IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

MORPHOSYS AG, Plaintiff, v. JANSSEN BIOTECH, INC., GENMAB US, INC. and GENMAB A/S, Defendants.	: : : : : : : : : :	C.A. No. 16-221-LPS-CJB

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MEMORANDUM OPINION

October 23, 2017
Wilmington, Delaware

STARK, U.S. District Judge:

In this patent infringement action, Plaintiff MorphoSys AG alleges that Defendants Janssen Biotech, Inc., Genmab US, Inc., and Genmab A/S (collectively, "Janssen"), and specifically Janssen's Darzalex (daratumumab) anti-CD38 antibody used for the treatment of patients with multiple myeloma, infringe MorphoSys' U.S. Patent Nos. 8,263,746 and 9,200,061, which generally describe and claim anti-CD38 human antibodies and methods of treating hematologic cancer with such antibodies. Presently before the Court is the issue of claim construction.[1] The parties submitted technology tutorials (D.I. 85, 88) and claim construction briefs (*see* D.I. 147, 150, 168, 169). Both parties also submitted expert declarations (*see* D.I. 148, 151, 170, 171), which the Court has considered. The Court held a claim construction hearing on August 28, 2017. (*See* D.I. 196 ("Tr."))

I. LEGAL STANDARDS

The ultimate question of the proper construction of a patent is a question of law. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 135 S. Ct. 831, 837 (2015) (citing *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 388-91 (1996)). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (internal quotation marks omitted). "[T]here is no magic formula or catechism for conducting claim construction." *Id.* at 1324. Instead, the court is free to attach the appropriate weight to appropriate sources "in light of the statutes and policies that inform patent law." *Id.*

[1]The Court previously construed the terms "human," "humanized," and "specifically binds within" in an early claim construction process. (D.I. 102)

"[T]he words of a claim are generally given their ordinary and customary meaning . . . [which is] the meaning 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." *Id.* at 1312-13 (internal citations and quotation marks omitted). "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted). The patent specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996).

While "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding words of the claim also must be considered. *Phillips*, 415 F.3d at 1314. Furthermore, "[o]ther claims of the patent in question, both asserted and unasserted, can also be valuable sources of enlightenment . . . [b]ecause claim terms are normally used consistently throughout the patent . . . ." *Id.* (internal citation omitted).

It is likewise true that "[d]ifferences among claims can also be a useful guide . . . . For example, the presence of a dependent claim that adds a particular limitation gives rise to a presumption that the limitation in question is not present in the independent claim." *Id.* at 1314-15 (internal citation omitted). This "presumption is especially strong when the limitation in dispute is the only meaningful difference between an independent and dependent claim, and one party is urging that the limitation in the dependent claim should be read into the independent claim." *SunRace Roots Enter. Co., Ltd. v. SRAM Corp.*, 336 F.3d 1298, 1303 (Fed. Cir. 2003).

It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the

inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. It bears emphasis that "[e]ven when the specification describes only a single embodiment, the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)) (internal quotation marks omitted).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). The prosecution history, which is "intrinsic evidence," "consists of the complete record of the proceedings before the PTO [Patent and Trademark Office] and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he 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.*

In some cases, "the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 135 S. Ct. at 841. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. For instance, technical dictionaries can assist the court in determining the meaning of a term to those of skill in the relevant art because such dictionaries "endeavor to collect the

accepted meanings of terms used in various fields of science and technology." *Phillips*, 415 F.3d at 1318. In addition, expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Id.* Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* Overall, while extrinsic evidence "may be useful" to the court, it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

Finally, "[t]he construction that stays true to the claim language and most naturally aligns with the patent's description of the invention will be, in the end, the correct construction." *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998). It follows that "a claim interpretation that would exclude the inventor's device is rarely the correct interpretation." *Osram GmbH v. Int'l Trade Comm'n*, 505 F.3d 1351, 1358 (Fed. Cir. 2007) (quoting *Modine Mfg. Co. v. U.S. Int'l Trade Comm'n*, 75 F.3d 1545, 1550 (Fed. Cir. 1996)).

II. CONSTRUCTION OF DISPUTED TERMS

A. "at least [five/two]-fold better efficacy"[2]

MorphoSys "at least [five/two]-fold lower EC50"
Janssen plain and ordinary meaning, i.e., not limited to EC50
Court "at least [five/two]-fold lower EC50"

The parties dispute whether the claims require a specific method for determining efficacy. MorphoSys contends that the claims require efficacy to be measured by EC50, while Janssen counters that the claims cover any method for evaluating efficacy. The Court agrees with MorphoSys.

Considering the claim language in context, claim 1 recites in relevant part an antibody that "mediates killing of a CD38+ target cell by antibody dependent cellular cytotoxicity with at least five-fold better efficacy than chimeric OKT10 antibody (SEQ ID NOS: 23 and 24) under the same or substantially the same conditions when a human PBMC cell is employed as the effector cell." '746 patent col. 67 ll. 29-35. The claims give specific, detailed parameters for the efficacy testing that must be performed: the claimed antibody must mediate killing of a particular type of cell (e.g., CD38+ target) by a particular mechanism (e.g., antibody dependent cellular cytotoxicity) under particular conditions. *See also* col. 67 ll. 63-67 (claim 8: "said antibody mediates killing of a CD38-transfected CHO cell by cell dependent cytotoxicity with at least two-fold better efficacy than chimeric OKT10 antibody (SEQ ID NOS: 23 and 24) under the

[2]This term appears in claims 1, 6-8, 12, and 13 of the '746 patent.

same or substantially the same conditions"). Claim 1 also requires the CD38+ target cell to be one of two cell lines: LP-1 or RPMI-8226. *See* col. 67 ll. 36-38.

The specification, in turn, presents data collected in accordance with the recited efficacy testing for the four representative antibodies of this invention. In particular, "Table 2 provides a summary of the determination of EC50 values of representative antibodies of the invention in both ADCC [antibody-dependent cellular cytotoxicity] and CDC [complement-dependent cytotoxicity]." Col. 10 ll. 4-6. Thus, the underlying data supporting the claims measures efficacy exclusively in terms of EC50. Moreover, during prosecution, the patentees pointed to Table 2 as the written description support for these functional limitations of the claims. (*See* D.I. 75 at JA83) Thus, the claims, specification, and prosecution history support MorphoSys' position that it used the term "efficacy" in the claims to describe EC50 measurements.

Janssen's argument that EC50 is merely one way to measure antibody efficacy is not persuasive. Janssen contends that the patent describes maximum specific killing as a different method for determining how effective an antibody is at killing certain cells. For example, Figure 14 of the '746 patent sets forth maximum specific killing values for a number of cell lines – with no mention of EC50. But, as described above, the claims require LP-1 or RMPI-8226 cells to be used. The data presented in Figure 14 for the RMPI-8226 cell line shows that the reference antibody OKT10 has a maximum specific killing in ADCC of 46%, and no data is provided for LP-1. Thus, under Janssen's view, an antibody would have to kill 230% of cells (i.e., five times 46%) in order to satisfy the limitation that an inventive antibody has five-fold better efficacy than OKT10. This cannot be correct, of course, as an antibody can kill no more than 100% of cells in a sample.

Janssen also points to disclosures in the '061 patent. (*See, e.g*, Tr. at 21-22) The '061 patent is a continuation-in-part of the '746 patent, and the disclosures on which Janssen relies are some of the new material that was added to the '061 patent. While "statements made by the inventor during continued prosecution of a related patent application can, in some circumstances, be relevant to claim construction," here the '061 patent does not compel a different construction. *Ventana Med. Sys., Inc. v. Biogenex Labs., Inc.*, 473 F.3d 1173, 1184 (Fed. Cir. 2006). In particular, Janssen contends that Figure 20 and the accompanying description demonstrate that the patentee used efficacy to mean more than comparison of EC50 values. But in describing Figure 20, the '061 patent summarizes that "only minor differences among the HuCAL® hCD38 antibodies were found except for MOR03100 which was ***less efficient as judged from its EC50 values***." '061 patent col. 30 ll. 6-15 (emphasis added). This statement, then, leaves the Court continuing to believe the patentee was not using the term efficacy more broadly than to refer to EC50.

B. "isolated"[3]

MorphoSys "essentially free from other immunoglobulins"
Janssen "essentially free from impurities"
Court "essentially free from antibodies that do not bind to CD38"

The parties dispute what type of unwanted material is excluded from an isolated antibody. MorphoSys contends that the use of "isolated" in the patents is consistent with how this term is

[3]This term appears in claims 1, 5, 6, 11, 12, and 15 of the '061 patent and claims 1, 6-8, 12-15, 18, 27, and 28 of the '746 patent.

used in the art – it simply means that the desired antibody is free from other immunoglobulins that exhibit different antigen specificities. (*See* Tr. at 35-37) In the context of the asserted patents, an isolated antibody excludes antibodies that do not bind to CD38. (*See id.*) Janssen counters that "isolated" is essentially synonymous with "purified," meaning that an isolated antibody is free from impurities.

The Court is not persuaded that isolation and purification necessarily represent the same concept. Although Janssen identifies portions of the specification that seem to use the terms interchangeably, those passages refer to certain types of blood cells. (*Compare* '061 patent col. 27 ll. 28-31, *with* col. 28 ll. 20-24) Purification and isolation techniques for cells are different from the techniques required for purification or isolation of antibodies. (*See* Tr. at 51; D.I. 180 at ¶ 24) Thus, the Court agrees with MorphoSys that an isolated antibody means that the antibody excludes antibodies that do not bind to CD38 – as is consistent with the ordinary usage in the art.[4]

C. "binds an epitope of CD38 that contains one or more amino acid residues within 192-206 of SEQ ID NO:22"[5]

MorphoSys plain and ordinary meaning, i.e., interactions outside of residues 192-206 are permitted
Janssen "binds an epitope of CD38 at only one or more amino acid residues within 192-206 of SEQ ID NO: 22 (and not elsewhere)"

[4]The Court deems it helpful and appropriate to specify in its construction that what is excluded are antibodies that do not bind to CD38, as opposed to more generally "other immunoglobulins."

[5]This term appears in claims 1, 5, 6, 11, 12, and 15 of the '061 patent.

Court
plain and ordinary meaning, i.e., interactions outside of residues 192-206 are permitted

The parties dispute whether this term requires the isolated antibody to bind only to CD38 within residues 192-206 or whether the antibody can bind outside those residues as well. The Court construed a similar term in the '746 patent during the early claim construction. (*See* D.I. 102) (construing "specifically binds within" to have its plain and ordinary meaning, rejecting Janssen's proposed construction of "binding only within the recited amino acid region") Janssen's arguments regarding both terms are based on prosecution history (*see, e.g.*, D.I. 108 at 25), which is potentially unique to each patent. Therefore, the Court's early construction of the '746 patent does not preclude Janssen from arguing for a different construction of this term in the '061 patent.

The Court, however, finds that the prosecution history does not support Janssen's position. The disputed term uses the word "contains," which in both ordinary usage and patent-specific usage is an open-ended term that is generally synonymous with "comprises" or "includes." *See Mars, Inc. v. H.J. Heinz Co., L.P.*, 377 F.3d 1369, 1375 (Fed. Cir. 2004). In order for the Court to adopt a more narrow construction, the patentee's actions or statements during prosecution must amount to a clear and unmistakable disavowal. *See Avid Tech., Inc. v. Harmonic, Inc.*, 812 F.3d 1040, 1045 (Fed. Cir. 2016). Janssen relies on two events in the prosecution history, but neither meets the high standard for disclaimer.

The first concerns an amendment, and corresponding explanation, made by MorphoSys in response to the examiner's determination that MorphoSys was not entitled to its earliest claimed priority date. (*See* D.I. 143 at 4617) In that amendment, MorphoSys added specific ranges for

binding (*see id.* at 4615) and told the examiner that those ranges "correspond to the epitopes bound by the antibodies designated in the specification as 'MOR03077' and 'MOR03079'" (*id.* at 4617). MorphoSys then argued that it was entitled to the earlier priority date because the claims were amended to be "directed to the antibodies disclosed in the priority application." (*Id.*) These actions, however, do not establish that the claimed antibodies must bind to the recited ranges and nowhere else. Instead, MorphoSys simply demonstrated to the examiner how and why its claims were supported by disclosures in the priority application such that it was entitled to an earlier priority date.

The second event relates to a new matter rejection by the examiner. MorphoSys had amended its claims to recite "the list of amino acids stretches 44-66, 82-94, 110-122, 142-154, 148-164, 158-170, 186-200, 192-206, 202-224, and 280-296." (*Id.* at 4621) These stretches correspond to every location at which the four exemplary antibodies of the '061 patent bind. *See* '061 patent Figure 7. The examiner rejected this claim for containing new matter. (*See* D.I. 143 at 4630) The examiner explained that the claim language "combines four individual epitopes to create new epitopes that 'mix-and-match' residues from the four epitopes described in the specification." (*Id.* at 4631) For example, the examiner stated that "the specification does not describe an epitope containing amino acids from stretches 192-206 ***and*** 280-296," so the claims could not specifically recite such combination. (*Id.* at 4631-32) (emphasis added) But this history does not clearly and unmistakably show that only binding within stretches 192-206 is now claimed; it just shows that there was not textual support for MorphoSys' "mix-and-match" claim.

III. CONCLUSION

The Court construes the disputed terms as explained above. An appropriate Order follows.

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ORDER

At Wilmington, this **23rd** day of **October, 2017**:

For the reasons set forth in the Memorandum Opinion issued this date,

IT IS HEREBY ORDERED that the disputed claim terms of U.S. Patent Nos. 8,263,746 and 9,200,061 are construed as follows:

Claim Term	**Court's Construction**
at least [five/two]-fold better efficacy [claims 1, 6-8, 12, and 13 of the '746 patent]	at least [five/two]-fold lower EC50
isolated [claims 1, 5, 6, 11, 12, and 15 of the '061 patent and claims 1, 6-8, 12-15, 18, 27, and 28 of the '746 patent]	essentially free from antibodies that do not bind to CD38

binds an epitope of CD38 that contains one or more amino acid residues within 192-206 of SEQ ID NO:22 [claims 1, 5, 6, 11, 12, and 15 of the '061 patent]	plain and ordinary meaning, i.e. interactions outside of residues 192-206 are permitted

HON. LEONARD P. STARK
UNITED STATES DISTRICT JUDGE