NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

2009-1023

AMGEN, INC., IMMUNEX CORPORATION,
AMGEN USA, INC., AMGEN MANUFACTURING LIMITED,
and IMMUNEX RHODE ISLAND CORPORATION,

Plaintiffs/Counterclaim Defendants-Appellees,

and

WYETH,

Counterclaim Defendant,

v.

ARIAD PHARMACEUTICALS, INC.
and THE WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH,

Defendants/Counterclaimants-Appellants,

and

MASSACHUSETTS INSTITIUTE OF TECHNOLOGY
and THE PRESIDENT AND FELLOWS OF HARVARD COLLEGE,

Counterclaimants-Appellants.

Mark A. Pals, Kirkland & Ellis LLP, of Chicago, Illinois, argued for plaintiffs/counterclaim defendants-appellees. With him on the brief were Marcus E. Sernel and Jamie H. McDole. Of counsel on the brief were Siegmund Y. Gutman, Hogan & Hartson LLP, of Washington, DC, and J. Drew Diamond, of Los Angeles, California. Also on the brief were Melanie K. Sharp, Young Conaway Stargatt & Taylor, of Wilmington, Delaware; Stuart L. Watt, Wendy A. Whiteford, Monique L. Cordray, Gail A. Katz, Erica S. Olson, Amgen Inc., of Thousand Oaks, California, and Kathleen Fowler, of Seattle, Washington.

Evan R. Chesler, Cravath, Swaine & Moore LLP, of New York, New York, argued for defendants/counterclaimants-appellants and counterclaimants-appellants. With him on the brief were Keith R. Hummel, David R. Marriott, and David Greenwald.

Appealed from: United States District Court for the District of Delaware

Magistrate Judge Mary Pat Thynge

NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

2009-1023

AMGEN INC., IMMUNEX CORPORATION,
AMGEN USA INC., AMGEN MANUFACTURING LIMITED,
and IMMUNEX RHODE ISLAND CORPORATION,

Plaintiffs/Counterclaim
Defendants-Appellees,

and

WYETH,

Counterclaim Defendant,

v.

ARIAD PHARMACEUTICALS, INC.
and THE WHITEHEAD INSTITUTE FOR BIOMEDICAL RESEARCH,

Defendants/Counterclaimants-
Appellants,

and

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
and THE PRESIDENT AND FELLOWS OF HARVARD COLLEGE,

Counterclaimants-Appellants.

Appeal from the United States District Court for the District of Delaware in case No. 06-CV-259, Magistrate Judge Mary Pat Thynge.

DECIDED: June 1, 2009

Before MICHEL, Chief Judge, DYK and MOORE, Circuit Judges.

MOORE, Circuit Judge.

The Plaintiffs/Counterclaim Defendants-Appellees (collectively, Amgen) sued the Defendants/Counterclaimants-Appellants (collectively, Ariad) in the United States District Court for the District of Delaware for a declaratory judgment of invalidity and noninfringement of U.S. Patent No. 6,410,516 (the '516 patent). Ariad counterclaimed for infringement of claims 6, 18, 70-72, 183, and 184 of the '516 patent (the asserted claims). The district court construed a number of terms in the asserted claims, largely in accordance with Amgen's proposed constructions. In light of its claim construction, the district court granted Amgen's motion for summary judgment of noninfringement. Amgen, Inc. v. Ariad Pharms, Inc., 577 F. Supp. 2d 695 (D. Del. 2008). Ariad appeals. For the reasons set forth below, we affirm.

BACKGROUND

We previously discussed the technology at issue in this case with regard to different claims of the '516 patent. See Ariad Pharms., Inc. v. Eli Lilly & Co., 560 F.3d 1366, 1369-70 (Fed. Cir. 2009). The '516 patent concerns a protein known as NF-κB, and claims methods comprising "reducing NF-κB activity." All of the asserted claims include that limitation:

> 6. A method for diminishing induced NF-κB-mediated intracellular signaling comprising reducing NF-κB activity in cells such that NF-κB-mediated intracellular signaling is diminished.
>
> 70. The method of claim 6, carried out on mammalian cells.
>
> 71. The method of claim 6, carried out on human cells.
>
> 72. The method of claim 70 or 71, carried out on immune cells.
>
> 18. A method for reducing Interleukin-1 or Tumor Necrosis Factor-α activity in mammalian cells comprising reducing NF-κB activity in the cells so as to reduce intracellular signaling caused by Interleukin-1 or Tumor Necrosis Factor-α in the cells.

183. The method of claim 18, carried out on human cells.

184. The method of claim 18 or 183, carried out on immune cells.

The district court determined that "NF-κB activity" means "the ability of NF-κB to act as an intracellular messenger by being released from IκB; translocating into the nucleus; and regulating the transcription of particular genes by binding to specific DNA recognition sequences in those genes." Amgen, 577 F. Supp. 2d at 727. The parties do not appeal this construction. NF-κB activity may arise when it is induced by extracellular influences such as tumor necrosis factor-alpha (TNF-α)—an "inducing substance" in the language of the specification. TNF-α interacts with receptors on the surface of the cell and thereby initiates a chain of events that eventually releases NF-κB from IκB—the first step of NF-κB activity. The parties' arguments on appeal focus on the meaning of "reducing NF-κB activity in cells." The reduction of NF-κB activity is desirable because NF-κB increases the harmful expression of certain genes.

Because NF-κB also induces the expression of its own inhibitor, IκB, NF-κB activity will decrease naturally if the external inducing substance (e.g., TNF-α) is removed. Exogenous agents may also be able to decrease NF-κB activity, and it is helpful to consider several examples of such agents. The '516 patent proposes several classes of molecules potentially capable of reducing NF-κB activity, such as specific inhibitors, dominantly interfering molecules, and decoy molecules, all of which were discussed in greater detail in Ariad, 560 F.3d at 1374-76. These classes of molecules are meant to act inside the cell. For example, decoy molecules are "designed to mimic a region of the gene whose expression would normally be induced by NF-κB. In this case, NF-κB would bind the decoy, and thus, not be available to bind its natural target."

'516 patent col.37 ll.51-54. In contrast, the accused drug—Amgen's Enbrel—acts outside the cell. Enbrel acts by binding to free TNF-α outside the cell, thus interfering with the TNF-α's ability to reach the receptors on the cell and induce NF-κB activity. Amgen, 577 F. Supp. 2d at 700. The prior art also contains example agents that act outside the cell. For example, antibiotics act by killing bacteria, which consequentially reduces the amount of TNF-α released by macrophages in response to the bacterial infection. The use of decoy molecules, Enbrel, or antibiotics all may ultimately result in a decrease of NF-κB activity, but the question remains what is included in the properly interpreted scope of "reducing NF-κB activity in cells."

The district court agreed with Amgen that the asserted claims are limited to actions that reduce NF-κB activity wherein those actions occur within the cell. As such, the district court adopted Amgen's construction of "reducing NF-κB activity in cells": "taking action inside cells to directly inhibit (interfere or block) an NF-κB activity." Id. at 728. Under the district court's construction, decoy molecules could infringe, but Enbrel cannot. This precipitated the district court's summary judgment of noninfringement. Id. at 700-02. On October 3, 2008, the district court stayed Amgen's invalidity claims and entered final judgment on the noninfringement claim pursuant to Fed. R. Civ. P. 54(b). We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

DISCUSSION

Ariad argues that the district court erred in its construction of "reducing NF-κB activity in cells," and that under the proper construction, we should reverse the summary judgment of noninfringement. Claim construction is a question of law reviewed de novo. Cybor Corp. v. FAS Techs., Inc., 138 F.3d 1448, 1455-56 (Fed. Cir. 1998) (en banc).

"Claim terms should generally be given their ordinary and customary meaning and . . . such meaning is one 'that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application.'" ICU Med., Inc. v. Alaris Med. Sys., 558 F.3d 1368, 1374 (quoting Phillips v. AWH Corp., 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc)). "[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." Phillips, 415 F.3d at 1313; see id. at 1317 ("It is therefore entirely appropriate for a court, when conducting claim construction, to rely heavily on the written description for guidance as to the meaning of the claims."). Furthermore, "the prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." Id.

Amgen prevailed in the district court by arguing that the outer boundary of the asserted claims' scope is the cell membrane. The district court agreed with Amgen that agents that act outside the cell do not infringe, but that agents that act inside the cell may. This is not to imply that Ariad argues in response that the reducing act could occur anywhere. Rather, Ariad would place the boundary at some indefinite place outside of the cell such that accused drugs such as Enbrel are captured but certain prior art drugs, such as antibiotics, are left out of the claim scope. Ariad is correct that the asserted claims have a limited scope, but its particular choice of boundary lacks foundation in the intrinsic evidence. For our analysis, we begin with the claim language.

The ordinary meaning of "reducing NF-κB activity in cells" is unclear. The phrase cannot simply reflect that the NF-κB activity must occur within cells because this would be redundant. There is no dispute NF-κB activity can occur only within cells, and this limit is already included in the claim construction of "NF-κB activity." Amgen, 577 F. Supp. 2d at 727. As Amgen argues, "reducing NF-κB activity in cells" could mean that the reducing act must occur within the cell. But as Ariad suggests, it could also mean simply that the method must be performed on cells in which NF-κB is present, without regard to the situs of the reducing agent.

The specification of the '516 patent divides external influences (e.g., TNF-α) and intracellular transducers (e.g., NF-κB). That division is at the cell membrane, and the claim language "reducing NF-κB activity in cells" is consistent with this division. The specification repeatedly frames NF-κB as an intracellular transducer of external influences:

> As a result of this finding, it is now possible to alter or modify the activity of NF-κB as an intracellular messenger and, as a result, to alter or modify the effect of a variety of external influences, referred to as inducing substances, whose messages are transduced within cells through NF-κB activity. Alteration or modification, whether to enhance or reduce NF-κB activity or to change its binding activity (e.g., affinity, specificity), is referred to herein as regulation of NF-KB activity. The present invention relates to a method of regulating or influencing transduction, by NF-κB, of extracellular signals into specific patterns of gene expression and, thus, of regulating NF-κB-mediated gene expression in the cells and systems in which it occurs.
>
> In particular, the present invention relates to a method of regulating (enhancing or diminishing) the activity of NF-κB in cells in which it is present and capable of acting as an intracellular messenger, as well as to substances or composition useful in such a method.

'516 patent col.3 l.59 – col.4 l.9. For example, TNF-α is an "inducing substance" because its "messages are transduced within cells through NF-κB activity." Decoy

molecules are designed to "alter or modify the activity of NF-κB as an intracellular messenger" by binding active NF-κB and preventing it from inducing DNA expression. Consequently, the administration of decoy molecules would "alter or modify the effect of" TNF-α by blocking, within the cell, the signal that was initiated by TNF-α at the receptor on the surface of the cell.

Thus, the specification assumes the existence of an external influence whose effect can be modified by acting within the cell. In contrast, Enbrel acts to stop the external influence (TNF-α) from reaching the cell. Enbrel does not "alter or modify the activity of NF-κB as an intracellular messenger and, as a result, . . . alter or modify the effect of a variety of external influences." Rather, it directly blocks one of the "variety of external influences." While the specification proposes several agents that act within the cell to reduce NF-κB activity, there is no mention whatsoever of agents that act outside the cell to reduce NF-κB activity.

In its arguments made to the PTO during reexamination of the '516 patent, Ariad further reinforced the division between actions taken inside and outside of the cells:

> Broadly speaking, there are the two types of methods to obtain a cell exhibiting reduced NF-κB activity [which are] as follows: (a) reducing the induced NF-κB activity by intervening in the signaling pathway by which NF-κB activity is manifested including particularly intervening intracellularly at a specific segment within the signaling pathway; and (b) preventing the external inducing stimuli from inducing the intracellular signaling pathway through which NF-κB activity is manifested. Certain claims of the '516 patent as issued covered both types of methods. However, as discussed further in this response applicants maintain that the rejected claims now pending [which include claims 6, 18, 70-72 and 183-184] are directed only to type (a) above.

The category (a) methods described above indisputably include decoy molecules and the other examples in the specification because those agents "interven[e]

intracellularly." And the category (b) methods indisputably include antibiotics because they "prevent[] the external inducing stimuli from inducing" NF-κB activity. Enbrel, which acts outside the cell, and acts by blocking the external inducing stimuli from reaching the cell, would seem a far better fit in category (b) than category (a). Ariad's difficulty in making its argument to the PTO, and in this case, is that it lacks a basis in the specification to distinguish Enbrel from antibiotics. Rather, the patent creates a category of "external influences" that are simply the backdrop for the invention, and Enbrel and antibiotics impact only this category. Ariad argues that the "signaling pathway" should include the event of TNF-α binding to the receptor on the outside of the cell, and as such Enbrel should fit into category (a). But again, there is nothing whatsoever in the specification to support this view—not even a single mention of an NF-κB signaling pathway.

Although the ordinary meaning of the term "reducing NF-κB activity in cells" admits alternative views, the specification and prosecution history unequivocally point to the conclusion that the term limits the asserted claims to methods wherein the action that reduces NF-κB activity is taken inside the cell. As such, we conclude that "reducing NF-κB activity in cells" means "taking action inside cells to inhibit (interfere or block) an NF-κB activity." We therefore affirm the summary judgment of noninfringement. Ariad also appealed the construction of numerous other claim terms, but the parties agree that none of these has any impact on the summary judgment of noninfringement on appeal. Therefore, we decline to reach them.

On appeal, Amgen filed a motion for affirmance on the alternative ground of collateral estoppel in view of our decision in Ariad, which invalidated claims 80, 95, 144,

and 145 of the ’516 patent for lack of written description. 560 F.3d at 1376-77. In its motion, Amgen argued that Ariad is now precluded from asserting any claims of the ’516 patent that recite methods comprising the single step of “reducing NF-κB activity.” We decline to reach this issue. The motion is denied.

CONCLUSION

We agree with the district court that the term “reducing NF-κB activity in cells” limits the claims to acts within the cell to reduce NF-κB activity. Because there is no dispute of fact that Enbrel does not infringe the asserted claims as construed, the judgment below is affirmed.