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

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OPINION

February 16, 2018
Wilmington, Delaware

STARK, U.S. District Judge:

In this patent infringement case involving groundbreaking work by both parties in the field of treatments for the Hepatitis C virus ("HCV") infection, Plaintiffs Idenix Pharmaceuticals LLC and Universita Degli Studi di Cagliari (together, "Idenix") sued Defendant Gilead Sciences, Inc. ("Gilead"). Prior to trial, Gilead stipulated that, under the Court's claim construction, its accused products, Harvoni and Sovaldi, infringe the asserted claims of Idenix's patent, U.S. Patent No. 7,608,597 ("'597 patent").[1] (D.I. 452 at 8 n.2) After a two week-trial in December 2016, a jury found that Gilead failed to prove that the asserted claims are invalid and awarded Idenix $2.54 billion in damages. (D.I. 518)

Gilead now renews its motion for judgment as a matter of law ("JMOL") (D.I. 535), which the Court took under advisement during trial and later denied as moot and with the opportunity to renew following entry of judgment (D.I. 533). In its JMOL motion, Gilead urges the Court to set aside the jury's verdict on the basis that Idenix's asserted patent claims are invalid for failure to meet 35 U.S.C. § 112's written description and enablement requirements. Gilead alternatively asks the Court to reduce the jury's damages award as unsupported by the evidence.

The Court addresses each of Gilead's JMOL arguments in turn, beginning with damages and then moving on to validity.[2] For the reasons that follow, the Court finds that, while

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[1]The '597 patent is entitled "Methods and Compositions for Treating Hepatitis C Virus." It was issued on October 27, 2009. (D.I. 1 Ex. B)

[2]Gilead challenged the sufficiency of Idenix's evidence of willfulness during trial (*see* Trial Transcript (D.I. 539-50) ("Tr.") at 2029, 2043; D.I. 509), but did not renew this challenge in its post-judgment motion (D.I. 536). While Gilead summarily references in a footnote of its brief that it is renewing this challenge, and purports (improperly) to incorporate by reference its prior

judgment as a matter of law is improper on damages and written description, the '597 patent is invalid for lack of enablement. Accordingly, the Court will grant in part and deny in part Gilead's motion.

I. BACKGROUND

HCV is a serious chronic liver disease that affects millions of people around the world. Cirrhosis and liver cancer caused by HCV infection claim thousands of lives every year in the United States alone. Until recently, the best treatment available for HCV infection involved use of interferon and ribavirin. In addition to the significant side-effects of interferon treatment, this course of treatment often failed to cure the disease. (*See generally* '597 patent; Carter Tr. at 770-71; McHutchison Tr. at 1234-38)

HCV is a member of the *Hepacivirus* genus and *Flaviviridae* family. Because its genetic material consists of ribonucleic acid, it is referred to as an RNA virus. Throughout the 1990s and into the new millennium, scientists were carrying out significant research on the use of modified nucleosides as antiviral agents. Some antivirals are developed as chain terminators, which bind to (and block off) the enzymes that allow the target virus to replicate. HCV was among the viruses being targeted for a possible cure that would act directly against the virus itself. (*See generally* Sommadossi Tr. at 365-74; McHutchison Tr. at 1239-40)

In 2000, Idenix discovered an important modification and filed a provisional patent application at the United States Patent and Trademark Office ("PTO"). (*See* Provisional

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briefing on this issue (*see* D.I. 536 at 24-25 nn.14-16), under this Court's practice this was insufficient to renew the challenge (for reasons including that, if permitted, it would evade the Court's page limits on briefs). Hence, no challenge to the sufficiency of Idenix's evidence of willfulness is before the Court.

application No. 60/206,585, filed May 23, 2000 (PX311)) Idenix's work addressed the placement of a methyl group (CH_3) at the nucleoside's 2' (pronounced "two prime") up position. The application eventually led to, among others, U.S. Patent Nos. 6,914,054[3] ("'054 patent") and the '597 patent.

Around the same time, a company called Pharmasset was pursuing similar research. Pharmasset was eventually acquired by Gilead. It worked on modified nucleosides that, like Idenix's, included a methyl group at the 2' up position. Pharmasset's work also involved placing a fluorine atom at the 2' down position. This compound – 2'-methyl up 2'-fluoro down – led to the groundbreaking "miracle" treatment that has cured HCV for millions who are afflicted with it, without the debilitating side effects that resulted from interferon treatments, and has produced billions of dollars in revenue for Gilead. Gilead named its drug containing 2' methyl up 2' fluoro down – which acts on HCV's NS5B polymerase – sofosbuvir, which Gilead markets under the trade name Sovaldi. Gilead also markets a combination of sofosbuvir and ledipasvir, which also inhibits the virus's NS5A protein activity, under the trade name Harvoni. (*See generally* McHutchison Tr. at 1238-70)

Given the importance of these medical breakthroughs, as well as the massive revenues Gilead has earned, it is perhaps unsurprising that Idenix and Gilead have for years been fighting patent disputes against one another all around the world. The instant suit began in 2013, when Idenix sued Gilead for infringement of the '054 and '597 patents in the United States District Court for the District of Massachusetts. (*See generally* D.I. 1) The case was later transferred to

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[3]The '054 patent is entitled "Methods and Compositions for Treating Hepatitis C Virus." It was issued on July 5, 2005. (D.I. 1 Ex. A)

this Court. (*See* D.I. 39)

The parties engaged in extensive discovery and the Court construed the relevant disputed claim terms. (*See* D.I. 237) On June 1, 2016, Gilead moved for summary judgment on several issues, including lack of written description in both the '054 and '597 patents. (*See* D.I. 287) The Court denied the motion. (*See* D.I. 367) Among the Court's reasons for denying summary judgment based on lack of written description was that there remained unresolved claim construction disputes. The Court ordered supplemental claim construction briefing, held a supplemental claim construction hearing, construed two additional disputed claim terms, and, on November 16, 2016, denied Gilead's renewed motion for summary judgment of invalidity due to lack of written description. (*See* D.I. 371, 410, 447)

Thereafter, as the parties prepared for trial, Gilead stipulated to infringement of the '597 patent based on the Court's claim constructions, and Idenix dropped the '054 patent from the case. (D.I. 452 at 4-5, 8 n.2) The parties proceeded to trial on willfulness, damages, and invalidity with respect to several claims of the '597 patent. (*See id.* at 4-5)

The trial lasted nine days. The parties called a total of 27 witnesses, including four experts. Idenix's expert witnesses included Dr. Chris Meier, a professor of organic chemistry, and Dr. Raffaele De Francesco, a virologist. Gilead's expert witnesses included Dr. John Secrist, a medicinal chemist, and Dr. Christoph Seeger, a virologist. The parties also moved 179 exhibits into evidence. (*See* D.I. 586 ("Arg. Tr.") at 34)

During trial, both parties moved for judgment as a matter of law (*see* D.I. 509, 514), which the Court took under advisement (Tr. at 2043). The jury then returned a verdict finding that Gilead's infringement was willful, that Gilead had failed to prove the patent claims are

invalid, and that Idenix is entitled to $2.54 billion in damages. (*See* D.I. 518)

The Court entered judgment on the verdict. (D.I. 533) Thereafter, both parties filed post-trial motions. Idenix's motion – which is addressed in a separate Opinion (D.I. 587) – sought enhanced damages for Gilead's willful infringement, a higher ongoing royalty than the royalty on which the damages for past infringement were based, an award of attorney fees, and prejudgment interest at the prime rate. (D.I. 538) Gilead's motion, which is addressed here, asks the Court to find the '597 patent invalid for lack of enablement and/or written description. Gilead also contends that Idenix presented a legally insufficient damages case and seeks remittitur to a damages figure of no greater than $380 million. (D.I. 535 at 1) Alternatively, Gilead seeks a new trial.[4]

After the parties completed their principal briefing on Gilead's motion (*see* D.I. 536, 554, 565), the parties submitted several letters notifying the Court of subsequent authority (*see* D.I. 570, 572, 576-79, 583-84). At the Court's direction, the parties also submitted letter briefs addressing the impact of two of this Court's recent decisions in other cases finding patents invalid due to lack of enablement. (*See* D.I. 581, 582) The Court heard extensive argument during a hearing on September 7, 2017. (*See* Arg. Tr.)

On September 22, 2017, the Court issued its Opinion on Idenix's motion, denying Idenix's request to enhance damages for willful infringement as well as its request to declare this case exceptional and award Idenix attorney fees. (D.I. 587 at 3-17) The Court granted Idenix's

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[4]Gilead's motion also seeks severance and a stay of "any ongoing royalty claim." (D.I. 536 at 25) This request is unripe, in light of the parties' joint request to stay their disputes relating to ongoing royalties. (*See* D.I. 574 at 1; *see also* D.I. 575 (granting "parties' joint request to stay"))

request that the pre-judgment interest it was being awarded be compounded at 3.25 - 3.75 % (prime rate) instead of 0.10 - 0.14 % (T-bill rate). (*Id.* at 17-18) The Court expressly stated that its rulings on Idenix's motion were based on the assumption – which it emphasized was by no means a ruling – that Gilead's pending motion would be denied in full. (*See id.* at 2 n.4)

The Court now turns to the issues raised in Gilead's motion.

II. LEGAL STANDARDS

A. Judgment as a Matter of Law

Judgment as a matter of law is appropriate if "the court finds that a reasonable jury would not have a legally sufficient evidentiary basis to find for [a] party" on an issue. Fed. R. Civ. P. 50(a)(1). "Entry of judgment as a matter of law is a sparingly invoked remedy," one "granted only if, viewing the evidence in the light most favorable to the nonmovant and giving it the advantage of every fair and reasonable inference, there is insufficient evidence from which a jury reasonably could find liability." *Marra v. Phila. Hous. Auth.*, 497 F.3d 286, 300 (3d Cir. 2007) (internal quotation marks omitted).

To prevail on a renewed motion for judgment as a matter of law following a jury trial, the moving party "must show that the jury's findings, presumed or express, are not supported by substantial evidence or, if they were, that the legal conclusions implied [by] the jury's verdict cannot in law be supported by those findings." *Pannu v. Iolab Corp.*, 155 F.3d 1344, 1348 (Fed. Cir. 1998) (internal quotation marks omitted). "'Substantial' evidence is such relevant evidence from the record taken as a whole as might be accepted by a reasonable mind as adequate to support the finding under review." *Perkin–Elmer Corp. v. Computervision Corp.*, 732 F.2d 888, 893 (Fed. Cir. 1984).

In assessing the sufficiency of the evidence, the Court must give the non-moving party, "as [the] verdict winner, the benefit of all logical inferences that could be drawn from the evidence presented, resolve all conflicts in the evidence in his favor, and in general, view the record in the light most favorable to him." *Williamson v. Consol. Rail Corp.*, 926 F.2d 1344, 1348 (3d Cir. 1991); *see also Perkin–Elmer Corp.*, 732 F.2d at 893. The Court may not assess the credibility of witnesses nor "substitute its choice for that of the jury between conflicting elements of the evidence." *Perkin–Elmer Corp.*, 732 F.2d at 893. Rather, the Court must determine whether the evidence reasonably supports the jury's verdict. *See Dawn Equip. Co. v. Ky. Farms Inc.*, 140 F.3d 1009, 1014 (Fed. Cir. 1998); *Gomez v. Allegheny Health Servs. Inc.*, 71 F.3d 1079, 1083 (3d Cir. 1995) (describing standard as "whether there is evidence upon which a reasonable jury could properly have found its verdict"); 9B Wright & Miller, Federal Practice & Procedure § 2524 (3d ed. 2008) ("The question is not whether there is literally no evidence supporting the party against whom the motion is directed but whether there is evidence upon which the jury properly could find a verdict for that party.").

B. New Trial

Federal Rule of Civil Procedure 59(a) provides in pertinent part, "[t]he court may, on motion, grant a new trial on all or some of the issues – and to any party – as follows: . . . after a jury trial, for any reason for which a new trial has heretofore been granted in an action at law in federal court." New trials are commonly granted where "the jury's verdict is against the clear weight of the evidence, and a new trial must be granted to prevent a miscarriage of justice," where "newly-discovered evidence exists that would likely alter the outcome of the trial," where "improper conduct by an attorney or the court unfairly influenced the verdict," or where the

jury's verdict was "facially inconsistent." *Zarow–Smith v. N.J. Transit Rail Operations*, 953 F. Supp. 581, 584-85 (D.N.J. 1997) (internal citations omitted).

The decision to grant or deny a new trial is committed to the sound discretion of the district court. *See Allied Chem. Corp. v. Daiflon, Inc.*, 449 U.S. 33, 36 (1980); *Olefins Trading, Inc. v. Han Yang Chem Corp.*, 9 F.3d 282, 289 (3d Cir. 1993) (reviewing "district court's grant or denial of a new trial motion" under "abuse of discretion" standard). Although the standard for granting a new trial is less rigorous than the standard for granting judgment as a matter of law – in that the Court need not view the evidence in the light most favorable to the verdict winner – ordinarily a new trial should only be granted "where a miscarriage of justice would result if the verdict were to stand," the verdict "cries out to be overturned," or the verdict "shocks [the] conscience." *Williamson*, 926 F.2d at 1352-53.

III. DAMAGES

With respect to damages, Gilead requests judgment as a matter of law, remittitur of the jury's damage award – to an amount not to exceed $380 million, which was the figure Gilead's expert, Dr. Putnam, testified was the maximum fully-paid-up royalty for the life of the patent that Gilead could owe Idenix – or a new trial. Gilead contends that Idenix's damages presentation was fatally deficient in two respects. First, Idenix's damages expert, Andrew Carter, failed to establish that the patent license agreements on which he relied were sufficiently comparable. Second, Carter and Idenix's damages case violated the Entire Market Value Rule ("EMVR"). The Court disagrees with Gilead.

A. Applicable Law

Under 35 U.S.C. § 284, patentees are entitled to damages "adequate to compensate for the

infringement, but in no event less than a reasonable royalty." Under the "hypothetical negotiation" approach to calculating a reasonable royalty, the finder of fact "attempts to ascertain the royalty upon which the parties would have agreed had they successfully negotiated an agreement just before infringement began." *Asetek Danmark A/S v. CMI USA Inc.*, 852 F.3d 1352, 1362 (Fed. Cir. 2017). For purposes of this calculation, the negotiating parties are assumed to carry a mutual understanding that the asserted patent is valid and infringed. *See Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1325 (Fed. Cir. 2009).

In litigating this issue, parties often point to "[t]he rates paid by the licensee for the use of other patents comparable to the patent in suit." *Georgia–Pacific Corp. v. U.S. Plywood Corp.*, 318 F. Supp. 1116, 1120 (S.D.N.Y. 1970). The "licenses relied upon" must be "sufficiently comparable to the hypothetical license at issue." *Lucent*, 580 F.3d at 1325. The comparability analysis must account for relevant "technological and economic differences." *Wordtech Sys., Inc. v. Integrated Networks Solutions, Inc.*, 609 F.3d 1308, 1320 (Fed. Cir. 2010) (internal quotation marks and citation omitted). "[A]lleging a loose or vague comparability between different technologies or licenses does not suffice." *LaserDynamics, Inc. v. Quanta Computer, Inc.*, 694 F.3d 51, 79 (Fed. Cir. 2012).

To prevail on its JMOL, Gilead must show that the jury's damages award "is, in view of all of the evidence . . . so outrageously high . . . as to be unsupportable as an estimation of a reasonable royalty." *Spectralytics, Inc. v. Cordis Corp.*, 649 F.3d 1336, 1345 (Fed. Cir. 2011). In evaluating Gilead's motion, the Court must remain mindful that "a reasonable royalty analysis necessarily involves an element of approximation and uncertainty." *Ironworks Patents, LLC v. Apple, Inc.*, 255 F. Supp. 3d 513, 528 (D. Del. 2017) (internal quotation marks omitted).

B. Comparability

At trial, Idenix sought (and the jury awarded) a 10% royalty on net sales of Gilead's Harvoni and Sovaldi products. During his testimony, Carter supported this royalty rate by pointing to two "Roche licenses" – one between Pharmasset and Roche, and another between Merck (which is now Idenix's parent company) and Roche. (*See* PX1132; PX1606; Carter Tr. 742-44) Gilead argues that Carter's comparability analysis was improper because he failed to "account[] for the technological and economic differences between each agreement and the hypothetical license" Idenix and Gilead are presumed to have negotiated with respect to Gilead's use of Idenix's '597 patent. (D.I. 536 at 18) More specifically, Gilead asserts that Carter did not: (i) account for the Roche licenses' inclusion of a patent portfolio, as opposed to the single patent that would have been involved in the hypothetical negotiation; (ii) specifically identify the licensed patents; (iii) properly address the relative timing and risks involved (e.g., whether FDA approval had been obtained); and (iv) account for the inclusion in the Roche licenses of non-patent assets. (*See id.* at 18-19)

Idenix responds that the Roche licenses were both "entered into before the 2013 hypothetical negotiation and relatively close in time" to the date of the hypothetical negotiation between Idenix and Gilead. (D.I. 554 at 19-22) The Roche licenses also both involved similar technology to that covered by the '597 patent and "similarly situated parties with similar bargaining power." (*Id.*) Further, in Idenix's view, the distinctions Gilead points to – such as the number of patents involved, timing and risks, and inclusion of non-patent assets – were all presented to the jury, and substantial evidence supports the jury's implicit decision to credit Carter's comparability opinion. (*See id.*) Nor, according to Idenix, has Gilead identified any

basis to conclude as a matter of law that the Roche licenses are not comparable to the hypothetical license Idenix and Gilead would have negotiated. (*See id.*)

While Gilead has leveled powerful factual attacks on Carter's analysis, they are just that: factual attacks. None of them, individually or collectively, renders Carter's analysis flawed as a matter of law. *See ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1333 (Fed. Cir. 2012) (affirming denial of motion to strike damages expert, stating the "degree of comparability of [certain] license agreements as well as any failure on the part of [the] expert to control for certain variables are factual issues best addressed by cross examination and not by exclusion."). The jury was free to accept Carter's opinion that the Roche licenses were technologically and otherwise comparable to the hypothetical license, notwithstanding hearing Gilead's (and its expert's) strong critiques of that opinion. The jury's implicit finding is supported by substantial evidence, including Carter's own testimony on each of the topics on which Gilead's motion is based. (*See, e.g.*, Carter Tr. at 779-80 (portfolio), 788-91 (identifying specific patents), 785-87 (timing and risks, including FDA approval), 800-01, 809-13 (non-patent assets))[5] Furthermore, Carter supported his 10% royalty rate with testimony about several *Georgia-Pacific* factors. (*See* Carter Tr. at 752-57)

While Gilead is correct that comparability "cannot focus just on the covered ***product***,"

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[5]To the extent Gilead is arguing that a damages expert is prohibited from opining that the reasonable royalty can be the same regardless of the number of patents that are the subject of the hypothetical license (*see* Arg. Tr. at 104-11), the Court disagrees. Carter's opinion that Idenix and Gilead would have agreed to the same royalty rate for a license to just the '597 patent as they would have for a license to the '597 patent as well as other patents, while certainly vulnerable to factual attack, is not an improper opinion as a matter of law. Carter's testimony that in real-world negotiations the parties ignore the number of patents was properly admitted and without (at trial) any objection. (*See* Carter Tr. at 790-91)

but must also "describe the relationship between the ***patented technology licensed therein*** and the licensee's products" (D.I. 536 at 19 n.11) (quoting *Uniloc USA, Inc. v. Microsoft Corp.*, 632 F.3d 1292, 1316 (Fed. Cir. 2011) (emphasis added)), substantial evidence was present to support a finding of sufficient comparability between the '597 patent's technology and Gilead's accused products. Moreover, the jury could reasonably have found comparability between the technology involved in the hypothetical license – a license to compounds useful in the treatment of HCV – and the technology involved in the Roche licenses – one between Pharmasset and Roche and another between Merck (Idenix's parent company now) and Roche. (*See* PX1132; PX1606)

In sum, comparability issues do not provide a basis for granting Gilead any relief.

C. Entire Market Value Rule

Infringement damages must "'separate or apportion the defendant's profits and the patentee's damages between the patented feature and the unpatented features.'" *LaserDynamics*, 694 F.3d at 67 (quoting *Garretson v. Clark*, 111 U.S. 120, 121 (1884)). For that reason, reasonable royalties must generally "be based not on the entire product, but instead on the smallest salable patent-practicing unit." *Id.* (internal quotation marks omitted). The Entire Market Value Rule ("EMVR") allows for an exception to this general requirement when the patentee shows that "the patented feature drives the demand for an entire multi-component product," in which case the patentee may obtain damages "as a percentage of revenues or profits attributable to the entire product." *Id.*

Gilead contends that Carter's use of a royalty base consisting of "Gilead's adjusted net sales" of Harvoni and Sovaldi was improper and violated the EMVR. Gilead's position is based on its contention that Carter failed to account for, among other things, Gilead's substantial

contribution of placing fluorine at the 2' down position as well as Gilead's development of the prodrug[6] necessary for the accused product's administration. (D.I. 536 at 20-24)

Idenix counters that the EMVR does not apply in cases where, as here, the accused products are pharmaceuticals "covered in full by the claim" and the "active ingredient . . . provides the claimed therapeutic benefit." (D.I. 554 at 23) For this proposition, Idenix cites to *AstraZeneca AB v. Apotex Corp.*, 782 F.3d 1324 (Fed. Cir. 2015). *AstraZeneca* involved a branded pharmaceutical patentee's suit against a generic competitor. The patent on the drug's active ingredient had expired, but the plaintiff still held "formulation patents claim[ing] three key elements – the drug core, the enteric coating, and the subcoating," which encompassed the "complete omeprazole product" accused of infringement. *Id.* at 1338. The generic manufacturer defendant argued that, unless the active ingredient was excluded from the damages calculation, the EMVR would be violated. The Federal Circuit declined to apply the EMVR because "the [asserted] patents cover the infringing product as a whole, not a single component of a multi-component product." *Id.* It further concluded that, because the "formulation . . . created a new, commercially viable omeprazole drug . . . previously unknown in the art and . . . novel in its own right," the district court did not err in declining to "exclude the value of the active ingredient when calculating damages." *Id.* at 1340.

In response, Gilead correctly observes (*see* D.I. 565 at 9) that *AstraZeneca* explicitly refused to adopt a rule making the EMVR "*per se* inapplicable in the pharmaceutical context," *AstraZeneca*, 782 F.3d at 1337-38, and it further notes that the facts in this case are very different

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[6]A prodrug is a biologically inactive compound that, when metabolized in the body, produces a "drug," allowing the active ingredient in a medication to be delivered to its target. (*See* Sofia Tr. at 1073)

from those relating to the infringing generic product in *AstraZeneca*. Nevertheless, the Court agrees with Idenix that under the circumstances presented in this case, the EMVR does not apply, a conclusion that is supported by *AstraZeneca*. Here, there is substantial evidence to support the jury's implicit findings that the '597 patent covers sofosbuvir (which, at trial, was undisputed) and that "there is no unpatented or non-infringing feature in the [accused] product[s]," as their active ingredient is sofosbuvir. *Id.*

Gilead further contends that Carter's analysis was legally flawed because it failed to "apportion his base to account for the relative value of 2' methyl up," Idenix's contribution to the accused products, "in comparison to 2' fluoro down and the prodrug," which were Gilead's contributions. (D.I. 565 at 10) Gilead is correct that, even now that the Court has found that the EMVR does not apply, *AstraZeneca* still requires a "related inquiry" if the asserted claims "recite both conventional elements and unconventional elements." *AstraZeneca*, 782 F.3d at 1337. In particular, one must "account for the relative value of the patentee's invention in comparison to the value of the conventional elements recited in the claim, standing alone." *Id.*

Carter sufficiently performed this analysis, in a manner on which the jury was free to rely – conclusions the Court reached even before trial. In denying Gilead's motion to exclude Carter's opinions (*see* D.I. 297; D.I. 298 at 13-17), the Court explained:

> . . . [W]ith respect to damages and the Entire Market Value Rule, the Court finds that plaintiffs' expert [Carter] gives a reasonable reliable opinion that fits and is consistent with the law, including that for use of the medication to treat an ailment, the smallest saleable unit may be the pill with the patented active ingredient. The patented feature may not, under the circumstances, be segregated out and that the patented feature may be found to drive demand. Really on all of these points, the plaintiffs' expert expresses an opinion that is consistent with the law and is based on inferences that may reasonably be drawn in plaintiffs' favor on the

evidence.

(D.I. 368 at 145-46; *see also* Tr. at 535 (Gilead's counsel remarking that "this was the subject of Gilead's Daubert motion with respect to Mr. Carter," which the Court denied))

Gilead argues that the Court's pre-trial decision relied on representations made by Idenix but subsequently broken at trial. In Gilead's telling, Idenix made "a promise" to establish at trial that the '597 patent's "cover[age of] the active metabolite . . . was the basis of customer demand" (D.I. 536 at 21), something Idenix never proved. But, even assuming that Gilead's portrayal of the pre-trial litigation is correct, the failure to fulfill that "promise" does not mean the Court should grant the relief Gilead now seeks, because Carter did not ask the jury to award damages based on the EMVR. (*See* Carter Tr. at 792-95) An unfulfilled promise that does not also render an expert's analysis deficient, which at most is what occurred here, is not a meritorious basis for JMOL, remittitur, or a new trial.

Gilead's motion with respect to damages will be denied.

IV. INVALIDITY

Gilead's motion asks the Court to conclude that Idenix's '597 patent is invalid due to its failure to comply with the requirements of 35 U.S.C. § 112,[7] which provides, in pertinent part:

> The specification shall contain a written description of the invention and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . . .

[7]The patent statute was amended in September 2011 by the America Invents Act ("AIA"). *See* Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284, 300-01 (2011). The pre-AIA version of § 112 applies in this case. The post-AIA version of this portion of the statute (§ 112(a)) is identical to the pre-AIA verison.

Section 112 sets out separate requirements for written description and enablement. *See Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1344 (Fed. Cir. 2010) (holding that written description and enablement requirements are separate). Still, these requirements "often rise and fall together." *Id.* at 1352.

Gilead challenges the jury's finding that the '597 patent sufficiently described and enabled its claimed subject matter. With respect to written description, which is a factual issue, the Court finds that there was substantial evidence to support the jury's conclusion that clear and convincing evidence does not support a finding of lack of written description. Just as the Court twice declined to grant Gilead summary judgment on lack of written description, so, too, does the Court again conclude that this was an issue on which a factfinder could have found for either side. With respect to enablement, which presents a question of law, the Court concludes, as a matter of law, that no reasonable factfinder could find anything other than that the '597 patent is not enabled. This being the Court's first occasion to evaluate whether any genuine disputes of material fact preclude resolution of the enablement issue as a matter of law, the Court concludes – based on the trial record – that no such disputes exist.

A. Written Description

1. Applicable Law

Whether a specification satisfies the written description requirement is a question of fact. *See GlaxoSmithKline LLC v. Banner Pharmacaps, Inc.*, 744 F.3d 725, 729 (Fed. Cir. 2014); *see also Alcon, Inc. v. Teva Pharms. USA, Inc.*, 664 F. Supp. 2d 443, 468 (D. Del. 2009) ("Satisfaction of the written description requirement is a fact-based inquiry, depending on 'the nature of the claimed invention and the knowledge of one skilled in the art at the time an

invention is made and a patent application is filed.'") (quoting *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008)). To comply with the written description requirement, a patent's specification "must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed." *Ariad*, 598 F.3d at 1351 (internal brackets and quotation marks omitted).

"[T]he test for sufficiency is whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* "[T]he hallmark of written description is disclosure. Thus, 'possession as shown in the disclosure' is a more complete formulation" of the written description requirement. *Id.* "[T]he test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art." *Id.* "[T]he written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Id.* at 1352. However, "a description that merely renders the invention obvious does not satisfy the requirement." *Id.*

2. The Jury's Verdict is Supported by Substantial Evidence

Gilead contends that the '597 patent is invalid for lack of written description because the "closed, defined list of substituents at 2' (and 3') down" disclosed in the specification fails to describe the full scope of the claims, which – at Idenix's urging – includes ***all*** non-hydrogen substituents at these positions. (D.I. 536 at 12-14) Further, Gilead contends that the specification "does not show possession beyond certain 2' methyl up, 2'/3' OH down molecules," and asserts that Idenix's expert, Dr. Meier, failed to testify as to Idenix's "possession of a definite

class of compounds . . . useful to inhibit HCV polymerase." (D.I. 536 at 17) (internal quotation marks omitted)

Idenix responds that the specification's disclosures are not "closed" in the way Gilead suggests, pointing to Dr. Meier's testimony regarding "'clear indication[s]' in the specification that the HCV polymerase should be targeted in identifying effective compounds" as well as the patent's examples showing testing data for 2'-methyl ribonucleosides. (D.I. 554 at 14) (quoting Meier Tr. at 1854-56) That is, Idenix suggests that the scope of the claims is limited by the functional limitation and guidance in the patent with respect to the polymerase target.[8]

The Court has on two prior occasions considered this identical dispute. In connection with denying Gilead's original and renewed motions for summary judgment of invalidity based on lack of adequate written description, the Court twice concluded that the record, taken in the light most favorable to Idenix, does not require a reasonable factfinder to find, by clear and convincing evidence, that the challenged patent claims are invalid for lack of adequate written description. (*See* D.I. 368, 446) The core question posed by the written description requirement is whether the specification "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter." *Ariad*, 598 F.3d at 1351. The jury was entitled to credit Idenix's evidence, including its expert's opinion, and resolve this genuine dispute of material fact in Idenix's favor. Substantial evidence supports the jury's implicit finding that the record did not contain clear and convincing evidence of lack of written description.

Hence, the Court will deny this portion of Gilead's motion.

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[8]Idenix also contends that Gilead's argument was waived, by virtue of its failure to argue this particular theory to the jury and failure to present it in its Rule 50(a) motion at trial. The Court disagrees and has considered all of Gilead's arguments with respect to written description.

B. Enablement

1. Applicable Law

"Enablement is a question of law based on underlying factual findings." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation." *Id.* (internal quotation marks omitted). "Enablement serves the dual function in the patent system of ensuring adequate disclosure of the claimed invention and of preventing claims broader than the disclosed invention." *Id.* at 1380-81. "Thus, a patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *Id.* at 1381. "The scope of the claims must be less than or equal to the scope of the enablement to ensure that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims." *Id.* (internal quotation marks omitted).

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). These factors include: "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." *Id.* Although "a specification need not disclose what is well known in the art," "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). A patent "cannot simply rely on the

knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification." *ALZA Corp. v. Andrx Pharm., LLC*, 603 F.3d 935, 941 (Fed. Cir. 2010).

2. The '597 Patent Is Invalid Due to Nonenablement

a. Claim construction

As already noted, the Court found it necessary to resolve multiple claim construction disputes and, eventually, to hear claim construction arguments on two separate occasions. The resulting constructions – which are essentially the constructions Idenix proposed – have important implications for the Court's conclusions as to enablement.

At trial, Idenix asserted claims 1, 2, 4-7, 9-10, 16, 19, 23, and 28-31 of the '597 patent. Claim 1, the key independent claim, reads as follows:

> A method for the treatment of a hepatitis C virus infection, comprising administering an effective amount of a purine or pyrimidine ß-D-2'-methyl-ribofuranosyl nucleoside or a phosphate thereof, or a pharmaceutically acceptable salt or ester thereof.

Two limitations are of particular significance in resolving Gilead's enablement challenge.

First, the claim includes structural limitations (hereinafter, the "Structural Limitations"). The term "ß-D-2'-methyl-ribofuranosyl nucleoside" encompasses any ß-D-nucleoside that includes "a five member sugar ring with a methyl group in the 2' up position and non-hydrogen substituents at the 2' down and 3' down positions." (D.I. 237 at 12; D.I. 516 at 22)

Second, at Idenix's urging, the Court construed the claims to contain a functional limitation, through claim 1's preamble ("A method for the treatment of a hepatitis C virus infection") and its "effective amount" term. (*See* D.I. 446 at 8-13) Specifically, the Court concluded that claim 1's preamble is limiting and that the term "effective amount" means "an amount [of the . . . ribofuranosyl nucleoside . . .] that is effective to treat HCV" (hereinafter, the

"Functional Limitations") (D.I. 447).

Combining these two limitations, the claims cover all those nucleosides, but ***only*** all those nucleosides, that meet the Structural Limitations – including a methyl group at the 2'-up position – ***and*** the Functional Limitations of exhibiting effective anti-HCV activity. (*See, e.g.*, D.I. 446 at 8-13; Secrist Tr. at 1576-77; Meier Tr. at 1865-66) Thus, as further explained below, the claims as construed combine Structural Limitations that are satisfied by an enormous number of compounds with Functional Limitations that are satisfied by an unknown, but far smaller, number of undisclosed compounds.

Also pertinent to the Court's analysis is what is ***not*** in its claim construction. Targeting the NS5B polymerase – which Idenix contends is the key to a compound demonstrating effectiveness in the treatment of HCV (*see, e.g.*, D.I. 554 at 8) (identifying "a defined target (NS5B)") – is not an explicit claim limitation. The patent claims are not limited to compounds that are effective in treating HCV ***due to*** their acting on the NS5B polymerase. Nor does the patent specification even teach that to identify effective compounds a person of ordinary skill in the art ("POSA") must or even should be looking for compounds that target the NS5B polymerase. Instead, the patent explains that effective compounds can act through "inhibiting HCV polymerase, by inhibiting other enzymes needed in the replication cycle, ***or*** by other pathways." ('597 patent col. 139 ll. 30-32) (emphasis added) The patent also discloses focus on kinase and protease activity. (*See* '597 patent col. 139 ll. 52-59)[9]

Further, the accused embodiment – 2' methyl up 2' fluoro down – which, undisputedly,

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[9]The jury was free to accept the opinion of Idenix's expert, Dr. Chris Meier, that a POSA, with the assistance of the '597 patent, would particularly focus on NS5B activity. (*See* Meier Tr. at 1918) But, as a matter of law, NS5B activity is ***not*** a claim limitation.

comes within the scope of the claims as construed (*see, e.g.*, D.I. 516 at 13), is not expressly disclosed in the '597 patent. While fluorine is disclosed as a candidate for the 2' up position, it is not disclosed as a candidate for the 2' down position. (*Compare, e.g.*, '597 patent col. 22 l. 41 (disclosing embodiment with fluorine at 2' up position) *with id.* at col. 22 ll. 44-49 (same embodiment without fluorine listed as option at 2' down position)) Notably, fluorine is a halogen, and other halogens are disclosed as candidates for the 2' down position, but, again, fluorine is not. Even the inventor of the '597 patent, Dr. Michael Somadossi, testified that there is no disclosure of the 2' methyl up 2' fluoro down nucleoside in either the May 2000 provisional patent application or the May 2001 patent application. (*See* Somadossi Tr. at 456)[10]

b. Pertinent undisputed facts

Gilead characterizes the trial record as largely devoid of genuine disputes of material fact, while Idenix contends that the ***only*** agreed-upon material issue is that the POSA had significant qualifications and experience. (*Compare, e.g.*, Arg. Tr. at 15-17, 89 *with id.* at 36-37; *see* Seeger Tr. at 1440 (defining POSA for this case); Meier Tr. at 1849-50 (same); *see also* Clark Tr. at 960) Having carefully reviewed the evidence and considered the parties' competing characterizations of it, the Court finds that Gilead's view of the record is far more accurate. More importantly, the Court concludes that several of the facts pertinent to addressing Gilead's

[10]Gilead contends that 2' methyl up 2' fluoro down is excluded from the claims, when properly construed. (*See, e.g.*, Secrist Tr. at 1613-14; Meier Tr. at 1931) At a minimum, in Gilead's view, the patent specification teaches away from placing fluorine at the 2' down position. (*See, e.g.*, Arg. Tr. at 96-97) Gilead made these arguments to the jury (*see, e.g.*, Tr. at 2172) but they were implicitly rejected. Substantial evidence supports the jury's finding. Accordingly, for purposes of resolving Gilead's JMOL motion, the Court takes as established that the 2'-fluoro down embodiment is within the scope of the claims and that the '597 patent's specification is silent about – and does not teach away from – this embodiment.

enablement defense are undisputed in the record. As importantly, the remaining facts pertinent to addressing enablement are ones that, while disputed, could, based on the trial record, only be resolved in favor of Gilead. In this subsection and the next, the Court addresses these undisputed and disputed (but not ***genuinely*** disputed, as they can reasonably be resolved only one way) facts, respectively.

(i) The structural limitations of the claims are satisfied by billions of compounds

In the Court's view, it is undisputed that the Structural Limitations of the claims are satisfied by billions of compounds. (*See* Secrist Tr. at 1577; *see also* Meier Tr. at 1917-18 (discussed further below)) That is, the Structural Limitations allow for a vast number of substituent combinations. Since the compounds of the claims include multiple locations for binding, and each binding site can be filled by numerous substitutions, when all of the possible combinations are counted up, the sum is an indeterminate number measured in billions. (*See* Secrist Tr. at 1577)

As Gilead correctly puts it, "the structural limitations in the claims encompass nucleosides with a methyl group in the 2' up position, ***any*** substituent other than hydrogen at the 2' and 3' down positions, any substituent at other substituent positions on the nucleoside, and any purine or pyrimidine base." (D.I. 536 at 5 (emphasis added); *see also id.* at 3 ("The claims recite a β-D-nucleoside with a five-membered sugar ring having, among other features, a methyl group in the 2' up position and ***any*** substituent other than hydrogen at the 2' and 3' down positions . . . .") (emphasis added)) The patent discloses as "principal embodiments" a number of formulas, each containing a large number of acceptable modifications. For instance, even holding the 2' up (R^6) position constant (by, say, directing that it be filled with methyl, which is ***not*** required of all

the disclosed formulas), the "eleventh principal embodiment" (Formula XVII) all by itself discloses ***at least*** (i) 12 options at the R^1 position; (ii) 12 options at the R^7 (2' down) position (excluding hydrogen); (iii) 12 options at the R^9 (3' down) position (again excluding hydrogen); and (iv) either a purine or pyrimidine base, which has multiple options, as the patent defines the term purine or pyrimidine base very broadly. (*See* '597 patent col. 37 l. 59 - col. 38 l. 10) (noting "[t]he term purine or pyrimidine base includes, but ***is not limited to***," multiple listed compounds) (emphasis added) In other words, Formula XVII on its own constitutes at least a minimum of approximately 7,000 unique configurations (1 x 12 x 12 x 12 x 4).[11] And the patent expressly discloses 18 similar formulas.

Idenix derides this fact as merely a "theoretical" point. (*See* D.I. 554 at 9) Idenix states that one of skill in the art would know not to fill in each compound variable with just any element that would meet the literal terms of the Structural Limitations. For example, no one disputes that placing radioactive plutonium at the 2' down position would meet the pertinent structural limitation, but it is also undisputed that a POSA would never use plutonium for this purpose, given that the patent is directed to compounds effective as medicines for human beings (whereas a plutonium pill would presumably kill humans). (*See* Secrist Tr. at 1722-23)

Still, Idenix's point only effectively reduces the "scope" of the structural limitations from billions of compounds to, likely, millions or at least many, many thousands. Even Idenix's interpretation of its own expert witness' testimony, Dr. Meier, does not undermine Gilead's

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[11]This assumes the purine or pyrimidine base is one of four options – the commonly found bases: adenine, thymine, cytosine, and uracil – listed in the patent. (*See* '597 patent col. 37 ll. 60, 65, 67; *see also* Rachakonda Tr. at 823-25) The number of possible configurations increases considerably (by an order of magnitude) when all the compounds the patent defines as a purine or pyrimidine base are taken into account. (*See* '597 patent col. 37 l. 59 - col. 38 l. 10)

portrayal of the undisputed evidence. Idenix writes:

> Dr. Meier expressly disputed the notion that the claims implicate "a lot of compounds." He testified that if a skilled artisan followed Gilead's "theoretical approach" and considered every conceivable combination (even those no ordinary skilled artisan would consider), then there would have been "a lot of compounds." (Tr. 1917:20-1918:11.) But Dr. Meier reasoned that scientists "would not approach a patent" this way; instead, they "would take into account the patent as a whole and the description of the patent and what is mentioned in" it and arrive at a number "significantly smaller." (Tr. 1918:11-19.)

(D.I. 554 at 9)

Through all this what remains undisputed is that the Structural Limitations of the claims are literally satisfied by billions of compounds. Even fully crediting Idenix's view (and Meier's testimony) on this point, the "significantly smaller" number still leaves a POSA with a very large (and unspecified) number of compounds, measured at least in the thousands. Both numbers – the billions and the at least many thousands – are relevant to the enablement analysis.

In the remainder of this Opinion, the Court will use the term "Structural Limitations" to refer to the billions of compounds that literally satisfy the claims' structural limitations and will use the term "Refined Structural Limitations" to refer to the at least many thousands of those compounds – from among those billions – on which a POSA, relying on her experience and "common sense," would focus in attempting to practice the patent.[12]

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[12]While the Functional Limitations are satisfied by far, far fewer compounds, no reasonable factfinder – for reasons fully explained below – could have found that the '597 patent enabled all of the embodiments that fully meet the claims; i.e., those that satisfy the Structural (or even Refined Structural) ***and*** Functional Limitations.

(ii) POSAs were capable of working with billions of compounds

It is undisputed that, at the pertinent time, POSAs were capable of working from baseline classes containing potentially billions of compound variations to identify subsets of potentially interesting arrangements. (Secrist Tr. at 1709) Idenix notes that Dr. Secrist, one of Gilead's experts, is the inventor on a patent for HCV compounds that he characterized as claiming billions of compounds but as disclosing only a small number. (Secrist Tr. at 1708-10; *see also id.* at 1562-63 (discussing number of compounds and rate at which they can be synthesized))[13]

(iii) The functional limitations greatly reduce the scope of the claims

The claims do not, of course, consist solely of the Structural Limitations or even just the Refined Structural Limitations. They also include the Functional Limitations. It is undisputed that far, far fewer compounds also satisfy the Functional Limitations of being effective for the treatment of HCV.

Relatedly, in analyzing the '597 patent, POSAs would not "check their common sense at

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[13]Neither Gilead nor its experts have endorsed the position that inventions in this area of art – or even inventions in this area of art having structural limitations that are literally satisfied by billions of compounds – are automatically non-enabled or inherently suspect. As is made clear throughout the remainder of this Opinion, the required enablement analysis must take into account numerous factors, facts, and circumstances, leading to an ultimate conclusion as a matter of law. A wide disparity between the number of compounds satisfying the Refined Structural Limitations and those also satisfying the Functional Limitations, combined with only a little bit of guidance given in the patent for how to navigate from the larger to the smaller category, are big factors (though not the sole considerations) in rendering the '597 patent invalid for lack of enablement. *See generally Wands*, 858 F.2d at 737 ("Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations."); *but see also generally In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970) ("In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.").

the door." (Secrist Tr. at 1723) Instead, POSAs would interpret the structural limitations in light of the patent's disclosure as a whole and while considering the purpose of the claimed compounds. (*See* Meier Tr. at 1918; *see also* Secrist Tr. at 1723-24 (Gilead expert Secrist agreeing that one would not "choose tractor tires" in "build[ing] a [rolling] suitcase," adding that POSAs "are going to bring their knowledge and they're going to look at what's in the patent, which doesn't include a hundred carbon chain")) In essence, then, a POSA's common sense and experience will do some work in narrowing the scope of the claims to a set of compounds substantially less than all embodiments that merely satisfy the structural limitations stated in the claims. Again, the Court's defined term of "Refined Structural Limitations" captures this reduction from the far broader scope of compounds that meet the literal "Structural Limitations" of the claims.

Hence, the Functional Limitations greatly reduce the scope of the claims.

(iv) While 2'-methyl up was "key" to curing HCV, it was not sufficient, as not all 2'-methyl up compounds are effective against HCV

It is undisputed that not all 2' methyl up compounds are active against HCV or effective in treating HCV.[14] In other words, it is undisputed that something more (and something more specific) than just 2' methyl up is needed for a compound to be effective in treating HCV. While placing methyl at the 2' up position was "key" to curing hepatitis C (Meier Tr. at 1908), this placement was necessary but not nearly sufficient to result in the invention. The claims do not provide – nor does the specification disclose – that the "key" structural limitation is the 2'-methyl

[14]Like the parties, the Court sometimes includes a hyphen after 2' (e.g., 2'-methyl up) and sometimes does not (e.g., 2' up). No significance should be attributed to this minor discrepancy in nomenclature.

up. (*See* D.I. 536 at 9; D.I. 565 at 5 (citing '597 patent col. 139 ll. 30-32))

Relatedly, it is undisputed that there are many "inoperable embodiments" that contain 2' methyl up, and otherwise satisfy the claims' Structural Limitations, but do not satisfy the claims' Functional Limitations. Indeed, it is undisputed that many 2'-methyl up nucleosides are inactive or toxic. (*See* McHutchison Tr. at 1215-17, 1245-47, 1251-52) Nor does the patent even focus on methyl at the 2'-up position, and it includes examples that do not even allow methyl at that position. (*See, e.g.*, '597 patent col. 11 ll. 1-17)

It is further undisputed that not even all of the compounds expressly disclosed in the patent specification are effective to treat HCV. Therefore, it is undisputed that the specification is replete with embodiments that are not within the scope of the claims.

c. Factual disputes that, based on the trial record, could only reasonably be resolved in Gilead's favor

The Court now turns from the undisputed facts to those facts that are disputed but which, in the Court's view, present disputes on which a reasonable jury, taking the trial record in the light most favorable to Idenix and drawing all reasonable inferences in favor of Idenix, could only have found in favor of Gilead. "The rule that a jury verdict is reviewed for support by 'substantial evidence' does not mean that the reviewing court must ignore the evidence that does not support the verdict. . . . That is, the court should give credence to the evidence favoring the nonmovant as well as that evidence supporting the moving party that is uncontradicted and unimpeached." *Integra Lifesciences I, Ltd. v. Merck KGaA*, 496 F.3d 1334, 1345 (Fed. Cir. 2007).

The Court concludes that while each of the following topics were disputed, they are not genuinely in dispute, in that a reasonable factfinder could only have found for Gilead on these

disputes. Nor does the Court find that there are any other material factual disputes regarding enablement that are in genuine dispute. Instead, Gilead has shown that "the record is critically deficient of the minimum quantity of evidence to sustain the verdict." *Accumed LLC v. Advanced Surgical Servs., Inc.*, 561 F.3d 199, 211 (3d Cir. 2009) (internal quotation marks omitted).[15]

(i) Many embodiments were not readily available and would have required *synthesis*, which takes substantial time and effort

While not undisputed, a reasonable factfinder at trial could only have found that a great deal of time and effort (i) ***would have been required*** if a POSA wanted to synthesize ***every*** compound that met the Refined Structural Limitations of the claims (that is, if a POSA wanted to have in hand all of the compounds satisfying the Refined Structural Limitations); and (ii) ***may also have been required*** to synthesize ***any particular*** compound that met the Refined Structural Limitations of the claims, including the embodiment that is now called sofosbuvir (i.e., 2' methyl up 2' fluoro down). Many – if not the vast majority – of these compounds were not readily available to a POSA "off the shelf."

In order to determine which compounds were embodiments of the claims, synthesis

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[15]Idenix contends that the Court must apply what is essentially a summary judgment standard, taking the "full and rich" record (Arg. Tr. at 34-35) and resolving all disputed facts in its favor and also drawing all reasonable inferences in favor of Idenix as the verdict winner. The analysis the Court is undertaking in this section is entirely consistent with such an approach. Indeed, it is the type of analysis the Court would have undertaken had either side filed a motion for summary judgment regarding enablement. *Cf. Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371, 1372, 1379 (Fed. Cir. 2007) (affirming summary judgment of invalidity for lack of enablement where, among other things, "inventors admitted that they [had] tried unsuccessfully to produce a pressure-jacketless system and that producing such a system would have required more experimentation and testing").

would have been necessary. This conclusion – which a reasonable factfinder, even taking all of the evidence in the light most favorable to Idenix, and drawing all reasonable inferences in Idenix's favor – arises from a related finding a reasonable factfinder would also have had to have made. That is, while some limited number of compounds meeting the Structural Limitations of the claims were already available – for instance, in "libraries" of compounds maintained by a pharmaceutical companies – only relatively few of the billions of compounds meeting those Structural Limitations were available at the pertinent date.

Idenix's expert, Dr. Meier, acknowledged that not all compounds of interest were commercially available. (*See* Meier Tr. at 1855) Instead, they needed to be synthesized (before they could be screened for whether they meet the Functional Limitations of the claims, which is discussed in detail in the next section). (*Id.*) Idenix's Dr. Gosselin agreed with the proposition that "you don't know whether or not a nucleoside will have activity against HCV until you ***make it*** and test it." (Gosselin Tr. at 1334) (emphasis added)

No witness contradicted Gilead's Dr. Secrist's opinion that "an average chemist could make only 2-3 nucleosides a month." (Secrist Tr. at 1562-63, 1601) Other witnesses testified about the existence of compound libraries, but without describing their size – leaving no basis to find that their size even began to approach billions or even many thousands of compounds. (*See* La Colla Tr. at 498, 502-03 (noting library without characterizing its size); Stuyver Tr. at 657-58 (testifying that Kyo Watanabe, VP of chemistry at Pharmasset, came with a library of nucleoside compounds, including a 2' down fluoro cytosine, but none of which had 2' methyl up, and not knowing "complete content" of that library); Hasan Tr. at 947-48 (noting Pharmasset had library of compounds); Cook Tr. at 1336 (noting existence of library with 2' modified compounds

without characterizing its size))

It is not reasonable to infer from the specific numbers of compounds said to be in the libraries, or from the testimony about libraries that did not even describe the size of the libraries, that any large proportion of the compounds meeting the Structural Limitations or Refined Structural Limitations of the claims was available without synthesis. To the contrary, the only conclusion supported by substantial evidence is that a POSA would have had to synthesize a significant number of candidate compounds, which would have required a substantial amount of time. (*See* Secrist Tr. at 1728) (stating that number of readily-available compounds was "a pretty small number. Very small number, I would say," adding that compounds contained in library "don't last forever") Thus, the availability of compounds to screen was a substantial rate-limiting factor. A large percentage of the compounds a POSA would want to test – as they plainly met the Structural Limitations of the claims, and might be predicted to have potentially satisfied the Functional Limitations as well – were not readily available and needed to be synthesized before they could be studied. (*See also generally* Arg. Tr. at 38) (counsel for Idenix: "Well, certainly, to practice the invention, one has to make the compound.") And, as set out immediately below, synthesis of just one candidate compound (indeed, the compound presently accused of infringement) might be a multi-year pursuit on its own.

(ii) Synthesis of 2' methyl up 2' fluoro down was neither routine nor simple

The parties and their experts disputed whether synthesis of the embodiment that is contained in Gilead's accused products, 2' methyl up 2' fluoro down, was simple and routine. Despite the amount of competing evidence presented, the Court concludes that a reasonable factfinder could only have found that synthesis of this particular compound was neither routine

nor simple but, instead, required extensive experimentation.

This conclusion is most vividly demonstrated by the experience, and repeated failures, of Idenix's Dr. Jean-Francois Griffon. Dr. Griffon first began to attempt making 2'-methyl up 2'-fluoro down in March 2002. (*See* DX189.0002) By February 2003 he was reporting multiple failures in completing his task. (*See* DX1129.0001) In November of that year, Idenix abandoned the effort. (DX268.0002) Idenix reinstated the project in February 2004. (DX2184.0002) Throughout that year, Dr. Griffon reported more failures. (DX2186.0007 (June 2004); Griffon Tr. at 1183 (admitting that as of June 2004 "all the strategies that were attempted to introduce a methyl group at the 2' up position and a fluorine atom at the 2' down position failed"); DX1171.0002 (Sept 2004); Griffon Tr. at 1181-82 (Sept. 2004)) Only in March 2005 – two months after the publication of U.S. Patent Application No. 2005/0009737 (DX371), issued to ***Pharmasset's*** Jeremy Clark (more on him below), had been distributed at Idenix – did Idenix first succeed in making and testing 2'-methyl up 2'-fluoro down. (DX359; DX0274.0119, .0122; Wang Tr. at 1196, 1198-1200 (stating that in March 2005 Idenix first successfully synthesized "an unprotected 2'-methyl-2'-fluoro nucleoside" and recognized it had done so); Standring Tr. at 1831-33) In short, the undisputed record shows that, between 2002 and 2005, Idenix tried and failed to make and test a 2'-methyl up 2'-fluoro down nucleoside, and only succeeded when Dr. Griffon "***us[ed] information from a published Pharmasset patent application.***" (Griffon Tr. at 1172-83 (emphasis added); *see also* Stewart Tr. at 1188-94; Standring Tr. at 1831; DX268.002; DX2184; DX359)

Idenix's response to this devastating evidence is that it is "possible" (Griffon Tr. at 1187) that Dr. Griffon "may have actually [and unknowingly] formed the target [compound]" at some

earlier point. (D.I. 554 at 12) Dr. Griffon did not test each of the reaction products he obtained from his experiments, so he could not rule out the possibility that maybe he had synthesized what he intended sometime before he recognized he had done so. (Griffon Tr. at 1184-87) The suggestion that Dr. Griffon may have actually formed the target compound without realizing it is pure speculation. More importantly, if an experienced scientist like Dr. Griffon worked for several years intentionally trying to synthesize the particular accused compound and actually succeeded but only ***wrongly*** thought he failed, such "facts" would provide no basis for a reasonable factfinder to find that this synthesis is easy or routine.

As an alternative response to Dr. Griffon's failures Idenix points to the success of Pharmasset's Jeremy Clark, mentioned just above. It is undisputed that Clark does not have a doctoral degree, but just a master's degree, and, accordingly, does not meet the Court's definition of a POSA. (*Compare* Clark Tr. at 960 *with* Seeger Tr. at 1440 and Meier Tr. at 1849-50) Idenix presented evidence that Clark, despite his lack of qualifications, was confident that he would be able to make a modified nucleoside with a fluorine atom at the 2' down position (*see* Otto Tr. at 694; Clark Tr. at 996) and managed to produce the compound in relatively short order by "following a well-known synthetic route (of the type disclosed in the '597 patent) [DAST] and using a common fluorinating reagent" (D.I. 554 at 11-12) (citing Otto Tr. at 696; Clark Tr. at 977-80, 992-95). At Pharmasset, Clark developed compound PSI 6130, which is a 2'-methyl up 2'-flouro down modified nucleoside. (*See* Clark Tr. at 977-80, 992-95) Accepting all of this as true does no more for Idenix than, at best, neutralize the evidence of Dr. Griffon's failure. It does not, however, provide substantial evidence that synthesizing the target methyl-fluoro compound was easy or routine.

Idenix relatedly contends that the jury could have reasonably found that Clark's success was based on his reliance on Idenix's PCT patent application, providing strong support that the asserted patent claims are enabled, because the '597 patent shares the same specification as the PCT patent application. (*See, e.g.*, Arg. Tr. at 46-47) A reasonable jury could not have made such a finding.

Pharmasset's Dr. Otto testified that when Clark came to him with the idea for the compound that became 6130, Otto told Clark to conduct a literature search, and thereafter Clark "did bring with him to my office" a copy of a Novirio (i.e., Idenix) patent application. (Otto Tr. at 696) However, in response to being asked at trial "did he present you with any literature that ***guided*** him to 6130," Otto responded, "Well, he didn't say what necessarily guided him to that idea." (Otto Tr. at 696) (emphasis added)

Idenix argues: "So the jury could reasonably infer from this that [the] Novirio application, the Idenix patent application, and this was the specification that is the '597 patent, is what guided Mr. Clark to 2'-methyl, 2' fluoro, and aided him in his synthesis, which he was able to do with ease during this time frame with clearly having Idenix's patent application in hand." (Arg. Tr. at 46-47) But this is not a reasonable inference to draw from either the specific testimony on which Idenix relies or the overall evidentiary record created at trial.

Contrary to Idenix's suggestions, Clark did not say he used Idenix's patent as a guide, and Otto did not say that Clark said he did. When asked how it is that he thought of using 2'-methyl up 2'-fluoro down, Clark answered: "Probably from reading the literature. If you go back to the old literature of the 2'-methylcytidine, those compounds were made in the late '60s. . . . So I can't say for certain, but I would almost certainly say that it had to do with reading the old

literature. . . ." (Clark Tr. at 961-62) He came to use methyllithium because it "was analogous to work by Matsuda . . . at the nuleoside level." (Clark Tr. at 977) While Clark stated that the reaction took only 15 minutes (Clark Tr. at 979-80), the only reasonable interpretation of his testimony, as a whole is that the process of conceiving and creating the compound took far longer, weeks in fact. The synthesis with the sugar he described as "the spawn of the devil. This took me many, many times of going back and doing the same steps over and over, and the reason was in part because this reaction here was extremely messy and for some reason it would not scale up . . . ." (Clark Tr. at 976-77)[16]

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[16]In denying Idenix's motion to enhance damages based on Gilead's willful infringement, the Court stated:

> When Pharmasset's Jeremy Clark was describing to his boss, Dr. Michael Otto, Clark's breakthrough – the synthesis of a 2'-methyl up 2'-fluoro down compound, later labeled PSI-6130 – he had Idenix's patent application in hand. (*See, e.g.*, Tr. at 1006) The jury implicitly found that Clark and others at Pharmasset copied (and were assisted by) Idenix's work.

(D.I. 587 at 6) The Court further held that "substantial evidence was presented at trial" to support the jury's implicit finding that Gilead deliberately copied Idenix's invention. (*Id.* at 7) In describing the interactions between Clark and Otto, when Clark had "Idenix's patent application in hand" (*id.* at 8), the Court further stated that "the jury presumably found that at some point in time Pharmasset or Gilead acted in bad faith" (*id.* at 8-9).

These were appropriate conclusions in the context of assessing the "*Read* factors" and exercising discretion as to whether damages should be enhanced. Importantly, in that analysis the Court was assuming, without deciding, that Gilead's pending motion would be denied in full. (*See* D.I. 587 at 2 n.4) In the context now of evaluating Gilead's motion, the Court can only credit ***reasonable*** inferences that a reasonable jury could have drawn based on the evidence it heard. In this context, the Court has determined that it would not have been reasonable for the jury to have found that Clark used the '597 patent application as the basis for his compound or that Clark's experience supports a conclusion of enablement. In making the conclusion as a matter of law whether the claims are enabled, the Court cannot consider an unreasonable finding of fact. At bottom, the only reasonable finding one can make from the Clark evidence is that it does not defeat Gilead's showing that the patent claims lack enablement.

Idenix's expert, Dr. Meier, opined that the experimentation required to make nucleosides was routine at the pertinent date. (*See* Meier Tr. at 1922, 1936) But given Idenix's own well-documented failures to intentionally synthesize the specific relevant compound for several years, and the entire record, the Court concludes that no reasonable factfinder could find that it was easy or merely routine to synthesize the 2'-methyl up 2'-fluoro down compound.[17]

(iii) While nucleoside synthesis was well-known, the use of modified ribonucleosides for treatment of HCV was in its infancy

A reasonable factfinder could only find that while nucleoside synthesis, in general, was not a new field in 2000 – indeed, synthesizing and modifying nucleosides was a well-known and routine art at this pertinent date (*see* Secrist Tr. at 1725, 1727-28; Meier Tr. at 1921-25, 1936) – the more specialized task of synthesis of modified nucleosides for the treatment of HCV was in its infancy.

The patent discloses "multiple synthetic routes for making at least several members" of

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[17] Limited, further support for this conclusion is found in the Federal Circuit's recent decision in *Storer v. Clark*, 860 F.3d 1340 (Fed. Cir. 2017), which addresses an Idenix patent related to the '597 patent-in-suit. In *Storer*, Idenix appealed the Patent Trial & Appeal Board's (PTAB) finding that a 2002 provisional application did not enable Idenix's claim in a patent (issued subsequent to the '597 patent) for use of a 2'-methyl-fluoro nucleoside. The Federal Circuit affirmed the PTAB's invalidity determination, holding that "substantial evidence supports the finding that 'a high amount of experimentation is necessary to synthesize' the target compound." *Id.* at 1352.

Storer is distinguishable because it involved a different patent, having different claims as well as a different specification than the '597 patent. Also, the evidentiary record here is far more developed than that which was before the PTAB and the Court of Appeals, and the legal standard applicable here (on Gilead's challenge to a jury verdict in favor of Idenix) is far more favorable to Idenix than it was on appeal from a loss in the PTAB. Clearly, then, *Storer* by no means compels a conclusion that the '597 patent is also invalid due to lack of enablement. But it is consistent with this Court's conclusion that the experimentation involved with the '597 patent is neither routine nor simple.

the "small class" of compounds effective active against HCV. (D.I. 554 at 4; *see also* Secrist Tr. at 1594; Meier Tr. at 1922-25; '597 patent Scheme 3) Modifications involving prodrugs and hydroxy or phosphate groups at the 3' and 5' positions were routine and within a POSA's skillset. (*See* Secrist Tr. at 1726-27) (acknowledging that "nucleoside synthesis" was not in its infancy) However, research involving the use of modified nucleosides ***as treatments for HCV*** was "in its infancy" in the 2000-2001 period. (Meier Tr. at 1927-28; *see also* Arg. Tr. at 56 (Idenix conceding that use of nucleosides to treat HCV "was in an early stage" at pertinent date))

Idenix's expert, Dr. Meier, admitted that, even as of 2012, nucleoside activity against HCV remained unpredictable. (*See* Meier Tr. at 1928-29) Indeed, unrebutted evidence at trial demonstrated that even seemingly minor changes to active or effective compounds can – unpredictably – render the modified compounds inactive or even toxic. (*See, e.g.*, Sofia Tr. at 1116; McHutchison Tr. at 1252-53)

Moreover, even though POSAs would have been informed by the pursuit of compounds acting on HCV polymerase, they could not simply and readily ascertain with any certainty which structures would have that activity.

(iv) Determining whether a compound meeting the structural limitations also satisfied the functional limitations required *screening*, which takes substantial time and effort

Because the activity of a modified nucleoside, and especially its effectiveness in treatment of HCV, is unpredictable – even for compounds satisfying the Structural Limitations or Refined Structural Limitations of the claims – a reasonable factfinder could only have found that it was necessary to screen these compounds in order to determine if they also met the Functional Limitations of the claims. This ***screening*** would have taken additional substantial time and

effort, on top of the time and effort required to synthesize the compounds.

The '597 patent discloses: "The βD- and βL-nucleosides of this invention ***may inhibit HCV polymerase activity***. Nucleosides can be ***screened for their ability to inhibit HCV polymerase activity*** in vitro according to screening methods set forth more particularly herein." ('597 patent col. 13 ll. 42-49) (emphasis added) The patent discloses several methods for screening compounds that meet the claims' Structural Limitations, methods that would allow a POSA to determine if such compounds also satisfy the Functional Limitations. (De FrancescoTr. at 1980-81; *see also* '597 patent col. 139 ll. 29-50) Other methods were also known in the art. (*See* Meier Tr. at 1855-56; De FrancescoTr. at 1982-88; *see generally* Seeger Tr. at 1488-90; PDX9)

Based on the record presented at trial, a reasonable jury would have to have found that, as of the pertinent date, a POSA would have understood that, in the context of the pertinent art, "very small changes . . . create a new molecule" so "it's impossible to predict whether that molecule is active or not." (Seeger Tr. at 1436; *see also id.* Secrist Tr. at 1584-85 ("[T]he smallest change can have a dramatic effect not only on the activity of that compound but on the toxicity of the compound."); DX338; Arg. Tr. at 15-17) Further testing, that is, screening, would have been necessary to determine if any particular compound met the claims' Functional Limitations.

Idenix's witnesses concurred. Dr. De Francesco, Idenix's virology expert, explained, "[N]ucleosides can be screened for ability to inhibit HCV polymerase activity in vitro. . . . We use the screening because that is the way you actually cut down the number of compounds, by removing all inactive ones to a few interesting ones." (De Francesco Tr. at 1969-70; *see also id.*

at 1979-89; Meier Tr. at 1855 (testifying about screening methods)) Idenix's Dr. Gosselin agreed with the proposition that "you don't know whether or not a nucleoside will have activity against HCV until you make it and ***test it***." (Gosselin Tr. at 1334) (emphasis added) Consistent with this testimony, at the motions hearing Idenix's counsel acknowledged "[c]ertainly" one would "have to do some screening," at least "[s]ometimes." (Arg. Tr. at 39)

Idenix contends that testimony from Dr. Raffaele De Francesco provided substantial evidence for the proposition that screening methods either disclosed in the patent or known in the art "could test a large amount of compounds in a relatively short period of time." (D.I. 554 at 6; *see also* D.I. 582 at 3 ("Dr. De Francesco testified that, as of 2000, his lab [had] tested over 100,000 compounds in the HCV polymerase assay and, in only a three-month period in 2000, tested 18,000-20,000 compounds in the HCV replicon assay.") (citing Tr. at 1984-85, 1988-89); De Francesco Tr. at 1984 ("[I]t was possible to screen thousands or even tens of thousands of compounds in a relatively short time frame, and without any undue experimentation"))[18] Taking Dr. De Francesco's testimony as true does not support a finding that screening was not required, nor does it support a finding that anything less than a great deal of screening would have been necessary in order to identify all of the compounds meeting the Refined Structural Limitations and also satisfying the Functional Limitations. It may, at best for Idenix, only mean that the rate at which ***screening*** limited a POSA's ability to "make and use the full scope of the claimed invention," *MagSil*, 687 F.3d at 1380, was less than Gilead contended and maybe less than the rate at which ***synthesis*** limited a POSA's ability to do the same. Still, however, a reasonable jury

[18]By contrast, Dr. Tausek, a biologist in Idenix's HCV group, testified that testing 37 compounds of interest in a month is considered a lot. (*See* Tausek Tr. at 1202-03)

could only have found that screening would have been a significant rate-limiting factor, as screening would have been necessary, takes time, yields unpredictable results, and would need to be undertaken repeatedly. (*See* Seeger Tr. at 1486-94)

(v) Whether a compound satisfying the structural limitations would also meet the functional limitations could not be predicted nor "visualized"

Idenix's contrary position – that a POSA could visualize embodiments that would meet all of the limitations of the claims (including the Structural and Functional Limitations) without screening – is not supported by substantial evidence. No reasonable factfinder could have made such a finding.

Idenix insists that it presented substantial evidence that screening was ***not*** required in order for a POSA to be able to discover active compounds meeting the claims' Functional Limitations. Instead, Idenix views the evidence as having established the viability (and existence) of a "visualize . . . and confirm" process for identifying effective compounds. (D.I. 554 at 9) Specifically, the patent's disclosure, in combination with the knowledge of a POSA, would have allowed a POSA to "visualize the 'other compounds' expected to have anti-viral activity." (D.I. 554 at 4) For support, Idenix points to the patent's disclosure that the "invention may inhibit HCV polymerase activity" (Meier Tr. at 1855) (quoting '597 patent col. 13 ll. 43-44), which means, according to Idenix, that POSAs would "focus on 2'-methyl compounds that are likely to inhibit that enzyme" (D.I. 554 at 4; *see also* Meier Tr. at 1854), particularly compounds with a hydroxy group at 2' down.

In the Court's view, substantial evidence does not support Idenix's contention. Idenix's characterization of screening as merely "confirmatory" (D.I. 554 at 10 n.3) ignores both its

experts' testimony and the patent itself. De Francesco testified that "one can readily determine the spectrum of activity by evaluating the compound in the assays described in the patent ***or*** with confirmatory assays." (De Francesco Tr. at 1970) (emphasis added) Almost immediately thereafter, he unambiguously noted that screening is like a "filter," and is used "because that is a way ***you actually cut down the number of compounds, by removing all inactive ones to a few interesting ones***." (De Francesco Tr. at 1970) (emphasis added) Further, Dr. Gosselin testified that "you don't know whether or not a nucleoside will have activity against HCV until you make it and test it." (Gosselin Tr. at 1334) Also, as Gilead points out, the patent "instructs a POSA to discover active compounds using screening," and that screening ***is*** "the tool to determine if a compound inhibits NS5B polymerase." (D.I. 536 at 6-7) All of this is reinforced by the undisputed novelty and infancy of the field at the relevant time (described above). And, notably, no witness testified at trial that a POSA could "visualize" all embodiments of the claims.[19]

Hence, even assuming that a POSA would have chosen to focus exclusively on NS5B, the range of possibilities and unpredictability of the art foreclosed mere deductive "visualization" as

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[19]Idenix further points to testimony suggesting that a POSA, informed by knowledge of "steric hindrance and electronegativity," might also pursue only substituents that "mimic hydroxy in some way," which would include fluorine. (Hassan Tr. at 954; Storer Tr. at 1155-58) Idenix premises this contention principally on the testimony of its expert, Dr. Storer, who joined Idenix after the '597 patent application had been filed. Dr. Storer's testimony does not support the conclusions Idenix is drawing from it. In order to help enable the patent claims, the information about which Storer testified must be contained in the patent specification, which it is not; it cannot solely rest within the knowledge of a POSA. *See ALZA*, 603 F.3d at 941 ("To satisfy the plain language of § 112, ¶ 1, [plaintiff] was required to provide an adequate enabling disclosure in the specification; it cannot simply rely on the knowledge of a person of ordinary skill to serve as a substitute for the missing information in the specification."); *MagSil*, 687 F.3d at 1380 ("To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.") (internal citation omitted).

a successful strategy.

Hence, a reasonable factfinder could only reach one conclusion: that the range of potential candidates is and was substantial, and that testing played an indispensable and exploratory – rather than confirmatory – role in a POSA's attempts to practice the '597 patent's claims.

d. Application of *Wands* factors

In contrast to the billions of compounds satisfying the claims' Structural Limitations, and in contrast to the at least many thousands of compounds satisfying the Refined Structural Limitations, only a very small number of those compounds also satisfy the claims' Functional Limitations. That is, taking the evidence in the light most favorable to Idenix, a reasonable jury had to find that "not a large class" of the compounds meeting the Structural Limitations are active against HCV. (D.I. 582; *see generally* Seeger Tr. at 1486-88, 1578, 1918) In other words, the number of effective compounds is far smaller than (a) the number of compounds meeting just the Structural Limitations, (b) the number of compounds meeting just the Refined Structural Limitations, and (c) the range of compounds disclosed as potential embodiments in the patent's specification.

This fact, however, would leave a POSA asking herself the crucial question: which of the compounds meeting the Refined Structural Limitations also satisfy the Functional Limitations? A reasonable factfinder could only conclude that the patent fails to provide this necessary information. (*See* D.I. 516 at 31) (Jury Instruction on Enablement, including: "A patent specification must contain a sufficiently full and clear description of how to make and use the full scope of the claimed invention. . . . In order to be enabling, the patent must permit persons

having ordinary skill in the field of technology to make and use the full scope of the claimed invention at the time of original filing without having to conduct undue experimentation.") As a matter of law, based on the undisputed facts and the facts that, although disputed, a reasonable factfinder would have to have found (by clear and convincing evidence), the '597 patent is invalid due to lack of enablement.

This is the conclusion compelled by application of the *Wands* factors to the record before the Court. Consistent with *Wands*, the Court instructed the jury:

> In deciding whether a person having ordinary skill would have to experiment unduly in order to make and use the invention, you may consider several factors:
>
> (1) the quantity of experimentation necessary;
>
> (2) how routine any necessary experimentation is in the relevant field;
>
> (3) whether the patent discloses specific working examples of the claimed invention;
>
> (4) the amount of guidance presented in the patent;
>
> (5) the nature and predictability of the field;
>
> (6) the level of ordinary skill; and
>
> (7) the scope of the claimed invention.
>
> No one of these factors is alone dispositive. Rather, you must make your decision as to whether the degree of experimentation required is undue based upon all of the evidence presented to you with regard to all of the factors above. You should weigh these factors and determine whether or not, in the

> context of this invention and the state of the art at the time of the relevant application, a person having ordinary skill would need to experiment unduly to make and use the full scope of the claimed invention.

(*Id.* at 31-32)

First, with respect to "the quantity of experimentation necessary," significant work is necessary to synthesize and screen the full scope of the compounds that fall within the claims, or even to synthesize and screen any particular compound coming within the scope of the claims. Second, while some of that experimentation was routine, much of it was not, as is demonstrated at least by Dr. Griffon's failures. The next factors – the disclosure in the patent of "specific working examples" and the "amount of guidance presented in the patent" – also favor a finding of nonenablement. While the patent discloses working embodiments, routes for making the claimed nucleosides, and assays for screening candidates, the claims' Structural Limitations are enormously broad, the Refined Structural Limitations are also quite broad, and the patent's examples disclose a significant number of possible arrangements. The claims do not require a focus on the NS5B polymerase, many embodiments with a 2'-methyl up are inoperable or at least ineffective for the treatment of HCV, and the embodiment with fluorine at the 2'-down position is not disclosed – even though it is disclosed as a candidate for other positions. These factors, then, support only a finding of nonenablement.[20] Turning to the "nature and predictability of the

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[20]As Idenix emphasizes, the '597 patent includes experimental data on four compounds, each with a 2'-methyl up and hydroxyl (OH) group at 2' down and 3' down. The tables listing this data at least implicitly suggest to a POSA that the tested compounds are antivirally active. (*See, e.g.*, Meier Tr. at 1862 (opining that POSA "would understand that this compound has antiviral activity because otherwise he would never run an *in vivo* assay in a monkey"); *see also id.* at 2003-06) While this data provided some limited additional "guideposts," neither this data (nor any other part of the patent) disclosed any teaching about the activity (or any other characteristic) of a 2'-fluoro down compound, and data for four compounds was inadequate to render

field," including the state of the prior art, and the level of ordinary skill, while nucleoside chemistry was a well-studied field populated with highly skilled POSAs, the use of such compounds to treat HCV constituted a novel, highly unpredictable endeavor at the pertinent time. Finally, while the scope of claimed compounds is drastically reduced by the claims' Functional Limitations, seemingly minute differences can alter whether compounds meeting the claims' Structural Limitations will also meet its Functional Limitations. Only through experimentation, not prediction, could a POSA determine if a particular compound would meet the Functional Limitations. In this way, the scope of the claims can only be found to support nonenablement.

Because the Structural Limitations are satisfied by such a large number of compounds, and because of the other *Wands* factors as applied here, the amount of experimentation to refine this broad set of compounds to those that also satisfy the Functional Limitations, given the limited teachings on this point in the patent and the state of the prior art, is an "undue" amount. *See generally Erfindergemeinschaft Uropep GBR v. Eli Lilly and Co.*, 2017 WL 3676736, at *21 (E.D. Tex. Aug. 25, 2017) ("In the context of a disclosure and a field that provides no guidance, aimless plodding through systematic experimentation of a single compound that would take

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predictable the activity of all compounds meeting the structural limitations of the claims.

Idenix also makes much of a Pharmasset grant application which credited Idenix's patent application for disclosing "modified nucleoside analogues with potent inhibition of the HCV NS5B polymerase," including 2'-methyl modified nucleosides. (*See, e.g.*, D.I. 554 at 7) (citing PX0764.0023) But the Pharmasset grant application does not call out Idenix as having disclosed a 2' fluoro down compound. As Gilead explains, "It's no more [of a] comment on the full scope of this claim as we transfer from OH down to anything else at 2' than [is] the patent." (Arg. Tr. at 92) Similarly, Idenix points to a 2003 De Francesco article that credited Idenix's application with disclosing 2'-methyl ribonucleosides compounds "for the treatment of HCV." (D.I. 554 at 7) (citing PX0702.0118) However, the article does not credit Idenix with having enabled the full scope of the claims or even for disclosing a 2'-fluoro down embodiment. Instead it refers to a single compound. (*See* D.I. 565 at 4 n.1) (summarizing evidence)

weeks may be undue."); *see also Ariad*, 598 F.3d at 1353 ("Patents are not awarded for academic theories, no matter how groundbreaking or necessary to the later patentable inventions of others."). Thus, the only conclusion that can be reached based on the trial record is that the asserted claims of the '597 patent are invalid for lack of enablement.

e. Comparison to *Wyeth*

The Court's conclusions are further supported by a comparison between this case and what the Federal Circuit confronted in *Wyeth and Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013). *Wyeth* considered the validity of patents relating to the use of a class of compounds called rapamycin for treatment of restenosis, which is the "renarrowing" of an artery due to vascular injury that may result from inflation of a balloon catheter to clear plaque blockages. *Id.* at 1382. The patent at issue claimed methods that involved "administering an antirestenosis effective amount of rapamycin." *Id.* While the claim was to this genus, the patent disclosed "only one rapamycin species, called sirolimus." *Id.* It was known that "sirolimus acts in part by binding two proteins at sites within the macrocyclic ring," and that there were four additional compounds that shared the same macrocyclic ring. *Id.* at 1383. The specification disclosed *in vivo* and *in vitro* testing data. *Id.* The term "rapamycin" was construed to include all compounds containing sirolimus's macrocyclic ring that had "immunosuppressive and anti-restenotic effects." *Id.*

The District Court found that practice of the full scope of the claims required undue experimentation and granted summary judgment of invalidity for lack of enablement. *Id.* On Wyeth's appeal, the Federal Circuit affirmed. *Id.* at 1386.

Wyeth argued that a POSA would "readily know how to practice the full scope of the

claims" by first "ascertain[ing] whether a candidate rapamycin compound has the same macrocyclic ring as sirolimus," and then using assays to determine whether that candidate is effective. *Id.* at 1384. Despite the existence of "millions of compounds" that could meet the claims' structural limitations, Wyeth continued, "the number of compounds that would exhibit the recited functional effects would be significantly smaller." *Id.* Wyeth further suggested that a POSA would reduce the range of candidates by focusing on permeability across cell membranes, which occurs in compounds having certain molecular weights. *See id.*

The Federal Circuit rejected Wyeth's contentions. The Court observed that, even accepting Wyeth's representations regarding an implicit molecular weight limitation, there were still "at least tens of thousands of candidates" to screen; the specification was "silent about how to structurally modify sirolimus;" it would be necessary to "first synthesize and then screen ***each*** candidate" to determine effectiveness; and the record and specification offered no guidance as to which "particular substitutions" at substituent positions might be "preferable" or would preserve sirolimus' effective properties. *Id.* at 1385-86 (emphasis added). In reaching these conclusions, the Court cited expert testimony that "until you test [compounds], you really can't tell whether they work or not." *Id.* at 1385 (alteration in original). The claims were invalid because "practicing the full scope of the claims would require synthesizing and screening ***each*** of at least tens of thousands of compounds." *Id.* at 1385. Even putting aside the challenges of synthesizing all these compounds, the amount of experimentation required would be excessive as "it would take technicians weeks to complete each of these assays." *Id.* at 1386.

The parallels between *Wyeth* and the instant case are striking. As in *Wyeth*, Idenix claimed a new use for an existing class of compounds, but the patent contains limited disclosure

of functional species. *See id.* at 1384. In other words, "the invention is a new method of use of [] known [disclosed] compound[s] . . . ***and*** any other compounds that meet the construction's structural and functional requirements." *Id.* at 1385. Although much was known about nucleoside chemistry at the pertinent date, the chemical arts remain generally unpredictable and, as with the "limited knowledge of treatment of restenosis using sirolimus at the time of the invention" in *Wyeth*, *id.* at 1384, the study of nucleoside treatments for HCV at the time of Idenix's patent application was "in its infancy" (Meier Tr. at 1927-28), and remained unpredictable for at least the ensuing decade (Meier Tr. at 1939-40). More particularly, as in *Wyeth*, the evidence here is that "even minor alterations to the . . . [candidate] molecule could impact its . . . [treatment] properties." *Wyeth*, 720 F.3d at 1385. Further, as Idenix's expert, Dr. Gosselin, testified, "you don't know whether or not a nucleoside will have activity against HCV until you make it and test it." (Gosselin Tr. at 1334) The amount of time and effort to synthesize and screen compounds potentially meeting the limitations of the claims of the '597 patent contributes to the finding of lack of enablement, just as it did in *Wyeth*. *See* 720 F.3d at 1385 ("The remaining question is whether having to synthesize and screen each of at least tens of thousands of candidate compounds constitutes undue experimentation. We hold that it does.").

As with the patent invalidated in *Wyeth*, Idenix's patent requires a "systematic screening process" to identify the ***full range*** of 2'-methyl ribonucleosides falling within the broad structural and functional scope of the claims Idenix pursued. *Wyeth*, 720 F.3d at 1386. To the extent that the jury's verdict was based on a factual finding that such an extended screening process was not required, it was unreasonable. To the extent that the jury found the specification to be enabling in spite of that fact, its conclusion was legally erroneous in light of the Federal Circuit's holding

in *Wyeth*. Like in *Wyeth*, here, too, a patent that merely provides "a starting point" "to engage in an iterative, trial-and-error process to practice the claimed invention," lacks enablement. *Id.* at 1386 (internal quotation omitted).[21]

f. Comparison to *Enzo*

Still further support for the Court's conclusion is found in a comparison of the instant case to this Court's recent decisions in the *Enzo* cases.

In *Enzo Life Sciences., Inc. v. Gen-Probe Inc.*, 2017 WL 2829625, at *7 (D. Del. June 28, 2017); *Enzo Life Sciences, Inc. v. Abbott Laboratories*, 2017 WL 3585618 (D. Del. Aug. 15, 2017) (collectively, "*Enzo*"), this Court found claims to be nonenabled because they were "far broader" than in *Wyeth*, the relevant disclosures were "far less" than in *Wyeth*, the "relevant field is even more unpredictable" than in *Wyeth*, and the trial-and-error screening process to practice

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[21]Idenix is generally correct that enablement does not require that a POSA be able to actually make and use every embodiment and to do so within some definite, short period. (*See generally* Arg. Tr. at 50-51) ("[T]he meaning of . . . enable[ment] for the full scope of the claim is that a skilled artisan can take this invention, 2'-methyl ribonucleosides, not specific to OH down, and can . . . make such compounds without undue experimentation. It doesn't mean that they can make them all simultaneously this week but if they wanted, if they set out to try to make a compound, they will be able to do that without undue experimentation.")) Still, an enabling disclosure is the "*quid pro quo* of the right to exclude," *J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Intern., Inc.*, 534 U.S. 124, 142 (2001) (emphasis in original), and Idenix was accordingly obliged to provide a disclosure that would enable every species of the broad genus it claims, *see Wyeth.*, 720 F.3d at 1385 (observing that "practicing the full scope of the claims would require synthesizing ***each*** of at least tens of thousands of compounds"). The Federal Circuit has held that, to be enabling, a patent specification must teach a POSA "how to make and use the ***full scope*** of the claimed invention without undue experimentation." *MagSil*, 687 F.3d at 1380 (internal quotation marks omitted; emphasis added). What this directive means in the context of any particular patent – including how long it may take a POSA to make and use every embodiment – before any particular patent is deemed to lack an adequately enabling disclosure, can vary. Here, as in *Wyeth*, given the unpredictability of the art, and the consequent reality that synthesis and screening were necessary before a POSA could determine if a given compound meeting the structural limitations is also active and effective for the purpose stated in the claim, the only reasonable conclusion is that the claims here are not enabled.

the entire scope of the broad claims "would have taken even longer" than in *Wyeth*. The comparison here to *Enzo* is difficult, as the total breadth of the claims of the '597 patent is unclear, the '597 patent's disclosures appear broader than those involved in *Wyeth*, the fields appear similarly unpredictable, and the evidence of record leaves it unclear as to just how long the relevant experimentation would take.

But, similarly to in *Enzo*, the '597 patent essentially discloses an iterative screening plan for isolating effective compounds, with one useful guidepost (2'-methyl up) and other markers that are not especially helpful.

In attempting to distinguish *Enzo*, Idenix falls back on the undisputed fact that it was "routine in this field for skilled artisans to arrange and work with classes of compounds on the order of a billion." (D.I. 554 at 10) Even so, it is clear that, as in *Wyeth*, exploring the claims' full scope would require synthesizing and screening a significant number of candidates, time-consuming processes with unpredictable results.

In sum, while the comparison to *Enzo* may not favor Gilead as strongly as Gilead contends, it does nothing to help Idenix.[22]

g. Conclusion with respect to enablement

For the reasons stated above, a reasonable jury, even taking all the evidence in the light most favorable to Idenix and drawing all reasonable inferences in favor of Idenix, could only

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[22]Idenix compares this case to *Uropep*, 2017 WL 3676736, in which Federal Circuit Judge Bryson, sitting by designation, rejected a JMOL motion following a jury verdict denying a nonenablement defense. While the Court has carefully considered *Uropep*, the Court concludes that the more pertinent comparisons are to *Wyeth* and *Enzo*. Each case, of course, must rise or fall on its own facts, and here these fully support Gilead's position (under the applicable law), and not Idenix's.

have concluded that Idenix's '597 patent is invalid due to lack of enablement. The only reasonable finding, based on the trial record, is that Gilead met its burden to prove nonenablement by clear and convincing evidence. The trial revealed that there are no genuinely disputed material facts with respect to enablement. Accordingly, Gilead is entitled to judgment as a matter of law that the asserted claims of the '597 patent are invalid due to lack of enablement.

V. CONCLUSION

For the reasons given above, the Court finds that the '597 patent is invalid for lack of enablement, and Gilead's renewed motion for judgment as a matter of law will be granted on that basis. The Court will deny Gilead's JMOL as to damages and written description. An appropriate Order follows.