IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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SANOFI-AVENTIS U.S. LLC,
GENZYME CORP. AND
REGENERON PHARMACEUTICALS, INC.,
Petitioners

v.

IMMUNEX CORPORATION,
Patent Owner

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Case IPR2017-01129
Patent 8,679,487

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**PATENT OWNER PRELIMINARY RESPONSE**
**UNDER 37 C.F.R. § 42.107(a)**

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Patent Trial and Appeal Board
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

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Patent Owner Immunex Corporation ("Immunex") provides this preliminary response to the Petition for *inter partes* review ("IPR") of claims 1-17 of U.S. Patent No. 8,679,487 ("the '487 Patent"; EX1001) filed by Petitioners Sanofi-Aventis U.S. LLC, Genzyme Corp., and Regeneron Pharmaceuticals, Inc. (collectively, "Sanofi"), in accordance with 37 C.F.R. § 42.107(a).

Sanofi's Petition fails to meet its burden to establish a reasonable likelihood of prevailing with respect to its challenge to claims 1-17 of the '487 Patent. The Board should exercise its discretion to deny the Petition because it fails to comport with the Board's rules, the America Invents Act ("AIA"), and the U.S. Constitution. 35 U.S.C. §314(a); 37 C.F.R. §42.5; U.S. CONST., amend. VII.

## I. Introduction

The Board should see this Petition for what it is: an improper §112 attack under the AIA. IPR petitions may request review of patent claims "only on a ground that could be raised under Section 102 or 103 and only on the basis of prior art consisting of patents or printed publications." 35 U.S.C. § 311(b). The only document Sanofi offers as an alleged prior art reference is Stevens (EX1006), Sanofi's own patent application covering anti-IL-4R antibodies. But Stevens, which published seven years *after* the priority date the Office has explicitly

accorded to the ’487 Patent, discloses that Sanofi used one of the antibodies in the ’487 Patent, as well as the teachings in the ’487 Patent, to generate and select Sanofi’s own anti-IL-4R antibodies. Therefore, Stevens’ later-developed anti-IL-4R antibodies cannot *anticipate* the challenged claims.

Unable to mount a proper art-based attack on the ’487 Patent, Sanofi instead attempts to deny priority to any filing date for the challenged claims so as to be able to argue that Stevens is properly considered as invalidating art. But as Sanofi admits, the disclosure of the ’487 Patent was made in 2001, seven years before Stevens, and it has not changed since that priority filing. Arguing that the claims lack support in the Common Specification[1] is no different than arguing that the claims are unpatentable under §112—a ground that is not permissible in IPR petitions. *See* 35 U.S.C. § 311(b).

To institute IPR based on this Petition would have the effect of opening the

[1] As Sanofi concedes, the ’487 Patent and each of its Priority Applications “share[] an original specification,” and the disclosures in each specification “are substantially the same.” Pet., at 4. The shared specification is referred to as the “Common Specification” throughout this Paper.

gate to §112 attacks in countless IPRs. Petitioners would simply assert that the claims are entitled to no priority date because they lack §112 support and cite later references, potentially including a parent of the patent itself. That is not the law nor the intent of Congress in limiting IPRs to certain prior art based attacks.

Moreover, the Office previously decided the same §112 issues in Immunex's favor during prosecution of the '487 Patent and stated that the claims were entitled to the May 1, 2001 priority date. In an Office Action, the Examiner affirmatively determined that the pending claims (nearly identical to those that issued in the '487 Patent) are supported in the Common Specification and are afforded the May 1, 2001 priority date "for purposes of art." EX1002, at 0116. Conveniently, the Petition neither discloses nor disputes this fact from the '487 Patent's prosecution history. Accordingly, the Board should reject Sanofi's Petition outright for presenting "the same or substantially the same arguments previously considered by the Office." 35 U.S.C. §325(d).

Sanofi's §112 arguments rest on several additional procedural defects. To begin, the Petition fails to clarify Sanofi's ambiguous position on claim construction. In federal court, Sanofi has alleged that the claims are extremely

narrow and cover only six antibodies and their equivalents under 35 U.S.C. §112, paragraph 6. IMX2001, ¶¶30-31; IMX2002, ¶¶66-67. In its Petition, however, Sanofi alleges that the claims are so broad to encompass "untold numbers" of antibodies, without offering any construction of the term "antibody." Pet., at 24-25, 29, 49. That overreading of the challenged claims necessarily rests on a different, yet unidentified claim construction. Accordingly, Sanofi has improperly "shift[ed] the burden of advancing a claim construction from the petitioner to the Board." *Palo Alto Networks v. Finjan, Inc.*, IPR2015-02000, Paper 9, at 4 (PTAB, May 20, 2016). This defect alone also warrants denial of institution. *See* 37 C.F.R. §42.104(b)(3).

The Petition is further defective because it relies on Dr. Robinson's declaration testimony for its §112 arguments when he fails to provide <u>any claim construction</u> for <u>any term</u> as part of his alleged §112 assessment. Dr. Robinson cannot credibly compare the scope of the challenged claims to the disclosure in the Common Specification without first construing the claims. Thus, the entirety of the Petition's §112 arguments rely on faulty testimony and should be rejected. It would be untenable for the Board to institute an IPR proceeding here where Sanofi has

created ambiguity regarding its position on claim construction and the sole expert upon whom Sanofi relies for its §112 arguments is completely silent on claim construction.

Although the Board need not reach the merits of the §112 arguments, the Petition fails to show a reasonable likelihood of prevailing on its written description or enablement arguments. The description within the four corners of the Common Specification shows that the inventors on the ’487 Patent were in possession of the claimed genus of antibodies. The ’487 Patent claims are directed to antibodies that compete in binding to IL-4R with a reference antibody disclosed in great detail in the specification. Competition claims are commonly used to claim antibodies beyond the specific examples illustrated in the patent. Competition assays are routinely performed in the field and Sanofi has pointed to no difficulties in carrying out such assays. Given that Sanofi used one of the antibodies disclosed in the ’487 Patent, Immunex’s 12B5 antibody, to generate and select the antibodies disclosed in the Stevens reference, Sanofi’s arguments that the Common Specification does not describe or enable a person skilled in the art to make and use the invention are inconsistent and simply not credible.

Sanofi's §112 analysis is further flawed because it improperly focuses only on six specific examples of monoclonal antibodies disclosed in the Common Specification while ignoring numerous other disclosures and references expressly incorporated therein that describe and enable making and using IL-4R antibodies falling within the scope of the challenged claims. The Petition thus fails to consider the scope of the teachings in the Common Specification in view of the prior art.

Even in making its priority arguments, the Petition fails to adequately assess §112 support as of the filing date of each Priority Application. Sanofi makes a conclusory statement that the same §112 analysis would purportedly apply to each of the '487 Patent's priority dates. This is insufficient to meet Sanofi's burden of showing that Stevens is prior art to each challenged priority date, particularly given that the state of the art is a factor that must be considered.

Finally, the Board should deny the Petition on the ground that institution of IPR of the '487 Patent would deprive Immunex of its right to a jury trial under the Seventh Amendment. This is especially true here where the Petition hinges on §112 arguments that are not permitted within the statutory scope of IPR petitions. IPR proceedings are a form of litigation over private property rights, and the

Seventh Amendment preserves a Patent Owner's right to have litigation over its private property take place in an Article III Court, not before an administrative agency of the Executive Branch. Adjudicating the validity of the '487 Patent in this forum, especially the §112 arguments presented by the Petition, would violate Immunex's Seventh Amendment rights.

In sum, the Board should deny Sanofi's Petition because it fails to show a reasonable likelihood of prevailing on its challenges to claims 1-17.

## II. Sanofi's Petition should be denied because it fails to cite any prior art to the '487 Patent.

### A. *The Stevens patent application is not prior art under §102.*

On its face, the Petition fails to cite any prior art under §102 as the Stevens reference was published seven years after the May 2001 priority filing of the '487 Patent. The Board should end the inquiry there and deny the Petition outright. Sanofi attempts to explain its citation of Stevens by asserting that the claims of the '487 Patent are not entitled to any priority filing because the claims lack §112 support in the patent specification. But in an IPR proceeding, the only time a §112 analysis is appropriate is in determining which priority filing the claims are entitled to so as to properly determine the relevant prior art.

Such a situation may arise when the patent claims priority to several provisional applications or involves a continuation-in-part application where information was added to the specification. But these circumstances do not apply here. The Petition does not challenge claim to an earlier priority application while admitting priority is properly claimed to a later one. Rather, the Petition asserts that the claims are not supported at all and thus not entitled to any priority filing date, laying bare the clear §112 attack on the patent.

Sanofi admits that the specification did not change in any material respect after the May 2001 filing. Pet., at 4, 43. Thus, that is the date to assess the prior art for IPR purposes. Selecting a later date for assessing the art has no basis under §102 without first holding that there is no support in the specification for the claimed invention.

### B. *The Petition is based on an impermissible §112 attack on the patentability of the '487 Patent.*

Sanofi's Petition should further be denied under 35 U.S.C. §311 because the Petition is an improper patentability challenge based on 35 U.S.C. §112. As Sanofi concedes, each of the '487 Patent's Priority Applications "share[s] the specification" of U.S. Application Serial No. 09/847,816 ("the '816 Application").

Pet., at 43. Thus, Sanofi's challenges to the '487 Patent's priority claim based on §112 are substantively identical to a §112 challenge to the '487 Patent itself—which is impermissible under 35 U.S.C. §311. For the Board to allow such priority attacks would be akin to sanctioning §112 challenges in IPRs of any patent that issued from a continuation or divisional application. This would defeat the purpose of the law limiting IPRs to grounds that can be raised under §102 and §103. *See* § 35 USC 311(b).

## III. The Petition should be denied because it presents the same or substantially the same issues previously decided by the Office.

### A. *The Office has already affirmatively determined that the '487 Patent is entitled to its 2001 priority date "for purposes of art."*

Sanofi's Petition should be denied under 35 U.S.C. §325(d) because the Office already decided that the claims are entitled to claim a priority date of May 1, 2001. Section 325(d) gives the Board discretion to deny trial when the same or substantially the same issue was previously decided by the Office. 35 U.S.C. §325(d); *see also Prism Pharma Co., Ltd. v. Chongwae Pharma Corp.*, IPR2014-00315, Paper 14, at 13 (PTAB, July 8, 2014) (denying the Petition's priority challenge because the Examiner previously considered and decided the

challenged patent's priority date during prosecution).

Sanofi's Petition argues that the claims lack written description and enablement support in the '816 Priority Application, the earliest asserted priority date. Pet., pp. 26-56. But the Office has already considered and decided the '487 Patent's earliest priority date during prosecution when the Examiner afforded the '487 Patent its May 1, 2001 priority date "for purposes of art." *See* EX1002, at 0116 (emphasis added).

As Sanofi acknowledges in its Petition, Immunex adjusted inventorship and priority claims for the '487 Patent during its prosecution. EX1002, at 0145; Pet., at 21-22. Sanofi fails to inform the Board, however, that the Examiner reviewed the Priority Applications after the inventorship and priority updates and affirmatively stated in an Office Action that the claims are supported in the '816 Application:

> Based on the information given by Applicants and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in claims 1-16 and 34-35 is supported by the disclosure in U.S. Application Serial No. 09/847,816 filed on 01 May 2001, because, this application discloses antibodies that bind to IL-4 receptor, wherein said antibodies comprise the light

> chain of SEQ ID NO:10 and heavy chain of SEQ ID NO:12. Therefore, claims 1-16 and 34-35 are afforded an effective filing date of 05/01/2001 for purposes of art.

EX1002, at 0116 (emphasis added).

The claims the Examiner considered when making the above statement were nearly identical to the claims that ultimately issued in the patent. *See* EX1002, at 0124-0131; EX1001, 77:25-78:50. For reference, Immunex provides a comparison of pending claim 1 during prosecution (as of February 3, 2011) and issued claim 1 from the '487 Patent is shown below, with changes underlined:

| **Pending claim 1 on Feb. 3, 2011** | **Issued Claim 1** |
|---|---|
| 1. An isolated antibody that competes with a reference antibody for binding to human IL-4 receptor, | 1. An isolated human antibody that competes with a reference antibody for binding to human IL-4 interleukin-4 (IL-4) receptor, |
| wherein the light chain of said reference antibody comprises the amino acid sequence of SEQ ID NO: 10 | wherein the light chain of said reference antibody comprises the amino acid sequence of SEQ ID NO: 10 |
| and the heavy chain of said reference antibody comprises the amino acid sequence of SEQ ID NO: 12 | and the heavy chain of said reference antibody comprises the amino acid sequence of SEQ ID NO:12. |

*See* EX1001, claim 1; EX1002, at 0125 (underline indicates text added during

prosecution).

There are only two differences between the original claims and issued claims. First, the ’487 Patent’s issued claims include the term “human,” which was incorporated into issued claim 1 from previously canceled claim 11, which the examiner also had determined was afforded a priority date of May 1, 2001 “for purposes of art.” *See* EX1002, at 0068-0072, 0116. Moreover, the term “human” is supported in the Common Specification. *See, e.g.,* EX1008, at 0027:27. Claims 2-10, 12-16, and 34-35 submitted during prosecution are identical to issued claims 2-17 of the ’487 Patent, with the exception of the element “human” that was incorporated from canceled claim 11 during prosecution. *See* EX1001, claims 2-17; EX1002, at 0125-0128. The second difference between the examined and issued claims is a simple clarification of the abbreviated term “IL-4” to articulate the full name “interleukin-4.” Thus, the differences between the claims afforded the 2001 priority date during prosecution and the issued claims in the ’487 Patent are inconsequential for determining the priority date. Accordingly, the issue of §112 support in the Priority Applications for claims nearly identical to those in the ’487 Patent was already squarely before the Office during prosecution and decided

in Immunex's favor.

Because Sanofi asks the Board to consider the same or substantially the same issue that was already decided by the Office, the Board should "decline to revisit the Office's Decision" on priority and exercise its discretion to deny institution under Section 325(d). *Huawei Tech. Co., Ltd. v. Pabst Licensing GmbH & Co. KG*, IPR2017-00449, Paper 7, at 9 (PTAB, June 12, 2017). Instituting IPR would waste the Board's valuable time and resources in revisiting the priority issue. *Panacea Biotec, Ltd. v. Daiichi Sankyo Co. Ltd.*, IPR2015-01496, Paper 11, at 6 (PTAB, Jan. 7, 2016) (finding that the Board's "judicial resources are best spent elsewhere").

### B. *Because the Examiner found the claims entitled to claim priority, this case is distinguishable from other PTAB decisions.*

Since the Office has already affirmatively determined that claims nearly identical to the '487 Patent claims are entitled to the benefit of the earlier filed applications "for purposes of art," the present facts are distinguishable from those in *In re NTP, Inc*., 654 F.3d 1268 (Fed. Cir. 2011) (a reexamination case) and recent decisions in which the PTAB has determined "whether an involved patent is entitled to the benefit date of an earlier filed application when resolving whether a

reference is prior art." *Samsung Elec. Co., Ltd. v. Affinity Labs of Texas, LLC*, IPR2014-01181, Paper 16, at 49 (PTAB, Jan. 28, 2016); *HTC Corp. v. Adv. Audio Devices, LLC*, IPR2014-01158, Paper 6, at 12 (PTAB, Jan. 23, 2014).

In *NTP*, for example, NTP argued that the examiner "implicitly" afforded the claimed priority date to the patent at issue. But, there was no evidence in the file history "whether the examiner actually considered [the] issue." *In re NTP*, at 1278. The present facts are distinguishable from *NTP* because the Examiner actually considered the issue of priority during examination and expressly determined the priority date of May 1, 2001 in the prosecution history. EX1002, at 0116. The facts here are further distinguishable from *NTP* because Stevens, the purportedly "prior art" reference asserted in the Petition's anticipation argument, discloses that the allegedly anticipating aspects of Stevens were made by following the description and guidance from the Common Specification. *See, e.g.*, EX1006, ¶¶[0003], [0065] (citing U.S. Pat. No. 7,186,809, a parent patent to the '487 Patent which shares the Common Specification. *See* EX1001, at 0001).

Sanofi's improper §112 challenge to patentability is further illustrated by the Petition's attempt to misdirect the Board's attention to the prosecution history of

U.S. Patent Application No. 14/175,943 ("the '943 Application"), a divisional application filed from the '487 Patent. Pet., at 43-46. Sanofi's arguments are a red herring. First, Sanofi mischaracterizes the prosecution history of the '943 Divisional Application. Contrary to the Petition's portrayal of the prosecution history, there is no evidence in the record that the examiner of the '943 Divisional raised a §112 written description rejection based on *AbbVie Deutschland Gmbh & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285 (Fed. Cir. 2014)—indeed, the examiner did not discuss or even cite *AbbVie*. *See, e.g.*, EX1003, at 0090-0099. Second, as discussed below in Section V(C), the facts here are distinguishable from *AbbVie*.

Unmasked for what it is, Sanofi's Petition should be rejected by the Board as an improper challenge to patentability under §112. *See* 35 U.S.C. §§311(b), 325(d).

## IV. Sanofi's Petition should be denied because it fails to clarify Sanofi's ambiguous position on construction of the term "antibody."

Sanofi's Petition should also be denied because Sanofi fails to explain how the challenged claims are to be construed, as required by 37 C.F.R. §42.104(b)(3). In this proceeding, Sanofi attempts to avoid taking a stance on construction of the term "antibody," though in district court, Sanofi construes the term to be limited to

six specific antibodies and their equivalents. By failing to explain its position on claim construction in this proceeding, Sanofi improperly "shifts the burden of advancing a claim construction from the petitioner to the Board." *Palo Alto Networks v. Finjan, Inc.*, IPR2015-02000, Paper 9, at 4 (PTAB, May 20, 2016) (emphasis added). This defect is fatal to Sanofi's Petition, and the Board should deny the Petition on this basis.

### A. *Sanofi's extremely narrow construction of "antibody" in district courts creates unresolved ambiguity surrounding Sanofi's position on construction of "antibody" in this proceeding.*

Sanofi's Petition construes a single term ("human") and does not provide a construction for any other claim term. The Petition simply requests that "claim terms be given their broadest reasonable interpretation (BRI), as understood by a POSITA and consistent with the specification." Pet., at 24. The Petition also fails to articulate whether the remaining terms should be "given their ordinary and customary meaning" or any other meaning. *See In re Translogic Tech, Inc.*, 504 F.3d 1249, 1257 (Fed. Cir. 2007); *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005). Absent from Sanofi's claim construction in this proceeding is any explicit construction of the term "antibody."

Instead, Sanofi's Petition alleges, without offering any construction of the term "antibody," that the claims of the '487 Patent encompass a "staggeringly broad scope" that includes "untold numbers" of isolated human antibodies. *See* Pet., at 24-25, 29, 49. In contrast, merely three days before filing its IPR Petition, Sanofi represented to the U.S. District Court for the District of Massachusetts that the term "antibody" recited in the same claims of the same patent "must be construed in accordance with 35 U.S.C. § 112 ¶6" and that, "[p]roperly construed, none of the claims of the '487 Patent cover matter beyond the structures specifically disclosed in the specification, *i.e.*, the sequences of mAbs 6-2, 12B5, 27A1, 5A1, 63, or 1B7, the only structures conceivably capable of performing the 'compet[ing]' function, or their equivalents." IMX2001, at ¶¶30-31. Twelve weeks later, Sanofi repeated the same means-plus-function construction in U.S. District Court for the Central District of California. IMX2002, ¶¶66-67.

Immunex does not concede that any of Sanofi's conflicting statements regarding the scope of the claim term "antibody" are correct. Nevertheless, it is significant that Sanofi has created ambiguity regarding its position on construction of the term "antibody," and that its Petition leaves this ambiguity unresolved. As

the PTAB has recognized, a patent may not, like a "nose of wax," be twisted "as it suits [the parties'] infringement and invalidity cases." *Google, Inc. v. Koninklijke Philips N.V.*, IPR2017-00411, Paper 11, at 13 (PTAB, May 24, 2017) (citing *Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343, 1351 (Fed. Cir. 2001)). Moreover, the Petitioner may not avoid its burden under Rule 104(b)(3) by improperly "shift[ing] the burden of advancing a claim construction from the petitioner to the Board." *Palo Alto Networks*, IPR2015-02000, at 4 (emphasis added). In *Palo Alto*, the Board stated that, "our rules require the petition to set forth a claim construction … [h]aving failed to present a specific construction for "file cache" in its Petition, or to convince the Board that the term needed no further construction, Petitioner did not discharge its burden…." *Id* (emphasis added). Here, Sanofi has not discharged its burden under Rule 104(b)(3), and the Board should consequently reject the Petition.

Furthermore, though district courts apply the *Phillips* standard and the PTO applies the BRI, these methodologies are not so different as to permit Sanofi to argue that §112, ¶6 applies under one standard but not the other. Indeed, "no distinction is made in [§112] paragraph six between prosecution in the PTO and

enforcement in the courts … paragraph six applies … whether as part of a patentability determination in the PTO or as part of a validity or infringement determination in a court." *In re Donaldson Co., Inc*., 16 F.3d 1189, 1193 (Fed. Cir. 1994) (en banc) (emphasis added); *see also Euro-Pro Operating LLC v. Acorne Enterprises, LLC*, IPR2014-00351, Paper 19, at 6-7 (PTAB, July 10, 2014). Thus, Sanofi's unclear stance in this proceeding on construction of the term "antibody" cannot be brushed aside simply because the BRI applies here.

**B. *The ambiguity surrounding Sanofi's position on claim construction is fatal to Sanofi's §112 and §102 arguments because claim construction is a necessary predicate for each analysis.***

Given Sanofi's ambiguity on its position on the construction of the term "antibody" in this proceeding, the Petition cannot show a reasonable likelihood of prevailing on its unpatentability arguments. Claim construction is a fundamental tenet in written description, enablement, and anticipation. "In patent law, the name of the game is the claim," and the analysis must begin with claim construction. *ZTE Corp. v. Contentguard Holdings, Inc.*, IPR2013-00138, Paper 57, at 10 (PTAB, July 1, 2014) (quoting *In re Hiniker Co.*, 150 F.3d 1362, 1369 (Fed. Cir. 1998)). It is well established that "claim construction is inherent in any written

description analysis." *In re Katz Interactive Call Processing Patent Litigation v. Amer. Airlines*, 639 F.3d 1303, 1319 (Fed. Cir. 2011). Similarly, "an enablement inquiry typically begins with a construction of the claims." *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1254 (Fed. Cir. 2004). Likewise, "the first step in [an anticipation] analy[sis] is a proper construction of the claims…." *Medichem, S.A. v. Rolabo, S.L.*, 353 F.3d 928, 933 (Fed. Cir. 2003).

By failing to provide clarity regarding its position on claim construction in this proceeding, Sanofi's written description, enablement, and anticipation arguments all fail. Dr. Robinson's testimony provides no clarification on Sanofi's position because he failed to provide any claim construction for any term as part of his §112 analyses.[2] Without articulating or identifying any claim construction whatsoever, Dr. Robinson simply cannot provide credible testimony on whether the '816 Application provides adequate §112 support for the very claims he failed to construe. The Board should give his testimony no weight and reject the Petition's §112 arguments because Dr. Robinson cannot credibly compare the

[2] Nor does Dr. Robinson refer to or rely on Dr. Zurawski's claim construction, which construes only the term "human." *See* EX1004, ¶¶65-67.

scope of the claims to the disclosure in the Common Specification without first construing the claims. *See, e.g.*, Pet. at 31-32, 35-37, 39-40, 42, 44, 47, 49-56 (citing EX1012). Likewise, the Petition's anticipation arguments should be rejected because they rely on the same flawed §112 assessment, which ultimately fails to establish that Stevens is prior art to the '487 Patent. Pet., at 57-67; EX1004, ¶64.

The Board has routinely denied IPR petitions for similar claim construction defects in the Petition, and this Panel should do the same here. For example, in *Jiawei Tech. (HK) Ltd. v. Richmond*, IPR2014-00937, Paper 22 (PTAB, Dec. 16, 2014), the Board denied the Petition for failing to explain how the challenged claims were to be construed. The Board explained that "[i]t is Petitioner's burden to explain how the challenged claims are to be construed and how they read on the prior art. 37 C.F.R. §42.104(b)(3)–(5). Petitioner has not done so sufficiently on this record … [a]ccordingly, Petitioner has not demonstrated a reasonable likelihood of success in showing the [unpatentability of the challenged claims]." *Id.*, at 8 (emphasis added); *see also ams AG v. 511 Innovations, Inc.*, IPR2016-01793, Paper 15, at 15-16 (PTAB, March 15, 2017) (denying institution because Petitioner "has neither complied with 37 C.F.R. § 42.104(b)(3) nor adequately

proffered the 'minimal height' limitation for construction in this proceeding"); *Clickbooth.com, LLC v. Essociate, Inc.*, IPR2015-00464, Paper 9, at 11 (PTAB, July 9, 2015) (denying institution because "Petitioner does not explain how [a claim element] should be construed" and "[b]y failing to address this ambiguity, Petitioner has failed to explain sufficiently its contentions regarding the challenged claims").

Like the unsuccessful Petitioners in these cases, Sanofi has failed to advance a clear position on claim construction in this proceeding. *See* 37 C.F.R. §42.104(b)(3). The Board should accordingly deny the Petition.

## V. Sanofi's Petition fails to show that Stevens is prior art because the Petition fails to show that the challenged claims lack written description support in the Priority Applications.

Even assuming for the sake of argument the Board were to reach the merits of Sanofi's §112 arguments, the Board should deny the Petition because it fails to meet its burden of showing that the challenged claims lack written description support in the '487 Patent's Priority Applications.

### A. *Sanofi's Petition improperly focuses on six examples of monoclonal antibodies and ignores the specification as a whole.*

Sanofi's written description analysis is defective because it ignores

numerous disclosures throughout the Common Specification as well as numerous references incorporated therein that provide further description of the claimed antibodies. Instead, the Petition's §112 analysis rests on the erroneous assumption that there are only six examples of monoclonal antibodies described in the specification, and repeatedly emphasizes the same six monoclonal antibodies throughout its arguments. *See*, *e.g.*, Pet., at 40 ("The '816 Application's disclosure of the Six MAbs therefore does not provide sufficient support…."); *id.* at 42 ("Here, the '816 Application's disclosure of a mere 6 structurally similar IL-4R antibodies can hardly be sufficient to provide adequate written description…."); *id.* at 42-43 ("The '816 Application at best describes six structurally similar antibodies…."). Dr. Robinson also improperly limits his analyses to the same six antibodies, and expressly admits that he reached his conclusions regarding an alleged lack of antibody diversity in the Common Specification "based on [his] analysis of the six disclosed antibodies." EX1012, ¶117-120 (emphasis added).

But Sanofi relies on the wrong standard for written description. "[A]n actual reduction to practice is not required for written description." *Falkner v. Inglis,* 448 F.3d 1357, 1366-1367 (Fed. Cir. 2006) (emphasis added). The test for adequate

written description under 35 U.S.C. §112, first paragraph, is "whether the disclosure of the application relied upon reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharms., Inc. v. Eli Lilly & Co*., 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (emphasis added). The Petition's and Dr. Robinson's myopic written description analyses fail to demonstrate that the challenged claims lack written description support in the Common Specification, and thus fail to show a reasonable likelihood of prevailing on the Petition's anticipation arguments. *See*, *e.g.*, *Dr. Reddy's Labs. Ltd. v. Galderma Labs., Inc.*, IPR2015-01778, Paper 11, at 17-18 (PTAB, Feb. 16, 2016).

**1. Sanofi's Petition brushes aside the specification's explicit description of a genus of antibodies that compete with monoclonal antibody 12B5.**

The '816 Application explicitly discloses, and demonstrates that the inventors had possession of, a genus of antibodies: those that compete with monoclonal antibody 12B5 for binding to IL-4R. EX1008, at 0029:16-20; Pet., at 36. For example, the '816 Application describes antibodies that compete with 12B5 as follows:

> Particular monoclonal antibodies of the invention are selected from the group consisting of MAb 12B5; a Mab that is cross-reactive with 12B5; a MAb that binds to the same epitope as 12B5; a MAb that competes with 12B5 for binding to a cell that expresses human IL-4R; a MAb that possesses a biological activity of 12B5; and an antigen-binding fragment of any of the foregoing antibodies.

EX1008, at 0029:16-20 (emphasis added).

Sanofi's Petition brushes aside the above disclosure, ignoring its significance as an express disclosure of the genus of claimed antibodies. However, "the written description requirement does not demand either examples or an actual reduction to practice; a constructive reduction to practice that in a definite way identifies the claimed invention can satisfy the written description requirement." *Ariad*, 598 F.3d at 1352. The specification merely needs to "describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed." *Id.*, at 1351. The '816 Application's explicit disclosure of monoclonal antibodies that compete with a reference antibody (*i.e.*, 12B5 in the passage quoted above) is sufficient to identify a genus of antibodies in a "definite

way," and shows that the inventors possessed a genus of antibodies.

**2. Sanofi's Petition ignores disclosures in the Common Specification and references incorporated therein that describe diverse types of antibodies.**

Sanofi argues that the '816 Application "does not describe any examples of antibodies" with different heavy chain families, different light chain types, or different sequence similarities compared with six exemplary monoclonal antibodies disclosed in the specification. *See* Pet., at 40. But this argument is flawed because (i) Sanofi ignores explicit disclosures in the '816 Application relating to diverse types of antibodies; and (ii) techniques for making antibodies with different types of heavy chain or light chain families were known in the art and need not be described in detail in the specification. *Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366; *Chiron Corp.*, 363 F.3d at 1254.

For example, Sanofi ignores the fact that the '816 Application describes antibodies of different class and subclass types (*e.g.*, $IgG_1$, $IgG_4$, IgM) and thus demonstrates possession of the genus. The specification also describes techniques for generating the genus:

> Techniques are known for deriving an antibody of a different subclass or isotype from an antibody of interest,

> i.e., subclass switching. Thus, IgG1 or IgG4 monoclonal antibodies may be derived from an IgM monoclonal antibody, for example, and vice versa. Such techniques allow the preparation of new antibodies that possess the antigen-binding properties of a given antibody (the parent antibody), but also exhibit biological properties associated with an antibody isotype or subclass different from that of the parent antibody.

EX1008, at 0035:7-12 (emphasis added); *see also id.*, at 0029:30-35, 0053:31-36. Because antibody isotypes were well known, and "[t]echniques for altering (switching) the subclass/isotype of an antibody [were] known," the '816 Application need not write out every possible isotype and subclass of antibody within the scope of the challenged claims. EX1008, at 0053:31-33. Dr. Zurawski agrees with the inventors that techniques for isotype switching were well known. EX1004, ¶52. And Dr. Robinson cites to a 1988 reference when discussing the state of the art for antibody isotypes and subclasses. EX1012, ¶37 (citing Harlow & Lane, EX1017).

Sanofi's Petition ignores that the '816 Application describes using different types of exemplary immunoglobulin heavy chain genes from several different

heavy chain families, including $V_H1$ ("the germline human VH1-18 (DP-14) gene"), $V_H5$ ("the germline human VH5-51 (DP-73) gene"), and $V_H3$ ("the germline human VH3-23 (DP47) gene"). EX1008, at 0048:10-20. The description found within the four corners of the Common Specification therefore is more than enough to satisfy written description support for the challenged claims—it demonstrates clearly that the inventors had possession of the claimed genus.

Nonetheless, the Common Specification provides even further description and guidance through numerous disclosures incorporated by reference into the specification—disclosures that Sanofi fails to dispute or acknowledge. For example, Sanofi ignores references incorporated in the '816 Application such as U.S. Patent No. 5,569,825 ("the '825 Patent") that provides figures depicting the human kappa light chain locus and the human lambda light chain locus for generating transgenic mice with human antibody genes. *See* EX1008, at 0027:3-6; IMX2003, 4:38-39, Fig. 2, Fig. 3. The '825 Patent further describes that "[a] minilocus light chain transgene may be similarly constructed from the human λ or κ immunoglobulin locus." IMX2003, 17:39-40. U.S. Patent No. 5,545,806 ("the '806 Patent"), incorporated by reference in the '816 Application, also describes

creating transgenic mice using light chain transgenes from human lambda or human kappa light chains. EX1008, at 0027:3-6; IMX2005, 7:13-14, 25:65-66. Similarly, U.S. Patent No. 5,770,429, incorporated by reference in the '816 Application, describes, *inter alia*, creating transgenic mice through "Targeted Inactivation of the Murine Lambda Light Chain Locus," "Targeted Inactivation of the Murine Heavy Chain Locus," and "Introduction of Human Ig Genes into Mouse Ig Heavy and Kappa Light Chain Deficient ES cells." EX1008, at 0049:13-16, 0049:24-27; IMX2004, Exs. 28, 29, 31.

Sanofi cannot turn a blind eye to these disclosures in the '816 Application and meet its burden of showing that the challenged claims lack written description support. These disclosures squarely contradict Sanofi's and Dr. Robinson's assertions that the genus of antibodies described in the Common Specification is somehow limited to "the same heavy chain family (VH3), the same light chain type (κ), one of two light chain families (Vκ1 or Vκ3), and similar CDR lengths." EX1012, ¶118; Pet., at 39-40. And Dr. Robinson himself admits that different heavy and light chain gene families were well known in the art. *See, e.g.*, EX1012, ¶¶38, 44, 107-108 (citing references published in 1988 (EX1017), 1996 (EX1035),

1999 (EX1041), and 2001 (EX1045-1047); *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005). The disclosures in the Common Specification, in the art incorporated by reference, and in the knowledge of those skill in the art at the earliest priority date, demonstrate clearly that in the inventors were in possession of a genus of antibodies, not just six species.

Moreover, Dr. Robinson's testimony on antibody diversity should be entirely disregarded because his declaration fails to comply with 37 C.F.R. §42.65. EX1012, ¶116. Dr. Robinson testified that he used the "BLAST application" and the "Abysis 2.7 application" to analyze the heavy and light chain amino acid sequences of six example antibodies. EX1012, ¶¶117-118. But Dr. Robinson failed to explain *how* he performed the tests, *how* the data from the tests were generated, *how* the data were used to determine a value, or *how* the tests are regarded in the art. *See* 37 C.F.R. §42.65(b). Although Dr. Robinson testified that he used the "default values" for the online BLAST application, he failed to explain (i) *why* he selected the "default values," (ii) *what other values* are available for selection from the website, or (iii) *how* the "default values" are regarded in the art. EX1012, ¶117. Instead, Dr. Robinson merely cited to a URL hyperlink for the BLAST application,

with no explanation of how he performed his analysis or any evidence of the website's content. *Id.* This is insufficient to satisfy Rule 42.65.

Dr. Robinson likewise provided a paltry description of his analysis using the "Abysis" application. Here, Dr. Robinson merely stated that he "used the Abysis 2.7 application also available online" and provided what appears to be a URL hyperlink. EX1012, ¶117. But that URL hyperlink is currently defunct and has been defunct at each attempt to access it. If a user clicks on the hyperlink or pastes it into web browser, the browser provides an error message. *See, e.g.*, IMX2006, at 1. This makes it impossible for Immunex or the Board to even begin to understand how Dr. Robinson performed his analysis. *See, e.g.*, *Coalition for Affordable Drugs VIII, LLC v. Trustees of Univ. of Pennsylvania*, IPR2015-01836, Paper 58, at 20 (PTAB, March 6, 2017). Even assuming Dr. Robinson's hyperlink becomes functional at some point, Dr. Robinson still failed to explain "how the [Abysis] test was performed," "how the [Abysis] data is used to determine a value," or "how the [Abysis] test is regarded in the relevant art." 37 C.F.R. §42.65(b). And he again failed to provide any evidence of the website's content. Thus, the Board should give no weight to Dr. Robinson's testimony. *See, e.g.*, *Johns Manville Corp. v.*

*Knauf Insulation, Inc*., IPR2015-01527, Paper 17, at 13-14 (PTAB, Dec. 17, 2015); *Corning Inc. v. DSM IP Assets B.V.*, IPR2013-00049, Paper 88, at 40-41, 51 (PTAB, May 9, 2014).

**3. Sanofi's Petition ignores disclosures in the Common Specification relating to competition assays.**

Sanofi alleges that "[t]he '816 Application never describes how, or how to determine whether, an antibody 'competes' with a 'reference antibody.'" Pet., at 36. Again, Sanofi's argument ignores references incorporated in the '816 Application that describe examples of competition assays. These disclosures further bolster the description and guidance in the Common Specification. For example, the '816 Application discloses that "[e]xamples of procedures for preparing antibodies directed against human IL-4 (including monoclonal antibodies), assays by which blocking antibodies are identified, and techniques for generating humanized or genetically engineered derivatives of anti-IL-4 antibodies, are described in U.S. Patents 5,041,381, 5,863,537, 5,928,904, and 5,676,940, which are hereby incorporated by reference." EX1008, at 0036:3-7. Sanofi's Petition fails to acknowledge or explain any of these expressly incorporated references, which would have provided a POSA with further description of

techniques for preparing antibodies and assays for identifying blocking antibodies—including competition assays.

For example, Sanofi ignores the fact that U.S. Patent No. 5,863,537, incorporated by reference in the '816 Application, describes a "plate binding competition assay" used for anti-IL-4 antibodies. EX1008, at 0036:3-7; IMX2007, at 22:43-64. Similarly, Sanofi ignores that U.S. Patent No. 5,770,429, also incorporated by reference in the '816 Application, describes competition assays such as "competition binding flow cytometric experiments." *See* EX1008, at 0049:13-16, 0049:24-27; IMX2004, at 13:47-50, 132:19-22. Sanofi also ignores that a publication from its own declarant Dr. Zurawski—again, expressly incorporated in the '816 Application—describes cross-competition assays utilizing anti-IL-4R monoclonal antibodies. *See* EX1008, at 0024:18-23, 0025:29-32; EX1010, at 13871, 13874-13875.

"When a document is 'incorporated by reference' into a host document, such as a patent, the referenced document becomes effectively part of the host document as if it were explicitly contained therein." *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1329 (Fed. Cir. 2001); *see also Harari v. Lee*, 656

F.3d 1331, 1335-1336 (Fed. Cir. 2011). Although Rule 1.57(d) limits "essential material" incorporated into a patent for purposes of satisfying 35 U.S.C. §112, ¶1 to "a U.S. patent or U.S. patent application publication," those limitations do not apply for purposes of establishing an earlier priority date. "The limitations on the material which may be incorporated by reference in U.S. patent applications which are to issue as U.S. patents do not apply to applications relied on only to establish an earlier effective filing date under 35 U.S.C. 119 or 35 U.S.C. 120." *E-Trade Financial Corp. v. Droplets, Inc.*, IPR2015-00470, Paper 35, at 16 (PTAB, June 23, 2016) (quoting M.P.E.P. § 608.01(p)); *Ex parte Maziere*, 27 USPQ2d 1705, 1706-07 (BPAI, 1993). Thus, the disclosures are "effectively part of the [Common Specification] as if it were explicitly contained therein" for purposes of establishing an earlier filing date. *Telemac,* 247 F.3d at 1329; *Maziere*, 27 USPQ2d at 1706-07.

Sanofi's argument is further misplaced because the specification need not recite information that is well-known in the art, such as competition assays. "Because the specification is viewed from the perspective of one of skill, in some circumstances, a patentee may rely on information that is 'well-known in the art'

for purposes of meeting the written description requirement." *Boston Scientific Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1366 (Fed. Cir. 2011) (citation omitted). Moreover, "a patentee preferably omits from the disclosure any routine technology that is well known at the time of application." *Chiron Corp.*, 363 F.3d at 1254. In this case, Sanofi's declarant Dr. Robinson states that competition assays were well-known in the art as of May 1, 2001 "for assessing antibody-antibody competition with respect to a particular antigen like human IL-4R." EX1012, ¶¶47, 133 (Robinson); *see also* EX1004, ¶46 (Zurawski); EX1010, at 13871.

**4. Sanofi's Petition ignores structural aspects of the challenged claims.**

Sanofi alleges that the claims provide "no structural limitations" for the claimed antibodies. *See, e.g.*, Pet., at 30. But Sanofi concedes that an "antibody," by definition, has certain structural restrictions. *Id.*, at 14-15. For example, Sanofi states that "antibodies are generally understood as 'Y-shaped proteins,'" that "[t]hey are composed of two identical heavy chains and two identical light chains, which are bound together by disulfide bonds." *Id.*, at 14 (emphasis added). Dr. Robinson similarly admits that antibodies are "generally characterized by their 'Y' structure," and that the antibody "Y" structure is "a fair approximation of their

actual shape." EX1012, ¶¶29, 31 (emphasis added). Dr. Zurawski also admits that antibodies are "understood as 'Y-shaped proteins,'" and further testifies that the variable regions of an antibody (which would also include the variable regions of an Fab or $F(ab')_2$ fragment) have defined structures, comprising three complementarity determining regions (CDR) and four framework regions (FR). EX1004, ¶¶34-35 (emphasis added); *see also* EX1008, at 0026:10-15. And both Drs. Robinson and Zurawski provide figures depicting the understood structure of an antibody. EX1012, ¶32; EX1004, ¶34.

The challenged claims recite "antibodies"—a term that, by Sanofi's own admission, denotes structural limitations to the claimed subject matter. Sanofi's defective written description argument fails to acknowledge these structural aspects of the challenged claims.

### B. *Sanofi's arguments made in a European Opposition are at direct odds with Sanofi's arguments in the Petition.*

Sanofi's deficient written description challenges are further undermined because they are at direct odds with statements made by Sanofi and Regeneron in Opposition proceedings for a counterpart European Patent. European Patent No. 2292665 ("EP '665") claims priority to, *inter alia*, the '816 Application and has

similar claims to the ’487 Patent. *See* IMX2008, at 1, 53. For example, claim 1 of the EP ’665 Patent is copied below:

> 1. A human monoclonal antibody capable of inhibiting an IL-4 induced biological activity that competes with a reference antibody for binding to a cell that expresses human IL-4 receptor (IL-4R), wherein:
>
> a) the light chain of the reference antibody comprises the sequence of SEQ ID NO:10 and the heavy chain of the reference antibody comprises the sequence of SEQ ID NO:12; or … [the light and heavy chains of the variable regions of MAbs 27A1, 5A1, or 63].

IMX2008, at 53.

In the EP ’665 Opposition proceeding, Sanofi argued that “IL-4R specific antibodies that block IL-4 binding bind to one small well-defined epitope of the IL-4R and, thus two antibodies of this type will cross-compete.” IMX2009, at 31 (emphasis added). Similarly, in a parallel Opposition proceeding for the EP ’665 Patent, Regeneron argued that “[t]he claims encompass all inhibitory human anti-human IL-4R antibodies, because there is no room on the antigen (the extracellular domain of IL-4R) for an inhibiting antibody to bind without competing with one of

the reference antibodies recited in claim 1." IMX2010, at 4 (emphasis added).

Immunex does not concede that any anti-IL-4R antibody that blocks IL-4 binding to IL-4R will necessarily compete with 12B5. Nevertheless, Sanofi's and Regeneron's arguments in the EP '665 Oppositions are at direct odds with their argument in this proceeding that "[t]he '816 Application does not describe a single antibody that competes with any other antibody, including MAb 12B5." Pet., at 8; *see also id.* at 4, 35. The '816 Application explicitly discloses that working examples of monoclonal antibodies are each capable of binding to IL-4R and inhibiting its binding with IL-4. EX1008, at 0028:10-20, Exs. 6, 8-9. Thus, according to Sanofi's and Regeneron's statements in the Oppositions, the '816 Application describes antibodies that compete with MAb 12B5 because Sanofi argued that MAbs 6-2, 27A1, 5A1, 63, and 1B7—which are described in the '816 Application—will each compete with MAb 12B5. IMX2009, at 31; IMX2010, at 4. This is further evidence that the inventors on the '487 Patent were in possession of the claimed genus of antibodies.

### C. AbbVie *is distinguishable because the AbbVie patents provided only limited disclosures of a subset of the claimed antibodies*

Sanofi argues that the claims in this case lack written description support,

citing *AbbVie Deutschland Gmbh & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285 (Fed. Cir. 2014) for its improper §112 arguments. *See, e.g.*, Pet. at 2, 32-34, 39-42, 44, 54. But there are critical legal differences between the facts here and the facts in *AbbVie*. The patents at issue in *AbbVie* provided a limited disclosure of a subset of the claimed antibodies without any evidence that the inventors possessed other types of antibodies beyond the antibodies exemplified and described in the specification (*e.g.*, there were no disclosures of antibodies with kappa light chain genes or other heavy chain genes beyond $V_H3$).

As an initial matter, the Federal Circuit noted that AbbVie's own expert conceded that the patents at issue "[did] not disclose structural features common to the members of the claimed genus." *AbbVie.*, 759 F.3d at 1299. As such, *AbbVie*'s written description analysis only considered "whether the patents sufficiently otherwise describe representative species to support the entire genus." *Id.*

The Federal Circuit explained that AbbVie first identified a lead anti-IL-12 antibody ("Joe-9"), and then, "[i]n order to improve IL-12 affinity, AbbVie introduced mutations to the CDRs of Joe-9…." *Id.*, at 1291. Thus, as the court explained, all of the antibodies described in the AbbVie specification were derived

from the same Joe-9 parent antibody, with very little diversity:

> "All of the antibodies described in AbbVie's patents were derived from Joe–9 and have VH3 type heavy chains and Lambda type light chains. Although the described antibodies have different amino acid sequences at the CDRs, they share 90% or more sequence similarity in the variable regions and over 200 of those antibodies differ from Y61 by only one amino acid. The patents describe that other VH3/Lambda antibodies may be modified to attain IL–12 binding affinity."

*Id.*, at 1300 (emphasis added).

Nor did the AbbVie patents provide any examples—or even suggest the possibility—of antibodies having different heavy or light chain types outside of the working example antibodies:

> However, the patents do not describe any example, or even the possibility, of fully human IL–12 antibodies having heavy and light chains other than the VH3 and Lambda types."

*Id.*, at 1300 (emphasis added). The court also explained that there was "no evidence to show whether one of skill in the art could make predictable changes to

the described antibodies to arrive at other types of antibodies…." *Id.*, at 1301 (emphasis added).

In contrast to the AbbVie patents, the '816 Application describes, *inter alia*, antibodies of different isotypes, subclasses, heavy chain types, and light chain types. *See* discussion above in Section V(A)(2). And, unlike the patents at issue in *AbbVie*, the examples of monoclonal antibodies described in the '816 Application are not all derived from the same parent antibody—*e.g.*, five of them were independently created, resulting in greater diversity as compared to the *AbbVie* antibodies. EX1008, Exs. 4, 6, 8, 9. As explained above, the descriptions in the '816 Application and numerous references incorporated therein would have provided the artisan with further examples of "antibodies having heavy and light chains other than [those of the working examples of monoclonal antibodies]." *AbbVie*, 759 F.3d at 1300. Sanofi's Petition fails to show how the challenged claims purportedly lacks written description in the Common Specification given these critical differences between *AbbVie* and the present case.

**D. Ariad *is distinguishable because Ariad's patent was directed to "all substances" capable of achieving the desired result, but failed to provide an example of such a substance in its priority application.***

Sanofi's Petition also repeatedly relies on the Federal Circuit's decision in *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336 (Fed. Cir. 2010) for its improper §112 arguments. *See, e.g.*, Pet. at 32-33, 37-38, 42. But that case is distinguishable. Unlike the Common Specification, the patents at issue in *Ariad* encompassed any possible substance that achieved the desired result of reducing NF-κB binding to its target sites. As the Federal Circuit explained, Ariad's patent claims were "genus claims, encompassing the use of all substances that achieve the desired result of reducing the binding of NF-κB to NF-κB recognition sites." *Ariad*, 598 F.3d at 1341 (emphasis added). The Federal Circuit also explained that Ariad's specification provided only one specific example of a compound capable of achieving the desired result, and that the sole example compound (I-κB) was not present in the 1989 priority application at issue. *Id.*, at 1356.

Ariad's priority application specification did not describe a single exemplary substance that could achieve the desired result of inhibiting NFκB binding. This again is in marked contrast to the Common Specification, which describes a large

variety of antibodies that compete with a reference antibody, examples of making and using human antibodies, and incorporates numerous references that describe further examples different types of antibodies (and methods of making them). Moreover, the challenged claims in the '487 Patent recite antibodies (not "all substances," as in *Ariad*), which Sanofi concedes imposes structural restrictions on the claimed subject matter. Pet., at 14; EX1012, ¶¶29, 31; EX1004, ¶¶34-35.

### E. *Sanofi's Petition ignores the state of art as of Dec. 19, 2002; Oct. 27, 2006; and Nov. 13, 2008, failing to meet Sanofi's burden of showing that Stevens is allegedly prior art to these priority dates*

Sanofi's Petition purports to assess written description as of 2001 and then, with no support, asserts that the same conclusion would apply to 2002, 2006, and 2008. *See, e.g.,* Pet., at 19; EX1012, ¶25. But Sanofi's cursory statement fails to meet its burden of showing that Stevens is prior art to each of the '487 Patent's 2002, 2006, or 2008 priority dates because the law requires that one consider the state of the art as of the filing date of each application.

Factors to consider when assessing written description include "the existing knowledge in the particular field, the extent and content of the prior art," "the maturity of the science of technology," and "the scientific and technologic

knowledge already in existence." *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005) (emphasis added). And as the Federal Circuit stated in *Ariad*, "[t]he law [of written description] 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." *Ariad*, 598 F.3d at 1351 (emphasis added).

Sanofi's Petition attempts to assess the state of the art as of May 1, 2001, but failed to assess the state of the art as of the '487 Patent's other claimed priority dates: December 19, 2002; October 27, 2006; or November 13, 2008. Accordingly, Sanofi fails to meet its burden of showing that Stevens is prior art to each of the '487 Patent's claimed priority dates. *Ariad*, 598 F.3d at 1351.

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In sum, the evidence shows that the Common Specification describes the claimed genus of antibodies and that the inventors on the '487 Patent were in possession of the genus. Sanofi's Petition fails to show otherwise.

## VI. Sanofi's Petition fails to show that Stevens is prior art because the Petition also fails to show that the challenged claims lack enablement support in the Priority Applications.

Sanofi's Petition should also be denied because it fails to meet its burden of

showing that the challenged claims lack enablement support in the Common Specification, and thus further fails to meet its burden of showing that Stevens is prior art. And having failed to show that Stevens is prior art, the Petition fails to establish a reasonable likelihood of prevailing on its sole ground for unpatentability. *See, e.g., Dr. Reddy's Labs. Ltd. v. Galderma Labs., Inc.*, IPR2015-01778, Paper 11, at 17-18.

### A. *Sanofi's Petition ignores disclosures in the Common Specification and references incorporated therein.*

Sanofi's enablement challenges fail for several reasons. First, Sanofi's Petition fails to show that the challenged claims lack enablement support in the '816 Application because the Petition ignores disclosures throughout the Common Specification and references incorporated therein.

The Common Specification discloses (i) how to make transgenic mice for human antibody production; (ii) how to make hybridomas for human antibody production; (iii) how to screen for blocking antibodies and inhibition of IL-4 and IL-13 signaling; and (iv) how to conduct competition assays. *See, e.g.*, EX1008, at 0036:3-7; IMX2007, at 22:43-64; EX1008, at 0049:13-16, 0049:24-27; IMX2004, at 13:47-50, 132:19-22, Exs. 28, 29, 31; EX1008, at 0027:3-6; IMX2003, 4:38-39,

Fig. 2, Fig. 3; IMX2005, 7:13-14, 25:65-66; EX1008, at 0024:18-23, 0025:29-32; EX1010, at 13871, 13874-13875. The Petition ignores such disclosures in the Common Specification. But a document "incorporated by reference into a host document, such as a patent … becomes effectively part of the host document as if it were explicitly contained therein." *Telemac Cellular Corp. v. Topp Telecom, Inc.*, 247 F.3d 1316, 1329 (Fed. Cir. 2001) (internal quotation omitted); *see also Maziere*, 27 USPQ2d at 1706-1707.

Moreover, for enablement, "[a] patent need not disclose what is well known in the art." *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988). And, following the very holding in *Wands*, Sanofi admits that "MAbs can be screened by the appropriate functional assays for desirable features (*e.g.*, blocking IL-4R) … Each of these steps was described in the prior art." Pet., at 14; EX1012, ¶131 (emphasis added). Similarly, Dr. Robinson admits that "several different assays were known in the art for assessing antibody-antibody competition." EX1012, ¶47 (emphasis added); *see also id.*, ¶133; EX1004, ¶46; *Wands*, 858 F.2d at 740. Sanofi's admissions contradict its enablement arguments.

**B. *Sanofi's Petition uses the wrong standard for enablement***

Second, Sanofi's enablement challenges fail because Sanofi and Dr. Robinson use the wrong standard for enablement. Sanofi argues in its Petition that, to satisfy enablement, a POSA must be able to "generate all potential claimed antibodies … until the POSITA was satisfied that diverse antibodies were no longer being generated," all without engaging in undue experimentation. Pet., at 51 (emphasis added). And Dr. Robinson alleges that "one would have to make all the potential claimed antibodies that could be within the scope of the claims." EX1012, ¶143 (emphasis added); *see also id.*, ¶147 (referring to alleged amount of effort required to "produce every unique antibody covered by the '487 Claims" (emphasis added)).

The law of enablement does not require the artisan to make every possible embodiment within the scope of the claims in a single, continuous process, until the artisan is satisfied there are no more embodiments left to make, so that the entire process—from start to finish—does not require "undue experimentation." To the contrary, the test for enablement is that the specification must describe the invention so the artisan can make and use the invention without undue experimentation. *Wands*, 858 F.2d at 735. As the Board stated, *mutatis mutandis*,

in *Daiichi Sankyo Co., Ltd. v. Alethia Biotherapeutics, Inc.*, IPR2015-00291, Paper 75 (PTAB, June 14, 2016), to arrive at the invention, the artisan would have had to "generate anti-[IL-4R] antibodies, and then screen those antibodies until an antibody [*i.e.*, not every possible antibody] having the desired biological properties was identified." *Id.*, at 14. In other words, the specification must enable the artisan to make and use embodiments spanning the full scope of the claims, each without requiring undue experimentation.

### C. *Sanofi's Petition ignores the relevance of* In re Wands *and misapplies* Wyeth

Third, Sanofi's enablement challenges fail because the Petition ignores the relevance of *Wands* and misapplies the holding in *Wyeth*. The Petition cites *Wands* only in reference to the "*Wands* factors" for enablement. *See, e.g.*, Pet., at 48, 55, 56. Conspicuously absent from the Petition, however, is any acknowledgement that *Wands* squarely dealt with the issue of making and screening monoclonal antibodies—in an application filed in 1980—and that the Court of Appeals for the Federal Circuit found such methods to be routine. In *Wands*, the claims at issue were directed to an immunoassay using high-affinity IgM monoclonal antibodies that have a specific binding affinity for hepatitis B surface antigen (HBsAg). *Id.*, at

734. The issue before the court was "whether the specification enables one skilled in the art to make the monoclonal antibodies that are needed to practice the invention." *Id.*, at 735.

When considering the quantitative amount of experimentation needed to make and screen Wands' antibodies, the court acknowledged that the process involved "immunizing animals," "mak[ing] hybridomas, cloning the hybridomas, and screening the antibodies produced by the hybridomas for the desired characteristic." *Id.*, at 740. But "[t]he test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine…." *Id.*, at 737 (*quoting In re Jackson,* 217 USPQ 804, 807 (Bd. App. 1982)) (emphasis added). Indeed, the "key word is 'undue,' not 'experimentation.'" *Id.* ( emphasis added; citation omitted). The *Wands* court determined that an artisan armed with the disclosures and guidance in the specification, the "high level of skill in the [1980 monoclonal antibody] art," and the fact that "all the methods needed to practice the invention were well known," would have been able to make the library of antibodies without undue experimentation and have the antibodies readily available for screening. *Id.*, at 740 (emphasis added).

Many of these same facts in *Wands* align with the present proceeding. In *Wands*, there was a "high level of skill in the [monoclonal antibody] art." *Id.*, at 740. Here, Dr. Robinson testified that the "level of ordinary skill in the art … is relatively high." EX1012, ¶135. In *Wands*, "all the methods needed to practice the invention were well known." *Wands*, 858 F.2d at 740. Here, Dr. Robinson testified that "the state of the [monoclonal antibody] prior art was well-developed." EX1012, ¶128; *see also* ¶¶60, 130, 135. Similarly, Dr. Zurawski testified that "every step of making anti-hIL-4R blocking antibodies was 'conventional' in the prior art." EX1004, ¶44. In *Wands*, the specification provided "considerable direction and guidance." *Wands*, 858 F.2d at 740. Here, the specification of the '816 Application provides considerable direction and guidance, including numerous references incorporated therein, as well as disclosures providing methods of generating transgenic mice, making hybridomas, screening for blocking antibodies, and testing in competition assays. *See* discussion above in Section V(A). Sanofi fails to explain or distinguish the facts in *Wands* from the present case. And *Wyeth* did not overrule or replace *Wands*.

Rather than acknowledge the facts in *Wands*, Dr. Robinson spends nearly

four pages in his declaration discussing the so-called "technical facts" from *Wyeth.* EX1012, ¶¶149-151; *see also* Pet., at 47, 49, 52-54. But the technical facts in *Wyeth* dealt with chemically synthesizing small molecules, not making monoclonal antibodies. In *Wyeth*, the court concluded there was no enablement because making the library of rapamycin compounds to be screened required "a complicated and lengthy series of experiments in synthetic organic chemistry." *Wyeth*, at 1386. Thus, the court concluded that the library of rapamycin compounds could not be made and readily available for assay screening without engaging in excessive experimentation. *Id.* In contrast to the complex synthetic organic chemistry methods in *Wyeth*, Sanofi and its declarants assert that "every step of making anti-hIL-4R blocking antibodies was 'conventional' in the prior art." EX1004, ¶44 (emphasis added); *see also* EX1012, ¶¶60, 128, 130, 135. Moreover, the priority date at issue in *Wyeth* was 1992—nine years earlier than the earliest priority date of the '487 Patent, a fact that Dr. Robinson fails to acknowledge. *Id.*, at 1383. Therefore, Dr. Robinson's attempt to analogize the present case with the "technical facts" of *Wyeth* is misplaced.

The result in *Wyeth* is consistent with other Federal Circuit cases related to a

library or platform that could not be prepared without undue experimentation. *See, e.g.*, *Martek v. Nutrinova*, 579 F.3d 1363, 1378 (2009) (a genus of "euryhaline microorganisms"); *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1368 (Fed. Cir. 1999) (a genus of "prokaryotic or eukaryotic cell[s]"); and *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991) (a genus of "Cyanobacteria cells"). In *Martek*, there were no readily available methods of supplying the euryhaline microorganisms; in *Enzo Biochem*, there were no readily available methods of supplying the prokaryotic or eukaryotic cells; in *Vaeck*, there were no readily available methods of supplying the cyanobacteria; and in *Wyeth*, there were no readily available methods for supplying the rapamycin compounds. But such was not the case in *Wands*, and Sanofi's Petition fails to show that it is the case here.

**D. *Sanofi mischaracterizes* Daiichi.**

Sanofi's Petition alleges that *Daiichi* concerned "a priority application similar to the '816 Application." Pet., at 55. But this is simply wrong. In *Daiichi*, the claims at issue were directed to a method of impairing osteoclast differentiation using an antibody or antigen binding fragment which specifically binds to human Siglec-15 or murine Siglec-15. *Daiichi Sankyo Co., Ltd. v. Alethia Biotherapeutics,*

*Inc.*, IPR2015-00291, Paper 75, at 3 (PTAB, June 14, 2016). Far from being "similar to the '816 Application," the Board determined that the priority application in *Daiichi* did not expressly disclose any anti-Siglec-15 antibodies; and did not disclose any epitope or unique antigenic regions useful for generating antibodies with the desired functional properties. *Id.*, at 10-12.

Here, however, the '816 Application explicitly discloses examples of making and using human anti-IL-4R antibodies, including the heavy and light chain variable region sequences of the reference antibody which bind to a specific epitope on IL-4R. *See, e.g.*, EX1008, at 0029:16-24, 0029:36-0030:3, 0053:37-0054:7.

**E.** ***Sanofi's Petition ignores the state of art as of Dec. 19, 2002; Oct. 27, 2006; and Nov. 13, 2008, failing to meet Sanofi's burden of showing that Stevens is allegedly prior art to these priority dates***

Similar to the reasons discussed above regarding Sanofi's failed written description analysis, Sanofi's enablement challenges also fail to adequately address the state of the art as of each of the '487 Patent's December 19, 2002; October 27, 2006; or November 13, 2008 priority dates. *See, e.g.*, Pet., at 19; EX1012, ¶25. Again, Sanofi simply alleges that "[t]he priority analysis would be the same even if

the ’487 Patent claimed priority as late as November 13, 2008….” Pet., at 19.

Like written description, factors to consider when assessing enablement include “state of the prior art” and “relative skill of those in the art.” *Wands*, 858 F.2d at 737 (emphasis added). And as the Federal Circuit explained in *Chiron*, “[w]hether the earlier applications enable the claims of the [’487] patent is determined as of the filing date of each application.” *Chiron Corp.*, 363 F.3d at 1254 (emphasis added); *see also Rasmusson v. SmithKline Beecham Corp*., 413 F.3d 1318, 1322-1324 (Fed. Cir. 2005) (assessing enablement “as of each of the respective filing dates” of the priority applications (emphasis added)).

Sanofi’s Petition fails to adequately assess the state of the art as of each of the ’487 Patent’s claimed priority dates. *See* discussion above in Section V(E). Thus, Sanofi has not met its burden of showing a reasonable likelihood of success on the merits because its Petition has not shown that Stevens is prior art to each of the ’487 Patent’s claimed priority dates.

## VII. Summary of Sanofi’s failed §112 arguments

In summary, the Board must deny Sanofi’s Petition because the entire Petition hinges on an unsanctioned and defective §112 attack to the challenged

claims. Sanofi's Petition must be denied because it has the following defects:

- Stevens is not prior art to the '487 Patent (see Section II(A), *supra*);
- The Petition is based on an impermissible §112 attack on the patentability of the '487 Patent, in violation of 35 U.S.C. §311(b) (see Section II(B), *supra*);
- The same or substantially the same issue regarding the priority date for claims nearly identical to the challenged claims has already been squarely before the Office during prosecution—a fact Sanofi neither discloses nor disputes in its Petition (see Section III, *supra*);
- Sanofi fails to clarify its ambiguous position on claim construction in this proceeding—claim construction is a predicate to written description, enablement, and anticipation analyses (see Section IV(A), *supra*);
- Sanofi's entire Petition hinges on Dr. Robinson's §112 analysis—he failed to provide <u>any claim construction</u> for <u>any claim term</u> as part of this analysis (see Section IV(B), *supra*);
- Sanofi improperly focuses on six examples of monoclonal antibodies

in the ’816 Application, ignoring explicit disclosures throughout the specification and numerous references incorporated therein that provide ample description and guidance for §112 support (see Sections V(A)-(D) and VI(A)-(D), *supra*); and

- Sanofi fails to adequately assess the state of the art as of each filing date of the Priority Applications (see Sections V(E) and VI(E), *supra*).

## VIII. Should the Supreme Court Hold that *Inter Partes* Review trials are unconstitutional, the Board should vacate and terminate this proceeding

The Supreme Court recently granted a certiorari petition in *Oil States Energy Services LLC v. Greene’s Energy Group, LLC* to decide whether the IPR statute violates the U.S. Constitution by granting the Board the authority to extinguish private property rights in a non-Article III forum without a jury. *Oil States Energy Services, LLC v. Greene’s Energy Group, LLC*, 639 F. App’x 639 (Fed. Cir. 2016) (Mem.), *cert. granted*, 2017 WL 2507340 (U.S. June 12, 2017) (No. 16-712). Immunex respectfully objects to this tribunal’s exercise of jurisdiction to adjudicate the validity of the ’487 Patent because it would violate Immunex’s right to a jury trial under the Seventh Amendment. This is especially true here where

the Petition hinges on §112 arguments that the Board is not statutorily authorized to consider in the context of an IPR proceeding. If the Supreme Court disturbs the Federal Circuit's precedent in this area, Immunex will advise the Board and seek dismissal of this matter.

## IX. Conclusion

The Petition fails to show a reasonable likelihood that any of the challenged claims is unpatentable as anticipated by Stevens and, therefore, the Board should deny the petition.

The Patent Trial and Appeal Board is hereby authorized to charge any fee deficiency, or credit any overpayment, to Deposit Account 19-0036 (Customer I.D. is 45324).

Respectfully submitted,
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## CERTIFICATE OF WORD COUNT

Pursuant to 37 C.F.R. § 42.24(d), I certify that Immunex Corp.'s Patent Owner Preliminary Response contains 11,302 words as counted by the word-processing program used to generate this reply. This total does not include the table of contents, the table of authorities, appendix of exhibits, certificate of service, or this certificate of word count.

Respectfully submitted,
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## CERTIFICATE OF SERVICE (37 C.F.R. § 42.6(e))

The undersigned hereby certifies that the above-captioned "Patent Owner Preliminary Response" was served in its entirety on July 6, 2017, upon the following parties via electronic mail:

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