UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

CELLTRION, INC.,
Petitioner,

v.

REGENERON PHARMACEUTICALS, INC.,
Patent Owner.

Case: IPR2025-00456
U.S. Patent No. 11,084,865

PATENT OWNER'S PRELIMINARY RESPONSE

TABLE OF CONTENTS

TABLE OF AUTHORITIES iv

TABLE OF EXHIBITS viii

I. Preliminary Statement 1

II. Background 2

A. Parallel Proceedings 2

B. Celltrion's Petition 4

III. Celltrion's Petition Is Time-Barred Under 35 U.S.C. § 315(b) 15

IV. Celltrion Fails To Show a Reasonable Likelihood That the '865 Patent Claims Would Have Been Anticipated or Obvious 20

A. Technical Overview 21

1. Fusion Proteins 21

2. The '865 Patent 22

B. '865 Patent Priority Chain 25

C. Person of Ordinary Skill 26

D. Claim Construction 26

1. "wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4" 26

2. "wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography" 27

3. "glycosylated" and "native conformation" 32

E. Grounds 1-3: Celltrion Fails to Demonstrate That *US432* Is Prior Art, Because the '865 Patent Is Entitled to the Priority Date of Its Parent Application 33

1. The Specification Describes the 98% Native Conformation Limitation 33

2. The Specification Describes the Glycosylation Limitation 54

3. The Specification Describes the "No Phosphate" Limitation 55

F. Celltrion's Invalidity Grounds Rely on Non-Prior Art *US432* 57

V. Conclusion 58

TABLE OF AUTHORITIES

CASES

AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.,
759 F.3d 1285 (Fed. Cir. 2014) 51

Alcon Rsch. Ltd. v. Barr Labs., Inc.,
745 F.3d 1180 (Fed. Cir. 2014) 53

Allergan, Inc. v. Sandoz Inc.,
796 F.3d 1293 (Fed. Cir. 2015) 50, 54

Amneal Pharm., LLC v. Endo Pharm. Inc.,
No. IPR2014-00360, 2018 WL 446628 (P.T.A.B. Jan. 10, 2018) 20

Andersen Corp. v. Fiber Composites, LLC,
474 F.3d 1361 (Fed. Cir. 2007) 36, 38

Ariad Pharm., Inc. v. Eli Lilly & Co.,
598 F.3d 1336 (Fed. Cir. 2010) 47, 49, 55

AstraZeneca AB v. Mylan Pharm. Inc.,
19 F.4th 1325 (Fed. Cir. 2021) 43

Atlas Powder Co. v. E.I. du Pont De Nemours & Co.,
750 F.2d 1569 (Fed. Cir. 1984) 49, 51

Click-To-Call Techs., LP v. Ingenio, Inc.,
899 F.3d 1321 (Fed. Cir. 2018) 15, 16, 18, 19

Cordis Corp. v. Medtronic AVE, Inc.,
339 F.3d 1352 (Fed. Cir. 2003) 55

Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.,
689 F.3d 1368 58

Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.,
276 F. Supp. 3d 629 (E.D. Tex. 2017).....47

Falko-Guntner Falkner v. Inglis,
448 F.3d 1357 (Fed. Cir. 2006) 47, 53

Game & Tech. Co. v. Wargaming Grp. Ltd.,
942 F.3d 1343 (Fed. Cir. 2019) 16, 19, 20

Howard Assocs., Inc. v. Lunareye, Inc.,
No. IPR2014-01213, 2015 WL 495016 (P.T.A.B. Feb. 3, 2015).....20

In re Aflibercept Pat. Litig.,
2024 WL 3422971 (N.D.W. Va. June 24, 2024).....*passim*

In re Aflibercept Pat. Litig.,
2024 WL 3423047 (N.D.W. Va. July 9, 2024) .....*passim*

In re Aflibercept Pat. Litig.,
730 F. Supp. 3d 1374 (J.P.M.L. 2024) 2

In re Entresto,
125 F.4th 1090 (Fed. Cir. 2025) 55

In re Ethicon, Inc., Pelvic Repair Sys. Prods. Liab. Litig.,
2016 WL 1718826 (S.D.W. Va. Apr. 27, 2016).....19

In re Kaplan,
789 F.2d 1574 (Fed. Cir. 1986) 58

Indivior Inc. v. Dr. Reddy's Labs. S.A.,
930 F.3d 1325 (Fed. Cir. 2019) 38

Indivior UK Ltd. v. Dr. Reddy's Labs. S.A.,
18 F.4th 1323 (Fed. Cir. 2021) 12, 13, 40

Martek Biosciences Corp. v. Nutrinova, Inc.,
579 F.3d 1363 (Fed. Cir. 2009) 57

N. Telecom v. Samsung Elecs.,
215 F.3d 1281 (Fed. Cir. 2000) 30

Nalpropion Pharm., Inc. v. Actavis Labs. FL, Inc.,
934 F.3d 1344 (Fed. Cir. 2019) 36, 38

Phillips v. AWH Corp.,
415 F.3d 1303 (Fed. Cir. 2005) 31, 42, 44

Purdue Pharma L.P. v. Faulding Inc.,
230 F.3d 1320 (Fed. Cir. 2000) 39, 40

Regeneron Pharm., Inc. v. Mylan Pharm. Inc.,
127 F.4th 896 (Fed. Cir. 2025) .....*passim*

Regeneron Pharm., Inc. v. Mylan Pharm. Inc.,
2025 WL 324288 (Fed. Cir. Jan. 29, 2025).....*passim*

Regeneron Pharm., Inc. v. Mylan Pharm. Inc.,
2025 WL 706079 (Fed. Cir. Mar. 5, 2025).....*passim*

Regeneron Pharm., Inc. v. Mylan Pharm. Inc.,
714 F. Supp. 3d 652 (N.D.W. Va. 2024).....*passim*

Sensonics, Inc. v. Aerosonic Corp.,
81 F.3d 1566 (Fed. Cir. 1996) 50

Technology Licensing Corp. v. Videotek, Inc.,
545 F3d 1316 (Fed. Cir. 2008) 57

TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.,
529 F.3d 1364 (Fed. Cir. 2008) 53

Triller, Inc. v. TikTok Pte. Ltd,
No. IPR2022-00181, 2022 WL 1618057 (P.T.A.B. May 16, 2022) 58

Trs. of Cent. Laborers' Welfare Fund v. Lowery,
924 F.2d 731 (7th Cir. 1991) 18

United Servs. Automobile Ass'n v. Auto Telematics Ltd.,
No. IPR2023-00912, 2023 WL 8192060 (P.T.A.B. Nov. 27, 2023).....58

United Servs. Automobile Ass'n v. Auto Telematics Ltd.,
No. IPR2023-00858, 2023 WL 8653083 (P.T.A.B. Dec. 14, 2023) 58

United States v. Olano,
507 U.S. 725 (1993).....15, 17

Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.,
887 F.3d 1117 (Fed. Cir. 2018) 54

OTHER AUTHORITIES

35 U.S.C. § 312 48

35 U.S.C. § 315 ..... *passim*

TABLE OF EXHIBITS

Exhibit	Description
2001	Mylan Redacted Trial Decision, 22-cv-61, Dkt. 692 (N.D.W. Va.)
2002	SB Redacted PI Decision, 24-md-3103, Dkt. 194 (N.D.W. Va.)
2003	Formycon Redacted PI Decision, 24-md-3103, Dkt. 247 (N.D.W. Va.)
2004	Celltrion Redacted PI Decision, 24-md-3103, Dkt. 248 (N.D.W. Va.)
2005	SB Appeal Decision, 24-1965, Dkt. 76 (Fed. Cir.)
2006	Formycon Appeal Decision, 24-2009, Dkt. 67 (Fed. Cir.)
2007	Celltrion Appeal Decision, 24-2058, Dkt. 62 (Fed. Cir.)
2008	Exhibit A, Samsung Bioepis's Proposed Schedule, 24-md-3103, Dkt. 478-1 (N.D.W. Va.)
2009	Regeneron Pharmaceuticals, Inc.'s Response to Defendant Samsung Bioepis Co., Ltd.'s Motion for Entry of Scheduling Order Pursuant to Rule 16 or, in the Alternative, a Status Conference, 24-md-3103, Dkt. 483 (N.D.W. Va.)
2010	Celltrion's Opening Appeal Brief, 24-2058, Dkt. 25 (Fed. Cir.)
2011	Celltrion's Reply in Support of Celltrion's Motion for Status Conference, 24-md-3103, Dkt. 504 (Fed. Cir.)
2012	Celltrion's Redacted Brief in Opposition to Regeneron's Preliminary Injunction Motion, 23-cv-89, Dkt. 142-3 (N.D.W. Va.)
2013	Regeneron Pharmaceuticals, Inc.'s Memorandum in Support of its Motion for Alternative Service, Dkt. 43-1 (N.D.W. Va.)
2014	Defendant Celltrion, Inc.'s Response to Plaintiff's Motion For Alternative Service, Dkt. 52 (N.D.W. Va.)
2015	Order Setting Briefing Schedule on Motions to Dismiss and Setting Schedule for Preliminary Injunction Proceedings, Dkt. 61 (N.D.W. VA.)
2016	Order Granting Motions for Alternative Service, Dkt. 219 (N.D.W. Va.)
2017	Summons, Proof of Service of Complaint, Dkt. 223 (N.D.W. Va.)
2018	Returned Summons, Dkt. 224 (N.D.W. Va.)

2019	*Regeneron v. Mylan*, 22-cv-61, Trial Transcript (Public Excerpts) (N.D.W. Va.)
2020	J.L. Fast et al., *Physical Instability of a Therapeutic Fc Fusion Protein: Domain Contributions to Conformational and Colloidal Stability*, 48 Biochem. 11724 (2009) ("Fast")
2021	Appellant Celltrion's Reply Brief, Dkt. 33 (Fed. Cir.)

I. Preliminary Statement

Celltrion's Petition is unlikely to succeed because its central argument has already failed to succeed six times. *Four* decisions of the Northern District of West Virginia and *two* decisions of the Court of Appeals for the Federal Circuit already have rejected substantially similar validity challenges to Regeneron's U.S. Patent No. 11,084,865 ("'865 patent")—on appeal, after trial, and at the preliminary-injunction stage. Celltrion offers no reason to believe that the *seventh* time will be the charm.

To the contrary, Celltrion itself already has tried and failed to establish a likelihood of success on invalidity as to the '865 patent, in an unsuccessful bid to avoid a preliminary injunction. The District Court rejected Celltrion's invalidity theories and issued the injunction, Celltrion appealed, and the Federal Circuit affirmed. Remarkably, despite appealing (unsuccessfully) numerous aspects of the District Court's judgment, Celltrion *did not even bother* to appeal that Court's rejection of its written-description theory—the same theory (reformulated as a priority-based challenge) on which its entire Petition now rests. Incredibly, Celltrion fails to even challenge the numerous findings underpinning the detailed analyses of the District Court and the Federal Circuit, let alone show any error across all six of the courts' decisions. Because the claims of the '865 patent are supported by the

specification, as every court to consider that issue has held, institution should be denied.

II. Background

Regeneron has been litigating the '865 patent covering its Eylea® product against putative biosimilars, including Celltrion, for two-and-a-half years. That litigation has resulted in four decisions of the District Court and three decisions of the Federal Circuit addressing the validity of the '865 patent. Throughout these decisions, the District Court and Federal Circuit repeatedly have upheld the '865 patent's claims as not lacking adequate written description.

A. Parallel Proceedings

Regeneron sued Mylan, Samsung Bioepis ("SB"), Formycon, Celltrion, and Amgen for infringement of the '865 patent. These suits have been consolidated for pre-trial purposes as a multidistrict litigation in the Northern District of West Virginia. *In re Aflibercept Pat. Litig.*, 730 F. Supp. 3d 1374, 1377 (J.P.M.L. 2024). That Court has issued one bench-trial decision (*Mylan*) and four preliminary-injunction decisions (*SB*, *Formycon*, *Celltrion*, and *Amgen*), and in each other than *Amgen* (which did not address invalidity), the District Court rejected written-description challenges to the '865 patent.

On appeal, the Federal Circuit affirmed all three validity decisions, and one (*Mylan*) was dismissed upon the parties' broader settlement.

These decisions repeatedly have confirmed that:

(1) there is adequate written description of aflibercept formulations that achieve "at least 98% native conformation," including both the lower and upper ends of that range, *Regeneron Pharm., Inc. v. Mylan Pharm. Inc.*, 714 F. Supp. 3d 652, 751-54 (N.D.W. Va. 2024) ("*Mylan*"); *In re Aflibercept Pat. Litig.*, 2024 WL 3422971, at *34-35 (N.D.W. Va. June 24, 2024) ("*SB PI Decision*"); *In re Aflibercept Pat. Litig.*, 2024 WL 3423047, at *38-40 (N.D.W. Va. July 9, 2024) ("*Formycon PI Decision*"); Ex.2004 (*Celltrion PI Decision*) at 118-24;[1] *Regeneron Pharm., Inc. v. Mylan Pharm. Inc.*, 127 F.4th 896, 915-17 (Fed. Cir. 2025) ("*SB*"); *Regeneron Pharm., Inc. v. Mylan Pharm. Inc.*, 2025 WL 324288, at *7 (Fed. Cir. Jan. 29, 2025) ("*Formycon*");

(2) the "at least 98% native conformation" limitation does not require a comparison of the amount of intact aflibercept present at the time of measurement to the amount present at time zero, *Regeneron Pharm., Inc. v.*

[1] The district court's validity analyses in the *SB PI Decision*, *Formycon PI Decision*, and *Celltrion PI Decision* are substantially similar because the three defendants raised substantially similar double-patenting defenses. For brevity, Regeneron generally cites the *Celltrion PI Decision*.

Mylan Pharm. Inc., 2025 WL 706079, at *3 (Fed. Cir. Mar. 5, 2025) ("*Celltrion*"); *Formycon*, 2025 WL 324288, at *5; and

(3) there is adequate written description of "glycosylated" aflibercept, *SB*, 127 F.4th at 914-15; *Formycon*, 2025 WL 324288, at *7.

B. Celltrion's Petition

Celltrion filed its Petition on January 15, 2025, after over fourteen months of litigation between Regeneron and Celltrion in the District Court and the Federal Circuit on the '865 patent.

Although technically styled as raising anticipation and obviousness challenges, all grounds of the Petition rest on the premise that the '865 patent may not claim priority to its parent application, undisputedly containing "the same specification" as the '865 patent, due to lack of written description in the shared specification. Pet. 1; *see* Pet. 47-48. Thus, Celltrion's Petition hinges on written-description and claim-construction arguments already considered and rejected by decisions of the District Court and Federal Circuit. For instance, Celltrion principally asserts that there is inadequate written-description support for the native-conformation limitations, maintaining that the specification does not support the 98% and 99% lower limits, a purported 100% upper limit, or that "the broad range of formulations encompassed by the claims" can achieve the claimed stability. Pet. 2-3, 32-45. Celltrion also advances a twice-rejected claim construction of the native-

conformation limitations that would require a "comparison" of the amount of intact VEGF antagonist present after storage versus at time zero. Pet. 24-26, 32, 37, 39, 43. Celltrion further asserts that there is no written-description support for the "glycosylated" limitation. Pet. 2-3, 45-46.

Inexplicably, however, Celltrion's Petition wholly ignores these prior decisions. And as the table below sets forth, these prior court decisions undermine each of Celltrion's arguments:

Celltrion's Petition	**District Court and Federal Circuit**
"Despite the ***broad genus of glycosylated VEGF antagonist proteins*** covered by the challenged claims, *US865* mentions glycosylation only once, and only in the context of describing one specific glycosylated VEGF antagonist, aflibercept, which has a specific glycan structure. Similarly, despite Regeneron's ***broad claims to a genus of VEGF antagonists containing a buffer, a sugar, and an organic co-solvent covered by the challenged claims***, the specification discloses stability testing only for formulations containing a specific	"[Regeneron's expert] Dr. Trout testified that each of the claim limitations in the ['865] Patent have ***'common structural features,' including the 'very specific' VEGF antagonist*** and the categories of organic co-solvent, buffer, and stabilizing agent. He further testified that these structures were well known in the art…. The Court credits Dr. Trout's analysis and conclusion." *Mylan*, 714 F. Supp. 3d at 751-52 (emphasis added) (citations omitted).

VEGF antagonist, aflibercept, and only for a handful of formulations containing the specific buffer phosphate, the specific sugar sucrose, and the specific organic co-solvents polysorbate 20 and polyethylene glycol 3350 for specified lots of aflibercept." Pet. 2-3 (emphases added).	
"Accordingly, this claim phrase should be construed such that the 'at least 98% or 99%' is in ***comparison with the amount of VEGF antagonist that is in intact functional form at time zero***." Pet. 25 (emphasis added).	"***According to Celltrion, the common knowledge of a person of ordinary skill in that art and the intrinsic evidence make clear that the at least 98% limitation in the '865 patent defines a rate of aggregation over a particular time, under particular conditions. We disagree.*** Celltrion's argument contradicts the plain claim language, which states that 'at least 98% of the VEGF antagonist is present in native conformation following … storage for two months as measured by SEC.' ***Nothing in the claims or specification suggests that a rate must be calculated. Rather, the claim states that after two months, the formulation is measured***

	by SEC, and the result is either above 98%—within the scope of the claim—or below 98%—outside the scope of the claim. On this record and even under de novo review of the claim construction issue, we discern no error in the district court's analysis." *Celltrion*, 2025 WL 706079, at *3 (emphases added) (internal quotation marks omitted). "Formycon argues for inherency on the ground that the 'native conformation' limitation in the '865 patent … refer[s] not to the starting point but to the amount of change in the percentage of native conformation after the period of time specified in the claims…. ***[A] substantial argument would be needed to overcome the apparent meaning of the claim language on its face, which requires that at least 98% of the VEGF antagonist is present in native conformation following storage for two months—a reference simply to a***

	property at that time—without calling for a comparison to an earlier time." *Formycon*, 2025 WL 324288 at *5 (cleaned up) (emphasis added).
"Notably, nothing in the general disclosure, or even in the text accompanying the examples, discloses these end points, much less these ranges…. ***The disclosure as filed, however, does not disclose, discuss, or suggest the[] [98-100% or 99-100%] ranges or their end-points***, and thus again fails to provide support for the claim limitation in which at least 98% (or 99%) of a glycosylated VEGF antagonist comprising amino acids 27-457 is present in native conformation following storage at 5ºC for two months (or twenty-four months) as measured by SEC for the broadly claimed formulations. Moreover, the examples do not provide data that allow the skilled artisan to derive the lower 98% and 99% end points of the claimed ranges. ***Nothing in the general disclosure, the***	"***The ['865] Patent's multiple disclosures of native conformations less than 1% shy of 100% (the absolute upper limit for the claim term, which in general is not met for proteins) meets the Federal Circuit's [written description] standard***…. [T]he ['865] Patent contained multiple disclosures of native conformations throughout the range of 98% to 100%," such that "***it is clear to a POSA reading the ['865] Patent that inventors possessed the entirety of the claimed subject matter*** …." Ex.2004 (*Celltrion PI Decision*) at 122, 124 (emphases added) (internal quotation marks and citations omitted). "Here, the district court appropriately credited expert testimony that most proteins are not purified to 100% to

text accompanying the examples, the data, or anything else in the specification provide blaze marks to the % claimed stability limitations including the 98 and 99% lower end or 100% upper end of the claimed range." Pet. 3, 34 (emphases added) (citation omitted).	conclude that the maximum percent native conformation would be limited by what a relevant artisan would understand to be workable…. ***The district court relied appropriately on expert testimony—this time from Dr. Trout—to find that the results in the patent show between 98.5 and 99.2% native conformation for the liquid formulations tested after storage for 2–3 months and that those multiple disclosures of native conformations less than 1% shy of 100% (the absolute upper limit for the claim term, which in general is not met for proteins) showed possession of the claimed range***…. SB contends[] a relevant artisan cannot reasonably discern the 98% lower bound…. Here, no cobbling together of numbers is necessary—the '865 patent contains multiple disclosures of native conformations throughout the range of 98% to 100%. ***Thus, the district court could properly find that it is clear to a relevant artisan reading the '865***

	patent that inventors possessed the entirety of the claimed subject matter." *SB*, 127 F.4th at 916-17 (cleaned up) (emphases added).
"***And a POSA reading the narrow examples would not understand that the inventors possessed the broadly claimed formulations*** having the claimed stability range after storage for a defined amount of time given only the specifically reported data points of the examples having very similar formulations…. There are no blaze marks pointing the skilled artisan to the claimed stability ranges or indicating that the data points would also apply to the broad range of formulations encompassed by the claims…. Regeneron also ***never explained how the very similar formulations of the Examples provide written description support for these limitations given the broad range of formulations encompassed by the claims***." Pet. 35, 37, 39 (emphases added).	"Dr. Trout also testified that ***the POSA could recognize the formulations that were claimed in the ['865] Patent, could visualize the formulations within the claims, and could recognize from the specification that the inventors invented the claimed formulations***. As for the specific disclosures in the ['865] Patent that allowed the POSA to recognize these features, Dr. Trout pointed to the disclosure of column 2, lines 39 to 57, as well as each of the examples. ***Those disclosures conveyed what structures would fall within the scope of the claim, permitting the POSA to visualize the claimed formulations and to recognize that the inventors invented and possessed what the ['865] Patent claims***. He noted that ***all of the ['865] Patent's examples have at least 98 percent native***

	conformation as measured by SEC after two months…. Following this analysis, Dr. Trout testified that the ['865] Patent provided species or examples representative of the genus, claimed structures rather than function, and thus provided adequate written description for the asserted claims. The Court credits Dr. Trout's analysis and conclusion…. ***Here, in contrast, the evidence demonstrated that the examples in the specification were predictive of the performance of formulations that were not exemplified in the patent***. Regeneron pointed to several working examples of embodiments that were outside the disclosed examples (and the prior art) but nonetheless met the 98% native conformation [limitation]…. The Defendants did not dispute these results, nor did the Defendants point to any formulation within the claims that did not achieve the claimed functional properties…. [T]he evidence showed that the POSA would have pursued a

	more linear process that, the Defendants' expert agreed, would not require making and testing each permutation of the structural elements of the claim, and that the POSA could use formulation design systems…. Thus, the Court concludes that the Defendants have failed to demonstrate by clear and convincing evidence that the asserted claims of the ['865] Patent are invalid for lack of written description." *Mylan*, 714 F. Supp. 3d at 751-54 (emphases added) (internal quotation marks and citations omitted).
"A sufficient written description requires a statement of an invention, not an invitation to go on a hunting expedition to ***cobble together***, after the fact, a synthetic definition of an invention. *Indivior UK Ltd. v. Dr. Reddy's Labs. S.A.*, 18 F.4th 1323, 1329 (Fed. Cir. 2021) (***finding that PO's range was not described but was***	"In reaching its conclusion, ***the district court correctly distinguished the present cases from the case SB relied on***: *Indivior UK Ltd. v. Dr. Reddy's Laboratories S.A.*, 18 F.4th 1323 (Fed. Cir. 2021)…. ***Here, no cobbling together of numbers is necessary***—the '865 patent contains multiple disclosures of native conformations throughout the range of 98% to 100%.

merely 'cobbling together numbers after the fact')." Pet. 36 (emphases added).	Thus, the district court could properly find that it is clear to a relevant artisan reading the '865 patent that inventors ***possessed the entirety of the claimed subject matter***." *SB*, 127 F.4th at 917 (cleaned up) (emphases added).
"The disclosure mentions glycosylation only once, and only mentions one glycosylated VEGF antagonist variant. That one variant is glycosylated at each of Asn residues 62, 94, 149, 222, and 308…. ***Thus, to the extent that glycosylation in claim 1 is construed to mean anything other than glycosylation at each of Asn residues 62, 94, 149, 222, and 308, … the term 'glycosylated' lacks written description support*** …." Pet. 46 (emphasis added) (citations omitted).	"SB argues that there is no support in the '865 patent's specification for glycosylated aflibercept formulations with the claimed level of stability. SB states that the specification has only one generic disclosure of glycosylation that precedes the examples and is not connected in any way to them…. We disagree…. The '865 specification, in discussing the preparation of the VEGF trap, states that the VEGF trap in a specific embodiment comprises amino acids 27-457 of SEQ ID NO:4, *i.e.*, aflibercept, and is glycosylated at Asn residues 62, 94, 149, 222 and 308. The specification then provides several embodiments along with their stability data, including Examples 3 and 4, which

	comprise the same amino-acid sequence (SEQ ID NO:4) and have stability measurements that fall within the claimed range. Regeneron presented expert testimony that a relevant artisan reading those examples would look to the rest of the specification to see how the VEGF trap was made, would note the specification's disclosure that glycosylation results from a particular method of manufacture, and would understand the VEGF trap to be glycosylated at those specific residues. SB has not cited any evidence in rebuttal. ***The district court did not clearly err in finding, on this record, that a relevant artisan, reading the specification as a whole, would understand the specification to disclose glycosylation as claimed***." *SB*, 127 F.4th at 914-15 (cleaned up) (emphasis added).

Celltrion's Petition relies on the Declaration of Dr. Tessier (Ex.1002), the same expert Celltrion relied on in the District Court and whose testimony the District

Court previously considered in resolving the preliminary-injunction proceedings against Celltrion.

III. Celltrion's Petition Is Time-Barred Under 35 U.S.C. § 315(b)

Celltrion filed its Petition on January 15, 2025—more than fourteen months after Regeneron sued it for infringement of the '865 patent (in November 2023) and more than twelve months after Celltrion waived the issue of service of the complaint (on January 4, 2024). Its Petition is thus time-barred under 35 U.S.C. § 315(b), and the Board should deny institution.

"An inter partes review may not be instituted if the petition requesting the proceeding is filed more than 1 year after the date on which the petitioner … is served with a complaint alleging infringement of the patent." 35 U.S.C. § 315(b). The service requirement of § 315(b) may be satisfied through "official delivery" of a complaint. *Click-To-Call Techs., LP v. Ingenio, Inc.*, 899 F.3d 1321, 1330 (Fed. Cir. 2018), *vacated and remanded sub nom. on other grounds*, *Thryv, Inc v. Click-To-Call Techs., LP*, 590 U.S. 45 (2020), *and vacated sub nom. Click-To-Call Techs., LP v. Ingenio, Inc.*, 810 F. App'x 881 (Fed. Cir. 2020). However, service of process, like other rights and defenses, can be intentionally relinquished or abandoned. *See United States v. Olano*, 507 U.S. 725, 733 (1993) ("[W]aiver is the 'intentional relinquishment or abandonment of a known right.'" (citation omitted)). Thus, in the § 315(b) context, the Federal Circuit has held that "the service requirement is

satisfied by proper service of process" *or* by "consent, waiver, or forfeiture by the defendant." *Game & Tech. Co. v. Wargaming Grp. Ltd.*, 942 F.3d 1343, 1349 (Fed. Cir. 2019) (citing *King v. Taylor*, 694 F.3d 650, 655 (6th Cir. 2012)). And when "the service requirement is satisfied," whether "by proper service of process" or "waiver," *Game & Tech.*, 942 F.3d at 1349, "§ 315(b)'s time bar" is "trigger[ed]," *Click-To-Call*, 899 F.3d at 1332.

Celltrion waived service here. After suing Celltrion in November 2023, Regeneron moved for alternative service of the complaint on Celltrion in December 2023. Ex.2013 (Dkt. 43-1), 2-3. Celltrion responded to Regeneron's motion on January 4, 2024, asserting that Regeneron's "*Motion is moot* given that Celltrion intends to file a special appearance and motion to challenge venue in mid-January," such that "[t]he Court thus need not address Regeneron's Motion." Ex.2014 (Dkt. 52), 1 (emphasis added). Celltrion further represented that the court need not address the issue of service:

> Regeneron's Motion is moot, and the Court need not address it. In order to efficiently move this matter along, Celltrion intends to file its motion to dismiss for lack of personal jurisdiction and improper venue by January 17, even though Celltrion has not been served (and no answer will be due on that date). Even if the Court grants Regeneron's motion, which it should not, Celltrion's motion will be on file before Celltrion's answering date.

> The issue of service therefore need not be addressed by this Court.

Id. at 3. Accepting Celltrion's representation that it "will have filed a motion to dismiss on or before January 17, 2024," the District Court issued an order on January 9, 2024, setting the briefing schedule for that motion and for preliminary-injunction proceedings. Ex.2015 (Dkt. 61), 2.

Celltrion's response to Regeneron's alternative-service motion waived the issue of service as of January 4, 2024, such that Celltrion's Petition, filed over a year later on January 15, 2025, is untimely under § 315(b). Celltrion's *repeated* representations that the issue of service "*is moot*" and "*need not be addressed*," and its reassurance to the District Court that litigation may proceed "*even though Celltrion has not been served*," Ex.2014 (Dkt. 52), 1, 3 (emphases added), are a textbook example of a party intentionally abandoning a known right, *Olano*, 507 U.S. at 733. Had Celltrion intended to preserve the issue of improper service, whether in its motion to dismiss or at some later date, then it would have been necessary for "[t]he issue of service" (as well as Regeneron's alternative-service motion) to "be addressed by th[e] Court." Ex.2014 (Dkt. 52), 3. Celltrion, however, represented precisely the opposite to the District Court, confirming that Regeneron's motion and the issue of service were "moot" and "need not be addressed," and that litigation could proceed without Celltrion having been served (whether in

accordance with Rule 4 or by electronic means, as Regeneron's alternative-service motion sought). *Id*. Thus, on January 4, 2025, Celltrion waived service of process and started the § 315(b) clock. *Id.*; *Click-To-Call*, 899 F.3d at 1332.

Although Celltrion's response to Regeneron's alternative-service motion included a footnote purporting not to "waive any objections or defenses, including any of those identified in Rule 12 of the Federal Rules of Civil Procedure, and specifically objections and defenses based on the lack of personal jurisdiction and/or improper venue," Ex.2014 (Dkt. 52), 1 n.1, that statement did not preserve an inadequate service-of-process defense. As explained above, Celltrion represented that Regeneron's alternative-service motion was "moot" and "need not be addressed" by the District Court. Those express representations could be true only if Celltrion had committed to not contesting service; thus, Celltrion necessarily confirmed its waiver of an inadequate-service-of-process defense. Whatever "objections or defenses" Celltrion sought to preserve in this footnote, they could not have included the preservation of any service-of-process defense, as Celltrion's express representations to the court necessarily confirmed its waiver of that defense.

Celltrion's representations, moreover, led both Regeneron and the District Court to believe that Celltrion would not contest the adequacy of service—which further supports waiver. *See*, *e.g.*, *Trs. of Cent. Laborers' Welfare Fund v. Lowery*, 924 F.2d 731, 733 (7th Cir. 1991) ("Where a defendant leads a plaintiff to believe

that service is adequate and that no such defense will be interposed, for example, courts have not hesitated to conclude that the defense is waived."); *In re Ethicon, Inc., Pelvic Repair Sys. Prods. Liab. Litig.*, 2016 WL 1718826, at *2 (S.D.W. Va. Apr. 27, 2016) ("[M]any circuits agree that defendants can waive objections to personal jurisdiction by indicating a willingness to defend the suit or taking other action that would lead the plaintiff to believe service was adequate."). Relying expressly on Celltrion's representations, the District Court ordered that litigation proceed, in the form of motion-to-dismiss and preliminary-injunction briefing, without first addressing the adequacy of service.[2] Ex.2015 (Dkt. 61), 2-3 ("Assuming that all Defendants will have filed a motion to dismiss on or before January 17, 2024, as represented, the following briefing schedule shall govern the

[2] It is irrelevant that the district court later granted Regeneron's alternative-service motion and that Regeneron then prophylactically served a summons on Celltrion by email. Ex.2016 (Dkt. 219); Ex.2017 (Dkt. 223); Ex.2018 (Dkt. 224). As discussed above, Celltrion indisputably waived its right to contest service as of January 4, 2024. Once "the service requirement is satisfied," including by "waiver," *Game & Tech.*, 942 F.3d at 1349 (citation omitted), subsequent events are immaterial for purposes of § 315(b), *see Click-To-Call*, 899 F.3d at 1330 (confirming "subsequent events" are immaterial once service requirement has been satisfied).

motions to dismiss …. [T]he Court finds that it is appropriate here to allow preliminary injunction proceedings to take place at the same time as the briefing and resolution of the motions to dismiss ... [and] set[s] forth the following schedule for preliminary injunction proceedings ….”). Accordingly, Celltrion was “brought under [the] court’s authority” and was “obligate[d] … to engage in litigation in relation to th[e] [’865] patent,” underscoring that Celltrion, through its waiver, had been served for purposes of § 315(b). *Amneal Pharm., LLC v. Endo Pharm. Inc.*, No. IPR2014-00360, 2018 WL 446628, at *3 (P.T.A.B. Jan. 10, 2018); *see also Gordon * Howard Assocs., Inc. v. Lunareye, Inc.*, No. IPR2014-01213, 2015 WL 495016, at *10 (P.T.A.B. Feb. 3, 2015) (“[S]ufficiency of service for purposes of § 315(b) depends on whether the service was sufficient to place the petitioner under the authority of the court ….” (citation omitted)).

In sum, Celltrion waived its right to contest service of process on January 4, 2024. As a result, Celltrion was served on that day for purposes of § 315(b), *Game & Tech.*, 942 F.3d at 1349, and its January 15, 2025 Petition is thus time-barred. The Board should therefore deny institution.

IV. Celltrion Fails To Show a Reasonable Likelihood That the ’865 Patent Claims Would Have Been Anticipated or Obvious

Even if timely, the numerous prior District Court and Federal Circuit adjudications of the ’865 patent’s validity foreclose Celltrion’s likelihood of success. Remarkably, Celltrion proceeds as if these decisions do not exist. But those

decisions repeatedly have made numerous findings independently foreclosing Celltrion's arguments here.

A. Technical Overview

The '865 patent discloses and claims ophthalmic formulations of the fusion protein aflibercept, including Eylea®. Eylea® contains 40 mg/mL of a glycosylated form of aflibercept along with other ingredients. "Aflibercept is known as a 'VEGF antagonist' or 'VEGF trap' due to its ability to bind, or 'trap,' a protein called vascular endothelial growth factor (VEGF) before VEGF can bind to receptors in the human body and stimulate blood-vessel growth. Aflibercept formulations have been approved by the FDA for the treatment of several angiogenic eye diseases (*i.e.*, diseases related to blood-vessel growth in the eye) via intravitreal administration." *SB*, 127 F.4th at 903.

1. Fusion Proteins

Eylea® was the first fusion-protein ophthalmic drug product. Fusion proteins are formed by fusing together different domains of multiple proteins. Ex.2019, 448:1-12 (Furfine). At the time of the invention, the leading ophthalmic VEGF antagonist in development was Genentech's ranibizumab. Ex.2019, 448:18-449:6, 450:14-19 (Furfine). Whereas aflibercept is a synthetic fusion protein, ranibizumab is an antibody fragment. Ex.2019, 1035:4-9 (Rabinow), 451:5-14, 456:6-9 (Furfine).

"[F]usion proteins are fundamentally different from antibodies in that fusion proteins are synthetic molecules made by humans, while antibodies have evolved over time to be stable." *Mylan*, 714 F. Supp. 3d at 737 (citing Ex.2019, 2013:14-17, 2014:21-2015:16 (Trout), 448:1-6, 456:6-9 (Furfine)); Ex.2020 (Fast), 15 ("In comparison with native IgG proteins, wherein interdomain interactions presumably have evolved to provide mutual stabilization, fusion proteins may lack such stabilizing interdomain stabilization."); *SB PI Decision*, 2024 WL 3422971, at *31.

2. The '865 Patent

Claim 4 of the '865 patent is illustrative (emphases added):

> 4. A vial comprising an ophthalmic formulation suitable for intravitreal administration that comprises:
>
> a vascular endothelial growth factor (VEGF) antagonist
>
> an organic co-solvent,
>
> a buffer, and
>
> a stabilizing agent,
>
> ***wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4***; and
>
> ***wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two***

> ***months as measured by size exclusion chromatography***[;]
>
> ***wherein the concentration of said VEGF antagonist fusion protein is 40 mg/ml***[;]
>
> [and] wherein said organic co-solvent comprises about 0.03% to about 0.1% polysorbate 20.

The patent also includes claims requiring 99% stability for two months, *see, e.g.*, '865 patent, claim 16 ("The vial of claim 5, wherein at least 99% of said VEGF antagonist is present in native conformation after 2 month storage at 5° C. as measured by size exclusion chromatography."), and claims requiring 98% stability for 24 months, *see, e.g.*, *id.*, claim 17 ("The vial of claim 5, wherein at least 98% of said VEGF antagonist fusion protein is present in native conformation following storage at 5° C. for 24 months as measured by size exclusion chromatography.").

The patent discloses eight working examples of aflibercept formulations, with certain stability measurements reported after storage. One of these stability measurements is the fusion protein's "native conformation," which refers to "the original intact form of the VEGF antagonist, which is a form that does not exhibit chemical or physical instability." *Mylan*, 714 F. Supp. 3d at 696. Proteins not in their native conformation can aggregate, reducing therapeutic activity and

potentially leading to severe problems such as inflammation or an adverse immune response. *Id.* at 707; *SB PI Decision*, 2024 WL 3422971, at *33.

The patent's working examples vary in their ingredients and/or container systems. In each example, the formulations were evaluated based on several characteristics, including "Native Configuration." *E.g.*, '865 patent, 8:45-57, Tables 1-8. As relevant here, the reported "native configuration" (synonymous with "native conformation") in each example over 2-3 months is summarized below:

Example	**Native Conformation**	**Time (months)**
1	98.7	3
2	98.5	3
3	99.2	2
4	99.1	2
5	99.2	2
6	99.1	3
7	99.3	2
8	98.9	2

As the data illustrates, the native conformation in each example was over 98% after 2-3 months storage.

The specification provides examples of the different specific ingredients and amounts that fulfill each of the claimed limitations of the formulation. '865 patent, 2:39-57. For example, the specification states that "[i]n various embodiments . . . the stable liquid ophthalmic formulation comprises about 40-50 mg/ml of the VEGF antagonist." *Id.* 2:49, 2:53-54. As another example, the specification states that "the

buffering agent may be, *for example*, phosphate buffer." *Id.* 2:45-46 (emphasis added).

The specification also discloses that the VEGF antagonist may be glycosylated, including at specific amino acid residues. *Id.*, 6:34-37 ("In a specific embodiment, the fusion protein . . . is glycosylated at Asn residues 62, 94, 149, 222, and 308.").

B. '865 Patent Priority Chain

As Celltrion acknowledges, Pet. 28, the '865 patent has a priority chain tracing back to provisional application 60/814,484, filed on June 16, 2006.[3] '865 patent, Related U.S. Application Data. The earliest nonprovisional application in the continuation chain is application 11/818,463, filed on June 14, 2007. *Id.* Celltrion agrees that every application and patent in the continuation chain has a materially identical specification, Pet. 28, referred to herein as the specification or common specification. All of Celltrion's invalidity grounds center on US2007/0293432 as the primary reference (Pet. 28, 58, 64), which Celltrion refers to as *US432*. Pet. 1. As Celltrion again acknowledges, "*US432* is the published application of US App.

[3] Celltrion's representation that the filing date of the provisional application was June 14, 2006, Pet. 28, appears to be a typographical error.

11/818,463, an application in US865's priority chain, which has the same specification as [the '865 patent]." Pet. 1 (internal citation omitted).

C. Person of Ordinary Skill

The District Court applied the following POSA definition:

> [T]he POSA "would have held an advanced degree, such as a Master's in a biopharmaceutical science, or a related discipline, such as chemical engineering, and several years of experience in the development of biologics products. Alternatively, the POSA could have a Ph.D. in such discipline and less experience. The POSA may collaborate with others, including a medical doctor with experience treating ophthalmic diseases."

Mylan, 714 F. Supp. 3d at 702; Ex.2004 (*Celltrion PI Decision*) at 20. Celltrion advances the same level of ordinary skill. Pet. 12. Regeneron proposes that the Board adopt the same POSA definition that has consistently governed these cases.

D. Claim Construction

1. "wherein said VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4"

Celltrion asserts that the limitation "wherein said VEGF antagonist fusion protein is glycosylated and *comprises* amino acids 27-457 of SEQ ID NO:4" should be understood as "not limited to a protein comprising only amino acids 27-457 of SEQ ID NO:4," provided that the protein "still bind[s] VEGF to some degree." Pet.

22-23. Celltrion cites nothing in support of its vague "bind[s] VEGF to some degree" constraint. *Id.* Nonetheless, Regeneron assumes for purposes of this filing that "comprises" in this claim term is understood as open-ended.

2. "wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography"

Celltrion argues that the claim term "wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography" (the "98% native conformation limitation") should be construed such that 98% is "in comparison with the amount of VEGF trap in native conformation reported at time zero." Pet. 24. Celltrion presented a nearly identical construction to the Federal Circuit. Ex.2010, 57-58. It was squarely rejected there because it lacks any support in the claim language or the specification, and the Board should reject it again here. *Celltrion*, 2025 WL 706079, at *3.

Specifically, the Federal Circuit in *Celltrion* explained:

> Celltrion's argument contradicts the plain claim language, which states that "at least 98% of the VEGF antagonist *is present* in native conformation following storage ... for two months" as measured by SEC. '865 patent claim 1 (emphasis added). Nothing in the claims or specification suggests that a "rate" must be calculated. Rather, the claim states that after two months, the formulation is

> measured by SEC, and the result is either above 98%—within the scope of the claim—or below 98%—outside the scope of the claim. On this record and even under de novo review of the claim construction issue, we discern no error in the district court's analysis.

Id. Although once is enough, the Federal Circuit also observed in *Formycon* that the claim language "at least 98% of the VEGF antagonist *is present* in native conformation following storage ... for two months" is "a reference simply to a property at that time—*without calling for a comparison to an earlier time*." 2025 WL 324288, at *5 (second emphasis added). The Federal Circuit has thus twice made clear that, consistent with the claim's plain language, determining the amount of VEGF antagonist in native conformation does not require an unrecited calculation comparing the native conformation at a given time point to the native conformation at time zero.

The Federal Circuit's construction is consistent with the intrinsic evidence and the construction Celltrion originally advanced at the District Court. The claims and specification nowhere suggest, exemplify, disclose, or recite the calculation of a difference from time zero that Celltrion proposes. Instead, in every example, the patent reports measured values of "% VEGF Trap Native Configuration"—a term undisputedly synonymous with the "native conformation" recited in the claims, *see* Pet. 5—at "0" months, rather than arbitrarily assigning a native conformation of

100% at time zero. Every example also reports measured values of "% VEGF Trap Native Configuration" after various storage periods, not as a comparison with the time-zero measurement. For example, the "% VEGF Trap Native Configuration" in Example 6 at time zero is 99.2%. '865 patent, 10:41, 10:60. After one month, the "% VEGF Trap Native Configuration" is unchanged and the percentage is reported as 99.2%. *Id.*, 10:62. Celltrion's construction would result in a % native conformation of 100%, contrary to the values plainly described in the specification.

At the District Court, Celltrion and its expert Dr. Tessier originally, and correctly, understood the % native conformation limitation to not require a time-zero difference, and Celltrion relied on that understanding in support of its written-description arguments. Specifically, both argued, consistent with Regeneron, the District Court, and the Federal Circuit, that the "% native conformation data in the [patent's liquid formulation] examples ends at 99.2%"—*i.e.*, the specific two-month measured value reported in Examples 3, not a number reflecting the difference between time zero and two months. Ex.2012, 17 (citing testimony of Dr. Tessier); Ex.1001, 9:19-42. Critically, that understanding flatly contradicts Celltrion's interpretation advanced here requiring a time-zero difference.

Under the construction advanced in Celltrion's Petition, 99.2% is not the maximum native conformation after two months, nor is it even within the range of

disclosed values. Rather, Celltrion's interpretation would result in % native conformation values between 99.6% and 99.9%:

'865 Patent Example	Patent's Reported %N.C. (0 mo.)	Patent's Reported %N.C. (2-3 mo.)	Difference	%N.C. at 2-3 mo. under Celltrion's Original Construction	%N.C. at 2-3 mo. under Construction in Celltrion's Petition
1	98.8	98.7	0.1	98.7	99.9
2	98.9	98.5	0.4	98.5	99.6
3	99.5	99.2	0.3	99.2	99.7
4	99.4	99.1	0.3	99.1	99.7
5	99.3	99.2	0.1	99.2	99.9
6	99.2	99.1	0.1	99.1	99.9

Not until its preliminary injunction sur-reply did Celltrion alter its position and advance the claim construction argument it now advances in its Petition. Celltrion's about-face defies its own expert's prior sworn declaration and the intrinsic record, and should be rejected. *Cf. N. Telecom v. Samsung Elecs*., 215 F.3d 1281, 1290 (Fed. Cir. 2000) ("[The Court] look[s] with extreme disfavor on appeals that allege error in claim constructions that were advocated below by the very party now challenging them." (citation omitted)).

The portions of the specification cited by Celltrion do not refer to "native conformation" or "native configuration," nor do they set forth a comparison to time zero as its claim construction proposes. Pet. 24-25. Nowhere does Celltrion explain how the patent's discussion of "substantially free" somehow supports its construction. *Id.*; *see* '865 patent, 6:42-55 (neither referring to native conformation

nor setting forth comparison calculation with time zero). Thus, Celltrion's proposed comparison calculation is supported exclusively by the testimony of Dr. Tessier, Pet. 25 (citing Ex.1002), who himself agreed with the Federal Circuit's construction in the District Court. Ex.2012, 17. Dr. Tessier's irreconcilable constructions perfectly illustrate how expert testimony "generated at the time of and for the purpose of litigation … can suffer from bias that is not present in intrinsic evidence" and "pose[] the risk that it will be used to change the meaning of claims in derogation of the indisputable public records consisting of the claims, the specification and the prosecution history, thereby undermining the public notice function of patents." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1319 (Fed. Cir. 2005) (en banc). Dr. Tessier's testimony should be afforded no weight and rejected.

In summary, the Board should construe "wherein at least 98% of the VEGF antagonist is present in native conformation following storage at 5° C. for two months as measured by size exclusion chromatography" consistent with the Federal Circuit's decisions in *Celltrion*, 2025 WL 706079, at *3 ("[T]he claim states that after two months, the formulation is measured by SEC, and the result is either above 98%—within the scope of the claim—or below 98%—outside the scope of the claim."), and *Formycon*, 2025 WL 324288, at *5. In other words, this claim term should be construed to refer "simply to [native conformation] at [the claimed] time—

without calling for a comparison to an earlier time." *Formycon*, 2025 WL 324288, at *5.

3. "glycosylated" and "native conformation"

Celltrion does not dispute the claim constructions that were settled in the *Mylan* litigation as to the terms "glycosylated" and "native conformation" (in isolation). In *Mylan*, "the parties stipulated that the term 'glycosylated' in claim 1 of the ['865] Patent is construed as 'containing at least one amino acid residue with an attached carbohydrate.'" *Mylan*, 714 F. Supp. 3d at 695-96. The District Court also construed "native conformation" to mean "the original intact form of the VEGF antagonist, which is a form that does not exhibit chemical or physical instability." Id. at 696. These constructions are undisputed by Celltrion. Pet. 23, 26.

With no evident relevance to any of its arguments, Celltrion criticizes size-exclusion chromatography (SEC) as "not a true measurement of the amount of protein in native conformation." Pet. 23. But the claim language explicitly refers to "native conformation … *as measured by size exclusion chromatography*." '865 patent, claim 1. There is no "inconsistency," Pet. 23; SEC is simply how the claims instruct "native conformation" is measured.

E. Grounds 1-3: Celltrion Fails to Demonstrate That *US432* Is Prior Art, Because the '865 Patent Is Entitled to the Priority Date of Its Parent Application

Celltrion's Petition is premised on using the published application of the '865 patent's parent, from which the '865 patent claims priority, as prior art. As Celltrion agrees, Pet. 1, 28, 47-48, the specification of the '865 patent is identical to those of its parents (which are related through continuation applications). And as the District Court and Federal Circuit have repeatedly held, that common specification adequately describes the claims of the '865 patent. Accordingly, the priority claim of the '865 patent to its parent is proper and *US432* is thus not prior art, which forecloses any likelihood of success for each of Celltrion's Grounds (Pet. 21).

Celltrion's priority challenge simply re-packages the same written description arguments that Celltrion and its co-defendants previously advanced and which the District Court and Federal Circuit have rejected six times. Remarkably, even though Celltrion's written description challenges here focus on the same 98% native conformation and glycosylation limitations (*e.g.*, Pet. 27) that the District Court and Federal Circuit already have confirmed are adequately described, Celltrion fails to address these courts' repeated findings. *E.g.*, *SB*, 127 F.4th at 914-17; Ex.2004 (*Celltrion PI Decision*) at 118-124; *Mylan*, 714 F. Supp. 3d at 751-54. Celltrion's Petition shows no error in the courts' holdings.

1. The Specification Describes the 98% Native Conformation Limitation

Celltrion's written description arguments largely focus on the 98% native conformation limitation and, to a lesser extent, the related limitations set forth in claim 16 (requiring 99% native conformation after two months storage) and claim 17 (requiring 98% native conformation after 24 months storage). Pet. 32-45. As the District Court and Federal Circuit have repeatedly determined, written description is satisfied because the specification's multiple working examples of formulations all meet the 98% native conformation limitation. *E.g.*, *Mylan*, 714 F. Supp. 3d at 752; *SB*, 127 F.4th at 916. Specifically, the Federal Circuit affirmed the District Court's findings that "'the results in the patent show between 98.5 and 99.2% native conformation for the liquid formulations tested after storage for 2–3 months' and … those 'multiple disclosures of native conformations less than 1% shy of 100% (the absolute upper limit for the claim term, which 'in general' is not met for proteins)' showed possession of the claimed range" of "at least 98%" native conformation. *SB*, 127 F.4th at 916 (quoting *SB PI Decision*, 2024 WL 3422971, at *35); *Formycon*, 2025 WL 324288, at *7 (noting that there was "no material difference between Formycon's arguments and those presented by SB," which the Federal Circuit "held unpersuasive"); *see supra* IV.A.2 (summarizing reported native conformation for each example).

This disclosure goes well beyond what written description requires. As *SB* explained, "[t]he specification does not need to describe 'every conceivable and

possible future embodiment of [the] invention,'" 127 F.4th at 916 (quoting *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1365 (Fed. Cir. 2003)), and "[t]here is no rigid requirement that the disclosure contain 'either examples or an actual reduction to practice'; the proper inquiry is whether the patentee has provided an adequate description that 'in a definite way identifies the claimed invention' in sufficient detail such that a person of ordinary skill would understand that the inventor had made the invention at the time of filing," *id.* (quoting *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1308 (Fed. Cir. 2015)).

Celltrion nonetheless urges the Board to defy these well-established legal principles and the Federal Circuit's application of them to the '865 patent based on an argument that the specification does not disclose "the 98 and 99% lower end or 100% upper end of the claimed range." Pet. 34. But, as detailed below, the District Court and Federal Circuit have squarely rejected these arguments, and Celltrion provides no basis to overturn them.

a. The Specification Describes the Upper Bound of the 98% "Range"

Celltrion contends that the "100% upper end" of the 98% native conformation limitation is not described. Pet. 34. However, in five separate opinions, the District Court and Federal Circuit have held that there is adequate written description for the

upper bound of the claimed 98% range.[4] Ex.2004 (*Celltrion PI Decision*) at 118-124; *SB PI Decision*, 2024 WL 3422971, at *34-35, *Formycon PI Decision*, 2024 WL 3423047, at *38-40; *SB*¸ 127 F.4th at 914-17; *Formycon*, 2025 WL 324288, at *7. Celltrion does not address, much less refute, these decisions or the evidence underlying them. They are fatal to Celltrion's argument.

In *SB*, Celltrion's co-defendant SB argued that "the upper bound of the 'at least 98%'" native conformation limitation was not adequately described. 127 F.4th at 914. The Federal Circuit "reject[ed]" that argument. *Id.* The Court explained that open-ended claim terms, like "at least" 98% native conformation, have sufficient written description "where the upper bound 'would be limited by what a person skilled in the art would understand to be workable' and where the patent's specification adequately supported that range." *Id*. at 916 (quoting *Ralston Purina Co. v. Far-Mar-Co, Inc*., 772 F.2d 1570, 1576 (Fed. Cir. 1985)); *see also Andersen Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1376–77 (Fed. Cir. 2007) (affirming jury verdict of written description where there was evidence that a relevant artisan would recognize an inherent upper limit); *Nalpropion Pharm., Inc.*

[4] Celltrion's "upper end" arguments do not distinguish among the claims. Pet. 34. Because the claim limitations referring to native conformation are indistinguishable with respect to the purported "upper end," claim 4 is representative.

v. Actavis Labs. FL, Inc., 934 F.3d 1344, 1349–51 (Fed. Cir. 2019) (affirming adequate written description for an "at least 99% [dissolution]" limitation without disclosure of results at or above 99%). Applying this precedent to the '865 patent, the Court concluded that the upper bound was supported by the specification. The Court upheld the District Court's finding, based on the testimony of Dr. Tessier (who is also Celltrion's expert here), that "*most proteins* are not purified to [100%]." *SB*, 127 F.4th at 915-16. The Court then concluded that the specification adequately described what the '865 patent claimed, agreeing with the District Court that "'the results in the patent show between 98.5 and 99.2% native conformation for the liquid formulations tested after storage for 2–3 months' and that those 'multiple disclosures of native conformations less than 1% shy of 100% (the absolute upper limit for the claim term, which "in general" is not met for proteins)' *showed possession of the claimed range*." *Id.* at 916 (emphasis added) (quoting *SB PI Decision*, 2024 WL 3422971, at *35).

Celltrion offers no basis to reach a different outcome here. That is no surprise: Although it could have appealed the District Court's substantially identical written-description analysis, *see* Ex.2004 (*Celltrion PI Decision*) at 118-124, Celltrion lodged no challenge to that holding on appeal (thus only *SB* and *Formycon* addressed written description). Just as in *SB*, Celltrion "has not pointed to any evidence that aflibercept differs from 'most proteins'" which are not ordinarily purified to 100%

purity. *SB*, 127 F.4th at 916. Nor does Celltrion contend that "even a small change in native conformation above 99.2% would be both possible and so difficult to achieve that formulations with stability percentages within the 99.3–100% are significantly different inventions, making it improper to view the inventors as having invented them based on the 99.2% figure in the specification." *Id.*

Rather, Celltrion asserts that the specification conveys possession only of "the specifically reported data points of the examples having very similar formulations." Pet. 35. However, *SB* specifically rejected the theory that written description requires data points for every conceivable value between 98% and 100%. *See SB*, 127 F.4th at 915-16 ("The specification need not describe 'every conceivable and possible future embodiment of [the] invention.'" (quoting *Cordis*, 339 F.3d at 1365) (alteration in original)). And *SB* is in accordance with other Federal Circuit precedent finding sufficient written description for open-ended claim terms where the specification does not explicitly mention each and every theoretical point within the range. *See Andersen*, 474 F.3d at 1376-77 (upholding written description to a claim reciting "rating of greater than 500,000," despite no results greater than 1.2 million); *Nalpropion*, 934 F.3d at 1349-51 (upholding claims requiring "at least 99% [dissolution]" despite no results discussed between 99-100%); *Indivior Inc. v. Dr. Reddy's Labs. S.A.*, 930 F.3d 1325, 1347-48 (Fed. Cir. 2019) (upholding claim

requiring "about 60% or more" L-PEO despite the relevant application in the priority chain disclosing "50–75% L-PEO").

Accordingly, the patent adequately describes the upper bound of the 98% native conformation limitation. *SB*, 127 F.4th at 916-17.

b. The Specification Describes the Lower Bound of the 98% "Range"

The District Court and Federal Circuit also rejected Celltrion's argument (Pet. 34) that the specification lacks adequate written description for the lower bound of the 98% native conformation and 99% native conformation limitations. *SB*, 127 F.4th at 917; Ex.2004 (*Celltrion PI Decision*) at 122-124. As with the upper bound, Celltrion offers no basis for a different outcome here.

Here, the specification expressly discloses native conformations for the liquid formulation examples from 98.5 to 99.2% at 2-3 months. '865 patent, Examples 1-6; *SB*, 127 F.4th at 916. The 98% native conformation and 99% native conformation limitations thus claim what the specification describes. *See* Ex.2004 (*Celltrion PI Decision*) at 123. Celltrion relies on *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320 (Fed. Cir. 2000), in support of its argument that the specification does not sufficiently describe the 98% native conformation limitation. *See* Pet. 32-35. There, the claim limitation at issue was directed to a "C_{max}/C_{24}" ratio. *Purdue Pharma*, 230 F.3d at 1324. However, no C_{max}/C_{24} ratio *at all* was disclosed in the specification. Specifically, the Court observed that "neither the text accompanying the examples,

nor the data, nor anything else in the specification in any way emphasizes the C_{max}/C_{24} ratio," which could be derived only be "piec[ing] together" various data in the patent. *Id.* at 1326. The Federal Circuit thus held that there were "no blaze marks directing the skilled artisan to the C_{max}/C_{24} ratio or what value that ratio should exceed." *Id.* at 1326. As the Court explained, "there is nothing in the written description of Examples 1 and 3 that would suggest to one skilled in the art that the C_{max}/C_{24} ratio is an important defining quality of the formulation, nor does the disclosure even motivate one to calculate the ratio." *Id.* at 1327.

Unlike in *Purdue*, no such "cobbling together of numbers is necessary" here because "the '865 patent contains 'multiple disclosures of native conformations throughout the range of 98% to 100%.'" *SB*, 127 F.4th at 917 (quoting *SB PI Decision*, 2024 WL 3422971, at *35). Rather than the ratio nowhere mentioned in the patent in *Purdue*, or the similar defect in *Indivior*, 18 F.4th at 1329 (Pet. 36) where deriving the claim limitation required "select[ing] several components, add[ing] up the individual values, determin[ing] the aggregate percentages, and then coupl[ing] those aggregate percentages with other examples ... to create an otherwise unstated range," *SB*, 127 F.4th at 917 (quoting *Indivior*, 18 F.4th at 1329), here native conformation data is explicitly disclosed in *every* example in the '865 patent specification at multiple time points, and in every example native conformation is greater than 98% after 2-3 months storage as claimed, '865 patent, Tables 1-6.

Native conformation is not "a characteristic that is not even discussed in passing" as Celltrion falsely asserts (Pet. 35). Accordingly, *contra* Celltrion (Pet. 35), "it is clear to a [relevant artisan] reading the ['865 patent] that inventors possessed the entirety of the claimed subject matter." *SB*, 127 F.4th at 917 (quoting *SB PI Decision*, 2024 WL 3422971, at *35). The Federal Circuit has thus already rejected the exact argument raised by Celltrion here.

Celltrion raises no arguments particular to the 99% native conformation limitation. Claim 16, reciting this limitation, was already addressed by the District Court and affirmed on appeal, *SB PI Decision*, 2024 WL 3422971, at *3; Ex.2004 (*Celltrion PI Decision*) at 10 (asserting claim 16), and the patent includes working examples with native conformation above 99% after two months storage, *see SB*, 127 F.4th at 917 (noting the two-month native conformation for Examples 3 and 4 were 99.2% and 99.1%, respectively); *e.g.*, '865 patent, Tables 3-4. Accordingly, Celltrion's challenge to this claim likewise lacks merit.

c. Celltrion's Arguments Regarding "% VEGF Trap Recovered" Misconstrue the Claims

Celltrion's written description challenge also rests on an argument that the recited "native conformation" value in the claims somehow also requires reference to a different metric *not* recited in the claims, "% VEGF Trap Recovered." Pet. 42-44. Specifically, Celltrion asserts the novel theory that when the percent recovered decreases, the POSA would, in some unspecified way, "include the decreases" in

that metric in determining native conformation. Pet. 43. This is effectively a new claim-construction argument for the "native conformation" term, and Celltrion cites not a shred of intrinsic evidence in support of it. The Board should reject Celltrion's construction because it (1) has no support in the claim language, (2) defies the specification's teachings, (3) contradicts Celltrion's and Dr. Tessier's prior arguments to the District Court (like its proposed time zero calculation), and (4) is contrary to the Federal Circuit's *Celltrion* and *Formycon* decisions.

First, the claim language nowhere refers to "% VEGF Trap Recovered." The claims instead recite only a minimum percentage of "*native conformation* … as measured by [SEC]." *E.g.*, '865 patent, claim 1. Celltrion itself agrees that "native conformation" is referred to as "% VEGF Trap Native Configuration" in the specification. Pet. 5 (referring to "'% VEGF Trap Native Configuration,' (i.e., 'native conformation')"). Contrary to the claim language, Celltrion's construction would require a certain percentage of *both* (unrecited) percent recovered and (recited) percent native conformation, combined in some undescribed way. But that is simply rewriting the claim term, and should be rejected for that reason alone. Claim construction cannot "revise or ignore the explicit language of the claims." *Phillips*, 415 F.3d at 1327.

Second, every data table in the specification reports "% VEGF Trap Recovered" separately from "% VEGF Trap Native Configuration"; and the

specification nowhere suggests that percent native conformation is determined by factoring in percent recovered. '865 patent, Tables 1-8. In other words, the common specification describes, explicitly, exactly what the claim requires: % native conformation data as measured by size exclusion chromatography. Celltrion points to no teaching in the patent that % native conformation and % recovered values are combinable any way. Rather, the specification's consistent treatment of these quantities as distinct reinforces that they should not be conflated or combined in the claims. *See AstraZeneca AB v. Mylan Pharm. Inc.*, 19 F.4th 1325, 1334-35 (Fed. Cir. 2021).

Third, as explained above with respect to Celltrion's time-zero subtraction argument, *supra* IV.D.2, Celltrion's % recovered argument is contradicted by Celltrion's and Dr. Tessier's own positions in the District Court. Again, both argued that "the % native conformation data in the [patent's liquid formulation] examples ends at 99.2%"—i.e., the specific two-month measured value reported in Examples 3, not a number that somehow accounts for the % recovered at that time using a calculation nowhere described in the patent. Ex.2012, 17 (citing testimony of Dr. Tessier); '865 patent, 9:19-42. Indeed, even here, Celltrion agrees that it is inappropriate for a patent to claim a quantity which "the disclosure [does not] even motivate one to calculate," but that is precisely what its own construction requires by combining percent native conformation and percent recovery in some undefined

and undescribed way. Pet. 34-35 (quoting *Purdue*, 230 F.3d at 1326). Underscoring the ambiguity of Celltrion's farfetched construction, neither it nor its expert ever attempt to explain how percent recovery should be factored into the claimed percent native conformation metric. Pet. 42-44; Ex.1002, ¶¶ 126-131.

Fourth, the Federal Circuit had no difficulty construing the % native conformation limitation without reference to % recovery, consistent with the claim language and specification. *Celltrion*, 2025 WL 706079, at *3; *SB*, 127 F.4th at 916 (affirming District Court's finding that "the results in the patent show between 98.5 and 99.2% native conformation for the liquid formulations tested after storage for 2–3 months," corresponding to the native conformation values reported in Tables 1-6); *supra* IV.A.2.

Altogether, Celltrion's % recovered argument is utterly devoid of intrinsic support, contradicts Celltrion's own prior arguments, and flouts the judgment of every court that has considered this term. Again, Celltrion's only support is the reconsidered testimony of Dr. Tessier, Pet. 42-44, which merely parrots Celltrion's arguments and contradicts his prior testimony, Ex.1002, ¶¶ 126-131, and thus deserves no weight, *Phillips*, 415 F.3d at 1318-19; *supra* IV.D.2. Because the claims do not recite any limitations based on percent recovery, the percent recovery data in

the specification is irrelevant to written description of the native conformation limitation.[5]

d. The Specification Describes the Claimed Formulations Possessing 98% Native Conformation

Celltrion more generally criticizes the specification's examples as "narrow" in contrast to the "broadly claimed" formulations. Pet. 35. Mylan presented the same argument over the course of a two-week trial, and the District Court correctly rejected it in its thorough post-trial decision. *Mylan*, 714 F. Supp. 3d at 751-754. The Board should do the same.

As an initial matter, it is unclear what Celltrion's actual argument is. Celltrion does not explain how the claims are "broad[]" in comparison to the examples, and its criticisms are not directed at any particular claim limitations, Pet. 35; Regeneron thus treats claim 4 as representative. And while Celltrion accuses Regeneron of having "never explained" how the examples support the 98% native conformation limitation, Pet. 39, six decisions of the District Court and the Federal Circuit have

[5] Celltrion argues that differences in percent recovery in the specification suggest a "margin of error" "of at least 3%, and maybe as high as 13%." Pet. 44. However, even assuming that were correct, Celltrion offers no basis to impute the margin of error from percent recovery to percent native conformation, which does not show the same deviations.

explained that the ’865 patent is not invalid for lack of written description, yet Celltrion inexplicably ignores each one.

In *Mylan*, Mylan similarly criticized the claims as “open-ended and broad” and “for reciting the structural categories of ‘buffer’ and ‘stabilizing agent’ instead of specific chemical structures.” *Mylan*, 714 F. Supp. 3d at 750, 752. The District Court, after weighing the live testimony of five expert witnesses and inventors, rejected Mylan’s argument and found that “[b]ecause the claims are drawn to a specific protein at a specific concentration with specific concentration ranges of polysorbate 20, the Court holds that the specification allows the POSA ‘to visualize or recognize the identity of the subject matter purportedly described’ and thus meets the written description requirement.” *Id.* at 751 (quoting *Allergan,* 796 F.3d at 1308).

As the court in *Mylan* explained, the specification’s “multiple formulations with different combinations of excipients and corresponding stability data … and lists of suitable excipients and amounts” easily satisfied written description, which does not require “either examples or an actual reduction to practice.” *Id.* (quoting *Allergan*, 796 F.3d at 1308). More specifically, the specification’s examples as well as the specific disclosures at 2:39-57 of the ’865 patent allowed the POSA to “recognize from the specification that the inventors invented the claimed

formulations." *Mylan*, 714 F. Supp. 3d at 751-52; *see Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc).

Contrary to Celltrion's vague assertion of breadth, the District Court found that the claims were directed to formulations of a "a specific protein," i.e., a "VEGF antagonist fusion protein is glycosylated and comprises amino acids 27-457 of SEQ ID NO:4," along with other structures disclosed in the specification. *Mylan*, 714 F. Supp. 3d at 751. Although claim 4 recites the "structural categories of 'buffer' and 'stabilizing agent' instead of specific chemical structures," the District Court found—again based on the live testimony of experts and an inventor—that those categories were well known in the art and did not require detailed description. *Id.* at 751-52 (citing cases and testimony from Dr. Trout, Mylan's expert Dr. MacMichael, and Dr. Kenneth Graham, an inventor of the '865 patent); *see, e.g.*, *Falko-Guntner Falkner v. Inglis*, 448 F.3d 1357, 1368 (Fed. Cir. 2006) ("[T]he forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification."); *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629, 650 (E.D. Tex. 2017) (Bryson, J.) (patent did not need to describe "hundreds of" compounds already "known" and within the claims to satisfy written description), *aff'd*, 739 F. App'x 643 (Fed. Cir. 2018). Regardless, as the District Court found, the patent describes both categories and identifies specific substances for each. *E.g.*, '865 patent, 2:44-46.

Celltrion argues that Regeneron "never explained how the very similar formulations of the Examples provide written description support" for the native conformation limitation "given the broad range of formulations encompassed by the claims." Pet. 39. Even putting aside that it is Celltrion who must set forth the bases for unpatentability in its Petition, *see* 35 U.S.C. § 312, Celltrion is also wrong: in addition to the three District Court decisions addressing written description of the 98% native conformation limitation, all affirmed by the Federal Circuit, the parties addressed written description in the two-week *Mylan* bench trial. And in the *Mylan* decision, the court found specifically that the evidence demonstrated a "'correlation between structure and function' [that] may satisfy [the] written description requirement." *Mylan*, 714 F. Supp. 3d at 753 (quoting *Ariad*, 598 F.3d at 1350). The court found specifically that "the examples in the specification were predictive of the performance of formulations that were not exemplified in the patent." *Id.* at 753. Not only did all of the patent's examples achieve the claimed 98% native conformation at two months,[6] *id.* at 752, there were also "several working examples

[6] As Celltrion observes, multiple examples also possessed 99% native conformation at two months. Pet. 39 (citing '865 patent, Examples 3, 4); *see also, e.g.*, '865 patent, Examples 5, 6 (possessing 99.1 and 99.2% native conformation at 2-3 months).

of embodiments that were outside the disclosed examples (and the prior art) but nonetheless met the 98% native conformation" limitation, *id.* at 753 (citing Ex.2019, 1729:11-1732:3, 1732:4-1733:23 (testimony of Dr. Graham, a named inventor of the '865 patent)). This further supports the correlation between the structure of the claimed formulations and the 98% native conformation limitation. *Id.*

Celltrion points to a single formulation—made by the inventors during the course of developing the formulation described in the patent that ultimately became Eylea®—that did not possess 98% native conformation. Pet. 35-36. However, Celltrion points to no precedent requiring that every possible formulation possess 98% native conformation. To the contrary, written description requires only a "correlation between structure and function," not perfect correspondence. *Ariad*, 598 F.3d at 1350. The existence of a single formulation falling within the claim scope but lacking 98% native conformation does not demonstrate a lack of written description. *Id.*; *see also Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1576 (Fed. Cir. 1984) ("It is not a function of the claims to specifically exclude possible inoperative substances." (cleaned up)). The common specification,

---

Celltrion offers no arguments particular to the 99% native conformation limitation, which is described for the same reasons as the 98% native conformation limitation.

through its examples and guidance, disclosed a correlation between function and structure. This is all that is required for written description.

Contrary to the court's findings in *Mylan*, 714 F. Supp. 3d at 751-54, Celltrion argues the art is complex and unpredictable, which "support[s] the conclusion that the skilled artisan would not read the limited examples as demonstrating that the inventors had possession of the claimed invention." Pet. 41. Celltrion relies principally on expert declarations from Dr. Klibanov that Regeneron submitted in a different IPR addressing a different patent. *Id.* (citing Ex.1021). Critically, Dr. Klibanov's declarations exclusively addressed obviousness and anticipation, not written description. *See* Ex.1021, Ex.1027. Unlike written description, which focuses on POSA's understanding "after reading the *specification*," anticipation and obviousness address the POSA's understanding "in view of the *prior art*," *Allergan*, 796 F.3d at 1310, which necessarily excludes knowledge of the invention, *Sensonics, Inc. v. Aerosonic Corp.*, 81 F.3d 1566, 1570 (Fed. Cir. 1996) ("To draw on hindsight knowledge of the patented invention, when the prior art does not contain or suggest that knowledge, is to use the invention as a template for its own reconstruction—an illogical and inappropriate process by which to determine patentability."). Thus, Dr. Klibanov's testimony is irrelevant to written description.

Regardless, Dr. Klibanov's testimony lends no support to Celltrion's arguments. Celltrion cites Dr. Klibanov's testimony that "small structural

differences between two proteins of the same class can lead to significant stability differences." Pet. 41 (citing Ex.1027, ¶63). However, the claims here are all directed to a *particular glycosylated protein* with a specific amino acid sequence that is described in the specification, *Mylan*, 714 F. Supp. 3d at 754, '865 patent, 6:25-39, unlike cases involving claims to protein recited solely by function, *e.g.*, *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1292 (Fed. Cir. 2014). Celltrion asserts that the claims here are unlimited because the specifically recited sequence could include "additional amino acids at either or both of the C- and N-termini." Pet. 41. Even assuming Celltrion's open-ended claim construction, however, "[i]t is not a function of the claims to specifically exclude … possible inoperative substances." *Atlas Powder*, 750 F.3d at 1576 (quoting *In re Dinh-Nguyen*, 492 F.2d 856, 858-59 (C.C.P.A. 1974)); *Mylan*, 714 F. Supp. 3d at 752 (same). And Celltrion presents no evidence or concrete examples of different VEGF antagonists possessing the claimed amino-acid sequence but nonetheless lacking the claimed levels of native conformation in the claimed formulations.

Celltrion's arguments about the other formulation elements fare no better. Pet. 41. Celltrion cites Dr. Klibanov's testimony to argue that glycosylation, excipients, and protein concentration could generally affect the stability of a protein. *Id.* But again, Celltrion points to no evidence of variation within the claimed structures that would preclude achieving the 98% native conformation limitation *for*

the claimed aflibercept protein. To the contrary, *Mylan* explained that the patent's examples were predictive of the native conformation of other actual formulations. *Mylan*, 714 F. Supp. 3d at 753*; see also id*. (finding that "the POSA would not need to make and test every possible formulation in order to practice the claims"). And Celltrion itself has argued (in support of its double-patenting argument) that achieving 98% native conformation "would have required nothing more than ordinary skill," even based solely on the prior art. Ex.2021, 30. Celltrion's absence of any evidence specific to aflibercept, along with the detailed analysis in *Mylan* and Celltrion's own prior arguments, forecloses any reasonable likelihood of success of showing no written description.

e. The Specification Describes the 24-Month Native Conformation Limitations

In a single paragraph, Celltrion argues that claims 17, 25, 42, and 50 lack written description for the limitation requiring 98% native conformation after 24 months storage (the "24-month limitation"). Pet. 44-45. As with the 98% native conformation limitation in claim 1, the District Court and Federal Circuit have upheld the written description of these claims six times, in the post-trial *Mylan* decision and the preliminary-injunction decisions, all of which involved claim 17 and/or claim 42, *e.g.*, *Mylan*, 714 F. Supp. 3d at 677; Ex.2004 (*Celltrion PI Decision*) at 10.

Celltrion concedes that the specification describes a working embodiment

with over 98% native conformation after 24 months. Pet. 44; '865 patent, Table 1. This disclosure goes beyond what written description requires, which does not require "either examples or an actual reduction to practice." *Alcon Rsch. Ltd. v. Barr Labs., Inc.*, 745 F.3d 1180, 1190-91 (Fed. Cir. 2014); *see also Falko-Gunter*, 448 F.3d at 1366 ("A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language.") (cleaned up)).

Celltrion criticizes Example 1 as involving 50 mg/mL aflibercept instead of the claimed 40 mg/mL, Pet. 44, but the *Mylan* court considered this distinction and credited Regeneron's evidence that Example 1 nonetheless supported enablement, 714 F. Supp. 3d at 755 (citing Ex.2019 (2100:7-2103:18)), and it likewise supports written description, *see* Ex.2019 (2100:7-2103:18) (explaining that "the skilled person would understand that if this formulation with 50 mg/mL met that 98 percent or related limitations, then the similar formulation with 40 mg/mL would also meet those limitations, 98 percent, 99, and the different times").

Celltrion criticizes the disclosure by pointing to Example 2, which shows 97.6% stability after 24 months. Pet. 44-45. However, Celltrion's suggestion that the claims must encompass the scope of every example conflicts with precedent. *See TIP Sys., LLC v. Phillips & Brooks/Gladwin, Inc.*, 529 F.3d 1364, 1373 (Fed. Cir. 2008) ("[T]he mere fact that there is an alternative embodiment disclosed in [a]

patent that is not encompassed by [a] claim construction does not outweigh the language of the claim, especially when the court's construction is supported by the intrinsic evidence."); *Vanda Pharm. Inc. v. West-Ward Pharm. Int'l Ltd.*, 887 F.3d 1117, 1137 (Fed. Cir. 2018) ("The disclosure of a dose outside of the claimed range does not compel a finding that the asserted claims lack adequate written description."). Here, the specification describes a working example with greater than 98% native conformation at 24 months, and numerous other examples with greater than 98% native conformation at various other time points. As written description does not even require particular examples, *see Allergan*, 796 F.3d at 1308, the specification satisfies written description.

2. The Specification Describes the Glycosylation Limitation

Celltrion does not dispute that there is written description support for the glycosylation limitation in claims 14, 22, 39, 47, and 51-64. Pet. 45-46. Contrary to Celltrion's assertions, there is also written description support for the limitation in the other claims requiring that the claimed protein "is glycosylated" (claims 1-13, 15-21, 23-38, 40-46, and 48-50).

The Federal Circuit has already decided this exact issue and concluded that the glycosylation limitation is described. *SB*, 127 F.4th at 914-15. Specifically, the Court affirmed the District Court's finding that "a relevant artisan, reading the specification 'as a whole,' … would understand the specification to disclose

glycosylation as claimed." *Id.* at 915 (quoting *Allergan USA, Inc. v. MSN Labs. Private Ltd.*, 111 F.4th 1358, 1375 (Fed. Cir. 2024)). The Court pointed to the specification's disclosure of a VEGF antagonist "'in a specific embodiment' [which] 'comprises amino acids 27-457 of SEQ ID NO:4,' *i.e.*, aflibercept, '*and is glycosylated at Asn residues 62, 94, 149, 222 and 308*.'" *Id.* (emphasis added) (quoting '865 patent, 6:34-37).

Celltrion does nothing to undermine that decision, offering no reason why the term "is glycosylated" lacks written description, where, as the Federal Circuit held, the specification literally describes glycosylated aflibercept. Pet. 46; '865 patent, 6:34-37. Celltrion observes that the specification discloses just "one glycosylated VEGF antagonist variant," Pet. 46, but provides no basis for limiting the claims to that embodiment or running afoul of the written-description requirement. There is none. *See Cordis*, 339 F.3d at 1365 (the specification need not describe "every conceivable and possible future embodiment of [the] invention"); *In re Entresto*, 125 F.4th 1090, 1098 (Fed. Cir. 2025) (concluding written description was satisfied notwithstanding that claims encompassed an embodiment "not discovered until four years after the priority"). The specification conveys through its express language that the inventors were in possession of glycosylated aflibercept and thus satisfies the written description requirement. *Ariad*, 598 F.3d at 1351.

3. The Specification Describes the "No Phosphate" Limitation

Finally, Celltrion challenges the limitation in claims 18 and 43, which were not asserted or otherwise at issue against Celltrion during the preliminary injunction proceedings. These claims recite that the "formulation does not contain phosphate." Celltrion argues that the specification only specifically discloses phosphate buffer and thus cannot claim a formulation lacking phosphate. Pet. 47. But as courts have repeatedly found, the '865 patent is not limited to phosphate.

To be clear, this "no phosphate" limitation still requires a buffer—it just requires that the formulation not contain phosphate (a known buffer). The District Court has twice held a POSA would understand the common specification to disclose buffers beyond phosphate buffers. *Formycon PI Decision*, 2024 WL 3423047, at *15 (rejecting construction that would limit "buffer" to require a "phosphate buffer"); *Mylan*, 714 F. Supp. 3d at 755 (crediting Dr. Trout's testimony that the patent disclosed "a buffer such as phosphate and other known buffers that would achieve the disclosed pH range"). These decisions correctly recognized that the specification does not limit buffers to phosphate buffers and instead teaches that "the buffering agent may be, *for example*, phosphate buffer." '865 patent, 2:45-46. As the District Court explained, "[t]he specification's use of the phrase 'for example' indicates that the specification necessarily contemplates buffers other than phosphate." *Formycon PI Decision*, 2024 WL 3423047, at *15. Claims 18 and 43

are simply drawn to these other buffers, which were known in the art. *Id.* at *16 (describing multiple buffers known in 2006 other than phosphate).

Celltrion cites (Pet. 47) to *Novartis Pharm. Corp. v. Accord Healthcare, Inc.*, 38 F.4th 1013 (Fed. Cir. 2022), but that case does not support Celltrion's argument. *Novartis* makes clear that there is not a "heightened standard for negative claim limitations." 38 F.4th at 1020. "[A]s with positive limitations, the disclosure must only 'reasonably convey[] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.'" *Id.* (quoting *Ariad*, 598 F.3d at 1351). Here, it would be clear to a POSA that buffers other than phosphate, such as succinate or histidine, could be used as the buffer in the claimed "no phosphate" formulation, *Mylan*, 714 F. Supp. 3d at 755, and that these buffers are "necessarily present in [the] disclosure," *Novartis*, 38 F.4th at 1020.

F. Celltrion's Invalidity Grounds Rely on Non-Prior Art *US432*

As set forth above, the common specification adequately describes each of Celltrion's contested claim limitations. And as Celltrion admits (Pet. 1), *US432* is the published application of an application in the '865 patent's priority chain, and *US432* and the '865 patent share the aforementioned common specification. Therefore, the '865 patent's priority claim is proper and *US432* is not prior art. *See Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1369-70 (Fed. Cir. 2009); *Technology Licensing Corp. v. Videotek, Inc.*, 545 F3d 1316, 1327 (Fed. Cir.

2008); *cf. Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.*, 689 F.3d 1368, 1378-79; *In re Kaplan*, 789 F.2d 1574, 1580 (Fed. Cir. 1986).

All of Celltrion's invalidity grounds rely on *US432* as the principal reference. Pet. 48, 58, 64. Because *US432* is not prior art to the '865 patent, none of Celltrion's grounds have a likelihood of success. The Board should thus deny institution. *See United Servs. Automobile Ass'n v. Auto Telematics Ltd.*, No. IPR2023-00858, 2023 WL 8653083 (P.T.A.B. Dec. 14, 2023) (denying institution when Petitioner did not demonstrate a reasonable likelihood of showing that a prior art reference upon which all of Petitioner's grounds relied was prior art); *United Servs. Automobile Ass'n v. Auto Telematics Ltd.*, No. IPR2023-00912, 2023 WL 8192060 (P.T.A.B. Nov. 27, 2023) (same); *Triller, Inc. v. TikTok Pte. Ltd*, No. IPR2022-00181, 2022 WL 1618057, at *5-10 (P.T.A.B. May 16, 2022) (similar).

V. Conclusion

For the foregoing reasons, institution should be denied.

Date: May 14, 2025

/David I. Berl/
David I. Berl
Reg. No. 72,751
Williams & Connolly LLP
680 Maine Street SW
Washington, D.C. 20024
Lead Counsel for Patent Owner

CERTIFICATION UNDER 37 C.F.R. § 42.24(d)

In accordance with 37 C.F.R. § 42.24, as amended, the undersigned certifies that this Patent Owner Preliminary Response complies with the applicable type volume limitations of 37 C.F.R. §§ 42.24(a)(i) and 42.24(b)(1). Exclusive of the portions exempted by 37 C.F.R. § 42.24(a), this Patent Owner Preliminary Response contains 12,564 words as counted by the word processing program used for its preparation (Microsoft Word 2019).

Date: May 14, 2025

/David I. Berl/
David I. Berl
Reg. No. 72,751
Lead Counsel for Patent Owner

CERTIFICATE OF SERVICE
(37 C.F.R. § 42.6(e))

The undersigned hereby certifies that on May 14, 2025, I caused true and correct copies of the following materials:

- Patent Owner's Preliminary Response
- Patent Owner's Exhibit List
- Exhibits 2013-2021

to be served via e-mail on the following:

Name	E-Mail Address
Lora M. Green	lgreen@geminilaw.com
Robert Cerwinski	rcerwinski@geminilaw.com
Michael Johnson	mjohnson1@willkie.com
Keith A. Zullow	kzullow@geminilaw.com
Michael Cottler	mcottler@geminilaw.com
Yahn-Lin (Franklin) Chu	fchu@geminilaw.com
Aviv Zalcenstein	azalcenstein@geminilaw.com

Date: May 14, 2025

/David I. Berl/
David I. Berl
Reg. No. 72,751
Lead Counsel for Patent Owner