NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

PFIZER INC., WARNER-LAMBERT COMPANY LLC, AND C.P. PHARMACEUTICALS INTERNATIONAL C.V.,
Plaintiffs-Appellees,

AND

NORTHWESTERN UNIVERSITY,
Plaintiff-Appellee,

v.

TEVA PHARMACEUTICALS USA, INC. AND TEVA PHARMACEUTICAL INDUSTRIES, LTD.,
Defendants-Appellants,

AND

LUPIN, LTD. AND LUPIN PHARMACEUTICALS, INC.,
Defendants-Appellants,

AND

ACTAVIS, INC. AND ACTAVIS ELIZABETH, LLC,
Defendants-Appellants,

AND

COBALT LABORATORIES, INC. AND

COBALT PHARMACEUTICALS, INC.,
Defendants-Appellants,

AND

SUN PHARMA GLOBAL, INC.,
SUN PHARMACEUTICAL INDUSTRIES, LTD.,
AND SUN PHARMACEUTICAL INDUSTRIES, INC.,
Defendants-Appellants,

AND

WOCKHARDT LIMITED AND WOCKHARDT USA, LLC,
Defendants-Appellants,

AND

ALPHAPHARM PTY. LTD. AND
MYLAN PHARMACEUTICALS, INC.,
Defendants-Appellants.

2012-1576, -1601, -1602, -1603, -1604, -1605, -1607

Appeals from the United States District Court for the District of Delaware in Nos. 09-CV-0307, 09-CV-0308, 09-CV-0309, 09-CV-0310, 03-CV-0311, 09-CV-0312, 09-CV-0313, 09-CV-0315 and 10-CV-0853, Chief Judge Gregory M. Sleet.

Decided: February 6, 2014

DIMITRIOS T. DRIVAS, White & Case LLP, of New York, New York, argued for plaintiffs-appellees Pfizer

Inc., et al. With him on the brief were JEFFREY J. OELKE, ADAM GAHTAN, BRENDAN G. WOODARD, ROBERT E. COUNIHAN, and RYAN P. JOHNSON, for plaintiffs-appellees, Pfizer Inc., et al. Of counsel on the brief were KEVIN M. FLOWERS, MATTHEW C. NIELSEN and MARK H. IZRAELEWICZ, Marshall, Gerstein & Borun, LLP, of Chicago, Illinois, for plaintiff-appellee Northwestern University.

JAMES F. HURST, Winston & Strawn, LLP, of Chicago, Illinois, argued for defendants-appellants Sun Pharma Global, Inc., et al. Of counsel was GEOFFREY P. EATON, of Washington, DC.

TIMOTHY H. KRATZ, McGuireWoods LLP, of Atlanta, Georgia, argued for defendants-appellants Alphapharm Pty. Ltd., et al. With him on the brief were ROBERT L. FLORENCE and GEORGE J. BARRY, III. With him on the brief for defendants-appellants Cobalt Laboratories, Inc., et al. were E. ANTHONY FIGG, JOSEPH A. HYNDS, R. ELIZABETH BRENNER-LEIFER and CHRISTINA NICHOLE GIFFORD, Rothwell, Figg, Ernst & Manbeck, P.C., of Washington, DC; for defendants-appellants Actavis, Inc., et al. were FRANCIS H. MORRISON, III, and JONATHAN A. HARRIS, Axinn, Veltrop & Harkrider LLP, of Hartford, Connecticut; for defendants-appellants, Teva Pharmaceuticals USA, Inc., et al. were JAMES GALBRAITH, ANTONY PFEFFER, MATTHEW C. RUEDY, and LINNEA P. CIPRIANO, Kenyon & Kenyon, LLP, of New York, New York; for defendants-appellants Lupin Ltd., et al. were ROBERT F. GREEN, CARYN C. BORG-BREEN, CHRISTOPHER T. GRIFFITH, ELIZABETH M. CROMPTON, Leydig, Voit & Mayer Ltd., of Chicago, Illinois; for defendants-appellants Wockhardt Limited, et al. were JOSEPH M. REISMAN, JAY R. DESHMUKH, and THOMAS P. KRZEMINSKI, Knobbe, Martens, Olson & Bear, LLP, of San Diego, California.

Before RADER, *Chief Judge,* PROST and MOORE, *Circuit Judges.*

PROST, *Circuit Judge.*

Defendants-Appellants Teva Pharmaceuticals USA, Inc.; Teva Pharmaceutical Industries, Ltd.; Lupin, Ltd.; Lupin Pharmaceuticals, Inc.; Actavis, Inc.; Actavis Elizabeth, LLC; Cobalt Laboratories, Inc.; Cobalt Pharmaceuticals, Inc.; Sun Pharma Global, Inc.; Sun Pharmaceutical Industries, Ltd.; Sun Pharmaceutical Industries, Inc.; Wockhardt Ltd.; Wockhardt USA, LLC; Alphapharm Pty. Ltd.; and Mylan Pharmaceuticals, Inc. (collectively, "Appellants") appeal from a final judgment of the United States District Court for the District of Delaware that found various claims of the asserted patents[1] infringed and from the court's holdings regarding enablement,[2] written description,[3] and obviousness. *Pfizer Inc. v. Teva Pharm. USA, Inc.*, 882 F. Supp. 2d 643, 732 (D. Del. 2012) ("*District Court Opinion*").

Because we agree with the district court's claim construction, we affirm the finding of infringement. We also hold that challenged claim 2 of the '819 patent is not invalid for lack of enablement, insufficient written de-

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[1] The asserted patents are: U.S. Patent Nos. 6,197,819 ("'819 patent"); 5,563,175 ("'175 patent"); 6,001,876 ("'876 patent"); and U.S. Reissue Patent No. 41,920 ("RE '920 patent"), which is a reissue of the '876 patent.

[2] Defendants-Appellants Sun Pharma Global, Inc.; Sun Pharmaceutical Industries, Ltd.; and Sun Pharmaceutical Industries, Inc. (collectively, "Sun") do not join the other Appellants in challenging the district court's enablement determination.

[3] Sun, alone among the Appellants, asserted a written description invalidity defense below and now challenges the district court's finding on appeal.

scription, or obviousness. Accordingly, we affirm the judgment of the district court.

BACKGROUND

Plaintiffs-Appellees Pfizer Inc., CP Pharmaceuticals International C.V., Warner-Lambert Company LLC, and Northwestern University (collectively, "Appellees") sued each of the Appellants under 35 U.S.C. § 271(e)(2)(A) after they submitted Abbreviated New Drug Applications ("ANDAs") to the U.S. Food and Drug Administration ("FDA") seeking approval to market a generic version of Lyrica®, a prescription drug for treating seizures and certain types of pain. Although Appellees asserted four patents against Appellants below, only two patents, the '819 and the RE '920 patent, are relevant on appeal. Due to its claim scope and the breadth of the injunction entered, the disposition of this appeal rests entirely on a single claim: claim 2 of the '819 patent.[4]

The broadest in scope of the asserted claims, claim 2 recites: "4-amino-3-(2-methylpropyl) butanoic acid, or a pharmaceutically acceptable salt thereof." '819 patent col.

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[4] Prior to the bench trial, the parties stipulated that, to the extent the district court finds claim 2 to be valid and enforceable, the Appellants' respective ANDAs are covered by the claim under the court's claim construction and the proposed products infringe. *District Court Opinion*, at 662-63. Likewise, on appeal, the parties agree that Appellants' entire case is predicated upon claim 2, i.e., the other issues are moot and Appellants lose the appeal if we affirm the district court's findings with respect to claim 2. Oral Argument at 2:41-4:24, 16:50-17:09 *available a*t http://oralarguments.cafc.uscourts.gov/default.aspx?fl=2012-1576.mp3. Accordingly, we limit our review of the district court's findings and determinations to claim 2.

27 ll. 32-33. The district court construed the term "4-amino-3-(2-methylpropyl) butanoic acid"[5] to mean "the chemical compound 4-amino-3-(2-methylpropyl) butanoic acid," without limitation as to stereochemical form.[6] *Pfizer Inc. v. Teva Pharm. USA, Inc.*, No. 09-CV-307 (D. Del. Oct. 13, 2010), ECF No. 100 ("*Markman Order*").

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[5] 4-amino-3-(2-methylpropyl) butanoic acid is also known in the chemical nomenclature as 3-isobutylGABA.

[6] Stereochemical form refers to the three-dimensional structure of molecules. In organic chemistry, stereoisomers are compounds with the same molecular formula or atomic composition, but different spatial arrangements. Enantiomers are a pair of stereoisomers that are non-superimposable mirror images of each other and often have distinct physical properties. Enantiomeric pairs include compounds that have one or more stereogenic centers, i.e., carbon atoms with four non-identical substituent atoms or groups of atoms. These compounds are thus said to be chiral.

To distinguish between different enantiomers of the same compound, chemists use various naming conventions. Enantiomers are called optical isomers because they rotate plane-polarized light in a particular direction. If the light rotates clockwise, then that enantiomer is labeled (+); its counterpart will rotate the light counter-clockwise and is labeled (-). A different nomenclature labels each stereogenic center (R) or (S) according to a set of scientific rules. A racemate (or racemic mixture) is an equal mixture of two enantiomers and therefore is not optically active (i.e., will not rotate plane-polarized light in either direction because its constituent enantiomeric pairs cancel one another out). Racemates are typically designated (R, S) because they are comprised of both R-enantiomers and S-enantiomers.

Pregabalin, the active ingredient in Lyrica®, is the S-enantiomer of 3-isobutylGABA.[7] It is specifically disclosed by claim 1 of the '819 patent as "[a] compound of the formula S-(+)-4-amino-3-(2-methypropyl) butanoic acid as a single optical isomer." '819 patent col. 27 ll. 29-31. The district court construed the claim to mean "4-amino-3-(2-methylpropyl) butanoic acid in the single S-(+) isomer form only, free of the R-(-) isomer form." *Markman Order*, at 1.

After a bench trial in the consolidated Hatch-Waxman action, the district court held, inter alia, that claim 2 is not invalid for lack of enablement, insufficient written description, or obviousness. *District Court Opinion*, at 732. Because the Appellants stipulated to infringement, the court thereafter enjoined them from commercially manufacturing, using, offering for sale, or selling their proposed products prior to December 30, 2018—the expiration date of the '819 patent after the FDA's extension of its term under 35 U.S.C. § 156. *See id.* at 656, 730, 732.

This appeal followed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

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[7] In pharmacology, often only one enantiomer of a chemical compound is responsible for certain desired therapeutic effects, while the other enantiomer is less effective or inactive. This well-known phenomenon is attributable to the distinct physical structures of enantiomers. With respect to 3-isobutylGABA, the S-enantiomer is the pharmaceutically useful stereoisomer for the treatment of seizures and pain, while the R-enantiomer is less potent.

DISCUSSION

I. CLAIM CONSTRUCTION AND INFRINGEMENT

Claim construction is an issue of law that we review de novo. *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1454-55 (Fed. Cir. 1998) (en banc). In construing a claim term, we look at the term's plain and ordinary meaning as understood by a person of ordinary skill in the art. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (en banc). There are two exceptions to this general rule: (1) when a patentee sets out a definition and acts as her own lexicographer, or (2) when the patentee disavows the full scope of a claim term either in the specification or during prosecution. *Thorner v. Sony Computer Entm't Am., LLC*, 669 F.3d 1362, 1365 (Fed. Cir. 2012). The subsequent infringement analysis is reviewed for clear error after a bench trial. *Alza Corp. v. Mylan Labs., Inc.*, 464 F.3d 1286, 1289 (Fed. Cir. 2006).

Appellants argue that the district court erred in construing claim 2 of the '819 patent to cover 3-isobutylGABA generally. They contend that the proper construction of claim 2 is that it covers only racemic (i.e., a 50:50 mixture of S- and R-enantiomers of) 3-isobutylGABA. Appellants contend that the patent specification, prosecution history, and applicant declarations submitted to the U.S. Patent and Trademark Office ("PTO") support a narrower construction of the claimed compound as a racemic mixture. Finally, they argue that because their proposed products contain non-racemic mixtures, they do not infringe.

Appellees counter that a narrower construction would ignore the plain, clear, and specific language of the claim, which places no limitation on the claimed chiral compound. Appellees submit that the patentee's inclusion of test results of the compound's racemate in the specification, juxtaposed with the lack of a racemic limitation in the claim language, demonstrates the patentee's intent

not to limit the compound being claimed to its racemate. Appellees also point out that at trial, Appellants' own expert admitted that claim 2 covers "3-isobutylGABA in any isomeric form," that is, "the form is not defined." J.A. 20658.

We perceive no error in the district court's construction. The plain language of the claim does not include the narrowing limitation that the Appellants desire. The patent specification discusses 4-amino-3-(2-methylpropyl) butanoic acid as the "preferred compound" generally and without regard to its stereochemistry. *See, e.g.*, '819 patent col. 3 ll. 65-67. The specification makes clear that the patentee expressly used the word "racemate," "racemic," or its standard prefix (R, S) to refer to the chiral compound's racemate. *See, e.g.*, '819 patent col. 7 l. 39, col. 9 l. 25, col. 13 l. 23. Likewise, the patentee used standard prefixes (R) or (S) to designate a particular enantiomer of the compound. *See, e.g.*, '819 patent col. 4 ll. 7-15, col. 5 ll. 34-40, col. 7 l. 39, col. 13 l. 24. Because the patentee included no such references or prefixes in claim 2, it should not be so limited.

Appellants also note that Tables 1 and 2 in the specification report test results pertaining only to the compound's racemate, but not other mixtures with differing enantiomeric compositions. *See* '819 patent tables 1, 2. Appellants contend that this limited association of the subject matter of claim 2 with only racemic 3-isobutylGABA warrants a narrower construction. We disagree. Absent a clear disavowal or lexicographic definition in the specification or the prosecution history, the reporting of test results limited to a racemate does not warrant importing a racemic limitation into claim 2. Moreover, rather than listing 3-isobutylGABA in Tables 1 and 2 without specifying its form, the patentee used the prefix (R, S) to specify that the compound being tested was a racemic mixture. Contrary to Appellants' suggestion, the patentee's use of the prefix in the tables demon-

strates that it knew how to specify racemic 3-isobutylGABA as distinguished from the compound generally and chose not to do so in claim 2.

Indeed, the district court correctly observed in its claim construction order that "when the patentee identified the racemate in the specification, it used a prefix (R, S) that does not appear in the disputed claim." *Markman Order*, at 1 n.2. The court also correctly noted that the prosecution history cited to by the Appellants also "does not evince a disclaimer of non-racemic forms," *id.*, to warrant departure from the general rules of claim construction. There is no basis elsewhere in the intrinsic record to support Appellants' suggestion that the absence of an (R) or (S) prefix in claim 2 specifically signals the racemate, rather than the compound without limitation as to stereochemical form or composition. Accordingly, we affirm the district court's construction.

Because claim 2 was correctly construed to include 3-isobutylGABA regardless of its enantiomeric forms and infringement was stipulated to by the Appellants under this construction, we also affirm the finding of infringement.

II. ENABLEMENT

Enablement is a question of law that we review without deference, based on underlying factual inquiries that we review for clear error after a bench trial. *Cephalon, Inc. v. Watson Pharm., Inc.*, 707 F.3d 1330, 1336 (Fed. Cir. 2013). To be enabling under 35 U.S.C. § 112(a), a patent's specification must describe the invention and the manner and process of making and using it, in such full, clear, concise, and exact terms, as to allow any person skilled in the art "to make and use the full scope of the claimed invention without undue experimentation." *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377, 1380 (Fed. Cir. 2012) (internal quotation marks omitted).

The '819 patent, issued on March 6, 2001, claims priority to U.S. Patent Application Serial No. 07/618,692 ("'692 application"), which was filed on November 27, 1990. '819 patent col. 1 ll. 6-12. The district court held that, based on its construction, claim 2 is sufficiently enabled by the '692 application because "a person of skill in the art could have relied upon [the] application's disclosure to prepare 3-isobutylGABA . . . [with] no more than routine experimentation." *District Court Opinion*, at 655.

Appellants[8] contend that because claim 2 was construed to cover all compositions of 3-isobutylGABA, without limitation as to isomeric form, to be sufficiently enabling the '692 application must teach a skilled artisan how to prepare every conceivable mixture of 3-isobutylGABA's enantiomers. Although the parent application acknowledges that hundreds of permutations of non-racemic mixtures of 3-isobutylGABA exist, *see* J.A. 3010-13, Appellants assert that it fails to disclose how to prepare them. Appellants also contend that the '692 application provides nothing more than boilerplate language pointing to unspecified prior art as the basis for making the claimed invention, and fails to disclose the required starting materials, reaction conditions, and other working examples.

We are not persuaded by Appellants' arguments. First, there is no requirement that a specification must "disclose what is routine and well known in the art." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997). Second, as the district court found, there is no dispute in the record that the co-inventors of the '819 patent were the first to create and claim the chemical compound 3-isobutylGABA. *District Court Opinion*, at

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[8] Reference to Appellants in this section does not include Sun, who does not join the other Appellants in challenging the district court's enablement determination.

689. It is also undisputed that the parent application discloses the method for synthesizing the compound and states that the compound's "enantiomers may be prepared or isolated by methods already well known in the art." J.A. 3012-14. The district court found support for this fact in the prior art, the prosecution history, and witnesses' trial testimonies. *See District Court Opinion*, at 683-87; *see also* J.A. 3012-14, 21196-203, 21168-69, 21172-80, 20622-24, 21205-06. The court also acknowledged that the same conclusion was reached by the PTO Examiner, who withdrew an enablement rejection on that very basis during prosecution of the patent. *District Court Opinion*, at 689 n.41.

In view of the finding that enantiomer separation methods are well-known and routine to a person of ordinary skill, we agree with the district court that the inventors were not required to provide a detailed recipe for preparing every conceivable permutation of the compound they invented to be entitled to a claim covering that compound. Where a claim has been construed to cover a chemical compound, the specification is not deficient merely because it does not disclose how to prepare a particular form or mixture—among hundreds of possible permutations—of that compound. *See In re Hogan*, 559 F.2d 595, 606 (CCPA 1977) (noting that requiring such specific disclosures would "impose an impossible burden on inventors").

Instead, claim 2 satisfies the requirements under § 112(a) because the '692 application's disclosure, coupled with the methods for synthesis and resolution that were found to be well-known and routine in the art, is sufficiently enabling. The district court's legal determination of enablement was not incorrect. Its factual findings are not clearly erroneous. We therefore affirm the determination that claim 2 is not invalid for lack of enablement.

III. WRITTEN DESCRIPTION

Compliance with the written description requirement is a question of fact reviewed for clear error following a bench trial. *Lampi Corp. v. Am. Power Prods.*, 228 F.3d 1365, 1378 (Fed. Cir. 2002). A party alleging that a patent is invalid for lack of written description has the burden of establishing by clear and convincing evidence that a patent disclosure does not reasonably convey to a skilled artisan that the inventor was in possession of the claimed invention at the time of the patent application. *See Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

The district court found claim 2 of the '819 patent not invalid for lack of written description. The court found the '692 application to have expressly claimed 3-isobutylGABA in both racemic and non-racemic mixtures, and detailed the inventor's method for synthesizing the compound. *District Court Opinion*, at 702. The court also found the parent application to have included seven claims specifically directed to the compound or its use in pharmaceutical compositions or methods of treatment, as well as repeatedly identified it as the preferred embodiment of the invention. *Id.* The court noted the testimony of the other Appellants' enablement expert in which he admitted that "chemists would understand what the disclosure" in the '692 application meant, *id.*, as well as Sun's dearth of evidence at trial, before concluding that the application's descriptions were more than sufficient to meet the written description standard. *Id.*

Sun alone presses a written description argument on appeal. First, Sun argues that although the '692 application discloses a chemical synthesis method for the racemate of 3-isobutylGABA, *see* J.A. 21263-64, 20768, it discloses nothing towards the isolation of the enantiomers, even though claim 2 of the '819 patent has been construed to encompass all forms of the compound.

Second, according to Sun, despite the patentee describing the separation of the racemate (i.e., isolation of the enantiomers) as anything but routine in later applications, at the time of the '692 application, both inventors readily admitted that they had not yet separated the racemic mixture to obtain a purified enantiomer. *See* J.A. 20814-18. Taken together, Sun contends, these facts establish that the inventors had not actually invented 3-isobutylGABA in all of its forms in 1990.

Sun's position on written description is surprisingly similar to the other Appellants' position on enablement. Sun conflates the disclosure requirement for claim 2 with that for claim 1: it argues that because the inventors had not sufficiently described the narrower claim 1 (to pregabalin) they could not have sufficiently described the broader claim 2 (to 3-isobutylGABA).

But written description does not require inventors, at the time of their application for a patent, to reduce to practice and be in physical possession of every species (e.g., the S-enantiomer of 3-isobutylGABA) of a genus (3-isobutylGABA) claim. For claims to a chemical compound, an application satisfies the written description requirement when it details "relevant identifying characteristics" such that the compound can be distinguished from other compounds. *In re Wallach*, 378 F.3d 1330, 1333, 1335 (Fed. Cir. 2004). Here, the '692 application not only disclosed the structure of 3-isobutylGABA as the preferred embodiment of the invention, *see* J.A. 3018-19, 20764:11-14, 3011, but also set forth in vitro and in vivo data for the compound, J.A. 3025-29, 20766:19-21, and described a method of synthesizing the compound, J.A. 3012-14, 20900. As the district court correctly found, such a description is sufficient for persons of ordinary skill in the art to recognize that the inventor invented what is claimed. *Union Oil Co. of Cal. v. Atl. Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000)

We therefore affirm the finding that the '692 application provided an adequate written description for claim 2 under § 112(a).

IV. OBVIOUSNESS

The determination of obviousness is a legal conclusion based on underlying facts. *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1290-91 (Fed. Cir. 2013). After a bench trial, we review the district court's factual findings for clear error and its conclusions of law de novo. *Honeywell Int'l, Inc. v. United States*, 609 F.3d 1292, 1297 (Fed. Cir. 2010). A patent claim is invalid for obviousness if "the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103. The "underlying factual considerations in an obviousness analysis include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations[,]" which include "commercial success, long-felt but unsolved needs, failure of others, and unexpected results." *Allergan*, 726 F.3d at 1290-91 (citations omitted). Patent invalidity must be established by clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2242 (2011).

The district court concluded that the evidence presented by Appellants at trial was insufficient to render claim 2 invalid under § 103. The district court held that claim 2 would not have been obvious in view of the three prior art references cited by Appellants: U.S. Patent No. 4,322,440 ("Fish"), U.S. Patent No. 5,051,448 ("Shashoua"), and a 1962 article published at pages 598 through 603 in the *Bulletin de la Société Chimique de France* ("Colonge"). It found that these references did not teach

skilled artisans to select 3-isobutylGABA for its anticonvulsant activity. *District Court Opinion*, at 667. Specifically, the court found that Appellants provided neither "information detailing what [chemical] structures were important for anticonvulsant activity [research] in 1990" nor "teachings from the Colonge, Fish, and Shashoua references, which, individually or combined, would have directed one skilled in the art" to arrive at the claimed invention, i.e., to substitute alkyl groups[9] at GABA's 3-position.[10] *Id.* The court also determined that various secondary considerations—namely, unexpected results, long felt but unmet need, commercial success, and industry recognition—strongly supported the conclusion of nonobviousness. *Id.* at 667-72.

Appellants contend on appeal that the district court clearly erred in failing to make the following findings: (1) Fish, Shashoua, and Colonge taught that 3-isopropylGABA and other homologous compounds may have anticonvulsant activity; (2) one of ordinary skill in the art would have expected 3-isobutylGABA to have anticonvulsant activity due to its structural similarities to 3-isopropylGABA; and (3) gabapentin, a 3-alkylGABA compound in the prior art with demonstrated anticonvulsant efficacy, provided a motivation for persons skilled in the art to try other alkyl substituents at GABA's 3-position.

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[9] An alkyl group is a carbon chain of varying length and orientation. Isobutyl is a four-carbon alkyl group with a specific carbon configuration. There are potentially infinite alkyl groups.

[10] GABA stands for "gamma aminobutyric acid," which is a neurotransmitter that can cause seizures when its levels in the brain are abnormally low. GABA has a four-carbon structural backbone. The term "3-position" refers to the third carbon on GABA's backbone.

According to the district court and Appellees, Appellants failed to make an obviousness case because the evidence presented at trial was too sparse. We agree.

Whether a new chemical compound would have been prima facie obvious over particular prior art compounds follows a two-part inquiry under our precedent. First, the court determines whether a chemist of ordinary skill in the art would have selected the asserted prior art compound as a lead compound, or starting point, for further development. *Eisai Co. v. Dr. Reddy's Labs., Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008). A lead compound is a compound in the prior art that would be "most promising to modify in order to improve upon its activity and obtain a compound with better activity." *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). The selection analysis may be guided by evidence of the compound's pertinent properties, such as chemical activity or potency. *See Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1378 (Fed. Cir. 2006). Mere structural similarity between a prior art compound and the claimed compound does not inform the lead compound selection. *Otsuka Pharm. Co. v. Sandoz Inc.*, 678 F.3d 1280, 1292 (Fed. Cir. 2012); *see Daichii Sankyo Co. v. Matrix Labs., Ltd.*, 619 F.3d 1346, 1354 (Fed. Cir. 2010).

On the selection of a lead compound, the district court found that the Appellants "did not point to any evidence in the prior art indicating that a particular compound or class of compounds, including alkyl-substituted GABA analogs . . . would improve anti-seizure treatment." *District Court Opinion*, at 667. We agree that the record contains scant evidence that either gabapentin or 3-isopropylGABA would have been selected as a lead compound.

With respect to gabapentin, no evidence in the record firmly situates gabapentin in the prior art or otherwise

supports its selection as a lead compound. At most, Appellants established that gabapentin was being tested for its anticonvulsant effect contemporaneously with 3-isobutylGABA, *see* J.A. 20849, but there is no testimony establishing its being tested prior to the discovery of 3-isobutylGABA. Appellants note that Appellees' expert admitted that by 1990, gabapentin had entered Phase III clinical trials, *see* J.A. 20982-83, but no testimony indicates that the trials or results therefrom had been disclosed publicly by then.

Further, there is no evidence in the record of motivation for a skilled artisan to modify gabapentin for further anticonvulsant research. Appellees submit that Appellants have failed to provide the most basic details about gabapentin, such as a discussion of its advantages over other compounds, biological or other data, or mechanism of action—any of which would have aided the selection analysis. Instead, Appellants chose to emphasize that gabapentin was a solid choice for a skilled artisan based on its structural similarity to pregabalin, a fact the specification of the '819 patent acknowledged. *See* '819 patent col. 13 ll. 12-16. A patent challenger, however, must demonstrate the selection of a lead compound based on its "promising useful properties," not a hindsight-driven search for structurally similar compounds. *Daichii*, 619 F.3d at 1354.

Record evidence supporting 3-isopropylGABA's candidacy as a lead compound is just as meager. Appellants suggest that the disclosure of 3-isopropylGABA in the Fish, Shashoua, and Colonge references would have directed a skilled artisan to modify other substituent groups at GABA's 3-position. The district court found, however, that Appellants failed to make the case for why 3-isopropylGABA would have been selected for further research in the first place, because the record lacks any explanation for "what structures were important for anticonvulsant activity[.]" *District Court Opinion*, at 667.

Indeed, nothing in the Fish, Shashoua, and Colonge references single out 3-isopropylGABA, among the other compounds within the references' broad disclosures, as a promising compound to modify due to its anticonvulsant effect. In addition, these references fail to identify a lead compound because they disclose nothing concrete about 3-isopropylGABA or its mechanisms of action, including whether it has anticonvulsive properties. *See Daiichi*, 619 F.3d at 1352 (requiring a lead compound to have properties that are similar to or improvable by the new compound). Therefore, the district court did not clearly err when it concluded that "the evidence [Appellants] presented is insufficient to show clearly and convincingly that skilled artisans would have known to select 3-isobutylGABA in November 1990 based simply on the fact that it is a homologous compound" to 3-isopropylGABA. *District Court Opinion*, at 666-67.

Proof of obviousness of a chemical compound "clearly depends on a preliminary finding that one of ordinary skill in the art would have selected [a particular prior art compound] as a lead compound." *Takeda*, 492 F.3d at 1357. The second step of the obviousness analysis requires a showing that the prior art would have taught a skilled artisan to make "specific molecular modifications" to a lead compound so that the claimed compound may be made with a reasonable expectation of success. *Id*. at 1356-57.

Beyond Appellants' failure to establish a lead compound as a threshold, the record also supports the district court's finding that Appellants failed to identify the teachings required in the second step of the inquiry. According to Appellants, the disclosures in Fish, Shashoua, and Colonge would have taught a skilled artisan to modify "lower alkyl substitutes"—which includes isobutyl—at GABA's 3-position to achieve 3-isobutylGABA. However, it is quite evident that the Fish, Shashoua, and Colonge references together disclosed trillions of com-

pounds without calling out alkyl groups in particular or singling out isobutyl specifically. As the district court correctly found, the Appellants "did not point to any evidence in the prior art indicating that a particular compound or class of compounds" nor "identify any teachings as of the filing date that would have directed a skilled artisan to substitute [at GABA's 3-position] with an isobutyl group, as opposed to any other alkyl group[.]" *District Court Opinion*, at 667. Indeed, a vague suggestion in the prior art pointing to a broad class of compounds, without any teaching particularly identifying isobutyl among the millions of potential compounds, is not a teaching of "specific molecular modifications" required by our precedent. *Takeda*, 492 F.3d at 1356. Finally, the district court found Appellees to have credibly established that anticonvulsant drug discovery in 1990 was "complicated," "unpredictable," and "largely conducted through trial and error." *District Court Opinion*, at 667. This finding would have precluded any argument by Appellants that there would have been a "reasonable expectation of success" to achieve an anticonvulsant in 3-isobutylGABA even if Appellants were able to establish that the prior art taught the substitution of isobutyl at GABA's 3-position.

The district court did not err in finding that Appellants failed to establish that gabapentin or 3-isopropylGABA would have been selected as lead compounds, or that Appellants failed to set forth evidence identifying the necessary teachings for a skilled artisan to modify alkyl groups at GABA's 3-position to improve anticonvulsant activity. Because we agree with the district court that the Appellants failed to prove that claim 2 would have been prima facie obvious over the asserted prior art compounds, we need not address the court's findings regarding secondary considerations of nonobviousness. *See Otsuka*, 678 F.3d at 1296.

CONCLUSION

We have considered the Appellants' remaining arguments and do not find them to be persuasive. We hold that the district court did not err in its conclusion that claim 2 of the '819 patent has been infringed, and that Appellants failed to prove that the claim is not enabled, insufficiently described, or obvious. Based on the foregoing, the parties' arguments with respect to the other patent claims are moot. Accordingly, we affirm the district court's judgments of infringement and no invalidity.

AFFIRMED