanding of *Wyeth*. Rather, the inquiry turns on the specific facts of each case. Quoting *Wyeth*, Judge Bryson reiterated that "'[u]ndue experimentation is a matter of degree. Even a considerable amount of experimentation is permissible as long as it is merely routine or the specification provides a reasonable amount of guidance regarding the direction of experimentation.'" *UroPep* at 45 (quoting *Wyeth v. Abbott Labs.*, 720 F.3d 1380, 1385-86 (Fed. Cir. 2013)). For extensive experimentation to be "undue," the defendant must provide clear and convincing evidence such as "a disclosure and a field that provides no guidance, [and requires] aimless plodding through systematic experimentation of a single compound that would take weeks." *Id.* Those facts were present—and undisputed—in *Wyeth*. But such facts were not present in *UroPep*, and they are not present here, either: The jury heard copious evidence that contradicted Gilead's "undue experimentation" claim, including that Pharmasset scientists read and understood the value of the '597 patent disclosure and that Mr. Clark, with the '597 disclosure in hand, was able to practice the invention with ease. This case, like *UroPep*, has a rich trial record on enablement that is far removed from the undisputed record in *Wyeth*.

In short, *UroPep* is far more like this case than *Wyeth* or *Enzo*, and it is a far more salient decision both on the procedural posture of a jury's resolution of disputed facts and on its record. For reasons similar to Judge Bryson's decision upholding the verdict in *UroPep*—and on a record here that is in most relevant respects more compelling with respect to enablement than was the record in *UroPep*—the jury's well-supported verdict here should not be disturbed.

Respectfully,

/s/ John G. Day

John G. Day (#2403)