No. 2018-2362

United States Court of Appeals
for the Federal Circuit

GENZYME CORP. and SANOFI-AVENTIS U.S. LLC,

Plaintiffs – Appellees,

v.

ZYDUS PHARMACEUTICALS (USA) INC.,

Defendant – Appellant,

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE IN CASE NO. 1:16-CV-00540, JUDGE KENT A. JORDAN SITTING BY DESIGNATION

ZYDUS PHARMACEUTICALS (USA) INC'S COMBINED PETITION FOR REHEARING *EN BANC* AND PANEL REHEARING

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September 16, 2019

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CERTIFICATE OF INTEREST

Pursuant to Federal Circuit Rule 47.4, Counsel for Appellant Zydus Pharmaceuticals (USA) Inc. certifies the following:

1. The full name of every party or amicus represented by me is:

Zydus Pharmaceuticals (USA) Inc.

2. The name of the real party in interest represented by me is:

Zydus Pharmaceuticals (USA) Inc.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock of the party or amicus curiae represented by me are:

Cadila Healthcare Limited

4. The names of all law firms and the partners or associates that appeared for the party or amicus now represented by me in the trial court or agency or are expected to appear in this court (and who have not or will not enter an appearance in this case) are:

Axinn, Veltrop & Harkrider LLP: James T. Evans
Heyman Enerio Gattuso & Hirzel LLP: Dominick Gattuso

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal.

Genzyme Corporation, et al. v. Gland Pharma Limited, 1:18-cv-01071, U.S. District Court for the District of Delaware

Genzyme Corporation, et al. v. Fresenius Kabi USA, LLC, 1:18-cv-01934, U.S. District Court for the District of Delaware

Dated: September 16, 2019 /s/ Chad A. Landmon

Chad A. Landmon
Attorney for Appellant Zydus Pharmaceuticals (USA) Inc.

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Table of Abbreviations

Abbreviation	Description
Asserted Claims	Claims 8 and 19 of U.S. Patent No. 7,897,590 (and by extension/stipulation, claim 8 of U.S. Patent No. 6,987,102)
G-CSF	Granulocyte-colony stimulating factor
Genzyme	Genzyme Corporation and Sanofi-Aventis U.S. LLC
Hendrix	Hendrix, et al., *Pharmacokinetics and Safety of AMD-3100, a Novel Antagonist of the CXCR-4 Chemokine Receptor, in Human Volunteers*, 44 ANTIMICROBIAL AGENTS & CHEMOTHERAPY 1667 (June 2000)
Konopleva	Konopleva et al., *G-SCF Induces CXCR4 Expression on CD34+38- Peripheral Blood Progenitor Cells In Vivo*, 94(10) BLOOD 322b, Abstract 4663 (1999)
Lapidot	Lapidot et al., *A Single Dose of Human G-CSF Inhibited Production of SDF-1 in The Bone Marrow and Upregulated CXCR4 Expression on Immature and Mature Hematopoietic Cells Prior to Their Mobilization*, 94(10) BLOOD 606a, Abstract 2695 (1999)
Plerixafor	1,1'-[1,4-phenylene-bis-(methylene)]-bis-1,4,8,11-tetraazacyclotetradecane; a.k.a. AMD3100 or JM3100
POSA	Person of ordinary skill in the art. Unless otherwise specified herein, references to a POSA are as of September 2000.
SDF-1	Stromal derived factor 1
Stem cells	Stem and progenitor cells
Zydus	Zydus Pharmaceuticals (USA) Inc.

STATEMENT OF COUNSEL – FEDERAL CIRCUIT RULE 35(B)

Based on my professional judgment, I believe this appeal requires an answer to one or more precedent-setting questions of exceptional importance:

1. Whether a patent-challenger asserting obviousness must prove that a POSA would have had a reasonable expectation of success as to achieving unclaimed features, such as achieving alleged unexpected results that are not recited in the asserted claims.

Dated: September 16, 2019

/s/ Chad A. Landmon
Chad A. Landmon
Attorney for Appellant Zydus Pharmaceuticals (USA) Inc.

I. INTRODUCTION

Objective indicia of nonobviousness can in certain cases inform the reasonable expectation of success inquiry. For example, if others tried and failed to achieve the claimed invention, that bears on whether there was a reasonable expectation of success. But the link between objective indicia and the reasonable expectation of success inquiry is limited to *claimed* features. Thus, when asserted objective indicia are based on *unclaimed* features (as this Court permits), they are irrelevant to the reasonable expectation of success. The district court (and therefore the panel) erroneously decided this case because it required Zydus to prove a reasonable expectation of success for *unclaimed* features.

This Court has limited reasonable expectation of success to the claims as written. "'What matters in the § 103 nonobviousness determination is whether a person of ordinary skill in the art, having all the teachings of the references before him, is able to produce the structure defined by the claim.'" *Samsung Elecs. Co. v. Elm 3DS Innovations, LLC*, 925 F.3d 1373, 1382 (Fed. Cir. 2019) (quoting *Orthopedic Equip. Co., Inc. v. United States*, 702 F.2d 1005, 1013 (Fed. Cir. 1983).) "Failure to consider the appropriate scope of the patent's *claimed invention* in evaluating the reasonable expectation of success constitutes a legal error that is reviewed without deference." *Intelligent Bio-Sys., Inc. v. Illumina Cambridge Ltd.*, 821 F.3d 1359, 1367 (Fed. Cir. 2016) (emphasis in original)

(quoting *Allergan, Inc. v. Apotex Inc.*, 754 F.3d 952, 965-66 (Fed. Cir. 2014)). Tying the reasonable expectation of success inquiry strictly to the claims as written ensures that courts do not decide obviousness on hypothetical claims that are fundamentally narrower than the actual claims at issue.

This case demonstrates the error that results when objective indicia based on unclaimed features infect the reasonable expectation of success analysis. The claims at issue are directed to using plerixafor to "mobilize," i.e., move, stem cells from the bone marrow (where they normally reside) to blood vessels. They recite nothing about (1) the stem cells' ability to find their way back to the bone marrow (a process known as "engraftment") after they are reintroduced to the body in a stem cell transplantation procedure; (2) the number of stem cells that must be mobilized; or (3) improving on the leading stem cell mobilizer, G-CSF. Yet the district court and the panel relied upon each and every one of these unclaimed features in concluding there was no reasonable expectation of success. None of these considerations were legally relevant to whether a POSA would reasonably expect to achieve the sole claimed result of mobilizing any number of stem cells.

The Court should grant Zydus's petition, clarify that reasonable expectation of success should be based strictly on the claims themselves, and reverse or vacate the district court's judgment.

II. STATEMENT OF THE CASE

Stem cell transplantations help cancer patients rebuild their blood and immune systems after exposure to chemotherapy. In those procedures, stem cells are "mobilized" from the bone marrow to blood vessels, collected, frozen, and later reintroduced to the patient after chemotherapy. The reintroduced stem cells find their way back to the bone marrow where they repopulate the blood system. (Zydus Opening Appeal Brief, D.I. 31 at 8-10.)

Stem cell mobilization and engraftment are regulated by the interaction of CXCR4, a receptor on stem cells, and SDF-1, a signaling protein produced in the bone marrow. The SDF-1/CXCR4 interaction functions like a magnet to keep stem cells in the bone marrow, thereby preventing them from floating off into the bloodstream (i.e., mobilizing). (Appx258-259 (85:3-86:6) (referring to Appx2897), Appx3482, App3483-3484, Appx3493-3494.) The Asserted Claims encompass part of the stem cell transplantation process, but they are also broad enough to cover basic research and other methods involving stem cell mobilization and "harvesting," a term broadly referring to any method of isolating the stem cells from other blood components. They recite (1) the use of plerixafor, which was known to block the SDF-1/CXCR4 interaction, to mobilize stem cells in any

quantity, and (2) harvesting the stem cells in any quantity.[1] (Appx15-16 (¶11), Appx1710-1711 (¶¶17-19), Appx3472.)

At least six prior art references indicated that CXCR4 and SDF-1 played a role in stem cells' movement between the bone marrow and bloodstream. (Zydus Opening Appeal Brief, D.I. 31 at 14-23.) One of those references, Lapidot, concluded based on *in vivo* data that CXCR4 and SDF-1 had a "major role" in how the leading stem cell mobilizer, G-CSF, works to mobilize stem cells. (Appx3482.) A second reference, Konopleva, relying on different *in vivo* test results, concluded that administering an agent that blocks the CXCR4/SDF-1 interaction (e.g., plerixafor) with G-CSF would improve stem cell mobilization and that the mobilized cells would have "high engraftment capability."[2] (Appx3478.) Konopleva thus predicted the claimed invention.

The district court concluded that a POSA would have been motivated to combine the prior art to arrive at the claimed methods, a finding that Genzyme did not challenge on appeal. One member of the panel remarked during oral argument

[1] The district court erroneously concluded that some "sufficient number of stem cells [must be mobilized] to conduct a harvest" (Appx115-16), overlooking testimony from Genzyme's expert that any number of mobilized cells can be harvested (Appx976 (803:9-11)). In fact, the named inventors harvested stem cells from mice without administering *any* mobilizing agent. (Appx149 (19:34-49).)

[2] This Court previously found one of the Asserted Claims to be nonobvious, but the prior litigants did not point the Court to (and presumably were unaware of) either Lapidot or Konopleva. *Genzyme Corp. v. Dr. Reddy's Labs., Ltd.*, 716 F. App'x 1006 (Fed. Cir. 2017) (non-precedential).

that "reading through Judge Jordan's motivation analysis, [it] practically convinced me that the claims were obvious…." (Oral Argument at 19:26, *Genzyme Corp. v. Zydus Pharm, (USA)*, No. 2018-2362 (Fed. Cir. Aug. 16, 2019).) Nevertheless, the district court held that a POSA would not have had a reasonable expectation of success. This Court affirmed the district court's judgment without opinion pursuant to Federal Circuit Rule 36.[3]

III. POINTS OF LAW AND FACT OVERLOOKED OR MISAPPREHENDED BY THE PANEL

The district court based its finding of no reasonable expectation of success on the following errors of law and fact:

1. Finding that a POSA would not reasonably expect to achieve an unclaimed result, i.e., plerixafor-mobilized stem cells that are capable of engraftment (Appx105), where this Court has repeatedly held that the reasonable expectation of success inquiry is limited to the claims as written. *Intelligent Bio-Sys.*, 821 F.3d at 1367; *see also Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1292-93 (Fed. Cir. 2013).

[3] "'[A]ppeals whose judgments are entered under Rule 36 receive the full consideration of the court,[']…including thoughtful *en banc* review…." *Memorylink Corp. v. Motorola, Inc.*, 676 F.3d 1051, 1052-53 (Fed. Cir. 2012) (O'Malley, dissenting) (quoting *U.S. Surgical Corp. v. Ethicon, Inc.*, 103 F.3d 1554, 1556 (Fed. Cir. 1997)).

2. Contrary to *Intelligent Bio-Sys.*, 821 F.3d at 1367, finding that the failure of skilled artisans to find an efficacious, well-tolerated agent that could improve upon G-CSF supported its finding of no reasonable expectation of success, even though the claims do not require plerixafor achieve any level of clinical efficacy, let alone efficacy greater than G-CSF, and prior art agents indisputably achieved the only claimed result of mobilizing at least some stem cells.

3. Finding that a POSA "at the time of the invention" would not have expected plerixafor to mobilize stem cells because *only* post-effective filing date art disclosed that "various CXCR4 antagonists decreased stem cell mobilization compared to G-CSF" (Appx112-113 (¶51)), contrary to *Velander v. Garner*, 348 F.3d 1359, 1377 (Fed. Cir. 2003) ("While later publications may explain what was known earlier, it would be wrong to impute later-recognized…possible obstacles [to a POSA] at the time of the invention….") and *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 974 (Fed. Cir. 2014) (same).

4. Finding that general statements of uncertainty about the art trumped specific teachings in the prior art (Appx104-05), contrary to *Sandoz*,

726 F.3d at 1292-93 and *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1364 (Fed. Cir. 2007).

5. Requiring Zydus to prove certainty, rather than a mere reasonable expectation of success, by criticizing the prior art for failing "to resolve the mechanisms by which stem cells are mobilized" (Appx44 (¶69 n.22)) and failing to provide a "degree of certainty" regarding how blocking CXCR4 might impact mobilization (Appx104-105 (¶41)), contrary to *Sandoz*, 726 F.3d at 1292 and *Pfizer*, 480 F.3d at 1364.

6. Finding a POSA would not expect success because certain "known stem cell mobilizers [] increased CXCR4 expression" (Appx62-63 (¶93)) based on the unsupported assumption that blocking CXCR4 would decrease CXCR4 expression, where Genzyme's expert testified that he did not believe that blocking CXCR4 with plerixafor would be expected to decrease CXCR4 expression, and where the prior art uniformly taught that CXCR4 keeps stem cells in the bone marrow rather than facilitating their exit from the bone marrow.

The district court made numerous other errors of law and fact that the Court should consider addressing on rehearing, including:

7. Finding that the claims required something more than "mobilizing a small number of stem cells using plerixafor." (Appx115.)

8. Finding, for purposes of determining patentability, mobilizing less than 1 million stem cells "to be a negligible number that effectively represents an inability to mobilize stem cells under the circumstances" (Appx039 n.17), where the Asserted Claims do not require "any threshold quantity of stem cells that must be mobilized" (Appx973 (800:13-16).

9. Finding that "[w]hile Zydus is also correct that those agents [i.e., the alleged "failures"] technically succeeded in mobilizing some amount of stem cells, they were still failures because they did not exhibit clinical success compared to G-CSF" (Appx110), where there was no evidence that plerixafor exhibited clinical success compared to G-CSF, but rather was used in combination with G-CSF to improve mobilization compared to G-CSF alone.

10. Determining that G-CSF, rather than Zydus's primary prior art reference Konopleva, was the closest prior art for purposes of unexpected results, despite the fact that Konopleva proposed combining G-CSF with an agent that blocks the CXCR4/SDF-1

interaction (as plerixafor was known to do) to improve stem cell mobilization outcomes. (Appx74-75 (¶110).)

11. Dismissing the impact of blocking patents where there was direct evidence that researchers were blocked from obtaining plerixafor, contrary to *Acorda Therapeutics, Inc. v. Roxane Labs., Inc.*, 903 F.3d 1310, 1336-42 (Fed. Cir. 2018). (Appx109 (¶47).)

IV. ARGUMENTS IN SUPPORT OF PANEL REHEARING OR REHEARING *EN BANC*

A. The Court Should Grant Panel Rehearing or Rehearing *En Banc* to Clarify that the Requirement to Prove Reasonable Expectation of Success Does Not Extend to Unclaimed Features.

The district court based its nonobviousness finding on legal errors contrary to this Court's precedent. Most importantly, the district court required Zydus to prove reasonable expectation of success as to unclaimed features, which in turn precipitated the clearly erroneous factual finding that there was no reasonable expectation of success. This Court should grant rehearing to affirm that the reasonable expectation of success inquiry should focus strictly on the claims as issued, and further to correct the district court's other errors on important issues regarding reasonable expectation of success and objective indicia.

1. The District Court and the Panel Erroneously Required Zydus to Prove Reasonable Expectation of Success as to Unclaimed Features.

Directly contradicting this Court's precedent, the district court explicitly required a POSA to reasonably expect to achieve at least two results that are not recited or otherwise required by the Asserted Claims. *Intelligent Bio-Sys.*, 821 F.3d at 1367; *Allergan*, 754 F.3d at 965-66; *see also Sandoz*, 726 F.3d at 1292-93.

- *First*, the district court required a POSA to reasonably expect plerixafor to mobilize stem cells capable of engraftment, i.e., homing back to and embedding in the bone marrow post-transplantation. (Appx104-106 (¶41).) Because the Asserted Claims do not recite mobilizing stem cells capable of engraftment, the district court committed legal error.[4] *See, e.g.*, *Sandoz*, 726 F.3d at 1292-93. The correct question is not whether a POSA would expect plerixafor to accomplish the ultimate objective of improving stem cell transplantation, but whether it would mobilize *any* stem cells. *See id.* "That is what [the Asserted Claims] require." (Appx91-93 (¶¶16-17).)
- And *second*, the district court pointed to the failure of others to "find an efficacious, nontoxic agent that could serve as an improvement [upon G-

[4] The district court also committed clear *factual* error, as Konopleva explicitly predicted that stem cells mobilized by interfering with the CXCR4/SDF-1 interaction, as plerixafor was known to do, would have "high engraftment capability." (Appx54 (¶83), Appx3478.)

CSF]" as a reason why a POSA would lack a reasonable expectation of success. (Appx104-106 (¶41).) As Genzyme's expert admitted, the Asserted Claims do not explicitly or inherently require "any threshold quantity of stem cells that must be mobilized" (Appx973 (800:13-16); *see also* Appx976 (803:9-11)), let alone a clinically "efficacious" number of such cells. Nevertheless, the district court concluded that "the success a person of ordinary skill in the art would care about in this case is a clinical success compared to G-CSF." (Appx41-42 (¶67 n.19).) By focusing on what a POSA might ultimately "care about" in its reasonable expectation of success analysis, rather than what the claims actually require, the district court again committed legal error.

The district court's confusion appears to have resulted from this Court's conflicting guidance regarding the relationship between the so-called "*prima facie* case of obviousness" ((1) disclosing all claim elements, (2) motivation to combine, and (3) reasonable expectation of success) and the objective indicia. Whereas the Court has regularly treated the objective indicia as rebuttal evidence after a *prima facie* case is established, it has in recent years stressed that the *prima facie* case and objective indicia must be considered jointly when making obviousness

determinations.[5] For example, this Court stated in *In re Cyclobenzaprine Hydrocloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1081 (Fed. Cir. 2012), that "there can be little better evidence negating an expectation of success than actual reports of failure." Some members of this Court have similarly stated that an unexpected result "is the touchstone of nonobviousness" and may "by itself support a finding of nonobviousness." *Bristol-Myers Squibb Co. v. Teva Pharm. USA, Inc.*, 769 F.3d 1339, 1350 (Fed. Cir. 2014) (Newman, Lourie and Reyna, dissenting from denial of petition for *en banc* review).

But as this case demonstrates, evidence of "failure of others" and "unexpected results" is not always tied to claim limitations. The district court apparently attempted to consider the *prima facie* case and asserted objective indicia together, but it did so by erroneously treating the objective indicia as claim limitations for purposes of assessing reasonable expectation of success. The panel declined to correct that error, and thus unless corrected *en banc* or by panel rehearing, courts will likely make the same error that the district court made in this case.

[5] The lack of clarity in the obviousness standard has also been a repeated source of conflict within this Court. *See, e.g.*, *Merck Sharp & Dohme Corp. v. Hospira, Inc.*, 874 F.3d 724, 732 (Fed. Cir. 2017) (Newman, dissenting) ("[S]ome Federal Circuit decisions [have] converted three of the four *Graham* factors into a self-standing 'prima facie' case, whereby objective considerations must achieve rebuttal weight…. [I]t is incorrect to consign the objective evidence to rebuttal….").

Not only is the consideration of unclaimed features in the reasonable expectation of success analysis contrary to this Court's precedent, it is also bad policy. Specifically, it rewards overbroad claiming by creating asymmetries between the obviousness analysis and the infringement and written description analyses. During oral argument, for example, Genzyme's counsel defended the district court's finding by arguing that mobilizing engraftable stem cells is an "implicit" claim limitation (i.e., considered to be a limitation for purposes of obviousness) while simultaneously asserting that engraftment capability was not a claim limitation for purposes of infringement:

- The Court: "[Y]ou're not defending the no expectation of engraftment ground of no reasonable expectation of success…, is that right?"
- Genzyme's Counsel: "I'd like to [defend it]…. Engraftment is an implicit part of the claims…. [W]hen you come to the no reasonable expectation of success analysis, you can't [] lower the goal to something other than what the person of skill in the art was looking at."
- The Court: "So are you saying that your claims are limited to the method of not only mobilizing stem cells but also engrafting stem cells?"…
- Genzyme's Counsel: "They are not. [Engraftment] is implicit."…
- The Court: "Implicit in the claim but it's not a claim limitation?"
- Genzyme's Counsel: "It is not."
- The Court: "[Y]ou're not requiring an accused infringer to actually successfully engraft stem cells to infringe your claim?"
- Genzyme's Counsel: "Correct."

(Oral Argument at 13:08.) That asymmetry is problematic, as it allows patentees to narrow their claims *post hoc* to avoid obviousness – e.g., by focusing the inquiry on, per Genzyme's counsel, "what the [POSA] was looking at" rather than what the claims require – without limiting the right to exclude and without providing any advanced notice to the public regarding what is required to prove obviousness.

Zydus also pointed out that Genzyme has no written description support for mobilizing stem cells with engraftment capability, as the specification contains no data suggesting that stem cells mobilized with plerixafor will engraft. (Zydus Reply Appeal Brief, D.I. 43 at 15-16.) Accordingly, the claims would have been invalid for lack of written description had they actually recited mobilizing stem cells capable of engraftment. *See Nuvo Pharm. (Ireland) Designated Activity Co. v. Dr. Reddy's Labs. Inc.*, 923 F.3d 1368, 1384 (Fed. Cir. 2019) ("[W]hen the inventor expressly claims [a] result, our case law provides that that result must be supported by adequate disclosure in the specification."). The district court's decision allows patentees to avoid the written description issue while retaining broad coverage for purposes of infringement, simply by waiting until litigation – and even after claim construction – to assert "implicit" limitations as secret hurdles to proving obviousness.

This Court should grant rehearing *en banc* or panel rehearing in order to correct and contain this serious disconnect between the scope of the claims as written and how they are treated in an obviousness analysis.

2. The District Court and the Panel's Other Findings Concerning Reasonable Expectation of Success Were Also Erroneous.

a. The District Court Erroneously Credited General Statements of Uncertainty Over Specific Disclosures in the Prior Art.

This Court has repeatedly held that it is *reversible error* to credit general statements of uncertainty over specific teachings in the prior art pointing to a reasonable expectation of success. *Apotex Inc.*, 754 F.3d at 965 ("[I]t does not matter whether [the field] is generally [] unpredictable []—the question is more narrowly whether the success of [practicing the claims] would be reasonably unpredictable."); *Sandoz*, 726 F.3d at 1292. Yet that is precisely what the district court did here, basing its nonobviousness finding on nonspecific references to uncertainty in the field appearing in the introductions of various prior art references. (Appx42-44 (¶¶68-69).)

Uncertainty in the art was not the focus or thesis of any of these papers.[6] Rather, the prior art specifically disclosed that:

[6] As Zydus's expert explained, "This is how we introduce a scientific paper. We always point out what we don't know. We don't point out what we do know because then nobody reads the paper." (Appx349-350 (176:8-177:5).)

- CXCR4 and SDF-1 were understood to work together to keep stem cells in the bone marrow (Appx258-259 (85:3-86:6) (referring to Appx2897));
- interfering with the CXCR4/SDF-1 interaction played a "major role" in how the leading stem cell mobilizer worked (Appx3482);
- using another agent that blocked that interaction would increase mobilization (Appx3478);
- plerixafor completely inhibited that same interaction (Appx3472); and
- in clinical trials plerixafor mobilized white blood cells bearing the CXCR4 receptor (Appx3470).

The district court did not address any of these teachings in its reasonable expectation of success analysis, and instead focused on the general statements of uncertainty.[7] Accordingly, the district court "equat[ed] unpredictability to patentability" and thus committed reversible error. *Pfizer*, 480 F.3d at 1364.

b. The District Court Credited a Baseless Factual Argument that Not Even Genzyme's Expert Endorsed.

The district court also erroneously found the fact that "known stem cell mobilizers [] increase[d] CXCR4 expression"[8] to weigh against reasonable

[7] Elsewhere in its opinion, the district court criticized the prior art for failing "to resolve the mechanisms by which stem cells are mobilized." (Appx44 (¶69 n.22).) But that criticism, if valid, would require a standard approaching certainty. If the "mechanisms were resolved," there would be no question that an agent that acted on the mechanisms would cause stem cells to mobilize. This too cannot be reconciled with this Court's precedent: "the expectation of success need only be reasonable, not absolute." *Pfizer*, 480 F.3d at 1364.

[8] "CXCR4 expression" refers to the number of CXCR4 receptors on a cell's surface. It does not refer to CXCR4 function. A stem cell may have high CXCR4 expression but low CXCR4 function if, for example, its CXCR4 receptors are blocked/disabled.

expectation of success. (Appx104-106 (¶41).) According to the district court, a POSA "would not have reasonably expected something that blocks CXCR4, and thus counteracts CXCR4 expression, to succeed." (Appx104-106 (¶41).) But there was no evidence or suggestion in the prior art that blocking CXCR4 would counteract CXCR4 expression. Genzyme's expert Dr. Mohty even admitted that he did not believe blocking CXCR4 would decrease CXCR4 expression. (Appx892-893 (719:23-720:3).) This is because a stem cell with blocked CXCR4 may nonetheless exhibit high CXCR4 expression, as is evident from Konopleva's teaching that blocking CXCR4 would mobilize stem cells with "high engraftment capability" (i.e., high CXCR4 expression). (Appx285-286 (112:24-113:10), Appx3478.)

Moreover, the district court's finding rested on the flawed belief that a POSA would think that CXCR4 facilitates mobilization. (Appx284-285 (111:15-112:1).) The prior art uniformly taught the exact opposite: that CXCR4 works with SDF-1 to *impede* mobilization. (Appx3482, App3483-3484, Appx3493-3494.) As the district court itself observed, "Plaintiffs have identified nothing in the prior art expressly telling skilled artisans not to block CXCR4, and in fact, Konopleva expressly proposed the opposite." (Appx56-58 (¶87).)

As the district court's finding here was baseless, and in fact ran counter to all of the evidence, it is clearly erroneous and cannot save the district court's ultimate conclusion of nonobviousness.

B. The Court Should Correct the District Court's Multiple Legal Errors In Its Objective Indicia Analysis on Rehearing.

The district court made multiple legal errors when assessing alleged unexpected results, the objective indicia's nexus to the Asserted Claims, and the effect of Genzyme's blocking patents. (*See* Zydus's Opening Appeal Brief, D.I. 31 at 52-60; Zydus's Reply Appeal Brief, D.I. 43 at 21-27.) On rehearing, the Court should correct these errors and hold that none of Genzyme's alleged secondary considerations support nonobviousness.

CONCLUSION

For the foregoing reasons, Zydus requests the court grant rehearing *en banc* or a panel rehearing of this case, vacate the panel opinion, and rehear this appeal.

Respectfully submitted,

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September 16, 2019

ADDENDUM

NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

GENZYME CORPORATION, SANOFI-AVENTIS U.S., LLC,
Plaintiffs-Appellees

v.

ZYDUS PHARMACEUTICALS (USA) INC.,
Defendant-Appellant

2018-2362

Appeal from the United States District Court for the District of Delaware in No. 1:16-cv-00540-KAJ, Circuit Judge Kent A. Jordan.

JUDGMENT

PAUL HENRY BERGHOFF, McDonnell, Boehnen, Hulbert & Berghoff, LLP, Chicago, IL, argued for plaintiffs-appellees. Also represented by ALISON JAMEEN BALDWIN, NATHANIEL PAUL CHONGSIRIWATANA, DANIEL F. GELWICKS, NICOLE E. GRIMM, JAMES LEE LOVSIN, JEREMY E. NOE, KURT WILLIAM ROHDE; JEFFREY B. BOVE, Ratner Prestia, Wilmington, DE.

CHAD A. LANDMON, Axinn Veltrop Harkrider, LLP,

Hartford, CT, argued for defendant-appellant. Also represented by DAVID KEELER LUDWIG, EDWARD M. MATHIAS; DAN-FENG MEI, New York, NY.

THIS CAUSE having been heard and considered, it is

ORDERED and ADJUDGED:

PER CURIAM (NEWMAN, CHEN, and HUGHES, *Circuit Judges*).

AFFIRMED. See Fed. Cir. R. 36.

ENTERED BY ORDER OF THE COURT

August 16, 2019
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court

United States Court of Appeals for the Federal Circuit

Genzyme Corporation v. Zydus Pharmaceuticals (USA), 2018-2362

CERTIFICATE OF SERVICE

I, Robyn Cohco, being duly sworn according to law and being over the age of 18, upon my oath depose and say that:

Counsel Press was retained by AXINN, VELTROP & HARKRIDER LLP, counsel for Appellant to print this document. I am an employee of Counsel Press.

On **September 16, 2019,** counsel has authorized me to electronically file the foregoing **Zydus Pharmaceuticals (USA) Inc.'s Combined Petition for Rehearing *En Banc* and Panel Rehearing** with the Clerk of Court using the CM/ECF System, which will serve via e-mail notice of such filing to all counsel registered as CM/ECF users, including the following principal counsel for the other parties:

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Principal Counsel for Appellees

Paper copies will also be mailed to the above principal counsel at the time paper copies are sent to the Court.

Eighteen paper copies will be filed with the Court within the time provided in the Court's rules.

September 16, 2019

/s/ Robyn Cocho
Counsel Press

CERTIFICATE OF COMPLIANCE WITH TYPE-VOLUME LIMITATION, TYPEFACE REQUIREMENTS AND TYPE STYLE REQUIREMENTS

1. This petition complies with the type-volume limitation of Federal Rule of Appellate Procedure 35(b)(2)(A) or Federal Rule of Appellate Procedure 40(b).

The petition contains 3,889 words, excluding the parts of the petition exempted by Rule.

2. This petition complies with the typeface requirements of Federal Rule of Appellate Procedure 32.

__x__ The petition has been prepared in a proportionally spaced typeface using Microsoft word in a 14 point Times New Roman font or

____ The petition has been prepared in a monospaced typeface using _____in a ___ characters per inch_____ font.

Respectfully submitted,

/s/ Chad A. Landmon
Chad A. Landmon