Paper No. 13

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

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

v.

IMMUNEX CORPORATION,
Patent Owner.

Case IPR2017-01879
Patent 8,679,487

PETITIONERS' REPLY TO PATENT OWNER'S PRELIMINARY RESPONSE

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

CASES

STATUTES

OTHER AUTHORITIES

EXHIBIT LIST

Exhibit	Description
1001	U.S. Patent No. 8,679,487 ("the '487 Patent").
1002	Excerpts from the File History of U.S. Patent No. 8,679,487 (U.S. Patent Application No. 12/829,231 ("'231 Application")).
1003	Excerpts from the File History of U.S. Patent Application No. 14/175,943, which is a continuation of U.S. Patent No. 8,679,487 ("'943 Application").
1005	*Curriculum Vitae* of Dr. Gerald Zurawski, Ph.D.
1006	U.S. Patent Publication No. 2008/0160035 ("Stevens" or "'035 Publication").
1007	European Patent Application No. EP 0604693 ("Schering-Plough").
1008	U.S. Patent Application No. 09/847,816 ("'816 Application").
1009	PCT International Publication No. WO 96/33735 ("Kucherlapati").
1010	Zurawski, *et al.*, *The Primary Binding Subunit of the Human Interleukin-4 Receptor is Also a Component of the Interleukin-13 Receptor*, Journal of Biological Chemistry (June 9, 1995) ("Zurawski").
1011	Agosti, et al., *Novel Therapeutic Approaches for Allergic Rhinitis*, 20 Immunology and Allergy Clinics of North America 401–423 (2000) ("Agosti").
1014	Thorsten Hage, et al., *Crystal Structure of the Interleukin-4/Receptor a Chain Complex Reveals a Mosaic Binding Interface*, 97 Cell 271–281 (1999) ("Hage").
1015	Whitty, et al., *Interaction Affinity Between Cytokine Receptor Components on the Cell surface*, 95 Proc. Natl. Acad. Sci. USA, 13165–13170 (October 1998) ("Whitty").

1016	United States Patent Application Pub. No. 2002/0002132 ("Pluenneke" or "'132 Publication").
1026	Perez de la Lastra, et al., *Epitope Mapping of 10 monoclonal antibodies against the pig analogue of human membrane cofactor protein (MCP)*, Immunology 1999, 96:663-670 ("Perez de la Lastra").
1028	U.S. Patent Application No. 10/324,493 ("'493 Application").
1029	U.S. Patent No. 7,186,809 ("the '809 Patent").
1031	U.S. Patent No. 7,465,450 ("the '450 Patent").
1032	U.S. Application No. 12/291,702 (the "'702 Application").
1039	U.S. Patent No. 9,587,026 ("'026 Patent").
1049	*Curriculum Vitae* of Mike McKool.
1051	*Curriculum Vitae* of John F. Garvish, II.
1200	Declaration of Dr. Gerald Zurawski, Ph.D.
1201	Amgen's November 23, 2016 Response to the Oppositions requested regarding European Patent No. 2 292 665 ("Immunex's EU Opposition Response").
1202	U.S. Patent Publication No. 2002/0076409 ("March").
1203	Comparison of '132 Publication disclosure to '487 Patent specification using Microsoft Word compare feature.
1204	Hart, et al., *Diminished responses to IL-13 by human monocytes differentiated in vitro*, 29 Eur. J. Immunol. 1999, 2087–2097 ("Hart").
1205	PCT International Publication No. WO 98/08957 ("Penn State").
1206	MAb 230 technical information from R & D System's webpage circa 1996 and 1997 with Affidavit ("R&D Systems Catalog").

1207	Hefta, et al., (1996) *Measuring antibody affinity using biosensors, Antibody Engineering*. A Practical Approach, (McCafferty et al., eds.), pp. 99-117, Oxford Univ. Press, Oxford.
1208	Parks, D., Herzenberg, L., and Herzenberg L. (1989) *Flow cytometry and fluorescence-activated cell sorting*, in Fundamental Immunology (Paul, W., ed.). Raven, New York.
1209	Zurawski, et al., *Receptors for interleukin-13 and interleukin-4 are complex and share a novel component that functions in signal transduction*, 12 EMBO J. 1993, 2663–2670.
1210	Medarex Form S-3 dated March 3, 2000.
1211	Excerpts from U.S. Patent Application No. 09/785,934 ("'934 Application").
1212	Affidavit of Mike McKool in Support of Motion for *Pro Hac Vice* Admission.
1213	Affidavit of John F. Garvish, II in Support of Motion for *Pro Hac Vice* Admission.
1432	Excerpts of Defendants' Disclosure of Initial Invalidity Contentions in Case No. 2:17-cv-2613
1433	Transcript of Telephonic Hearing held December 11, 2017

As authorized by the Board, Petitioners submit this Reply to address 3 issues raised in Patent Owner's ("PO") Preliminary Response ("POPR"): (1) new inventor "declaration testimony;" (2) 35 U.S.C. § 325(d); and (3) 35 U.S.C. § 314(a). As this Reply and the Petition demonstrate, the Board should institute trial.

I. The '132 Publication is Prior Art By Another Under 35 U.S.C. § 102(e).

Trial should be instituted despite PO's "declaration testimony" because (1) Petitioners demonstrate that the '132 Publication is "by another" and excluding the reference would be improper without a fully developed record; and (2) PO's contradictory new evidence fails to disprove that the '132 Publication is "by another." At the very least, PO's new evidence demonstrates there is a factual dispute, which must be viewed in the light most favorable to Petitioners. *See* 37 C.F.R. § 42.108(c).

Petitioners have established the '132 Publication is prior art under § 102(e) because on its face the '132 Publication lists a different inventor from the '487 Patent inventors—Pluenneke. *Coalition for ADROCA v. ACORDA Therapeutics*, IPR2015-01850, Paper 72, at 41. Contrary to PO's arguments, Petitioners do not have to meet their "ultimate burden" of proving that '132 Publication is "by another" in the Petition. *See MaxLinear, Inc. v. Cresta Tech. Corp.*, IPR2015-00594, Paper 90, at 14-15. Accordingly, prior panels have found that it is premature to disqualify prior art under § 102(e) at the institution stage. *See id.*,

Paper 13, at 9-10 (refusing to disqualify without "relevant evidence that may be developed at trial"); *Nelson Prods., Inc. v. Bal Seal Eng'g, Inc.*, IPR2014-00572, Paper 10, at 11-12 (refusing to disqualify without a cross-examination of the named inventor). The decisions PO relies upon are inapposite because they are all final written decisions issued **after** the record was fully developed and the Board had evaluated both parties' evidence. POPR at 53-55.

Inconsistencies surrounding PO's "declaration testimony" highlight why a more developed record is needed and trial should be instituted. Pluenneke's new declaration asserts that he is the sole inventor of "what is *claimed* in the '132 Publication." Ex. 2011 at 2. But claim 3 of the '132 Publication claims "an antibody that inhibits binding of IL-4 to an IL-4R" and the only IL-4R antibody expressly disclosed is mAb 6-2. Ex. 1016 at 0032. Even more troubling, the claims of the '132 Publication are reproduced ***verbatim*** in the later-filed '816 Application (to which the '487 Patent claims priority), yet Pluenneke is listed not as the sole inventor but as a co-inventor with Armitage. *Compare* Ex. 1016, Claims *with* Ex. 1008, Claims. PO's declarations do not reconcile this inconsistency. Instead, PO embraces inconsistent positions that suit its needs—Armitage had to be a named inventor on the '816 Application for the '487 Patent to claim priority to it.

The March application further establishes that Pluenneke's declaration lacks credibility. Like the '132 Publication, March claims methods of treating cancer

using human IL-4R antibodies and the only human IL-4R antibody identified is mAb 6-2. Ex. 1202, Claims 19, 25, 39, ¶¶ [0219]-[0220]. Since Pluenneke is the only common inventor between the ’132 Publication and March, Pluenneke is the only possible inventor of this overlapping mAb 6-2 subject matter.

PO’s contradictory positions are further exposed because PO *expressly disclaimed* priority to the ’132 Publication during prosecution of the ’487 Patent. Ex. 1002 at 0145. PO does not address this express disclaimer in its POPR. To the contrary, PO now attempts to establish the named ’487 Patent inventors actually invented portions of the disclaimed ’132 Publication.

PO’s declarations also fail to establish that the relied upon portions of the ’132 Publication are ***solely*** the work of the named ’487 Patent inventors and not Pluenneke, as required under § 102(e). The declarations speak only to what the named ’487 Patent inventors ***made*** and ***analyzed***—not to what they allegedly ***invented*** or ***conceived***. *See In re DeBaun*, 687 F.2d 459, 463 (CCPA 1982) (“The question [] is whether what was constructively reduced to practice was [the named inventors’] own conception.”). Tellingly, the declarations in the decisions cited by PO address conception. *See* POPR at 40, 42. 54-55. PO’s declarations, however, provide no explanation of Pluenneke’s connection to the development of human IL-4R antibodies, but simply illustrate that the named ’487 Patent inventors reduced to practice the use of human IL-4R antibodies as therapeutics.

II. The Board Should Not Exercise Its Discretion Under § 325(d).

The Board should not exercise its discretion under § 325(d) based on March. Even PO acknowledges that the Examiner "chose not to rely on [March]." POPR at 34. Critically, PO does not identify any evidence that March was substantively considered during prosecution or applied to the claims. Under similar circumstances, the Board declined to exercise its discretion under § 325(d). *Intel Corp. v. Alacritech, Inc.*, IPR2017-01392, Paper 11, at 25; *cf. Cultec, Inc. v. Stormtech, LLC*, IPR2017-00777, Paper 7, at 11 ("The Examiner cited and applied [the reference] throughout the examination proceedings."). Moreover, March is not "the same prior art" because it lacks the evidence that PO argued the Office lacked to convince the Office to grant the '487 Patent—evidence that prior art anti-IL-4R antibodies practice the "competes" limitation.

III. The Board Should Not Exercise Its Discretion Under § 314(a).

The *General Plastic* factors weigh in favor of Petitioners. Most importantly, the instant Petition is not an example of a strategic serial filing. Rather, Petitioners filed this Petition immediately after the completion of relevant competition experiments that form the basis for the challenge. *See Great West Casualty Co. v. Intellectual Ventures II LLC*, IPR2016-01534, Paper 13, at 31-32 ("[A]n adequate explanation by Petitioner may be enough to outweigh all of the other factors.").

Prior to November 23, 2016, PO never provided any indication as to how the

"competes" limitation could be assessed experimentally. The '487 Patent does not specify which experiment should be used, and despite arguing the "competes" limitation as the point of novelty during prosecution, PO never indicated how this limitation could be determined experimentally. Ex. 1002 at 0028-30. However, on November 23, 2016 in a European Patent Office proceeding for a related patent, PO endorsed two competition assays disclosed in Perez as methods for determining competition. Ex. 1201 at 12-13. Apprised of how PO believed competition could be assessed, Petitioners identified and retained experts, prepared the relevant antibodies, and conducted experiments demonstrating that mAb 6-2 "competes" and anticipates the claims. These experiments were completed on July 19, 2017, and the instant Petition was filed only seven business days later. Ex. 1200 at ¶81.

The remaining *General Plastic* factors further weigh against denial. While Petitioners identified the '132 Publication in the first petition, Petitioners did not have the relevant data demonstrating that mAb 6-2 anticipates the Challenged Claims until testing was complete. Notably, the first petition was a priority date challenge to the '487 Patent and did not rely upon experiments conducted by Petitioners' expert. In addition, no Board decision was issued prior to filing of the instant petition and while the first POPR had been filed, it largely responded to 35 U.S.C. § 120 arguments that are not at issue in this Petition. Finally, because the initial petition was denied, the remaining factors are irrelevant.

Dated: December 18, 2017

Respectfully submitted,

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CERTIFICATE OF SERVICE

Pursuant to 37 C.F.R. § 42.6(e) and 37 C.F.R. § 42.105(a), the undersigned certifies that on December 18, 2017, a complete copy of Petition's Reply to Patent Owner's Preliminary Response was served via electronic mail to the following:

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