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VIA FEDERAL EXPRESS

TO:	Exelixis, Inc. Attn: Michael M. Morrissey, Ph.D. President and Chief Executive Officer 1851 Harbor Bay Parkway Alameda, CA 94502	Exelixis, Inc. Attn: Sandy Smith Senior Vice President, Regulatory Affairs 1851 Harbor Bay Parkway Alameda, CA 94502
	Exelixis, Inc. Attn: Jeffrey J. Hesekiel, J.D. Executive Vice President and General Counsel 1851 Harbor Bay Parkway Alameda, CA 94502	Honigman LLP Attn: Jonathan P. O'Brien, Ph.D./Exelixis 650 Trade Centre Way Suite 200 Kalamazoo, MI 49002-0402

FROM: Azurity Pharmaceuticals, Inc.

DATE: March 5, 2025

RE: NOTICE OF PARAGRAPH IV CERTIFICATION RE: AZURITY
PHARMACEUTICALS, INC.'S CABOZANTINIB TABLETS, 13 MG, 26
MG, AND 39 MG; U.S. PATENT NOS. 8,877,776, 11,091,439, 11,091,440,
11,098,015, 9,724,342, 10,039,757, 10,034,873, 11,298,349, AND 12,128,039

Dear Sirs and Madam:

Pursuant to § 505(b)(3)(B) and § 505(b)(3)(D) of the Federal Food, Drug and Cosmetic Act ("the Act") and § 314.52 of Title 21 of the Code of Federal Regulations ("C.F.R."), please be advised that Azurity Pharmaceuticals, Inc. ("Azurity") has filed a patent certification pursuant to § 505(b)(2)(A)(iv) of the Act and § 314.50(i)(1)(i)(A)(4) of Title 21 of the C.F.R. in support of its 505(b)(2) New Drug Application ("NDA") No. 220258 with respect to cabozantinib tablets, 13 mg, 26 mg, and 39 mg ("Azurity's proposed product"). Azurity seeks to obtain approval to engage in the commercial manufacture, use or sale of Azurity's proposed product before the expiration of U.S. Patent Nos. 8,877,776 ("the '776 patent"), 11,091,439 ("the '439 patent"), 11,091,440 ("the '440 patent"), 11,098,015 ("the '015 patent"), 9,724,342 ("the '342 patent"), 10,039,757 ("the

'757 patent"), 10,034,873 ("the '873 patent"), 11,298,349 ("the '349 patent"), and 12,128,039 ("the '039 patent"), (collectively "the OB patents"). We understand that the holder of application No. 208692 under § 505(b) of the Act ("New Drug Application" or "NDA") in connection with cabozantinib tablets, 20 mg, 40 mg, and 60 mg (reference listed drug: CABOMETYX®) is Exelixis, Inc. We further understand, based on the information available in the United States Patent and Trademark Office ("USPTO") patent assignment database, Exelixis, Inc. ("Exelixis") is the current assignee of the '776, '439, '440, '015, '342, '757, '873, '349, and '039 patents.

Pursuant to § 505(b)(3)(D) of the Act and 21 C.F.R. § 314.52(c), Azurity provides the following information:

- (1) The U.S. Food and Drug Administration ("FDA") has received a 505(b)(2) NDA submitted by Azurity containing any required bioavailability or bioequivalence data or information with respect to cabozantinib tablets, 13 mg, 26 mg, and 39 mg;
- (2) The NDA number is 220258;
- (3) The established name of the proposed drug product, as defined in § 502(e)(3) of the Act, is "cabozantinib tablets, 13 mg, 26 mg, and 39 mg";
- (4) The active ingredient in Azurity's proposed product is *N*-(4-(6,7-dimethoxyquinolin-4-yloxy)phenyl)-*N'*-(4-fluorophenyl)cyclopropane-1,1-dicarboxamide,(2*S*)-hydroxybutanedioate, commonly known as cabozantinib (*S*)-malate; the strengths are equivalent to 13 mg, 26 mg, and 39 mg of cabozantinib base respectively, and the dosage form is a tablet for oral use;
- (5) The U.S. Patent Numbers and expiration dates, as known to Azurity, of the patents alleged to be invalid, unenforceable, or not infringed are:

<u>U.S. Patent No.</u>	<u>Expiration Date</u>
11,091,439	January 15, 2030
11,091,440	January 15, 2030
11,098,015	January 15, 2030
8,877,776	October 8, 2030
10,034,873	July 18, 2031
10,039,757	July 18, 2031
11,298,349	February 10, 2032
12,128,039	February 10, 2032
9,724,342	July 9, 2033

- (6) Azurity has certified with the FDA pursuant to § 505(b)(2)(A)(iv) of the Act and 21 C.F.R. § 314.50(i)(1)(i)(A)(4) (“Paragraph IV Certification”) that the OB patents are invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of Azurity’s proposed product for which Azurity has submitted its NDA. Therefore, pursuant to § 505(b)(3)(D)(ii) and 21 C.F.R. § 314.52(c)(6), a detailed statement of the legal and factual basis for the Paragraph IV Certification is enclosed herewith (as Annexures A, B, and C) and is made a part hereof. The information detailed in this letter and the attached memoranda are supplied for the sole purpose of complying with the above-referenced statutes and regulations, and neither Azurity nor its attorneys waive any attorney-client privilege or attorney work product immunity concerning the subject matter of this communication; and
- (7) Azurity reserves its right to supplement this letter and the attached memoranda detailing the factual and legal basis for Azurity’s assertion of invalidity, unenforceability, or non-infringement of the above listed patents should subsequent investigations reveal additional grounds for asserting invalidity, unenforceability, or non-infringement.

Offer of Confidential Access: In addition to and not in lieu of the limitations contained in 21 U.S.C. § 355(c)(3)(D)(i)(III) and pursuant to 21 C.F.R. § 314.52(c)(7), Azurity hereby offers confidential access to Azurity’s 505(b)(2) NDA solely to permit Exelixis to determine whether an action under Section 355 should be filed within the statutory 45 days of the receipt of this letter. Samples of Azurity’s 505(b)(2) NDA product can be supplied upon request. Access to the above materials and information is and shall be limited to only those attorneys acting as outside counsel for Exelixis, and any experts, that are needed to evaluate the information, and such persons who are to have access shall be identified to Azurity’s outside counsel, Andrew J. Miller, Esq., Windels Marx Lane & Mittendorf, LLP, 1 Giralda Farms, Suite 100, Madison, NJ 07940 (e-mail: amiller@windelsmarx.com). Such persons so identified shall agree in writing that the information can and only will be used for the sole and limited purpose of evaluating whether an action under Section 355 on a patent that is the subject of Azurity’s Paragraph IV certification should be filed within the statutory 45 days of the receipt of this letter. Those persons receiving access to Azurity’s NDA materials and samples shall not, without further negotiation of terms, engage, formally or informally, directly or indirectly in: any work (prosecution or post-issuance) before any patent office, including the USPTO, relating to cabozantinib or its pharmaceutically acceptable salts; or in any counseling, litigation or other work before or involving a regulatory agency, including the FDA, relating to cabozantinib or its pharmaceutically acceptable salts.

Exelixis, Inc.
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Pursuant to 21 C.F.R. § 314.52(c)(7), by providing this Offer of Confidential Access, Azurity maintains the right and ability to bring and maintain a Declaratory Judgment action under 28 U.S.C. §§ 2201 *et seq.*, pursuant to 21 U.S.C § 355(c)(3)(D).

Attached hereto are memoranda setting forth Azurity's detailed factual and legal basis supporting its Paragraph IV Certification.

Very truly yours,
Windels Marx Lane & Mittendorf, LLP



Ajay Kayal, Ph.D., Esq.
Outside Counsel for Azurity Pharmaceuticals, Inc.

Enclosures:

- Detailed Factual and Legal Basis for Paragraph IV Certification for U.S. Patent Nos. 8,877,776, 11,091,439, 11,091,440, and 11,098,015 (**Annexure A**).
- Detailed Factual and Legal Basis for Paragraph IV Certification for U.S. Patent Nos. 9,724,342, 10,034,873, and 10,039,757 (**Annexure B**).
- Detailed Factual and Legal Basis for Paragraph IV Certification for U.S. Patent Nos. 11,298,349 and 12,128,039 (**Annexure C**).

Annexure C

DETAILED STATEMENT OF FACTUAL AND LEGAL BASIS FOR AZURITY PHARMACEUTICALS, INC.'S ASSERTION OF INVALIDITY, UNENFORCEABILITY, OR NON-INFRINGEMENT OF U.S. PATENT NOS. 11,298,349 ("THE '349 PATENT") AND 12,128,039 ("THE '039 PATENT")

I. INTRODUCTION

Pursuant to § 505(b)(3)(D)(ii) of the Federal Food, Drug, and Cosmetic Act ("the Act") (codified at 21 U.S.C § 355(b)(3)(D)(ii)) and 21 C.F.R. § 314.52(c)(6), given below is the detailed factual and legal basis for Azurity's Paragraph IV Certification alleging that the claims of the '349 and '039 patents are invalid, unenforceable, or will not be infringed by the manufacture, use or sale of Azurity's proposed product described in its 505(b)(2) NDA No. 220258.

II. LEGAL PRINCIPLES

A. The Law of Infringement

The test for direct infringement of a patent is stated in 35 U.S.C. § 271(a) as follows:

(a) Except as otherwise provided in this title, whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.

Determining if an accused product infringes the claims of a patent is a two-step process. First, the meaning and scope of the claim must be ascertained. Second, the claim as properly construed, must be compared to the accused device or process. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996). The patent owner bears the burden of proving infringement by a preponderance of the evidence. *See Tanabe Seiyaku Co. v. U.S. Int'l Trade Comm'n*, 109 F.3d 726, 731 (Fed. Cir. 1997).

1. Claim Construction

The first step in an infringement analysis is to ascertain the meaning and scope of the

claims. *See, e.g., Process Control Corp. v. Hydrex Corp.*, 190 F.3d 1350 (Fed. Cir. 1999). The “ultimate interpretation” of a patent claim “is a legal conclusion.” *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 841 (2015); *see also Markman v. Westview Instruments*, 52 F.3d 967, 976 (Fed. Cir. 1995) (*en banc*), *aff’d*, 517 U.S. 370 (1996).

a. Plain and Ordinary Meaning

Construction of a claim term involves evaluating “the term’s plain and ordinary meaning as understood by a person of ordinary skill in the art.” *Allergan, Inc. v. Apotex, Inc.*, 754 F.3d 952, 957 (Fed. Cir. 2014), *citing Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005) (*en banc*). The ordinary and customary meaning of a claim term is the meaning that a person of ordinary skill in the art in question, at the time of invention, would have understood the claim to mean. *Phillips*, 415 F.3d at 1313. The sources available to understand disputed claim language include the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence, including relevant scientific principles, the meaning of technical terms, and the state of the art. *Id.* at 1314.

b. Intrinsic Evidence

“[C]laim construction involves consideration of primarily the intrinsic evidence, *viz.*, the claim language, the specification, and the prosecution history.” *Biosig Instruments, Inc. v. Nautilus, Inc.*, 783 F.3d 1374, 1378 (Fed. Cir. 2015) (citation omitted). Indeed, “the best source for understanding a technical term is the specification from which it arose, informed, as needed, by the prosecution history.” *Phillips*, 415 F.3d at 1315, *quoting MultiForm Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1478 (Fed. Cir. 1998). Along with the specification and the prosecution history, in some cases, a court will be required “to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art

during the relevant time period.” *Teva*, 135 S. Ct. at 841. “Though the ultimate construction of a claim term is a legal question reviewed de novo, underlying factual determinations made by the district court based on extrinsic evidence are reviewed [by the appellate court] for clear error.” *Biosig*, 783 F.3d at 1378, *citing Teva*, 135 S. Ct. at 842.

c. Applicant’s Statements and Prosecution Disclaimer

Statements made by the applicant in the file history or in a related application (including applications in the family that preceded the application-at-issue, or even in subsequent related applications) have relevance to claim construction. *Please see Microsoft Corp. v. Multi-Tech Sys.*, 357 F.3d 1340, 1350 (Fed. Cir. 2004) (emphases added):

We have stated on numerous occasions that a patentee's statements during prosecution, whether relied on by the examiner or not, are relevant to claim interpretation. *Laitram Corp.*, 143 F.3d at 1462 (“The fact that an examiner placed no reliance on an applicant's statement distinguishing prior art does not mean that the statement is inconsequential for purposes of claim construction.”) ... [In *Georgia Pacific*] [w]e rejected the argument that the patentee was bound, or estopped, by a statement made in connection with a later application on which the examiner of the first application could not have relied. We did not suggest, however, that such a statement of the patentee as to the scope of the disclosed invention would be irrelevant. *Any statement of the patentee in the prosecution of a related application as to the scope of the invention would be relevant to claim construction, and the relevance of the statement made in this instance is enhanced by the fact that it was made in an official proceeding in which the patentee had every incentive to exercise care in characterizing the scope of its invention. Accordingly, we conclude that Multi-Tech's statements made during the prosecution of the '627 patent with regard to the scope of its inventions as disclosed in the common specification are relevant not only to the '627 and '532 patents, but also to the earlier issued '649 patent.*

See also Sprint Communs. Co. L.P. v. Vonage Holdings Corp., 518 F. Supp. 2d 1306, 1316 (D. Kan. 2007) (“the Federal Circuit recently stated that ‘[w]hen the application of prosecution

disclaimer involves statements from prosecution of a familial patent relating to the same subject matter as the claim language at issue in the patent being construed, those statements in the familial application are relevant in construing the claims at issue.’ *Ormco Corp.*, 2007 U.S. App. LEXIS 20185, 2007 WL 2404723, at *5. Taking this statement at face value, then, the court will consider the possibility that statements made during prosecution of the child '928 patent are relevant to construing the same claim terms in the ancestor '429 and '064 patent claims.”).

The Federal Circuit has noted that:

A prosecution history statement may inform the proper construction of a term without rising to the level of a clear and unmistakable disclaimer. *See, e.g., Shire Dev., LLC v. Watson Pharms., Inc.*, 787 F.3d 1359, 1366 (Fed. Cir. 2015) (“Although the prosecution history statements do not rise to the level of unmistakable disavowal, they do inform the claim construction.”).

Galderma Labs., L.P. v. Amneal Pharms. LLC, 806 F. App'x 1007, 1011 (Fed. Cir. 2020)

The Federal Circuit has explained that the doctrine of prosecution disclaimer as follows:

The prosecution history limits the interpretation of claim terms so as to exclude any interpretation that was disclaimed during prosecution. *ZMI Corp. v. Cardiac Resuscitator Corp.*, 844 F.2d 1576, 1580, 6 U.S.P.Q.2D (BNA) 1557, 1561 (Fed. Cir. 1988); *Senmed, Inc.*, 888 F.2d at 818-20, 12 U.S.P.Q.2D (BNA) at 1511-13 (rejecting patentee's interpretation of claim term "on" as inconsistent with position taken during prosecution of patent application). Claims may not be construed one way in order to obtain their allowance and in a different way against accused infringers. *Unique Concepts, Inc. v. Brown*, 939 F.2d 1558, 1562, 19 U.S.P.Q.2D (BNA) 1500, 1504 (Fed. Cir. 1991).

Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1576 (Fed. Cir. 1995).

2. Literal Infringement

Literal infringement is found when an accused product or method falls within the scope of properly construed asserted claims. *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1575 (Fed. Cir. 1995). The application of a patent claim to an accused product or process is a question

of fact. *Trilogy Commc 'ns, Inc. v. Times Fiber Commc 'ns, Inc.*, 109 F.3d 739, 741 (Fed. Cir. 1997). For literal infringement, each limitation in the asserted claim must be found in the accused product or method. *General Mills, Inc. v. Hunt-Wesson, Inc.*, 103 F.3d 978, 981 (Fed. Cir. 1997); *see also Litton Sys., Inc. v. Honeywell, Inc.*, 140 F.3d 1449, 1454 (Fed. Cir. 1998) (“Literal infringement requires that the accused device contain each limitation of the claim exactly; any deviation from the claim precludes a finding of literal infringement.”). “If even one limitation is missing or not met as claimed, there is no literal infringement.” *Mas-Hamilton Group v. LaGard, Inc.*, 156 F.3d 1206, 1211 (Fed. Cir. 1998) (citation omitted). *See also Atlantic Thermoplastics Co. v. Faytex Corp.*, 970 F.2d 834, 838-47 (Fed. Cir. 1992) (infringement requires the limitations of the process be present); *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1293 (Fed. Cir. 2009) (*en banc* in pertinent part) (““process terms in product-by-process claims serve as limitations in determining infringement”) (citation omitted).

3. Infringement Under the Doctrine of Equivalents

The judicially created doctrine of equivalents requires asking if an accused product contains element(s) equivalent to each claimed element of the patented invention. *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 29, 40 (1997). Infringement under the doctrine of equivalents can be established if there is no literal infringement where each of the claimed elements performs substantially the same function in substantially the same way to achieve substantially the same result. *Id.*; *Graver Tank & Mfg. Co. v. Linde Air Prods. Co.*, 339 U.S. 605, 608 (1950).

There are several limits on the use of doctrine of equivalents. Of relevance here are the following doctrines:

a) **Ensnarement**

The ensnarement doctrine – sometimes referred to as “the *Wilson Sporting Goods* doctrine” – holds that the doctrine of equivalents may not be used to expand the range of equivalents to impermissibly encompass or “ensnare” the prior art. *Jang v. Boston Scientific Corp.*, 872 F. 3d 1275, 1285 (Fed. Cir. 2017) (citing *Wilson Sporting Goods v. David Geoffrey & Assoc.*, 904 F.2d 677, 684-85 (Fed. Cir. 1990), *overruled in part on other grounds*). As the Federal Circuit has explained, this doctrine is tested by comparing a hypothetical claim with the prior art:

A doctrine of equivalents theory cannot be asserted if it will encompass or “ensnare” the prior art. ... “This limitation is imposed even if a jury has found equivalence as to each claim element.” ... A “[h]ypothetical claim analysis is a practical method to determine whether an equivalent would impermissibly ensnare the prior art.” ... We have explained:

Hypothetical claim analysis is a two-step process. The first step is “to construct a hypothetical claim that literally covers the accused device.” Next, prior art introduced by the accused infringer is assessed to “determine whether the patentee has carried its burden of persuading the court that the hypothetical claim is patentable over the prior art.” In short, [the court] ask[s] if a hypothetical claim can be crafted, which contains both the literal claim scope and the accused device, without ensnaring the prior art. ...

Jang v. Bos. Sci. Corp., 872 F.3d at 1285 (citations omitted).

b) **Argument-Based Estoppel**

Arguments made during prosecution may give rise to prosecution history estoppel. *Pharmacia & Upjohn Co. v. Mylan Pharms., Inc.*, 170 F.3d 1373, 1376-77 (Fed. Cir. 1999). “In order to invoke argument-based estoppel, the prosecution history must evince a clear and unmistakable surrender of the subject matter.” *Amgen Inc. v. Coherus BioSciences Inc.*, 931 F.3d

1154, 1159 (Fed. Cir. 2019) (citation omitted). Argument-based prosecution history estoppel applies to that subject matter a competitor would be reasonably entitled to conclude the applicant gave up during prosecution history to procure issuance of the claim. *See Hoganas AB v. Dresser Indus., Inc.*, 9 F.3d 948, 952 (Fed. Cir. 1993). Argument-based prosecution history estoppel applies where the applicant has made unmistakable arguments to distinguish the claim from the prior art in support of patentability. *See CAE Screenplates v. Heinrich Fiedler GmbH*, 224 F.3d 1308, 1319 (Fed. Cir. 2000); *Southwall Techs., Inc.* 54 F.3d at 1583 (“Clear assertions made during prosecution in support of patentability, whether or not actually required to secure allowance of the claim, may also create an estoppel.”).

As the Federal Circuit has explained:

Prosecution history estoppel precludes a patentee from obtaining under the doctrine of equivalents coverage of subject matter that has been relinquished during the prosecution of its patent application. ... A number of activities during prosecution may give rise to prosecution history estoppel, ... including arguments made to obtain allowance of the claims at issue, ... For an estoppel to apply, such assertions in favor of patentability must “evinced a clear and unmistakable surrender of subject matter”... not an “equivocal” one.

Pharmacia & Upjohn Co. v. Mylan Pharms., Inc., 170 F.3d at 1376-77 (citations omitted).

c) **Claim Vitiating**

The doctrine of claim vitiating holds that the doctrine of equivalents may not be used to disregard or effectively remove limitations from the claim. Where a claim limitation covers only one of two opposite embodiments, it would vitiate the claim limitation to use the doctrine of equivalents to expand the claim to cover the opposite embodiment. As the Federal Circuit has explained:

To succeed on a doctrine of equivalents theory, the patentee must demonstrate equivalence under one of these two tests. This will be more difficult when the accused structure has an element that is the opposite of the claimed element, especially where the specification or prosecution history highlights the differences. If the claimed and accused elements are recognized by those of skill in the art to be opposing ways of doing something, they are likely not insubstantially different. The concept of vitiation is an acknowledgement that each element in the claim must be present in the accused device either literally or equivalently. And we have applied this concept to cases where we have recognized that two alternatives exist that are very different from each other and therefore cannot be equivalents for infringement purposes. See, e.g., *Planet Bingo*, 472 F.3d at 1345 (concluding that determining a winning combination *after* a game starts was not equivalent to determining a winning combination *before* the game starts); *Moore U.S.A., Inc. v. Std. Register Co.*, 229 F.3d 1091, 1106 (Fed. Cir. 2000) ("[I]t would defy logic to conclude that a minority—the very antithesis of a majority—could be insubstantially different from a claim limitation requiring a majority, and no reasonable juror could find otherwise.").

Brilliant Instruments, Inc. v. GuideTech, LLC, 707 F.3d 1342, 1347-48 (Fed. Cir. 2013).

4. Infringement of Dependent Claims

Finally, if an independent claim is not infringed, then the narrower claims that depend from it cannot be infringed. An independent claim stands alone, while a dependent claim incorporates the limitations of the claim(s) from which it depends. "A claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all of the limitations of the claim to which it refers." 35 U.S.C. § 112. "It is axiomatic that dependent claims cannot be found infringed unless the claims from which they depend have been found to have been infringed." *Wahpeton Canvas Co., v. Frontier, Inc.*, 870 F.2d 1546, 1553 (Fed. Cir. 1989).

B. The Law of Invalidity

1. Presumption of Validity

Under 35 U.S.C. § 282, a U.S. patent is presumed valid, and overcoming that presumption requires clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 95 (2011). Nonetheless, a court may find an issued patent invalid when clear and convincing evidence of invalidity is presented.

2. Claim Construction

The first step in an invalidity analysis is to ascertain the meaning and scope of the claims. *See, e.g., Merck & Co. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1369-72 (Fed. Cir. 2005). This analysis, called claim construction, is an issue of law. *See supra*, Section II. A. 1. for the law of claim construction.

3. The Law of Written Description

To satisfy the written description requirement under 35 U.S.C. § 112,¹ “the patent specification must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.” *Gentry Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479 (Fed. Cir. 1998) (internal quotations and citation omitted). This means that “the disclosure must . . . convey with reasonable clarity to those skilled in the art that . . . [the inventor] was in possession of the invention.” *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000) (internal

¹ Pursuant to § 4(e) of the America Invents Act (“AIA”), Pub. L. No. 112-29, amended § 112 applies to patent applications with claims having an effective filing date on or after September 16, 2012. Because the applications from which the '349 and '039 patents issued were filed before this date, it is assumed herein that the pre-AIA version of § 112 apply. Accordingly, all references herein to § 112 should be understood to mean the pre-AIA version of § 112. However, if written description is lacking in the predecessor applications, then there would be no entitlement to the earlier priority date and the AIA version of § 112 would apply. Under either the pre- or post-AIA statutory sections, the analysis of invalidity under Section 112 is effectively the same.

quotations and citation omitted) (affirming district court's finding that the patent claims were invalid); *see also Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005); *In re Curtis*, 354 F.3d 1347, 1350-52 (Fed. Cir. 2004) (affirming Board's finding that a prior application "did not provide an adequate written description of the later-claimed genus of friction enhancing coatings"). Under this requirement, the patent's specification must describe what is claimed with sufficient detail such that a person of ordinary skill in the art can conclude 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) (citation omitted); *see also Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008) ("[T]he applicant must 'convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention,' and demonstrate that by disclosure in the specification of the patent." (citation omitted)).

"[T]he hallmark of written description is disclosure. Thus, 'possession as shown in the disclosure' is a more complete formulation." *Ariad*, 598 F.3d at 1351. The test for written description involves an objective inquiry into whether the specification describes the invention sufficiently to allow a person of ordinary skill in the art to understand it and know that the inventor actually invented the claimed invention. *Id.* The operative time for this determination is the date of the patent's filing. *Id.* ("The law must be applied to each invention at the time it enters the patent process, for each patented advance has a novel relationship with the state of the art from which it emerges."). The Federal Circuit has stated that, when determining whether a patent specification complies with the written description requirement:

The level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology. For generic

claims, we have set forth a number of factors for evaluating the adequacy of the disclosure, including “the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.”

Id. (quoting *Capon*, 418 F.3d at 1359). Finally, “actual ‘possession’ or reduction to practice outside of the specification is not enough . . . it is the specification itself that must demonstrate possession.” *Id.* at 1352.

4. The Law of Enablement

Whether a claim is enabled under 35 U.S.C. § 112 is a question of law. *In re Goodman*, 11 F.3d 1046, 1050 (Fed. Cir. 1993); *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). The enablement requirement is satisfied when the patent specification enables “those skilled in the art to make and use the full scope of the claimed invention without ‘undue experimentation.’” *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) (citations omitted). A patent claim is invalid for lack of enablement if the specification fails to teach those in the art how to make and use the invention as broadly as it is claimed without undue experimentation. *Warner Lambert Co. v. Teva Pharms. USA, Inc.*, 418 F.3d 1326, 1337 (Fed. Cir. 2005); *see also In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993) (“Although not explicitly stated in section 112, to be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’”) (citations omitted).

The determination as to whether “undue” experimentation is required to practice a claimed invention is analyzed with regard to the “*Wands* factors.” As the Federal Circuit has explained:

“To prove that a claim is invalid for lack of enablement, a challenger must show by clear and convincing evidence that a person of ordinary skill in the art would not be able to practice the claimed invention without ‘undue experimentation.’” *Alcon Research*, 745 F.3d at 1188 (quoting *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988)). “Whether undue experimentation is

needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations.” *Wands*, 858 F.2d at 737. Those factual considerations, which have come to be known as the “*Wands* factors,” are:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.*

As we have stated elsewhere, “[a]fter the challenger has put forward evidence that some experimentation is needed to practice the patented claim, the factors set forth in *Wands* then provide the factual considerations that a court may consider when determining whether the amount of that experimentation is either ‘undue’ or sufficiently routine such that an ordinarily skilled artisan would reasonably be expected to carry it out.” *Alcon Research*, 745 F.3d at 1188 (quoting *Wands*, 858 F.2d at 737).

Amgen Inc. v. Sanofi, 987 F.3d 1080, 1084-85 (Fed. Cir. 2021).

5. The Law of Indefiniteness

35 U.S.C. § 112 ¶2 requires that “the specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.” In *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 901, 134 S. Ct. 2120, 2124 (2014), the Supreme Court explained:

a patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.

The Court further noted that this requirement “entails a ‘delicate balance.’” *Nautilus, Inc.*, 572 U.S. at 909 (quoting *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 731 (2002)). While the statute recognizes “the inherent limitations of language” and permits “[s]ome modicum of uncertainty” it also requires that “a patent must be precise enough to afford clear

notice of what is claimed, thereby apprising the public of what is still open to them.” *Id.* at 909 (quoting *Markman*, 517 U. S., at 373). The Court held that a patent is invalid for indefiniteness “if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.” *Id.* at 901.

“The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe.” *All Dental Prodx, LLC v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002) (citing *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 28-29 (1997)). Thus, a patent claim must be “sufficiently precise to permit a potential competitor to determine whether or not he is infringing.” *Morton Int’l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1470 (Fed. Cir. 1993).

Definiteness, like claim construction, is a question of law sometimes involving subsidiary factual determinations. *Biosig*, 783 F.3d at 1382. In assessing definiteness, “claims are to be read in light of the patent’s specification and prosecution history,” and courts apply the “viewpoint of a person skilled in the art at the time the patent was filed.” *Nautilus*, 572 U.S. at 908 (alterations and citation omitted).

III. THE ’349 PATENT

A. Introduction

The ’349 patent entitled “Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds” issued on April 12, 2022, from U.S. Patent Application No. 17/170,275 (“the ’275 application”) filed on February 8, 2021, which is a

continuation of U.S. Patent Application No. 17/152,394 (“the ’394 application”), filed on January 19, 2021, now abandoned, which is a continuation of U.S. Patent Application No. 16/706,323 (“the ’323 application”), filed on December 6, 2019, now abandoned, which is a division of U.S. Patent Application No. 16/151,653 (“the ’653 application”), filed on October 4, 2018, now U.S. Patent No. 10,543,206 (“the ’206 patent”), which is a division of U.S. Patent Application No. 15/348,716 (“the ’716 application”), filed on November 10, 2016, now U.S. Patent No. 10,123,999 (“the ’999 patent”), which is a division of U.S. Patent Application No. 13/984,559 (“the ’559 application”), filed as application No. PCT/US2012/024591 on February 10, 2012, now U.S. Patent No. 9,717,720 (“the ’720 patent”). The ’275 application claims priority to Provisional Application No. 61/441,520 (“the ’520 provisional”) filed on February 10, 2011, and Provisional Application No. 61/441,527 (“the ’527 provisional”), filed on February 10, 2011.

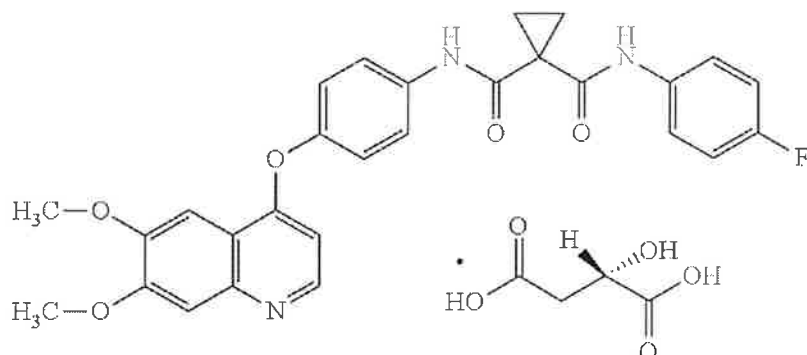
B. The Claims of the ’349 Patent

The ’349 patent issued with three claims, of which claims 1 and 3 are independent. Claim 2 depends directly from independent claim 1. The claims of the ’349 patent are generally directed to a tablet or capsule pharmaceutical composition for oral administration comprising cabozantinib (L)-malate (denoted “Compound IB”) in combination with generic categories of excipients (*i.e.*, fillers, disintegrants, glidants, and lubricants) that is “essentially free of process byproducts or contaminants” (claim 1) or “of 6,7-dimethoxy-quinoline-4-ol” (claims 2 and 3).

The claims of the ’349 patent are reproduced below:

1. A pharmaceutical composition for oral administration comprising Compound IB;

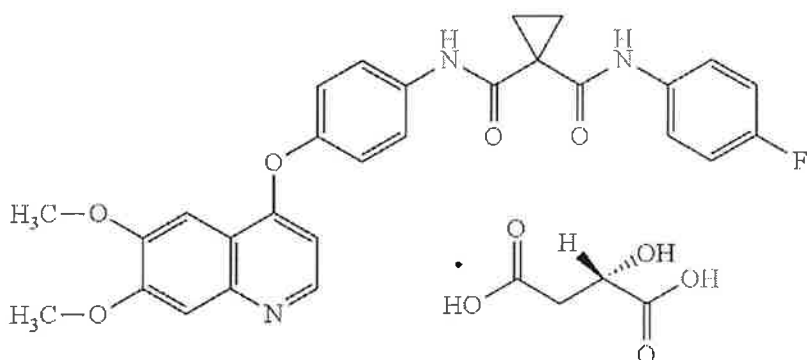
IB



one or more fillers; one or more disintegrants; one or more glidants; and one or more lubricants, wherein the pharmaceutical composition is a tablet or capsule pharmaceutical composition, and wherein the pharmaceutical composition is essentially free of process byproducts or contaminants.

2. The pharmaceutical composition of claim 1, wherein the process byproduct or contaminant is 6,7-dimethoxyquinoline-4-ol in the pharmaceutical composition.
3. A pharmaceutical composition for oral administration comprising Compound IB;

LB



one or more fillers; one or more disintegrants; one or more glidants; and one or more lubricants, wherein the pharmaceutical composition is a tablet or capsule pharmaceutical composition; and

wherein the pharmaceutical composition is essentially free of 6,7 - dimethoxy-quinoline-4-ol.

IV. THE '039 PATENT

A. Introduction

The '039 patent entitled “Processes for Preparing Quinoline Compounds and Pharmaceutical Compositions Containing Such Compounds” issued on October 29, 2024, from U.S. Patent Application No. 18/436,836 (“the '836 application”), filed on February 8, 2024, which is a continuation of U.S. Patent Application No. 18/462,739 (“the '739 application”), filed on September 7, 2023, which is a continuation of U.S. Patent Application No. 17/679,634 (“the '634 application”), filed on February 24, 2022, now abandoned, which is a continuation of the '275 application, filed on February 8, 2021, now the '349 patent, which is a continuation of the '394 application, filed on January 19, 2021, now abandoned, which is a continuation of the '323 application, filed on December 6, 2019, now abandoned, which is a division of the '653 application, filed on October 4, 2018, now the '206 patent, which is a division of the '716 application, filed on November 10, 2016, now the '999 patent, which is a division of the '559 application, filed as application No. PCT/US2012/024591 on February 10, 2012, now the '720 patent. The '836 application claims priority to the '520 and '527 provisionals both filed on February 10, 2011.

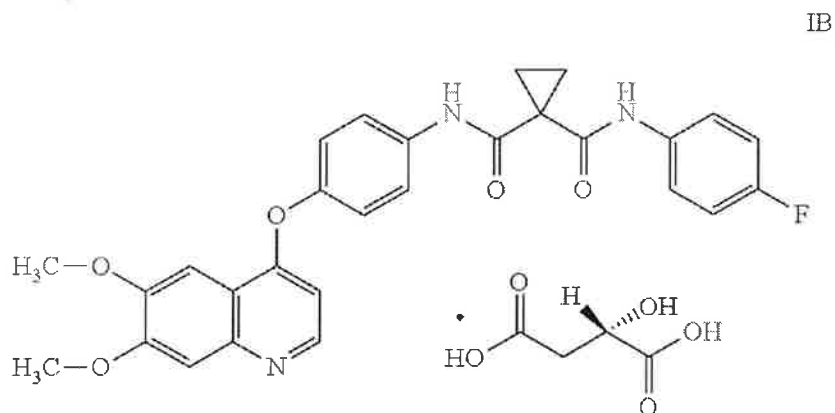
B. The Claims of the '039 Patent

The '039 patent issued with twenty-two claims, wherein claim 1 and 6 are independent claims. Claims 2-5 depend, either directly or indirectly, on independent claim 1. Claims 7-22 depend, either directly or independently, from independent claim 6. The independent claims of the '039 patent broadly relate to a tablet or capsule pharmaceutical composition of cabozantinib (L)-malate (denoted “Compound IB”) containing “100 ppm or less of 6,7-dimethoxy-quinoline-4-ol” or a method of treating cancer using the same composition. '039 patent at 34:2-24 (claim 1),

34:38-61 (claim 6). Additional claims restrict the permissible concentration range for 6,7-dimethoxy-quinoline-4-ol”) that may be present (claims 2-5 and 7-10) or specify a type of cancer for treatment (claims 11-22). *Id.*, 34:2-35:30

The claims of the '039 patent are reproduced below:

1. A pharmaceutical composition for oral administration comprising Compound IB:

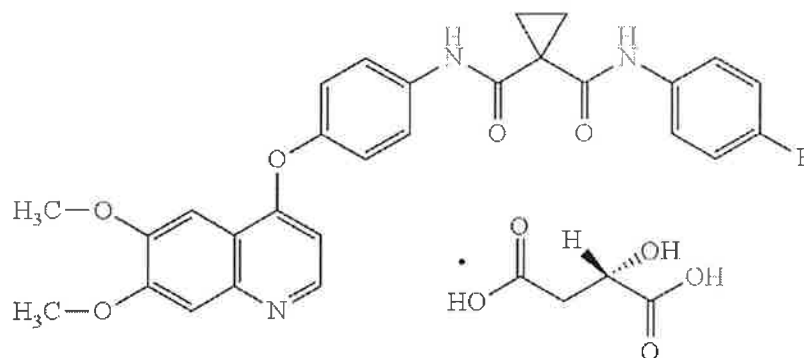


and a pharmaceutically acceptable carrier, wherein the pharmaceutical composition is a tablet or a capsule, and wherein the pharmaceutical composition contains 100 ppm or less of 6,7-dimethoxy-quinoline-4-ol.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition contains 50 ppm or less of 6,7-dimethoxy-quinoline-4-ol.
3. The pharmaceutical composition of claim 2, wherein the pharmaceutical composition contains 25 ppm or less of 6,7-dimethoxy-quinoline-4-ol.
4. The pharmaceutical composition of claim 3, wherein the pharmaceutical composition contains 10 ppm or less of 6,7-dimethoxy-quinoline-4-ol.
5. The pharmaceutical composition of claim 4, wherein the pharmaceutical composition contains 5 ppm or less of 6,7-dimethoxy-quinoline-4-ol.

6. A method of treating cancer, comprising administering to a subject in need thereof a pharmaceutical composition comprising Compound IB:

IB



and a pharmaceutically acceptable carrier, wherein the pharmaceutical composition is a tablet or a capsule, and wherein the pharmaceutical composition contains 100 ppm or less of 6,7-dimethoxy-quinoline-4-ol.

7. The method of claim 6, wherein the pharmaceutical composition contains 50 ppm or less of 6,7-dimethoxyquinoline-4-ol.
8. The method of claim 7, wherein the pharmaceutical composition contains 25 ppm or less of 6,7-dimethoxyquinoline-4-ol.
9. The method of claim 8, wherein the pharmaceutical composition contains 10 ppm or less of 6,7-dimethoxyquinoline-4-ol.
10. The method of claim 9, wherein the pharmaceutical composition contains 5 ppm or less of 6,7-dimethoxyquinoline-4-ol.
11. The method of claim 6, wherein the cancer is renal cancer.
12. The method of claim 6, wherein the cancer is prostate cancer.
13. The method of claim 6, wherein the cancer is hepatocellular carcinoma.
14. The method of claim 7, wherein the cancer is renal cancer.

15. The method of claim 7, wherein the cancer is prostate cancer.
16. The method of claim 7, wherein the cancer is hepatocellular carcinoma.
17. The method of claim 8, wherein the cancer is renal cancer.
18. The method of claim 8, wherein the cancer is prostate cancer.
19. The method of claim 8, wherein the cancer is hepatocellular carcinoma.
20. The method of claim 9, wherein the cancer is renal cancer.
21. The method of claim 9, wherein the cancer is prostate cancer.
22. The method of claim 9, wherein the cancer is hepatocellular carcinoma.

V. APPLICATION OF THE LAW

A. Claim Construction

Several potential claim construction issues may arise in the context of the non-infringement and invalidity analyses of the '349 and '039 patents. They are addressed below.

1. "Essentially Free of Process Byproducts or Contaminants"

The phrase "essentially free of process byproducts or contaminants" appears in claim 1 of the '349 patent and is defined in the '349 and '039 patents. *See* '349 patent, at col. 8, lines 15-20 ("‘Essentially free’ as used in the phrase ‘essentially free of process byproducts or contaminants,’ means that a compound or composition as disclosed here in is admixed with 200 parts per million (ppm) or less of such byproducts or contaminants."); '039 patent, at col. 8, lines 30-34. For the purposes of this Detailed Statement of Factual and Legal Basis, Azurity accepts this construction. However, Azurity reserves the right to amend, refine or otherwise alter this construction if a litigation ensues.

2. **“Essentially Free of 6,7-Dimethoxy-Quinoline-4-ol”**

There is no express definition of the term “essentially free of 6,7-dimethoxy-quinoline-4-ol” in the ’349 patent. Outside of claim 3, the ’349 patent does not utilize this phrase. However, the ’349 patent does identify “6,7-dimethoxy-quinoline-4-ol” as “a byproduct that may form during the synthesis of Compound IA or IB”² and something to be minimized in pharmaceutical compositions. ’349 patent at col. 22, lines 22-27; ’039 patent at col. 22, lines 14-26. Further, in prior litigation that patentee had with MSN, the district court applied a numerical limit of 200 ppm or less to 6,7-dimethoxy-quinoline-4-ol. *Exelixis, Inc. v. MSN Labs. Pvt. Ltd et al*, 22-cv-00228-RGA, slip. op. at 45, D.I. 186 (D. Del. 2024) at 45. For purposes of this Factual and Legal Basis Statement, Azurity accepts this construction. However, Azurity reserves the right to amend, refine or otherwise alter this construction if a litigation ensues.

a) **No Literal Infringement of the “Method of Treatment” Claims of the ’039 Patent**

Claims 6-22 of the ’039 patent, *inter alia*, recite a method of treating cancer using the pharmaceutical composition discussed above. As an initial matter, Azurity cannot directly infringe the method claims of the ’039 patent because it is a pharmaceutical company that will not treat any patients. *See Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1363 & n.7 (Fed. Cir. 2003) (finding no evidence of direct infringement under § 271(a), which is “hardly surprising” because “pharmaceutical companies do not generally treat diseases; rather, they sell drugs to wholesalers or pharmacists, who in turn sell the drugs to patients possessing prescriptions from physicians.”). Moreover, claims 12, 15, 18, and 21 of the ’039 patent are directed to the treatment of prostate

² Compound IA is cabozantinib. Compound IB is cabozantinib (L)-malate. *See*, the ’349 patent at col. 4, lines 1-28, depicting the structures of both Compound IA and Compound IB.

cancer. In contrast, Azurity's proposed product will not be indicated for the treatment prostate cancer and the prescribing information (label) of Azurity's proposed product does not contain any language regarding prostate cancer at all. Indeed, even Exelixis' Cabometyx[®] product is not approved for the treatment of prostate cancer. Thus there can be no claim of induced infringement of claims 12, 15, 18, and 21 of the '039 patent. *See Takeda Pharms. U.S.A. Inc. v. West-Ward Pharm. Corp.*, 785 F.3d 625, 631 (Fed. Cir. 2015).

Finally, the existence of substantial non-infringing uses defeats a claim for contributory infringement as a matter of law. *Vita-Mix Corp. v. Basic Holding, Inc.*, 581 F.3d 1317, 1328 (Fed. Cir. 2009). "[N]on-infringing uses are substantial when they are not unusual, far-fetched, illusory, impractical, occasional, aberrant, or experimental." *Id.* at 1327. The use of Azurity's proposed product for the indications set forth in its label is a substantial non-infringing use that would defeat a claim of contributory infringement with respect to claims 12, 15, 18, and 21 of the '039 patent.

3. No Infringement Under the Doctrine of Equivalents

The manufacture, use, sale, or offer for sale in the United States or importation into the United States of Azurity's proposed product cannot infringe the claims of the '349 and '039 patents under the doctrine of equivalents either.

An analysis of infringement under the doctrine of equivalents requires a limitation-by-limitation analysis. Infringement of each limitation must be shown to exist either literally or under the doctrine of equivalents. *See, e.g., Warner-Jenkinson*, 520 U.S. at 29, ("thus the doctrine of equivalents must be applied to individual elements of the claim, not to the invention as a whole."); *Eastcott v. Hasselblad USA, Inc.*, 564 Fed. Appx. 590, 596; 2014 U.S. App. LEXIS 10362 (Fed. Cir. 2014) ("Equivalence must be established on a limitation-by-limitation basis, not based on an assessment of the accused product as a whole. *See Aquatex*, 479 F.3d at 1328."). Similarly, for a

product-by-process claim, the process limitations also must be found – either literally or by equivalents. *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1293 (Fed. Cir. 2009) (“this court now restates that “process terms in product-by-process claims serve as limitations in determining infringement.” *Atl. Thermoplastics*, 970 F.2d at 846-47. As noted earlier, this holding follows this court’s clear statement in *In re Thorpe* that “product by process claims are limited by and defined by the process.” 777 F.2d at 697. *Warner-Jenkinson* thus reinforces the basic rule that the process terms limit product-by-process claims.”).

The “method of treatment” claims 12, 15, 18, and 21 of the ’039 patent do not infringe under the doctrine of equivalents. The differences between the accused product, and its label and usage, and the claims are substantial and preclude a finding of equivalents both factually and as a matter of law.

B. The Claims of the ’349 and ’039 Patents are Invalid Under 35 U.S.C. § 102 and/or 103

The claims of the ’349 and ’039 patents fail to satisfy the requirements of 35 U.S.C. § 102 and/or 103 for various independent reasons explained in Azurity’s petitions for *inter partes* review (IPR2025-00210 and IPR2025-00427 concerning the ’349 and ’039 patents, respectively). Azurity incorporates by reference the bases for invalidity as set forth in those petitions.

C. Alternatively, The Claims of the ’349 and ’039 Patents are Invalid Under 35 U.S.C. § 112

Alternatively, the claims of the ’349 and ’039 patents fail to satisfy the requirements of 35 U.S.C. § 112 for various independent reasons.

1. There is No Written Description for the Innumerable Permutations of Excipients Covered by the Overbroad Language in the ’349 Patent Claims

There is no written description in the specification, or in any of the preceding applications in the chain of alleged priority, for the '349 patent claims which all broadly claim any and all excipients falling into the categories of "one or more fillers; one or more disintegrants; one or more glidants; and one or more lubricants." Further, there is no written description support for the endless permutations of those excipients in a composition that is also "essentially free of process byproducts or contaminants."

A sufficient written description must "support[] all the limitations." *Technology v. Videotek*, 545 F.3d 1316, 1327 (Fed. Cir. 2008). If a claim includes more than what the specification describes there is no written description. Claims 1-3 of the '349 patent all require the inclusion of "one or more fillers; one or more disintegrants; one or more glidants; and one or more lubricants" in a tablet/capsule composition having less than 200 ppm of "process byproducts or contaminants" (claim 1) or less than 200 ppm of "6,7-dimethoxy-quinoline-4-ol" (claims 2 and 3). Thus, the claims encompass innumerable excipients and permutations of excipients.

The breadth of the final claims, is revealed by comparing the original very narrow claims that were broadened by the preliminary amendment in the '275 application (that led to the '349 patent). Compare the '275 Original Application Claims at 38-46 with Feb. 8 Preliminary Amendment at 2; and consider, as one example, cancelled claim 26, with its identification of very specific and particular excipients and recitation of amounts to the hundredth of a decimal place:

26. A pharmaceutical composition according to Table 5.

Table 5

	mg/unit dose
Ingredient	50mg
Compound IB (10 % drug load as Compound IA)	63.35
Microcrystalline Cellulose	95.39
Croscarmellose sodium	9.05
Sodium starch glycolate	9.05
Fumed Silica	0.54
Stearic acid	3.62
Total Fill Weight	181.00

By contrast, the final claims 1-3 of the '349 patent – recite very broad categories of excipients and innumerable combinations and permutations of these excipients. See Feb. 8 Preliminary Amendment at 2.

The specification does not justify such broad claims. To satisfy the written description requirement, the specification must convey possession of the full scope of those broad claims – including the innumerable permutations of excipients within a composition that achieves impurity levels below 200 ppm. *Nuvo Pharms. (Ireland) Designated Activity Co. v. Dr. Reddy's Lab'ys Inc.*, 923 F.3d 1368, 1384 (Fed. Cir. 2019) (“[W]hen the inventor expressly claims [a certain] result, our case law provides that [such] result must be supported by adequate disclosure in the specification.”).

Yet, the specification only identifies a particular set of “one or more fillers; one or more disintegrants; one or more glidants; and one or more lubricants”:

In this embodiment, the filler comprises microcrystalline cellulose.

In this embodiment, the disintegrant comprises croscarmellose sodium.

In this embodiment, the disintegrant comprises croscarmellose sodium and sodium starch glycolate.

In this embodiment, the glidant comprises fumed silica. In this embodiment, the lubricant comprises stearic acid.

(’349 patent at col. 21, lines 5-12). That is the only embodiment with any particular excipients.

Further, the specification only shows one example – a capsule – containing those same particular excipients that is stable and satisfies the “200 ppm” limitation.

But, Exelixis own experts admitted—in a litigation involving the ’349 patent—that the purity of the composition can be impacted by the interaction of cabozantinib malate with excipients in the composition; and that those interactions are unpredictable; and that none of this knowledge was in the prior art.³ However, the ’349 patent attempts to claim endless combinations and permutations of excipients with cabozantinib malate (Compound IB) and the purity limitation. Given the unknown interactions, and impurity-producing impacts, of these countless excipients,

³ See *Exelixis v. MSN*, 22-cv-00228-RGA, D.I. 163 (D. Del. 2024) at 712:19-713:2 (Exelixis expert answering “No, because as we’ve seen, the process of blending with excipients and making it into the drug product can result in increase in the [6,7-dimethoxy-quinoline-4-ol] impurity. Thus, it’s possible to start with an API that’s essentially free, but end up with a drug product that’s not essentially free due to the additional formation of the 1-1”); *id.* at 729:12-731:2 (Exelixis expert discussing important properties for formulating cabozantinib (L)-malate); *id.* at 739:3-740:5 (Exelixis expert indicating that to formulate cabozantinib (L)-malate into a drug product that was ‘essentially free’ of the claimed impurity one “would have to know about [the API’s] chemical stability . . . you would also have to know the list of physicochemical properties I mentioned before, including the excipient compatibility studies”); *id.* (Exelixis expert admitting that none of these properties were known in the prior art); *Exelixis v. MSN*, 22-cv-00228-RGA, D.I. 175 (D. Del. 2024) at 55 (“[A]chieving API with the claimed purity does not mean that any resulting formulation would have necessarily had the same purity.”); *Exelixis v. MSN*, 22-cv-00228-RGA, D.I. 176 (D. Del. 2024) at ¶68 (“Achieving API essentially free of the [6,7-dimethoxy-quinoline-4-ol] impurity does not necessitate that a formulation of that API would be similarly pure.”); See *Exelixis v. MSN*, 22-cv-00228-RGA, D.I. 163 at 712:15-713:14 (same); *id.* at 733:15-734:13 (Exelixis expert testifying to unpredictability); *id.* at 773:5-24 (Exelixis’s expert admitting that “[o]ther than disclosing a synthetic process that makes an API exceptionally low, [the ’349 patent] doesn’t then have an additional – anything additional that would control for [6,7-dimethoxy-quinoline-4-ol]”).

Applicant's attempt to claim the universe is not justified. Neither the specification in the '349 patent, nor any of its progenitor applications, provide sufficient information to justify a claim so broad.

Exelixis has failed to provide a written description of those excipients and manufacturing conditions that were needed to obtain compositions having the requisite purity. Stated differently, the inventors of the '349 patent did not possess the full breadth of the claims, and such possession is not shown in the written description. See *Idenix*, 941 F.3d at 1164 ("No written description can be found when "a POSA is deprived of any meaningful guidance into what [compositions] beyond the examples and formulas, if any, would provide the same result" as the claimed compositions.").

2. There is No Enablement for the Innumerable Permutations of Excipients Covered by the Overbroad Claims of the '349 Patent

For the same reason that there is no written description for any of the claims of the '349 patent with regard to the overbroad claiming of "one or more fillers; one or more disintegrants; one or more glidants; and one or more lubricants," there is also a lack of enablement for all claims of the '349 patent. It would take undue experimentation to sift through the innumerable permutations of these categories of excipients to determine which particular combinations of excipients will yield a composition that is "essentially free of process byproducts or contaminants." Exelixis's own experts in the MSN litigation testified that the stability of these compositions are unpredictable. *In re Curtis*, 354 F.3d 1347 (Fed. Cir. 2004) ("Under our precedent, a disclosure that names one species encompassed within a genus will adequately describe a claim directed to that genus only if the disclosure 'indicates that the patentee has invented species sufficient to constitute the genus.' . . . here, the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed.").

Applying the *Wands* factors, shows a lack of enablement where the claims are broad and the formulation science is unpredictable. Each *Wands* factor favors a finding of lack of enablement:

Wands Factor 1: quantity of experimentation necessary: Given the innumerable permutations of excipients, and formulations, and the time it takes to study the stability and “process byproducts and contaminants”, it would take enormous experimental efforts to determine which excipients result in less than 200 ppm and which do not. This factor favors lack of enablement.

Wands Factor 2: the amount of direction or guidance presented: There is no pointer or blaze mark in the specification that identifies particular types of excipients that would produce “less than 200 ppm”. This factor favors lack of enablement.

Wands Factor 3: the presence or absence of working examples: There is only one particular set of excipients that shows the “less than 200 ppm” limitation. This factor favors lack of enablement.

Wands Factor 4: the nature of the invention: The invention is not merely a formulation, but a stable formulation of a drug substance that can produce genotoxic impurities, and the claims that cover that invention purport to cover innumerable such formulations. This factor favors lack of enablement.

Wands Factor 5: the state of the prior art: The patents at issue explain that the prior art was in need of a process that would minimize the “process byproducts and contaminants.” Accepting this for purposes of this analysis, it would appear that the prior art does not provide guidance on what the full scope of excipients would be that would satisfy the less than 200 ppm limitation. This factor favors lack of enablement.

Wands Factor 6: the relative skill of those in the art: Pharmaceutical formulators often advance by trial and error experiments. Given the overbreadth of the claims, such trial and error skills would not allow for enablement without undue experimentation. This factor favors lack of enablement.

Wands Factor 7: the predictability or unpredictability of the art: Applicant's own experts in the prior litigation testified that the stability of Compound IB is impacted by excipients it is formulated with and that the impact is unpredictable. This factor favors lack of enablement.

and

Wands Factor 8: the breadth of the claims: As noted above, the claims are very broad with respect to the number of permutations of excipients purportedly covered. This factor favors lack of enablement.

Thus, claims 1-3 of the '349 patent are invalid for not being enabled under 35 U.S.C. § 112, ¶1.

3. No Written Description for the '039 Patent Claims With Regard to "Carriers" that Also Maintain the Less Than 100 ppm "1,1-Impurity" Limitation

The claims of the '039 patent require a cabozantinib pharmaceutical composition containing a "pharmaceutical carrier" that also satisfies the ≤ 100 ppm, ≤ 50 ppm, ≤ 25 ppm, ≤ 10 ppm, or ≤ 5 ppm 6,7-dimethoxy-quinoline-4-ol impurity requirements. As with the '349 patent's broad claims to innumerable excipients, those claims are overly broad in that they purport to cover innumerable "carriers." However, the examples only show a very small number of excipients that maintain the stability of the formulation and keep the 1-1 impurity levels low. Further, Applicant's own experts in the MSN litigation admitted that these formulations involve unpredictable stability. Therefore, the inventors of the '039 patent did not possess the full breadth of the claims, and such

possession is not shown in the written description. *Ariad*, 598 F.3d at 1351. Accordingly, the claims of the '039 patent are invalid for lack of written description.

4. The Claims of the '039 Patent are Not Enabled with Respect to All "Carriers"

The same absence of support in the specification of the '039 patent with regard to the overbroad claiming of "a pharmaceutical carrier" also requires a finding of lack of enablement for all of the claims of the '039 patent. It would take undue experimentation to sift through the innumerable permutations of these categories of excipients to determine which particular combinations of excipients will yield a pharmaceutical composition that contains ≤ 100 ppm, ≤ 50 ppm, ≤ 25 ppm, ≤ 10 ppm, or ≤ 5 ppm 6,7-dimethoxy-quinoline-4-ol impurity. Exelixis' own experts in the MSN litigation testified that the stability of these compositions are unpredictable. All of the claims of the '039 patent are invalid for not being enabled. The *Wands* factors discussed above with respect to the excipients claimed in the '349 patent also apply with respect to the '039 patent claims.

5. There is No Written Description for the Plural "byproducts" and "contaminants" in Claim 1 of the '349 Patent

There is no written description support for claim 1 of the '349 patent with respect to the use of the plural words "byproducts" or "contaminants" in the phrase "essentially free of process byproducts or contaminants." The '349 patent specification discloses only one such chemical: 6,7-dimethoxy-quinoline-4-ol. Indeed, the best the specification can say about any other "process byproduct or contaminant" is:

Minimizing the concentration of contaminants or byproducts such as 6,7-dimethoxy-quinoline-4-ol in pharmaceutical compositions destined for human administration is desirable.

(The '349 patent at col. 22, lines 24-27. *See also*, the '039 patent at col. 22, lines 27-30). The specification never identifies what specific compounds would fall into this "such as" category beyond 6,7-dimethoxy-quinoline-4-ol. Nor does the specification ever identify any "blaze marks" or common characteristics that would point out or otherwise help identify these "such as" chemicals. For this reason, claim 1 is invalid for lack of written description.

6. Claim 1 of the '349 Patent Is Indefinite

Claim 1 of the '349 patent is also indefinite under 35 U.S.C. § 112, ¶2 as to the plural phrase "essentially free of process byproducts or contaminants." For the reasons set forth above, there is no written description that defines what all of these "process byproducts or contaminants" are. In the absence of that disclosure, there is no way for a potential infringer to measure the particular "process byproducts or contaminants" in their accused product – *e.g.*, to know what compounds to include in that quantitative measurement – to determine if the product is, in fact, "essentially free" of them or not. As the U.S. Supreme Court said in the seminal case of *Nautilus*, 572 U.S. at 901:

a patent is invalid for indefiniteness if its claims, read in light of the specification delineating the patent, and the prosecution history, fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.

For these reasons, claim 1 of the '349 patent is invalid for being indefinite.

VI. CONCLUSION

The foregoing provides the detailed factual and legal basis in support of Azurity's position that the claims of the '349 and '039 patents are invalid, unenforceable, and/or will not be infringed by the manufacture, use, sale, or offer for sale in the United States or importation into the United States of Azurity's proposed product.

Azurity expressly reserves the right to modify or supplement this memorandum as additional information may become available, and to assert any other arguments or defenses relating to invalidity, unenforceability, and/or non-infringement of the claims of the '349 and '039 patents, including in the course of any future litigation involving Azurity's 505(b)(2) NDA submission.

Azurity may not have included in this memorandum information that may be made available pursuant to the foregoing Offer of Confidential Access. Please note that federal statute and regulation require certain information be provided to NDA holders and patent assignees in connection with an 505(b)(2) application and that 21 C.F.R. § 314.430 governs the availability for public disclosure of data and information in an 505(b)(2) application. Except as required by law, Azurity does not authorize the disclosure of any data or information in Azurity's 505(b)(2) NDA.