United States Court of Appeals for the Federal Circuit

BAXALTA INC., BAXALTA GMBH,
Plaintiffs-Appellants

v.

GENENTECH, INC.,
Defendant-Appellee

CHUGAI PHARMACEUTICAL CO. LTD.,
Defendant

2019-1527

Appeal from the United States District Court for the District of Delaware in No. 1:17-cv-00509-TBD, Circuit Judge Timothy B. Dyk.

Decided: August 27, 2020

WILLIAM R. PETERSON, Morgan, Lewis & Bockius LLP, Houston, TX, argued for plaintiffs-appellants. Also represented by NATALIE A. BENNETT, Washington, DC; MICHAEL J. ABERNATHY, CHRISTOPHER JOHN BETTI, MARIA DOUKAS, KARON NICOLE FOWLER, SANJAY K. MURTHY, Chicago, IL; JULIE S. GOLDEMBERG, Philadelphia, PA.

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appellee. Also represented by ALEXANDER ATKINS, MARISSA DORAN, JENNIFER GORDON, NICHOLAS P. GROOMBRIDGE, NAZ WEHRLI, JOSEPHINE YOUNG; DAVID COLE, KENNETH A. GALLO, Washington, DC.

Before MOORE, PLAGER, AND WALLACH, *Circuit Judges.*[1]

MOORE, *Circuit Judge*.

Baxalta Inc. sued Genentech, Inc. and Chugai Pharmaceutical Co. Ltd.,[2] alleging infringement of claims 1, 4, 17, and 19 of U.S. Patent No. 7,033,590. On December 3, 2018, the United States District Court for the District of Delaware issued a claim construction order, construing the terms "antibody" and "antibody fragment." Following the claim construction order, the parties stipulated to non-infringement of the asserted claims. The district court entered judgment based on its claim construction order and the parties' stipulation. Baxalta appeals the district court's judgment, arguing the district court's claim constructions were erroneous. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

Because the district court erred in construing the terms "antibody" and "antibody fragment," we vacate the district court's judgment of non-infringement and remand.

I. BACKGROUND

Baxalta sued Genentech, asserting that Genentech's Hemlibra® (emicizumb-kxwh) product used to treat the

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[1] Judge Stoll recused and took no part in this decision. Judge Plager replaced Judge Stoll on the panel following oral argument.

[2] Chugai was later voluntarily dismissed from the lawsuit pursuant to a joint stipulation between Chugai and Baxalta. J.A. 15946–47.

blood clotting disorder hemophilia infringes claims 1, 4, 17, and 19 of the '590 patent. Blood clotting occurs in the body through a series of enzymatic activations known as the "coagulation cascade." '590 patent at 1:7–10. One "key step" in the cascade is when an enzyme known as activated clotting factor VIII (FVIIIa) complexes with another enzyme known as activated clotting factor IX (FIXa) to form a complex that then activates factor X (FX). '590 patent at 1:17–19. Hemophilia A is a particular form of hemophilia where the activity of factor VIII is functionally absent, thereby impeding the coagulation cascade. This can occur in some Hemophilia A patients because they develop factor VIII inhibitors (i.e., antibodies against factor VIII), which hinder the effectiveness of factor VIII preparations administered as treatments. '590 patent at 1:24–32. The '590 patent relates to preparations used to treat hemophilia patients who have developed factor VIII inhibitors. '590 patent at 2:25–29. The preparations comprise antibodies or antibody fragments that bind to factor IX or factor IXa to increase procoagulant activity of factor IXa to compensate for the decreased factor VIII activity. *See, e.g.*, '590 patent at 2:29–34. Independent claim 1 and dependent claims 4 and 19 are illustrative and recite:

> 1. An isolated antibody or antibody fragment thereof that binds Factor IX or Factor IXa and increases the procoagulant activity of Factor IXa.
>
> 4. The antibody or antibody fragment according to claim 1, wherein said antibody or antibody fragment is selected from the group consisting of a monoclonal antibody, a chimeric antibody, a humanized antibody, a single chain antibody, a bispecific antibody, a diabody, and di-, oligo- or multimers thereof.
>
> 19. The antibody or antibody fragment according to claim 4, wherein the antibody is a humanized antibody.

The parties disputed the construction of the terms "antibody" and "antibody fragment," among other terms not at issue on appeal. Generally, antibodies are Y-shaped structures comprising two heavy chains (H chains) and two light chains (L chains). An antibody that has two identical H chains and two identical L chains is called "monospecific" because each H-L chain pair binds the same antigen. Bispecific antibodies, like Genentech's product Hemlibra® (emicizumb-kxwh), have different heavy chains and/or different light chains, allowing them to bind two different antigens. Baxalta argued "antibody" should be construed as "[a] molecule having a specific amino acid sequence comprising two heavy chains (H chains) and two light chains (L chains)." Genentech argued "antibody" should instead be construed as "[a]n immunoglobulin molecule, having a specific amino acid sequence that only binds to the antigen that induced its synthesis or very similar antigens, consisting of two identical heavy chains (H chains) and two identical light chains (L chains)."

The district court determined that "the term *antibody* standing alone without other structural terms can have different meanings to those skilled in the art," and that both Baxalta's and Genentech's proposed constructions were acceptable definitions. *Baxalta Inc. v. Genentech, Inc.*, No. 17-509, 2018 WL 6304351, at *4 (D. Del. Dec. 3, 2018). It determined, however, that the patentee "chose [Genentech's] narrower definition" by expressly defining antibodies in column 5 of the patent, which states:

> Antibodies are immunoglobulin molecules having a specific amino acid sequence which only bind to antigens that induce their synthesis (or its immunogen, respectively) or to antigens (or immunogens) which are very similar to the former. Each immunoglobulin molecule consists of two types of polypeptide chains. Each molecule consists of large, identical heavy chains (H chains) and two light, also identical chains (L chains).

Id. at *5 (quoting '590 patent at 5:56–63).

Although the district court recognized that the '590 patent claims and discloses "bispecific antibodies, which do not have identical heavy and light chains," and IgM and IgA antibodies, which "can have more than two heavy chains and more than two light chains," it determined that these claimed embodiments were "antibody derivatives" rather than "antibodies." *Id.* at *5–6. The district court likewise dismissed the "inconsisten[cy]" between Genentech's definition of "antibody" and "at least dependent claims 4 and 19" as insufficient to overcome what it considered to be the definitional language of column 5. *Id.* at *11. The district court therefore adopted Genentech's construction, construing "antibody" as "an immunoglobulin molecule, having a specific amino acid sequence that only binds to the antigen that induced its synthesis or very similar antigens, consisting of two identical heavy chains (H chains) and two identical light chains (L chains)." *Id.* at *12.

To support its construction, the district court cited an amendment Baxalta made during prosecution of the '590 patent. Original claim 1 recited "[a]n antibody or antibody derivative against factor IX/factor IXa which increases the procoagulant activity of FIXa." J.A. 15961. Original dependent claim 4 recited a list of "antibod[ies] or antibody derivative[s] according to claim 1" including "chimeric antibodies, humanized antibodies, single chain antibodies, bispecific antibodies, diabodies and di-, oligo- or multimers thereof." *Id.* During prosecution, the patent examiner rejected the term "antibody derivatives" as not enabled for "any antibody derivative against factor IX/factor IXa which increases the procoagulant activity of FIXa in claim 1" or any one of the enumerated list in dependent claim 4. J.A. 15987, 16008. Based on the examiner's suggestion, the patentee amended the claims to recite "antibody fragment" in place of "antibody derivative" and the examiner removed the enablement rejection. The district court determined that this amendment amounted to a

disclaimer of antibody derivatives "including bispecific antibodies, except *antibody fragments*." *Baxalta*, 2018 WL 6304351, at *7–8 (emphasis in original).

The parties also disputed the construction of "antibody fragment." Baxalta proposed that the term be construed as "[a] portion of a molecule having a specific amino acid sequence comprising two heavy chains (H chains) and two light chains (L chains)." *Id.* at *12. Genentech argued it should instead be construed as "[a] fragment of an antibody which partially or completely lacks the constant region; the term 'antibody fragment' excludes all other forms of antibody derivatives." *Id.* The district court, relying on a portion of the written description reciting that "antibody fragments . . . partially or completely lack the constant region" and identifying examples of fragments (Fv, Fab, Fab' [and] $F(ab)'_2$), construed "antibody fragment" as "a fragment of an antibody which partially or completely lacks the constant region; the term 'antibody fragment' excludes bispecific antibodies." *Id.* at *12–13 (citing '590 patent at 6:20–21).

Based on the district court's constructions, the parties stipulated to non-infringement of the asserted claims of the '590 patent. The district court entered final judgment of non-infringement of claims 1, 4, 17, and 19. Baxalta appeals, arguing that the district court erroneously construed the terms "antibody" and "antibody fragment."

II. DISCUSSION

We review a district court's claim construction de novo "[w]here, as here, the intrinsic evidence alone determines the proper claim construction." *Allergan Sales, LLC v. Sandoz, Inc.*, 935 F.3d 1370, 1373 (Fed. Cir. 2019) (citing *Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 332–33 (2015)). "The words of a claim are generally given their ordinary and customary meaning as understood by a person of ordinary skill in the art when read in the context of the specification and prosecution history." *Thorner v. Sony*

Comput. Entm't Am. LLC, 669 F.3d 1362, 1365 (Fed. Cir. 2012).

A. "Antibody"

i. The Claims of the '590 Patent

Claim 1 of the '590 patent recites "[a]n isolated antibody or antibody fragment thereof that binds Factor IX or Factor IXa and increases the procoagulant activity of Factor IXa." Therefore, contrary to the district court's construction, nothing in the plain language of claim 1 limits the term "antibody" to a specific antibody consisting of two identical heavy chains and two identical light chains or an antibody that only binds the antigen that induced its synthesis or very similar antigens.

The dependent claims confirm that "antibody" is not so limited. For example, dependent claim 4, recites "[t]he antibody or antibody fragment according to claim 1, wherein said antibody or antibody fragment is selected from the group consisting of . . . a chimeric antibody, a humanized antibody, . . . [and] a bispecific antibody." Each of these claimed "antibodies" falls outside of the district court's construction because each does not "only bind[] to the antigen that induced its synthesis or very similar antigens."[3] A

[3] The '590 patent explains that a humanized antibody has a structure of a human antibody but combines non-human antibody portions, such as the complement determining regions (CDRs), with human antibody portions. '590 patent at 6:50–7:1. It explains that a chimeric antibody differs from a humanized antibody in that it comprises the entire variable regions of non-human origin in combination with human constant regions. *Id.* Finally, it explains that a bispecific antibody has "two different binding specificities within one single molecule," i.e., it can bind two different antigens. *Id.* at 7:32–38. It is undisputed

"bispecific antibody" also does not satisfy the district court's construction of "antibody" because a bispecific antibody does not consist of two identical H chains and two identical L chains. Dependent claim 19 further limits claims 1 and 4 by claiming that the "*antibody* is a humanized antibody," which again does not fall within the district court's construction of "antibody."

The district court's construction which excludes these explicitly claimed embodiments is inconsistent with the plain language of the claims.[4] *See Intellectual Ventures I LLC v. T-Mobile USA*, Inc., 902 F.3d 1372, 1378 (Fed. Cir. 2018); *see also Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1362 (Fed. Cir. 2008) (rejecting a construction that would "render several dependent claims meaningless").

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that humanized antibodies, chimeric antibodies, and bispecific antibodies fall outside the district court's construction. *See* Genentech Resp. Br. at 1, 53; Baxalta Op. Br. at 12.

[4] Baxalta argues that the district court's claim construction is also inconsistent with dependent claims 7, 9, 11, 18, 21, and 22 because they require synthetic production methods that do not "only bind[] to the antigen that induced its synthesis or very similar antigens." Baxalta Op. Br. at 31–32. Baxalta also argues that the district court's construction excludes claimed embodiments in claims 3 and 20, which recite that the antibody is an "IgG, IgM, IgA or IgE antibody." Genentech agrees that IgM and IgA antibodies do not necessarily meet the district court's construction requiring that the antibody consist of two identical H chains and two identical L chains. Genentech Resp. Br. at 9, 36. We note that when a construction such as this is inconsistent with the plain language of the claims and the written description, it is incorrect.

The district court rejected this inconsistency, suggesting that the proper result here is "invalidation of the inconsistent claims rather than an expansion of the independent claims." *Baxalta*, 2018 WL 6304351, at *11. Similarly, Genentech invites us to assume that the examiner simply overlooked at least these dependent claim limitations when he allowed the claims. *See* Genentech Resp. Br. at 53 and *Baxalta Inc. v. Genentech, Inc.*, No. 19-1527, Oral Arg. at 34:44–35:12, *available at* http://oralarguments.cafc.uscourts.gov/default.aspx?fl=2019-1527.mp3 (counsel for Genentech explaining "we don't have an answer to why [bispecific antibodies are] there except that they stood rejected and somehow got allowed"). Genentech argues that because the patent defines the term "antibody" in column 5, we should invalidate all dependent claims which would not be consistent with that definition such as claims 4 and 19. We do not agree. The plain language of these dependent claims weighs heavily in favor of adopting Baxalta's broader claim construction. And as in *Intellectual Ventures I*, we reject the district court's construction which renders dependent claims invalid. 902 F.3d at 1378.

ii. The Written Description of the '590 Patent

Under the heading "Antibodies and Antibody Derivatives," the patentee explains:

> Antibodies are immunoglobulin molecules having a specific amino acid sequence which only bind to antigens that induce their synthesis (or its immunogen, respectively) or to antigens (or immunogens) which are very similar to the former. Each immunoglobulin molecule consists of two types of polypeptide chains. Each molecule consists of large, identical heavy chains (H chains) and two light, also identical chains (L chains).

'590 patent at 5:56–65. The district court determined that this portion of the written description defined the term "antibody." While this is a plausible reading of the excerpt in

isolation, claim construction requires that we "consider the specification as a whole, and [] read all portions of the written description, if possible, in a manner that renders the patent internally consistent." *Budde v. Harley-Davidson, Inc.*, 250 F.3d 1369, 1379–80 (Fed. Cir. 2001). When considered in the context of the remainder of the written description and the claims, we read the excerpt in column 5 as a generalized introduction to antibodies rather than as a definitional statement. We also note that these general statements do not include terms we have held to be limiting in other contexts such as "the present invention includes . . ." or "the present invention is . . ." or "all embodiments of the present invention are . . . ." *Luminara Worldwide, LLC v. Liown Elecs. Co.*, 814 F.3d 1343, 1353 (Fed. Cir. 2016).

Beyond this general description in column 5, the written description provides specific disclosures regarding bispecific, chimeric, and humanized antibodies and methods of production thereof, all of which do not comport with the district court's construction. For example, the written description explains that "[t]he inventive antibodies and antibody derivatives and organic compounds derived there from comprise . . . bispecific antibodies." '590 patent at 6:1–6. Both parties agree "bispecific antibodies" do not consist of two identical H chains and two identical L chains and thus fall outside the district court's construction. *See, e.g.*, Baxalta Op. Br. at 30 n.16; Genentech Resp. Br at 1. The written description further discloses that "antibodies and antibody derivatives may also include . . . 'technically modified antibodies' such as . . . chimeric or humanized antibodies . . . . In these technically modified antibodies, e.g., a part or parts of the light and/or heavy chain may be substituted." '590 patent at 6:15–24. And the written description explains that "[t]he *antibodies* of the present invention can be prepared by methods known from the prior art, e.g. by conventional hybridoma techniques, or by means of phage display gene libraries, immunoglobulin chain shuffling or humanizing techniques." *Id.* at 7:65–8:3 (emphasis

added). The written description, therefore, discloses synthetic techniques for preparing antibodies such as humanized or chimeric antibodies, which are inconsistent with the district court's claim construction requirement that the antibody "only binds to the antigen that induced its synthesis or very similar antigens." Recognizing that these disclosed techniques for preparing the claimed antibodies would result in antibodies excluded by the district court's construction, Genentech's response was "I hesitate to say that that's a typo." *Baxalta*, No. 19-1527 Oral Arg. at 37:02–38:26.

Genentech does not dispute that the written description discloses antibodies that fall outside the district court's construction, but rather argues that "there is no legal problem with a claim construction that excludes certain disclosed embodiments, where the specification otherwise supports that construction." Genentech Resp. Br. at 1, 60–61. To adopt Genentech's construction, we would need to invalidate several dependent claims, which according to Genentech, the examiner overlooked in allowing, and to conclude that preparation techniques for the claimed antibodies included in the written description were disclosed in error. *See Baxalta*, No. 19-1527 Oral Arg. at 31:37–32:26 (counsel for Genentech conceding that "[claim 19] and claim 4 are inconsistent with the notion that column 5 is a definition of 'antibody'"). As discussed, column 5 is not definitional, and the remainder of the written description and claims do not support the district court's construction. The claim construction excluding these disclosed and claimed embodiments is therefore incorrect.

iii. The Prosecution History of the '590 Patent

The prosecution history does not, as the district court suggests, "confirm[] the specification's definition of antibody." *Baxalta*, 2018 WL 6304351, at *7. We have recognized that the prosecution history "often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Phillips v. AWH Corp.*, 415 F.3d 1303,

1317 (Fed. Cir. 2005) (en banc). While a patentee cannot recapture specific constructions disclaimed during patent prosecution either through amendment or argument, we do not apply the doctrine of prosecution history disclaimer where the alleged disavowal is less than clear. *Avid Tech., Inc. v. Harmonic, Inc.*, 812 F.3d 1040, 1045 (Fed. Cir. 2016).

The district court's analysis centered around the patentee's amendment substituting the term "antibody fragment" for "antibody derivative," at the examiner's suggestion, to overcome an enablement rejection. *See* J.A. 15987, 16008, 16012, 16017–21. Based on its previous definition of "antibody derivatives" as "*antibodies* within the column 5 definition that had been altered in some significant way," e.g., bispecific antibodies, *Baxalta*, 2018 WL 6304351, at *6–7, the district court determined that the amendment from "antibody derivative" to "antibody fragment" amounted to a disclaimer of antibody derivatives "including bispecific antibodies, except *antibody fragments*." *Id.* at *7–8 (emphasis in original). Because we reject the premise that the excerpt of column 5 is definitional, and do not view the prosecution history as sufficiently clear and unmistakable, we conclude that the prosecution history is insufficient to overcome the meaning of "antibody" we discern from the claims and the written description.

First, there are no clear statements in the prosecution history regarding what scope, if any, was given up when the patentee substituted "antibody fragment" for "antibody derivative." "[I]n order for prosecution disclaimer to attach, the disavowal must be both clear and unmistakable." *3M Innovative Properties Co. v. Tredegar Corp.*, 725 F.3d 1315, 1325 (Fed. Cir. 2013). Both parties agree that the term "antibody derivative" is not a term that is commonly used in the art. *Baxalta*, 2018 WL 6304351, at *6. It is plausible, therefore, given the ambiguity regarding this amendment, that the patentee was substituting a known term at the suggestion of the examiner for a less commonly used term in the art. In fact, the written description

appears to use them almost interchangeably. *See, e.g.*, '590 patent at 6:20–22 (identifying Fv, Fab, Fab', and F(ab)'$_2$ as examples of antibody fragments); *id.* at 20:35–36 (identifying scFv and Fab as examples of antibody derivatives); *id.* at 30:15–17 (identifying Fab, F(ab)$_2$, and scFv as examples of antibody derivatives). The prosecution history, therefore, does not clearly establish disclaimer. Second, the district court's determination that the patentee disclaimed antibody derivatives "including bispecific antibodies, except *antibody fragments*" is inconsistent with the examiner's subsequent allowance of at least claim 4. As explained above, claim 4 explicitly claims "a bispecific antibody," a claimed embodiment directly at odds with a disclaimer theory. The prosecution history, therefore, does not support the district court's construction of "antibody."

The parties agree that Baxalta's and Genentech's proposed constructions are recognized meanings of "antibody." We hold that the district court erred in selecting the narrower construction, which is inconsistent with the written description and the plain language of the claim. Consistent with the claims and the written description, we instead construe "antibody" as "an immunoglobulin molecule having a specific amino acid sequence comprising two heavy chains (H chains) and two light chains (L chains)."

B. "Antibody Fragment"

The district court construed "antibody fragment" as "a fragment of an antibody which partially or completely lacks the constant region." The district court further specified that "the term 'antibody fragment' excludes bispecific antibodies." *Baxalta*, 2018 WL 6304351, at *12–13. Baxalta argues that the district court's construction improperly excludes bispecific antibodies and imports limitations from the written description. For reasons related to our construction of "antibody," we hold that the district court erred in construing "antibody fragment." We construe that term as "[a] portion of an immunoglobulin molecule having

a specific amino acid sequence comprising two heavy chains (H chains) and two light chains (L chains)."

The district court's construction relied on the following portion of the written description:

> The term factor IX/IXa activating antibodies and antibody derivatives *may also include* . . . *e.g.*, "technically modified antibodies" *such as* synthetic antibodies, chimeric or humanized antibodies, or mixtures thereof, or antibody fragments which partially or completely lack the constant region, *e.g.* Fv, Fab., Fab' or F(ab) *etc.*

'590 patent at 6:15–22 (emphases added). But this excerpt does not, as the district court suggests, define antibody fragments as necessarily "partially or completely lack[ing] the constant region." Indeed, the standard for lexicography is exacting, requiring the patentee to "'clearly express an intent' to redefine a term." *Thorner*, 669 F.3d at 1365–66. "[A]lthough the specification often describes very specific embodiments of the invention, we have repeatedly warned against confining the claims to those embodiments." *Phillips*, 415 F.3d at 1323. Here, the written description's use of "may also include," "e.g.," "such as," and "etc." makes clear the patentee did not intend this excerpt of the written description to define "antibody fragment." Instead, we construe "fragment" according to its plain and ordinary meaning in light of the written description as a whole. Accordingly, we construe "antibody fragment" to mean "a portion of an antibody" as we have defined above, that is: "a portion of an immunoglobulin molecule having a specific amino acid sequence comprising two heavy chains (H chains) and two light chains (L chains)."

III. CONCLUSION

We have considered the parties' remaining arguments and do not find them persuasive. Because the district court erred in construing the terms "antibody" and "antibody

fragment" and entered judgment of non-infringement based on its erroneous constructions, we vacate and remand for further proceedings consistent with the correct constructions of the terms.

VACATED AND REMANDED

COSTS

Costs to Baxalta.