MCDERMOTT WILL & EMERY LLP
THOMAS P. STEINDLER (*Pro Hac Vice*)
tsteindler@mwe.com
500 N. Capitol St., N.W.
Washington, DC 20001
Tel: (202) 756-8000
Fax: (202) 756-8087

(*Add'l counsel on signature page*)

IN THE UNITED STATES DISTRICT COURT

FOR THE NORTHERN DISTRICT OF CALIFORNIA

OAKLAND DIVISION

PLEXXIKON INC., Plaintiff, v. NOVARTIS PHARMACEUTICALS CORPORATION, Defendant.	Case No. 4:17-cv-04405-HSG **DEFENDANT'S MOTION FOR JUDGMENT AS A MATTER OF LAW** Date: Time: Judge: Hon. Haywood S. Gilliam, Jr. Ctrm: 2 – 4th Floor

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NOTICE OF MOTION AND MOTION FOR JUDGMENT AS A MATTER OF LAW

TO PLAINTIFF PLEXXIKON INC. and its attorneys of record:

PLEASE TAKE NOTICE that, pursuant to Fed. R. Civ. P. 50(a), on Tuesday, July 20, 2021, in Courtroom 2, 4th Floor of the Oakland Courthouse, 1301 Clay Street, Oakland, California 94612, Defendant Novartis Pharmaceuticals Corporation ("Novartis") will and does respectfully move for judgment as a matter of law of anticipation, obviousness, no written description, no enablement, limited damages, and no willfulness. The parties have been fully heard on these issues and no reasonable juror could find the patents not anticipated, non-obvious, containing sufficient written description and enablement, award the requested damages, or find the alleged infringement to be willful. Judgment should be entered for Novartis.

This motion is based upon this Notice of Motion and Motion, the Memorandum of Points and Authorities in support thereof, the evidence presented at trial, the briefing filed herein and in opposition hereto, and such other argument and evidence as may properly be presented to the Court.

MEMORANDUM OF POINTS AND AUTHORITIES

I. INTRODUCTION

Before Plaintiff Plexxikon, Inc.'s ("Plexxikon") priority date of July 17, 2007, GlaxoSmithKline plc ("GSK") reduced to practice three compounds (GSK1, GSK2, and GSK3) that, under 35 U.S.C. § 102(g)(2), anticipate claim 1 of the '640 patent and claims 1, 5, and 7 of the '539 patent, and render obvious claim 9 of the '640 patent. The only element of Novartis' § 102(g) defense that has been genuinely in dispute at trial is whether Plexxikon can establish an earlier invention date, specifically March 10, 2005. Plexxikon has been fully heard on the issue, and the record makes clear that no reasonable juror could find that Plexxikon is entitled to a March 10, 2005 invention date. Further, based on the evidence adduced, a reasonable juror must conclude the '640 and '539 patents (collectively, the "Asserted Patents") lack written description and/or enablement, that a royalty rate of no more than 7% would apply post-2018, and that any infringement was not willful. Accordingly, Novartis is entitled to judgment as a matter of law ("JMOL").

II. LEGAL STANDARD FOR JUDGMENT AS A MATTER OF LAW

A court may grant a motion for JMOL against a party on a claim or issue where the party has been "fully heard on [that] issue during a jury trial" and the court finds that a "reasonable jury would not have a legally sufficient evidentiary basis" to find for that party. Fed. R. Civ. P. 50(a). A JMOL motion should be granted "when the evidence permits only one reasonable conclusion as to the verdict." *McGonigle v. Combs*, 968 F.2d 810, 816 (9th Cir. 1992). "When an expert opinion is not supported by sufficient facts to validate it in the eyes of the law, or when indisputable record facts contradict or otherwise render the opinion unreasonable, it cannot support a jury's verdict." *Brooke Grp. Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209 (1993).

III. ARGUMENT

A. Anticipation

"It is [ ] an elementary principle of patent law that" when "a claim covers several compositions, the claim is 'anticipated' if *one* of them is in the prior art." *Titanium Metals Corp.*

v. Banner, 778 F.2d 775, 779 (Fed. Cir. 1985). Thus, a patent challenger invalidates a patent where "an earlier species reference anticipates a later genus claim." *Atofina v. Great Lakes Chem. Corp.*, 441 F.3d 991, 999 (Fed. Cir. 2006).

Under 35 U.S.C. § 102(g)(2), a party asserting invalidity "must prove facts by clear and convincing evidence establishing a prior invention that was not abandoned, suppressed, or concealed." *Apotex USA, Inc. v. Merck & Co. Inc.*, 254 F.3d 1031, 1035 (Fed. Cir. 2001). "[O]nce a challenger of a patent has proven by clear and convincing evidence that 'the invention was made in this country by another inventor,' 35 U.S.C. § 102(g), the burden of production shifts to the patentee to produce evidence sufficient to create a genuine issue of material fact as to whether the prior inventor has suppressed or concealed the invention." *Id.* at 1037. If "the patentee has satisfied its burden of production, the party alleging invalidity under § 102(g) must rebut any alleged suppression or concealment with clear and convincing evidence to the contrary." *Id.*

"The invention date is the date of conception." *Allergan*, 754 F.3d at 967. Conception requires "formation in the mind of the inventor, of a *definite* and *permanent* idea of the *complete* and *operative invention*, as it is hereafter to be applied in practice." *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1227 (Fed. Cir. 1994) (emphasis added). Conception is definite when the inventors have "a specific, settled idea" and a "particular solution to the problem at hand." *Dawson v. Dawson*, 710 F.3d 1347, 1352 (Fed. Cir. 2013). Conception is complete when "the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." *Id.*

It is well-established that conception must include each claimed limitation. *See Cumberland Pharm. Inc. v. Mylan Inst. LLC*, 846 F.3d 1213, 1218 (Fed. Cir. 2017); *REG Synthetic Fuels, LLC v. Neste Oil Oyj*, 841 F.3d 954, 962 (Fed. Cir. 2016); *Taurus IP, LLC v. DaimlerChrysler Corp.*, 726 F.3d 1306, 1323 (Fed. Cir. 2013).

For chemical inventions, conception requires both "(1) the idea of the structure of the chemical compound, and (2) possession of an operative method of making it." *Oka v. Youssefyeh*,

849 F.2d 581, 583 (Fed. Cir. 1998). "[C]onception of a chemical compound requires that the inventor be able to define [the compound] so as to distinguish it from other materials[.]" *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). In other words, the inventor must have "a mental picture of the structure of the chemical." *Vanderbilt Univ. v. ICOS Corp.*, 601 F.3d 1297, 1301 (Fed. Cir. 2010). And that mental picture "must be proven by evidence showing what the inventor disclosed to others and what that disclosure means to one of ordinary skill in the art." *In re Jolley*, 308 F.3d 1317, 1321 (Fed. Cir. 2002). This standard is exacting, as "[t]he conception analysis necessarily turns on the inventor's ability to describe his invention *with particularity*." *Burroughs*, 40 F.3d at 1228 (emphasis added).

Where a chemical compound is claimed the inventor must have "the compound with all of its components" not just "specific portions of a claimed compound." *Bd. Of Educ. Ex rel. Rd. of Trustees of Fla. State Univ. v. Am. Bioscience, Inc.*, 333 F.3d 1330, 1340 (Fed. Cir. 2003) ("*Am. BioSci.*"); *see also, e.g.*, *Bosies v. Benedict*, 27 F.3d 539, 543 (Fed. Cir. 1994) (holding that a laboratory notebook entry that disclosed that the length of a hydrocarbon chain in a generic formula for a compound should be "n" did not establish adequate conception of an invention in which the chain is 2-8). Where evidence of conception discloses compounds broader than the invention, the evidence must "fairly suggest to one of ordinary skill the subject matter of the [claim], without the need for extensive experimentation to ascertain whether the matter encompassed by the disclosure suggests that desirable features of compositions belonging to the [claim]." *Jolley*, 308 F.3d at 1323. While "conception of a species within a genus *may* constitute conception of the genus," *id.* at 1322n.2, for over half a century, the evidence of conception must "fairly suggest" to a POSA "*the particular composition claimed*[,]" *id.* at 1323 (emphasis added). "[A]n important factor to be considered in making the determination" is "the indication or lack of indication of a preference for the composition." *Id.* In order for a species to "fairly suggest" a "particular" and "prefer[red]" claimed compound "the determinative inquiry" is whether "the idea" was "sufficiently developed to support conception of the subject matter[.]" *Id.* at 1324.

When determining reduction to practice of a generic invention "[t]he question is whether the species which have been reduced to practice suffice to provide a basis for a reasonable inference of possession of the generic invention." *In re Rainer*, 390 F.2d 771, 774 (CCPA 1968). This question is answered by showing "generic applicability" such as "experiments of record." *Id.*; *In re Mantell*, 454 F.2d 1398, 1401 (CCPA 1972) (holding reduction to practice of relatively few species within the genus was insufficient "to establish possession of the *generic* invention"). Thus, when the entire genus is not reduced to practice, it is necessary that the species which were reduced to practice provide an adequate basis to demonstrate generic applicability. "[I]n order for an experiment to constitute an actual reduction to practice, there must have been contemporaneous appreciation of the invention at issue by the inventor." *Cooper v. Goldfarb*, 154 F.3d 1321, 1331 (Fed. Cir. 1998); *see Estee Lauder, Inc. v. L'Oreal S.A.*, 129 F.3d 588, 593 (Fed. Cir. 1997) ("[W]hen testing is necessary to establish utility, there must be recognition and appreciation that the tests were successful for reduction to practice to occur.").

For both conception and reduction to practice, conceiving and reducing to practice a single species generally is *not* sufficient to show earlier invention of a genus claim. *See Rainer*, 390 F.2d at 774; *In re Kyrides*, 159 F.2d 1019, 1020-23 (CCPA 1947). Although conceiving and reducing to practice a single species may be enough for the different issue of priority in an interference proceeding, patentability and validity under §§ 102 and 103 require a different analysis. *Kyrides*, 159 F.2d at 1020-23. Thus in *Kyrides*, the CCPA rejected the argument that an applicant claiming a genus could overcome prior art based on earlier conception and reduction to practice of a single species within the genus. *Id.* Even though the same applicant, based on the same evidence, had already been awarded priority in an interference to a count covering the genus based on the discovery of a single species, the single-species evidence was insufficient when the question was patentability. *Id.* (distinguishing *Kyrides v. Andersen*, 121 F.2d 514, 514-17 (CCPA 1941)).

All elements of Novartis' § 102(g) defense, except Plexxikon's prior invention, are uncontested. ***First***, Plexxikon stipulated that each of GSK1, GSK2, and GSK3 meet each element

of claim 1 of the '640 patent and claims 1, 5, and 7 of the '539 patent (collectively, the "Asserted Compound Claims"). TX510; Tr. 1355:4-7. Accordingly, each of GSK1, GSK2, and GSK3 anticipates the Asserted Compound Claims to the extent they are prior. *Titanium*, 778 F.2d at 779.

Second, Plexxikon stipulated that GSK1, GSK2, and GSK3 were synthesized by April 30, 2007, May 5, 2007, and July 9, 2007, respectively, TX510; Tr. 1355:8-10, and the unrebutted evidence is that GSK tested GSK1, GSK2, and GSK3 in its BRAF assay and determined them to be potent BRAF inhibitors on May 14, 2007 (GSK1 and GSK2) and July 16, 2007 (GSK3). TX1003; TX1004; Tr. 885:22-886:7, 1129:10-25. Because GSK reduced to practice each of GSK1, GSK2, and GSK3 before Plexxikon filed its priority application in this case, they are prior art unless GSK abandoned, suppressed, or concealed them.

Third**,** the unrebutted evidence is that GSK did not abandon, suppress, or conceal the GSK compounds. TX1006; TX1009; TX1011; TX438; Tr. 886:18-887:4, 1130:23-1131:6. The GSK compounds are thus prior art to the Asserted Compound Claims and thus anticipate them unless Plexxikon is entitled to an invention date of March 10, 2005. As a matter of law, Plexxikon is not.

Plexxikon's evidence of a prior invention is legally insufficient to antedate GSK's invention under § 102(g)(2). No reasonable juror could find that Plexxikon met its burden of production, and regardless, no reasonable juror could find that Plexxikon conceived the claimed genera on March 10, 2005, or reduced them practice before its constructive reduction to practice on July 17, 2007. Moreover, a reasonable juror could only conclude that Plexxikon was not diligent in reducing the claimed genera to practice in the period between GSK's reduction to practice of GSK1 and GSK2 (May 15, 2007) and Plexxikon's effective filing date (July 17, 2007) because the evidence shows no activity during that period.

No reasonable juror could find Plexxikon's alleged conception date to be March 10, 2005. The evidence adduced at trial is legally insufficient to meet Plexxikon's burden or establish conception of the claimed genus. The scope of the claimed invention encompasses trillions of hypothetical compounds, which were neither synthesized nor tested. Having heard the evidence

proffered at trial, no reasonable juror would have a legally sufficient evidentiary basis to find that Plexxikon conceived of the complete and operative invention claimed in the Asserted Compound Claims.

Absent appreciation of the substituents, the inventors were incapable of distinguishing the claimed compound from other compounds. Tr. 1514:11-23. And no reasonable juror could find that Plexxikon's inventors conceived of the specific compounds being claimed, with all of their component substituents. Tr. 890:18-891:17.

Claim 1 of the '640 patent, for example, permits R^1 to be an "optionally substituted lower alkyl or optionally substituted heteroaryl." Tr. 852:18-21; TX1 at col. 150:39-40. The patent sets out a definition of "optionally substituted lower alkyl" that includes a long list of possible options, many of which are defined generically. TX1 at col. 45:5-41. The patent also sets out a similarly lengthy list of options for "optionally substituted heteroaryl." TX1 at col. 49:5-34. No legally sufficient evidence supports a finding, and no reasonable juror could find that that the inventors conceived this specific list of possible options for R^1 in March 2005. Tr. 852:14-17. Moreover, claim 1 provides that there can be up to five R^1 groups by specifying that "*m*" in $(R^1)_m$ can be "0, 1, 2, 3, 4, or 5." Tr. 802:21-25. There is no evidence the inventors conceived of the options for this limitation as of March 2005 either. Claim 1 further provides that R^2 can be either hydrogen or halogen. There are multiple different species of halogens. Tr. 798:25-799:2. There is no evidence that the inventors conceived of these possible options for R^2 in March 2005.

Claim 1 further provides that R^3 can be "optionally substituted lower alkyl or optionally substituted aryl." Tr. 860:6-12. This definition is different from the definition for R^1, as it includes "optionally substituted aryl" rather than "optionally substituted heteroaryl." The patent sets out a long list of options for "optionally substituted aryl." Tr. 860:6-861:3; TX1 at col. 48:23-50. There is no evidence that the inventors conceived of the long lists of options for R^3 in March 2005, or that the options for R^3 would be different than for R^1. A reasonable juror would thus lack legally sufficient evidentiary basis to find the inventors had conceived of the generic invention claimed.

At trial, Plexxikon generally proffered evidence indicating the inventors' idea was a

chemical "scaffold." But identification of the "scaffold idea"—alone—which is precisely what Dr. Metzker testified that Plexxikon scientists conceived as of March 14 or 15, 2005, is insufficient to distinguish the claimed chemical genus from other materials, which is the touchstone of conception. *Amgen, Inc.*, 927 F.2d at 1206-07 ("Conception does not occur unless one has a mental picture of the structure of the chemical . . . so as to distinguish it from other materials."). Because there are compounds with the claimed scaffold that are *not* within the claimed genus, the scaffold itself is insufficient to "distinguish" the claimed genus "from other materials."

Further, no reasonable juror could find that Plexxikon's inventors possessed the idea of the invention's structure *and* an operative method of making it. Tr. 890:18-891:17. Plexxikon's evidence of conception does not "fairly suggest" to a POSA a preference for (or otherwise point toward) compounds or the particular composition claimed without the need for extensive experimentation. Tr. 879:22-880:9. Similarly, more than ordinary skill would be required to determine the equivalence of compounds within the scope of the claim. *See Dawson*, 710 F.3d at 1353; Dkt. No. 450. For example, even though Plexxikon claimed compounds with L_1 as a bond, the evidence failed to support a finding that the Plexxikon inventors were in possession of an operative method of making compounds of the claimed chemical genera where L_1 is a bond by March 2005. Tr. 458:9-21, 880:3-9. As it must, Plexxikon admits it never made a compound of the asserted claims where L_1 is a bond prior to filing its provisional application on July 17, 2007. Tr. 460:4-19. There is no disclosure as of March 14 or 15, 2005 of an operative method of making compounds of the asserted claims where L_1 is a bond. Tr. 457:18-458:21. Prosecution history and testimony of Dr. Baran established that over the course of the prosecution, Plexxikon repeatedly identified as elected compounds ones that fell outside the scope of what are now the Asserted Claims. *See* TX3; TX4; TX5; TX6; TX7; TX8; Tr. 805:7-822:1.

Where a patentee claims a broad genus but indicates no preference for (nor otherwise points toward) the particular compositions claimed and can neither provide evidence of "conception of the specific compounds being claimed, with all of their component substituents," as *Am. BioSci.*

requires, nor provides evidence of the requisite generic "appreciation" and "generic applicability," as *In re Walsh* requires, the patentee cannot avail itself to a prior invention date. The evidence presented at trial is legally insufficient to support a finding of conception for the broad genus claimed as of March 10, 2005. Novartis respectfully submits no reasonable juror would have a legally sufficient evidentiary basis to find that Plexxikon conceived the chemical genera of the asserted claims by March 10, 2005. Plexxikon fails to meet the conception test and thus is not entitled to an invention date earlier than July 17, 2007.

Plexxikon also fails to meet the conception test for two independent reasons. First, even assuming *arguendo* that Plexxikon evinced a preference for particularized subject matter falling within the scope of the claims—which it did not—such subject matter would be insufficient to support conception of the full scope of the claimed invention. *Price v. Symsek*, 988 F.2d 1187, 1195 (Fed. Cir. 1993). Second, Plexxikon's reliance on a single document to corroborate its alleged conception fails in light of the totality of the evidence, the only reasonable conclusion from which is that Plexxikon did not conceive compounds heaving a monocyclic heteroaryl and L_1 as a bond on March 10, 2005. Plexxikon's failure to establish conception is case dispositive.

No reasonable juror could find the reduction to practice of three compounds sufficient to establish possession of the generic invention claiming trillions of compounds. Even if there were a legally sufficient basis for a juror to find Plexxikon conceived of its invention as of March 10, 2005—which there is not—the claims are still anticipated because Plexxikon's alleged reduction to practice is legally insufficient. The evidence presented at trial does not provide a legally sufficient basis to find that Plexxikon had a generic appreciation of its claimed invention and determined that the invention would work for its intended purpose with "generic applicability." *Rainer*, 390 F.2d at 774. "[R]arely, if ever" can reduction to practice of a single species afford sufficient support for a generic claim. *In re Clarke*, 356 F.2d 987, 992 (CCPA 1966). Accordingly, when a patentee makes the strategic prosecution decision to claim a broad genus and later desires to establish an invention date earlier than its constructive reduction to practice, it bears the burden

of production to show "a considerably larger number of reductions to practice" to support conception of the generic invention. *Id.*

Legally sufficient evidence does not support finding that Plexxikon had a generic appreciation that the "compounds broadly would yield the desired results" and hence "considered their invention to be a generic one." *In re DaFano*, 392 F.2d 280, 283-84 (CCPA 1968). As of March 10, 2005, Plexxikon had no appreciation for whether the hypothetical compounds would yield the desired results. Tr. 890:18-891:17. Plexxikon had an idea for aspirational research, but no appreciation for whether the plan would or could come to fruition. *Id.*

For example, Plexxikon's identification of the "scaffold idea" is legally insufficient to distinguish the chemical genus from other materials and show a generic appreciation of compounds that would broadly yield desired results. Specifically, Plexxikon's azaindole compounds have the identical scaffold structure, but are explicitly excluded from the scope of the asserted claims. The scaffold alone thus cannot be the measuring stick to distinguish the chemical genera of the alleged conception from compounds outside the scope of the alleged conception (and asserted claims).

Moreover, Plexxikon's reduction to practice of three compounds is legally insufficient to support an inference of generic conception. Legally sufficient evidence does not support a finding that "the species which were reduced to practice provide an adequate basis for inferring that the invention has generic applicability." As Dr. Baran testified, properties such as the activity level of Plexxikon's P-0001, P-0007, and P-00012 compounds do not show generic applicability of the claimed genus. *See* TX1; TX2; Tr. 882:25-883:3. Additionally, Plexxikon never reduced to practice any compound with L_1 as a bond. Tr. 457:18-458:21. No legally sufficient evidence exists establishing the generic applicability of the compounds Plexxikon alleges it reduced to practice. Similarly, the evidence does not support a finding that a POSA would sufficiently understand the limited disclosure of reduction in order to practice the full scope of the claimed invention with only ordinary skill, rather than extensive experimentation. Tr. 879:20-880:9, 1040:9-24.

B. Obviousness

"A patent for a claimed invention may not be obtained . . . 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. Obviousness requires assessing (1) the level of ordinary skill in the pertinent art, (2) the scope and content of the prior art, (3) the differences between the prior art and the claims at issue, and (4) secondary consideration of non-obviousness such as commercial success, long-felt need, and failure of others. *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18 (1966); *KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 399, 406 (2007).

"When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. *KSR*, 550 U.S. at 421. "[I]n appropriate circumstances, a patent can be obvious in light of a single prior art reference if it would have been obvious to modify that reference to arrive at the patented invention." *Arendi S.A.R.L. v. Apple Inc.*, 832 F.3d 1355, 1361 (Fed. Cir. 2016). Section 102(g) prior art can serve as prior art for obviousness purposes under Section 103. *Tyco Healthcare Grp. LP v. Ethicon Endo-Surgery, Inc.*, 774 F.3d 968, 976-77 (Fed. Cir. 2014).

Just as GSK1, GSK2, and GSK3 anticipate claim 1 of the Asserted Compound Claims, they also render obvious claim 9 of the '640 patent, which recites "[a] pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier or excipient." The ultimate question of obviousness is one of law, determined against the background of "the scope and content of the prior art," "the differences between the prior art and the claim[] at issue," and "the level of ordinary skill in the pertinent art." *Graham*, 383 U.S. at 17. The prior art includes GSK1, GSK2, and GSK3, which are potent BRAF inhibitors falling within the scope of claim 1 of the '640 patent. *See supra*. The only difference between the prior art and claim 9 of the '640 patent is the combination of the compound with a pharmaceutically acceptable carrier or excipient.

Dkt. 502-1 ¶ 11. "A person of ordinary skill in the art with respect to the Asserted Patents would have a Ph.D. or equivalent degree in organic or medicinal chemistry and 2-3 years of post-graduate experience working in medicinal chemistry, synthetic organic chemistry, and/or kinase chemistry, including the development of potential drug candidates." *Id.* ¶ 8.

Dr. Rheault's unrebutted testimony establishes that persons of ordinary skill in the art test potent BRAF inhibitors by, *inter alia*, dosing them to mice. Tr. 1125:22-1126:5. The identification of a potent BRAF inhibitor like GSK1, GSK2, and/or GSK3 thus motivates persons of skill to formulate such compounds for testing. The formulations are "pharmaceutical compositions" that include "carriers or excipients, which may be chosen to facilitate administration of the compound by a particular route," TX1 at col. 65:20-21, particularly "oral administration[,]" *id.*, col. 65:32; Tr. 1133:5. "Carriers" include "physiologically compatible liquids as solvents," TX1 at col. 65:26-27, and "excipients" include "hydroxypropylmethyl-cellulose," TX1 at col. 65:46. Dr. Rheault's unrebutted testimony establishes that industry-standard formulations include water (a physiologically compatible liquid as a solvent) and HPMC (the acronym for **h**ydroxy**p**ropyl**m**ethyl-**c**ellulose). Tr. 1133:2-7. A reasonable juror could only conclude that a POSA would be motivated to use potent BRAF inhibitors in "pharmaceutical compositions" (as defined by the '640 patent). Moreover, a reasonable juror could only find that a POSA would have expected success in making the claimed compounds. Because there is no evidence of unexpected results or other objective indicia of nonobviousness, a reasonable juror could only conclude that the claims would have been obvious.

C. Lack of Written Description

35 U.S.C. § 112(a) provides that "[t]he specification shall contain a written description of the invention." "[T]he description must clearly allow persons of ordinary skill in the art to recognize that the inventor invented what is claimed. In other words, the 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." *Ariad Pharm.,*

Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

Where a claim recites a specific combination of variables, the specification must direct the person of ordinary skill to that specific combination with "blaze marks"; a general disclosure that encompasses the specific combination is not sufficient to satisfy the written description requirement. As explained in *In re Ruschig*, "[a]ppellants are pointing to trees. We are looking for blaze marks which single out particular trees." 379 F.2d 990, 995-96 (CCPA 1967). Where the claimed invention is not "specifically named or mentioned in any manner [in the application as filed], one is left to selection from the myriads of possibilities encompassed by the broad disclosure, with no guide indicating or directing that this particular selection should be made rather than any of the many others which could also be made." *Id.* at 995; *see also Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326-27 (Fed. Cir. 2000) ("[O]ne cannot disclose a forest in the original application, and then later pick a tree out of the forest and say here is my invention. In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure.").

This analysis has been applied to claims that cover subgenera. A claim to a particular subgenus is not adequately supported where the specification discloses only a broader genus and fails to sufficiently describe the subgenus. As the Federal Circuit explained in *Fujikawa v. Wattanasin* "the compounds of the [subgenus] were not [ ] preferred, and that his application contained no blazemarks as to what compounds, other than those disclosed as preferred, might be of special interest." *Fujikawa v. Wattanasin,* 93 F.3d 1559, 1571 (Fed. Cir. 1996). "In the absence of such blazemarks, simply describing a large genus of compounds is not sufficient to satisfy the written description requirement as to particular species or subgenuses." *Id.*; *see also Quake v. Lo*, 928 F.3d 1365, 1374 (Fed. Cir. 2019); *Bos. Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353 (Fed. Cir. 2011); *Fujikawa*, 93 F.3d at 1571. Thus, when a specification discloses a large genus or broad definitions for a series of variables, it is not permissible to work backward with the claims in hand "to derive written description support from an amalgam of disclosures plucked selectively

from the [ ] application." *Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349 (Fed. Cir. 2013) (holding patent invalid for lack of written description because although specification separately disclosed three individual claim limitations, it did not disclose a compound that had at once all three limitations).

In addition, to show possession of an invention to a genus or subgenus, the specification must set forth "either a representative number of species falling within the scope of the genus or structural features common to members of the genus so that one of skill in the art can visualize or recognize members of the genus." *Ariad*, 598 F.3d at 1351. The Federal Circuit has held claims invalid for lack of written description where a patent "does not define any structural features commonly possessed by members of the genus that distinguish them from others," allowing one of skill in the art to "visualize or recognize the identity of the members of the genus." *Regents of Univ. of Cal. v. Eli Lilly & Co.,* 119 F.3d 1559, 1568 (Fed. Cir. 1997). Moreover, those representative species must reflect the variance in that genus. *See AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1300 (Fed. Cir. 2014) (the disclosure must adequately reflect the structural diversity of the claimed genus, either through the disclosure of sufficient species that are "representative of the full variety or scope of the genus," or by the establishment of "a reasonable structure-function correlation"). As the Federal Circuit further explained, "[o]ne factor in considering the question [of the adequacy of the disclosure] is how large a genus is involved and what species of the genus are described in the patent." *AbbVie Deutschland* 759 F.3d 1285, 1299-1301 (Fed. Cir. 2014). "To satisfy the written description requirement in the case of a chemical or biotechnological genus, more than a statement of the genus is normally required. One must show that one has possession, as described in the application, of sufficient species to show that he or she intended and disclosed the totality of the genus." *Carnegie Mellon Univ. v. Hoffman-La Roche Inc.*, 541 F.3d 1115, 1300-01 (Fed. Cir. 2008); *In re Gosteli*, 872 F.2d 1008, 1088, 1012 (Fed. Cir. 1989) (disclosure of two chemical species was insufficient to support claims to 21 chemical species).

"[M]erely drawing a fence around the outer limits of a purported genus is not an adequate substitute for describing a variety of materials constituting the genus and showing that one has invented a genus and not just a species." *Ariad*, 598 F.3d at 1350. Three judges of the Federal Circuit recently summarized the requirements for a broad genus, explaining "Invention of a genus means to conceive and reduce to practice a reasonable number and distribution of species constituting the genus." *Amgen Inc. v. Sanofi, Aventisub LLC,* 850 F. App'x 794, 796 (Fed. Cir. 2021). "Mere statement of a genus does not demonstrate that one has invented a generic concept, without the enablement of constituent species." *Id.*

No reasonable juror could conclude that the Asserted Patents' specification "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad*, 598 F.3d at 1351.

The Asserted Patents fail to disclose sufficient representative species to support the claims. The uncontested evidence shows that the Asserted Patents claim, at minimum, a genus of trillions of compounds. *Compare* Tr. 801:1-10 (the patents claim a "near infinite" number of compounds), *with* Tr. 357:2-3 ("I have not done the math. I haven't counted."). Plexxikon admits that the specification discloses only three compounds—P-0001, P-0007, and P-00012—that fall within the scope of some, but not all, of the Asserted Claims. Thus, claim 1 of the '640 patent and claim 1 of the '539 patent each have three disclosed species, claim 7 of the '539 patent has two, and claim 5 of the '539 patent has none. TX1 at cl. 1; TX2 at cls. 1, 5, 7. Claim 9 of the '640 patent also has none, as the Asserted Patents fail to disclose any example of a pharmaceutical formulation. TX1 at cl. 9. In any event, the disclosed species are not representative of the claimed genuses because they are insufficiently diverse to represent the claims' vast scope. For example, while the Asserted Claims are each divisible into two distinct sub-classes (*i.e.*, compounds where L_1 is a bond and those in which it is an amide), all three of P-0001, P-0007, and P-00012 have an amide linker. The three compounds also fail to represent the vast diversity of the other claimed variables.

Nor could a reasonable juror find the Asserted Patents disclose sufficient common

structural features. To the extent the claimed compounds share a common feature, the specification fails to disclose any relationship between such feature and a common function. To the contrary, the limited activity data reported in the specification establishes only that the three example compounds falling within the claims' scope have vastly different function notwithstanding their high degree of structural similarity. One of the three compounds (P-0007) is not disclosed as having any activity at all. Moreover, the alleged common structural feature is insufficient to distinguish between the claimed subgenus and unclaimed compounds disclosed with the same specification.

Further, no reasonable juror could conclude that there are sufficient blaze marks that would lead a person of ordinary skill from the broad disclosure of the specification to the specific claimed sub-genuses. It is undisputed that Formula I and each of the sub-formulas Ia-Ij disclosed in the specification are much broader than the claimed sub-genus. Tr. 1425:4-10, 1429:9-12. Dr. Metzker admitted there is no embodiment in the specification that is co-extensive with the claims. *Id.* And nothing in the specification would lead the person of ordinary skill to the particular combination of options for the seven different variables that define the claims. For example, nothing in the Asserted Patents would lead a person of ordinary skill to select the claimed options for L_1, especially in combination with all of the other specific selections for the claimed variables.

This case is unlike *In re Driscoll*, in which a generic structure that had a single variable disclosing 14 possible options was held to adequately disclose one of the fourteen, *see* 562 F.2d 1245, 1250 (CCPA 1977)); here (more analogous to *Fujikawa*), there are innumerable combinations of claimed options in Formula I (or Formula Ia), and the Asserted Claims represent a haphazard selection of only some of only a tiny fraction of those options. The uncontested evidence shows that the Asserted Patents claim, at minimum, a genus of trillions of compounds. *Compare* Tr. 801:1-10 (the patents claim a "near infinite" number of compounds), *with id.* 357:2-3 ("I have not done the math. I haven't counted."). The written description inquiry in this case thus turns on "whether the disclosure of the application relied upon reasonably conveys to those

skilled in the art that the inventor had possession of the claimed [trillions of compounds] as of the filing date." *Ariad*, 598 F.3d at 1351. The record evidence requires finding that the inventors "had possession" of such claimed subject matter. *Id.* at 1349.

The '640 and '539 patents disclose the outer boundaries of an even broader genus than the trillion+ compound sub-genus claimed. Tr. 853:1-23. In such circumstances the patent's description must provide adequate direction that would reasonably lead persons of skill in the art to the sub-genus. *Fujikawa*, 93 F.3d at 1571. Here, the evidence establishes that the Asserted Patents lack such direction as a matter of law. *E.g.*, Tr. 838:2-8, 848:13-19. The specifications of the Asserted Patents identify several subgenera compounds, but none of them is coextensive with the claimed subgenus. There is nothing in the specifications to guide a POSA to pick and choose the particular claimed options for each of L1, R1, R2, R3, R4, m, and Ar, or the combination of those variables, and so the specifications fail to satisfy the written description requirement as to the claimed sub-genera. *See Fujikawa*, 93 F.3d at 1571; *Novozymes*, 723 F.3d at 1349.

Based on the trial evidence, a reasonable juror could only find that the specifications disclose a "representative number of species" or "structural features common to the members of the genus." *Ariad*, 598 F.3d at 1350 ("[A]n adequate written description of a claimed genus requires more than a generic statement of an invention's boundaries."). The Asserted Patents disclose 120 exemplary compounds, only three of which fall within the scope of the Asserted Claims. Tr. 831:25-832:17. The Asserted Patents do not include any representative compound for which L1 is a bond (one of the two claimed options) or show the inventors even knew how to make such compounds. *See* TX1; TX2; Tr. 842:14-19; *infra* at 21-22. The Asserted Patents also do not include any representative compound for which R_2 is a hydrogen (one of the two claimed categories of options). *See* TX1; TX2; Tr. 850:14-19. And the Asserted Patents do not include any representative compound for which R_1 is an optionally substituted heteroaryl (one of the two claimed categories of options). *See* TX1; TX2. No reasonable juror could find that P-0001, P-0007, and P-00012 are representative of the full scope of the claimed genera.

Moreover, as Dr. Baran testified, at length, he could not visualize or recognize the members of the genus because of all "the possible R groups." Tr. 927:19-25. Dr. Baran explained that the written description is of no support because it lacks "blaze marks" of what compounds, other than those disclosed as preferred, might be of interest. *E.g.*, Tr. 838:2-8, 848:13-19. Absent legally sufficient evidence of such blaze marks the specifications are "simply describing a large genus of compounds [which] is not sufficient to satisfy the written description requirements as to particular species or subgenera." *Bos. Scientific*, 647 F.3d at 1353. Finally, the trial evidence requires finding that the patents fail to disclose a correlation of the structure and function for the claimed compound genera and no such correlation was known in the art. For example, the Asserted Patents do not provide any disclosure of activity for compounds with, *e.g.*, aryl groups, groups having hydrophilic substituents, or very large groups at R3 and also fails to disclose a structure-function relationship for substituents at that position. Tr. 860:6-863:18.

Nor on the facts here could a reasonable juror conclude from the patents' disclosure of broad, generic formulas with many variables and many possibilities for each variable that the inventors possessed the entire genus or a specific sub-genus of compounds encompassed by such formulas. Given the number of and options for such variables here, the patents' formulas are at most "a generic statement of [the] invention's boundaries," which is insufficient as a matter of law. *Ariad*, 598 F.3d at 1349.

D. Lack of Enablement

35 U.S.C. § 112(a) provides that a patent's specification must "enable any person skilled in the art . . . to make and use" the patented invention. "The purpose of the enablement requirement is to ensure that the public is told how to carry out the invention, *i.e.*, to make and use it." *Amgen Inc. v. Sanofi*, 987 F.3d 1080, 1084 (Fed. Cir. 2021). Thus, "enablement requires that 'the specification teach those in the art to make and use the invention without undue experimentation.'" *Idenix Pharm. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1154 (Fed. Cir. 2019) (quoting *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)). "A claim is not enabled when, at the effective filing

date of the patent, one of ordinary skill in the art could not practice their full scope without undue experimentation." *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." *Amgen*, 987 F.3d at 1084. Those factual considerations, which have come to be known as the "*Wands* factors," are (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. *See id.*; *Idenix*, 941 F.3d at 1156; *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

"[A] patentee chooses broad claim language at the peril of losing any claim that cannot be enabled across its full scope of coverage." *MagSil Corp. v. Hitachi Glob. Storage Techs., Inc.*, 687 F.3d 1377, 1381 (Fed. Cir. 2012); *Liebel-Flarsheim Co. v. Medrad, Inc.*, 481 F.3d 1371, 1380 (Fed. Cir. 2007) ("The irony of this situation is that Liebel successfully pressed to have its claims include a jacketless system, but, having won that battle, it then had to show that such a claim was fully enabled, a challenge it could not meet.").

The specification must teach a person of ordinary skill in the art how "to make" the invention. 35 U.S.C. § 112(a). "The inquiry is whether the patent's specification taught one of skill in the art how to make such a device without undue experimentation as of the patent's effective filing date." *Trustees of Bos. Univ. v. Everlight Elecs*. Co., 896 F.3d 1357, 1363 (Fed. Cir. 2018). While "a specification need not disclose what is well known in the art[,]" it is "the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement." *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997); *see Nat'l Recovery Techs., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1195-96 (Fed. Cir. 1999) ("The enablement requirement ensures that the public knowledge is enriched by the patent specification to a degree at least commensurate with

the scope of the claims."). To the extent knowledge of one skilled in the art fills gaps, it "is merely supplemental; it cannot substitute for a basic enabling disclosure." *Trustees of Bos. Univ.*, 896 F.3d at 1364 (citing *Genentech*, 108 F.3d 1366) (reversing denial of defendant's motion for JMOL). Of course it is "[t]he *specification* that shall . . . enable any person of skill . . . to make" the invention. 35 U.S.C. § 112(a) (emphasis added).

In addition to teaching those in the field how to *make* the invention, the specification must also teach those in the field how to *use* the invention. A patent that claims subject matter that is not useful or operative fails to disclose how to use the invention and is invalid for lack of enablement. *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1323-24 (Fed. Cir. 2009).

The U.S. Constitution empowers Congress "[t]o promote the Progress of Science and *useful* Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective . . . Discoveries." U.S. Const. art. I, § 8, cl. 8 (emphasis added). Pursuant to that grant of power, Congress enacted the Patent Act of 1790 during the second session of the First Congress, requiring that patents may be granted only for "new and *useful*" inventions. This requirement is currently codified in multiple ways, including in both 35 U.S.C. § 101 *and* § 112. For example, § 101 "has been interpreted as embodying a fundamental requirement of American patent law, dating back some two-hundred years, 'that one may patent only that which is 'useful.'"" *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180 (Fed. Cir. 1991) (quoting *Brenner v. Manson*, 383 U.S. 519, 528-29 (1966)). As the Supreme Court stated in *Brenner* "[u]nless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." 383 U.S. at 534-35.

The "how-to-use" prong of the enablement requirement under § 112 includes the same requirement: it "incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention." *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1323 (Fed. Cir. 2005). An enabling disclosure must

disclose a "substantial utility" and "specific benefit existing in currently available form" for claimed matter. *In re '318*, 583 F.3d at 1323-24 (alteration omitted).

A patent disclosure lacks substantial utility, and so does not enable those skilled in the art to "make" and "use" the full scope of the claimed invention, if the claims read on significant numbers of inoperative embodiments. As the Federal Circuit noted in *Fujikawa*, it is well-established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed. 93 F.3d at 1563; *see also Brenner v. Manson*, 383 U.S. at 536 ("Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing . . . a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."). In addition, showing utility for only part of a genus is not sufficient to meet the utility requirement when an artisan would not reasonably believe the entire genus would have the stated utility based on the limited disclosure. *In re Fouche*, 439 F.2d 1237, 1242-43 (CCPA 1971).

Even aside from § 112's utility requirement, it is well-settled that a patent claim may be too broad to the point of invalidity by reading on significant numbers of inoperative embodiments. *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 336 U.S. 271, 276-77 (1949); *Atlas Powder Co. v. E. I. du Ponte de Nemours & Co.*, 750 F.2d 1560, 1576-77 (Fed. Cir. 1984) ("Of course, if the number of inoperative combinations becomes significant, and in effect forces one of ordinary skill in the art to experiment unduly to practice the claimed invention, the claims might indeed be invalid"); *In re C*, 734 (CCPA 1971) ("In 1949 the Supreme Court held [in *Graver Tank*] that claims may be too broad 'to the point of invalidity' by reason of reading on significant numbers of inoperative embodiments . . . . We see no reason why the Patent Office as well as courts deciding infringement litigation should not 'have authority to reject a broad claim merely because it . . . (reads on a significant number of) inoperative species.'" (third alteration in original)).

If a claim covers significant numbers of inoperative embodiments or there would be a need to make and test at least many, many thousands of compounds to determine which compounds

within a genus can actually be used for any specifically identified benefit in the patent, the claim is invalid. *Idenix*, 941 F.3d at 1162-63 (having to make and test "at least many, many thousands of candidate compounds" to determine whether they work for their intended purpose constitutes undue experimentation); *see Pac. Biosciences of Cal., Inc. v. Oxford Nanopore Techs., Inc.*, 996 F.3d 1342, 1350-51 (Fed. Cir. 2021) *Wyeth & Cordis Corp. v. Abbott Labs*, 720 F.3d 1380, 1385 (Fed. Cir. 2013) ("We hold that . . . having to synthesize and screen each of at least tens of thousands of candidate compounds constitutes undue experimentation"); *In re '318*, 583 F.3d at 1323-25. This is so even for claims that lack functional requirements because a patent that claims matter that is not useful or operative fails to disclose how to make and use the invention and so is invalid for lack of enablement. *Brenner*, 383 U.S. at 535-36. Were it otherwise "a patent may confer power to block off whole areas of scientific development, without compensating benefit to the public." *Id*. Thus, a "[m]ere statement of a genus does not demonstrate that one has invented a generic concept, without the enablement of constituent species. *Amgen*, 850 F. App'x at 796.

No reasonable juror could conclude that a person of ordinary skill in the art could make and use the full scope of the Asserted Compound Claims without undue experimentation. The genera of the Asserted Compound Claims include two distinct classes of compounds: those for which L_1 is an amide and those for which L_1 is a bond. *See, e.g.*, '640 patent, cl. 1. As acknowledged by the specification of the Asserted Patents, the two classes require fundamentally different methods of making. *Compare* TX1 at col. 68:30-70:30 (Scheme 1, prescribed for compounds for which L_1 is an amide), *with* TX1 at col. 70:31-71:67 (Scheme 2, prescribed for compounds for L_1 is an amide).

The Asserted Patents' synthetic scheme for compounds for which L_1 is a bond (Scheme 2) does not enable the person of ordinary skill to make the full scope of such compounds. Neither Plexxikon nor anyone else has never used Scheme 2 to synthesize a compound of the Asserted Compound Claims. Indeed, the first time Plexxikon ever synthesized such a compound occurred in 2010; the compound was GSK's dabrafenib, and Plexxikon instructed its contract laboratory to

use a different method.

Novartis expert Dr. Baran opined extensively that Scheme 2 would be difficult or impossible to use for making a large proportion of the compounds where L_1 is a bond. Tr. 871:9-878:4. Plexxikon expert Dr. Winkler's nominally contrary testimony only established (if credited) that the scientific literature (*not* the specification) provided many avenues for a person of ordinary skill to attempt to derive a suitable synthetic scheme. But Dr. Baran offered unrebutted testimony that the trillions of different combinations of options for the Ar-$(R^1)_m$, R^2, and R^3 variables of the Asserted Compound Claims would require the development of a vast number of synthetic schemes (with no guidance from the specification as to how to develop or modify any synthetic scheme so that it would be suitable for making a particular compound). And his further unrebutted testimony established that even if the synthetic methods disclosed in the 2007 literature might ultimately be helpful in developing such schemes, extensive experimentation would be required to adapt such methods to the specific context of the synthesizing compounds of the Asserted Compound Claims. Thus, even crediting *arguendo* Dr. Winkler's testimony, the person of ordinary skill would be left to scour the literature in the hopes of developing a scheme that may or may not ultimately work.

Moreover, the trillions of options for, *e.g.*, the Ar-$(R^1)_m$ moiety would themselves require undue experimentation to synthesize even notwithstanding the difficulty or impossibility of forming the L_1 bond. It is undisputed that the Asserted Patents include within their scope Ar-$(R^1)_m$ and R^3 moieties that include up to six *layers* of one or more "optional substituents" with radically different size, shape, and chemical functionality. The Asserted Patents provide no guidance on how to synthesize such complex intermediates; again, the person of ordinary skill is left entirely to her own devices.

In sum, Scheme 2 does not enable persons of skill to make the full scope of the Asserted Compound Claims. Plexxikon's reliance on the knowledge of the person of ordinary skill is insufficient at least because it exceeds the permissible gap-filling role of such knowledge.

But the undue experimentation necessary to make the full scope of claimed compounds

would not be nearly the end of POSA's troubles in practicing the claimed invention. Rather, it would only be the beginning of an experimental campaign to determine whether and how the compounds might be used. The undue experimentation necessary to determine the scope of operable compounds and the specific uses for which such compounds might be operable provides an independent reason why the Asserted Compound Claims are not enabled.

It is undisputed that a subset of the claimed compounds would be inoperable, for example, because they lack any kinase inhibition activity. *E.g.*, Tr. 515:23-516:7, 1003:19-24 1423:8-12, 1484:10-13. Dr. Jennings, the only expert in the case to attempt to quantify that subset as a proportion of the scope of the Asserted Compound Claims, found that the subset of inoperable compounds would constitute the majority of the claimed genus. Tr. 1003:19-24. The vast scope of inoperable compounds independently invalidates the claim.

But even among the compounds which are "operable," *e.g.*, have activity on one or more kinases, undue experimentation would *still* be required for the person of ordinary skill to determine how to use them. It is undisputed that there are over 500 different kinases (not including mutant forms, of which there are many, many more) in the human body alone (and the patent is not limited to humans); any given "operable" compound may be operable for inhibiting a wide array or just one of these kinases (indeed, such "selectivity" is considered desirable). In order to determine which kinase(s) a compound is active upon, the person would have to not only synthesize, but then purify and screen the compound against the full set of known kinases.

Moreover, determining which compounds within the broadly claimed genera exhibit kinase inhibition or other pharmacological activity and which do not would require extensive and undue experimentation. For example, the patents provide no structure-activity relationship that would help a person of ordinary skill even guess as to which compounds would be active on which kinase(s). This is nowhere better demonstrated than in vastly disparate behavior of the three example compounds falling within the scope of the Asserted Compound Claims (P-0001, P-0007,

and P-00012), *see* Tr. 725:24-726:3, notwithstanding their high degree of structural similarity, *i.e.*, failure to represent more than a tiny sliver of the claimed genera.

Finally, Novartis has adduced clear and convincing evidence under *Wands* that the claims are not enabled. By way of non-limiting example, Dr. Baran testified that the claims are "very broad." Tr. 866:22-24. He further testified that the specification of the Asserted Patents provides "[e]xtremely limited guidance." *Id.* at 866:25-867:3, 868:7-11. He explained that, notwithstanding the Suzuki reaction having been the subject of Nobel Prize, "[t]here are very important limitations of that reaction." Tr. 871:4-5. And he further explained that, in his expert opinion, it would not "be possible to make the compound we've identified as dabrafenib or Tafinlar® with the Suzuki reaction disclosed in the asserted patents." Tr. 872:7-10; *see also* Tr. 872:15-874:3. Dr. Baran relied on the lack of working examples in the patents. Tr. 880:3-9. Dr. Baran also opined, based in part on "papers from top groups in the country" that doing the Suzuki reaction "is very unpredictable to even decide what conditions you should use." Tr. 880:10-19. Dr. Bridges (whose skill, especially in combination with Dr. Bao's, greatly exceeds that of the POSA) "spent 40 days and 40 nights[,] $80,000 in materials and time[, and] failed 25 times at least" before achieving "less than 1 percent yield of the product." *E.g.*, Tr. 875:1-25.

E. Limited Damages

A plaintiff bears the burden of proving damages with substantial evidence by a preponderance of the evidence. *Minco, Inc. v. Combustion Eng'g, Inc.*, 95 F.3d 1109, 1118 (Fed. Cir. 1996). Attorney argument alone is not evidence, cannot amount to substantial evidence, and is insufficient to rebut evidence. *See, e.g., ArcelorMittal Atlantique et Lorraine v. AK Steel Corp.*, 908 F.3d 1267, 1275 (Fed. Cir. 2018). In seeking a reasonable royalty, the plaintiff bears the burden of proffering legally sufficient evidence supporting the royalty sought. *Trell v. Marlee Elecs. Corp.*, 912 F.2d 1443, 1447 (Fed. Cir. 1990). "[T]he trial court must carefully tie proof of damages to the claimed invention's footprint in the market place." *ResQNet.com, Inc. v. Lansa, Inc.*, 594 F.3d 860, 869 (Fed. Cir. 2010); *Grain Processing Corp. v. Am. Maize-Prods. Co.*, 185

F.3d 1341, 1350 (Fed. Cir. 1999).

Plexxikon's post-2018 royalty rate is not tied to economic reality and is unsupported by record evidence. Plexxikon's damages theory invites the jury to speculate as to the economic circumstances post-2018—accordingly, any damages award must be limited as a matter of law. The only evidence presented at trial by Plexxikon supports a royalty rate of 6.26% to 12.52% from October 18, 2016, through 2018. Tr. 678:10-19. Consistent with the Court's Order regarding Novartis' Motion in Limine No. 5, Dkt. 490, Novartis proffered evidence supporting a reasonable royalty rate of 0.5% throughout the damages period, *see* Tr. 1239:17-1240:4, while Plexxikon proffered no evidence of a reasonable royalty rate after the end of 2018. While the jury is permitted "to determine what royalty is supported by the record," *Apple Inc. v. Motorola, Inc.*, 757 F.3d 1286, 1327 (Fed. Cir. 2014), a damages award that simply extrapolates Plexxikon's expert's proffered pre-2018 royalty rate of 6.26% to 12.52% post-2018 would not be tied to economic reality and would be unsupported by record evidence. Accordingly, any damages award must be limited as a matter of law to no more than 7% post-2018.

F. No Willfulness

Novartis renews its Rule 50(a) motion filed after the close of Plexxikon's case-in-chief. Dkt. No. 545. For the reasons in that motion, and upon considering all the evidence through the end of trial, no reasonable juror could find that Novartis had pre-suit knowledge of the Asserted Patents or the requisite specific intent to knowingly infringe the Asserted Patents. *See* Waibel Dep. Tr. 20:25-21:03, 21:06-21:15; Schwarz Dep. Tr. 12:18-12:20, 12:21-13:03; TX23.

IV. CONCLUSION

For all the foregoing reasons, based on the trial evidence, a reasonable juror could conclude only that the Asserted Patents are invalid for at least one of three independent reasons: anticipation and obviousness, lack of written description, and lack of enablement. Also, there is no legally sufficient evidence to support an ongoing post-2018 royalty greater than 7%; and any infringement was not willful.

Respectfully submitted,

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MCDERMOTT WILL & EMERY LLP

By: */s/ Thomas P. Steindler*
Thomas P. Steindler

THOMAS P. STEINDLER (*Pro Hac Vice*)
tsteindler@mwe.com
NICOLE M. JANTZI (*Pro Hac Vice*)
njantzi@mwe.com
PAUL M. SCHOENHARD (*Pro Hac Vice*)
pschoenhard@mwe.com
MICHAEL S. NADEL (*Pro Hac Vice*)
mnadel@mwe.com
IAN B. BROOKS (*Pro Hac Vice*)
ibrooks@mwe.com
JENNIFER B. ROUTH (*Pro Hac Vice*)
jrouth@mwe.com
500 N. Capitol St., N.W.
Washington, DC 20001
Tel: (202) 756-8000
Fax: (202) 756-8087

MCDERMOTT WILL & EMERY LLP
WILLIAM G. GAEDE III (SBN: 136184)
wgaede@mwe.com
415 Mission Street, Suite 5600
San Francisco, CA 94105
Tel: (628) 218-3800
Fax: (628) 877-0107

MCDERMOTT WILL & EMERY LLP
SARAH C. COLUMBIA (*Pro Hac Vice*)
scolumbia@mwe.com
DAVID MLAVER (*Pro Hac Vice*)
dmlaver@mwe.com
200 Clarendon Street, Floor 58
Boston, MA 02116
Tel: (617) 535-4000
Fax: (617) 535-3800

Attorneys For Defendant
Novartis Pharmaceuticals Corporation

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