United States Court of Appeals for the Federal Circuit

SANOFI-AVENTIS,
Appellant,

v.

PFIZER INC.,
Appellee.

2012-1345

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences in No. 105,757.

Decided: November 5, 2013

Thomas J. Vetter, Lucas & Mercanti, LLP, of New York, New York, argued for appellant.

Z. Ying Li, Ropes & Gray, LLP, of New York, New York, argued for appellee. With her on the brief was James F. Haley, Jr.

Before NEWMAN, and LOURIE, *Circuit Judges,* and DAVIS, *District Judge.*[1]

NEWMAN, *Circuit Judge*.

Sanofi-Aventis ("Sanofi") appeals the decision of the United States Patent and Trademark Office ("PTO") Board of Patent Appeals and Interferences ("the Board"),[2] awarding priority of invention to Pfizer Inc. ("Pfizer") based on the following interference count:

> Count 3. The isolated protein of 6,268,480 claim 4;
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> OR
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> The isolated polynucleotide of 5,710,023 claim 1, selection (b) (an isolated polynucleotide comprising a nucleotide sequence of SEQ ID NO:3 from nucleotide 103 to nucleotide 1242).

Nucleotides 103 to 1242 constitute the protein-encoding portion of the complementary deoxyribonucleic acid ("cDNA") for the human interleukin-13 receptor binding chain ("IL-13bc").

The parties disagree as to the dispositive question in the interference. As summarized by Pfizer, the question is "who first had in hand the actual isolated DNA of the count and appreciated its IL-13bc function." Pfizer Br. 1. As summarized by Sanofi, the question is "the date each party first knew the complete sequence" of nucleotides

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[1] The Honorable Leonard Davis, Chief Judge, United States District Court for the Eastern District of Texas, sitting by designation.

[2] *Sanofi-Aventis v. Pfizer Inc.*, Patent Interference No. 105,757 (Bd. Pat. App. & Int. Jan. 5, 2012). Pfizer was substituted for Genetics Institute as the real party in interest.

103 to 1242. Sanofi Br. 4. The Board agreed with Pfizer that possession and appreciation of the actual isolated DNA is the dispositive question for priority of conception for an interference count directed to the isolated DNA, and on that basis awarded priority to Pfizer.

BACKGROUND

IL-13 is a regulatory molecule called a cytokine. Cytokines function by interacting with cytokine receptors located on target cells. The subject of this patent interference is a DNA polynucleotide that encodes the protein binding chain of the IL-13 receptor. Both Sanofi and Pfizer were conducting research in this field of scientific endeavor, for therapeutic and diagnostic purposes, and both Sanofi and Pfizer discovered and filed patent applications directed to the polynucleotide encoding the relevant IL-13 binding chain.

In accordance with the applicable law,[3] the patent is awarded to the first party to conceive and reduce to practice the invention represented by the interference count. *See Cooper v. Goldfarb*, 154 F.3d 1321, 1327 (Fed. Cir. 1998) ("[P]riority of invention goes to the first party to reduce an invention to practice unless the other party can show that it was the first to conceive of the invention and that it exercised reasonable diligence in later reducing that invention to practice."). This law is implemented in accordance with rules and precedent, administered by the PTO Board ("Board"). On appeal to the Federal Circuit, we review the Board's rulings of law for correctness, and factual findings for support by substantial evidence. *See Dawson v. Dawson*, 710 F.3d 1347, 1353 (Fed. Cir. 2013) ("The issue of conception turns in large

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[3] The America Invents Act ("AIA"), Pub. L. No. 112-29, obviated patent interferences. Pursuant to AIA §3(n)(2)(A), this interference remains governed by the prior laws.

part on the facts, and we review the Board's many factual findings in this case for substantial evidence.").

Sanofi was awarded the benefit of its December 6, 1995 priority date. Pfizer's filing date is March 1, 1996; Pfizer thus bore the burden of proving a date of conception earlier than the Sanofi benefit date. Pfizer presented documentary and testimonial evidence that it had isolated and identified the desired cDNA before the Sanofi benefit date. However, due to sequencing errors, Pfizer did not then have a completely accurate analysis of the entire nucleotide sequence. The Board found that Pfizer had "the claimed polynucleotide in hand with some additional identifying information including at least a partial sequence," and ruled that Pfizer "established conception and actual reduction to practice of a polynucleotide within the scope of count 3" before the Sanofi benefit date. Bd. Op. at 17.

On appeal, Sanofi argues that Pfizer cannot be credited with conception because although Pfizer's sequence analysis before the Sanofi date was correct as to 1135 of the 1143 nucleotides, the analysis was in error as to eight nucleotides. The Board found that Pfizer corrected this analysis by February 7, 1996. The Pfizer patent application filed on March 1, 1996 contained the correct analysis. Sanofi argues that conception of the claimed cDNA could not be established for priority purposes until the fully correct nucleotide sequence was determined, because the interference count is directed to the isolated polynucleotide. Sanofi argues that until Pfizer had correctly analyzed the polynucleotide, neither conception nor reduction to practice could occur. Sanofi states that Federal Circuit precedent requires the full and correct nucleotide sequence to establish conception, because reduction to practice, whether actual or constructive, requires the full and correct nucleotide sequence.

The Board did not share Sanofi's view of law and precedent. The Board held that Pfizer had established conception of the subject matter of the count when it selected, isolated, and obtained the desired IL-13bc full-length polynucleotide and verified that it was the desired product, regardless of whether the fully correct sequencing of the polynucleotide was complete. Sanofi argues on this appeal that the Board erred in law.

DISCUSSION

As junior party with the burden of proof, Pfizer presented evidence of its research with murine and human IL-13 starting in early 1995. The Board found that co-inventor Lori Fitz performed binding assays with commercially supplied human IL-13 in conjunction with recombinant murine IL-13bc protein fused to an antibody fragment known as the Fc domain. Ms. Fitz verified that the murine IL-13bc protein bound human IL-13 and that the interaction was specific, conducting experiments that showed that the protein could be blocked with excess murine IL-13bc fusion protein or with anti-human IL-13 antibody.

After isolating the murine IL-13bc, by October 16, 1995 Pfizer scientists isolated the human IL-13bc, called clone 11, from a human cDNA library. Co-inventor Matthew Whitters testified that he aligned the sequence of clone 11 with the respective sequences of the murine IL-13bc, and summarized his conclusions:

> [G]iven the size of the clone 11 insert (it corresponded to the mouse A25 full-length clone [*i.e.*, murine IL-13bc]), the significant sequence identity and similarity between the amino acid sequence deduced from the nucleotide of the 5' end of the cDNA of the clone 11 insert and the mouse A25 protein, the identification of the 5' end of the cDNA and the confirmation that it encoded the N-terminus of the protein and the fact that the

> cDNA contained the 3' end of the coding sequence, on October 25, 1995, I was highly confident, and virtually positive, that the clone 11 insert contained the full-length nucleic acid coding sequence for the human homolog of the mouse A25 protein.

Whitters Decl. 6, Feb. 25, 2011. Mr. Whitters also testified that on November 15, 1995 he was provided with a computer printout of the nucleotide sequence of clone 11, and the next day he was provided with the deduced amino acid sequence encoded by that clone. He testified that the nucleotide sequence and amino acid sequence were checked for errors by comparison with the sequences for additional human IL-13bc products that Pfizer had isolated from its cDNA library.

Whitters testified that for the polynucleotide sequence eight possible errors were found out of 1143 nucleotides, and that the encoded amino acid sequence was correct for 379 out of 380 residues. He testified that correction of these sequences was completed by December 12, 1995 and confirmed by February 7, 1996.

It was not disputed that clone 11 was the desired product. Pfizer argued that its initial sequence was 99.3% accurate, and that the sequencing errors were routinely detected and corrected. The Board held that Pfizer had established conception and reduction to practice before the Sanofi benefit date.

Sanofi argues that as a matter of law Pfizer did not have a complete conception until Pfizer had the full correct nucleotide sequence, citing Federal Circuit precedent including *Amgen Inc. v Chugai Pharmaceutical Co.*, 927 F.2d 1200 (Fed. Cir. 1991). *Amgen* does not support Sanofi's position. The court in *Amgen* held that when "an inventor is unable to envision the detailed constitution of a gene" there may nonetheless be conception and reduction to practice of the gene when the inventor is in possession of the gene and a method for its preparation, *i.e.*

"after the gene has been isolated," accompanied by knowledge of "other characteristics sufficient to distinguish it from other genes." *Amgen*, 927 F.2d at 1206. The Pfizer activity meets these criteria.

Sanofi argues that *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993) established a *per se* rule that conception of an isolated DNA requires the full and correct nucleotide sequence, and that this court limited Fiers to the filing date of his application that described the complete nucleotide sequence, and no earlier conception date. Sanofi states that this court recognized that "conception of DNA, like conception of any chemical substance, requires a definition of that substance other than by its functional utility" and that "[c]onception of a substance claimed *per se* without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties." Sanofi Br. 17-18, quoting *Fiers*, 984 F.2d at 1169. Sanofi states that in *Burroughs Wellcome Co. v. Barr Laboratories, Inc.*, 40 F.3d 1223, 1229 (Fed. Cir. 1994) this court clarified that *Fiers* requires knowledge of the complete nucleotide sequence as a condition of conception. Sanofi argues that Pfizer did not have a "definite and permanent idea" of the complete and operative invention, as required by *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1376 (Fed. Cir. 1986).

The Board held that Pfizer met the requirements of precedent. The Board found that Pfizer had isolated clone 11 and appreciated that it encoded the full-length human IL-13bc, had identified clone 11's structural characteristics, and had correctly analyzed over 99% of the nucleotide sequence. The Board found that the inventors had obtained the operative DNA and had described the method for obtaining it. It is not disputed that the Pfizer scientists had isolated and obtained the IL-13bc DNA; the issue is whether conception is negated because the nucleotide sequence was not corrected until after the Sanofi benefit date of December 6, 1995.

The Board distinguished *Fiers* and *Amgen* as holding that conception and reduction to practice did not occur until the gene was isolated, for in those cases neither structure nor definitive properties had been established for the isolated gene. Bd. Op. at 16. *Burroughs Wellcome* did not change these requirements, in holding that conception requires that the claimed DNA is possessed as a physical embodiment. Knowledge of the specific nucleotide sequence was not required in *Burroughs Wellcome*.

The Board elaborated that in this precedent the issue was not identification of the operative DNA by full nucleotide analysis, but isolation of the operative DNA and identification by distinguishing properties of the isolate. *Amgen*, 927 F.2d at 1206; *Fiers*, 984 F.2d at 1169. *Amgen* and *Fiers* did not hold, as Sanofi asserts, that conception requires the complete and correct sequencing of the isolated DNA; the court instead referred to "whatever characteristics sufficiently distinguish it." *Amgen*, 927 F.2d at 1206. The Board was not persuaded by Sanofi's argument that since the interference count is in terms of the nucleotide structure, Pfizer could not be credited with conception of the IL-13bc product until it knew the complete correct nucleotide sequence. Thus the Board held that Pfizer had achieved conception and reduction to practice before the Sanofi benefit date.

Precedent illustrates a variety of circumstances in which this requirement was met although the complete nucleotide sequence was not known. In *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956 (Fed. Cir. 2002) this court upheld claims for certain DNA probes that were made available by deposit in a public depository, as provided by the Rules and PTO practice, although the nucleotide sequence had not been determined. In *University of New Mexico v. Knight,* 321 F.3d 1111, 1122 (Fed. Cir. 2003), the court explained that "a chemical structure is simply a means of describing a compound; it is not the invention itself." The court stated in *In re Wallach*, 378

F.3d 1330, 1333 (Fed. Cir. 2004) that when a protein was described by a partial amino acid sequence in addition to other characteristics sufficient to identify it, the inventors were in possession of the protein.

We conclude that the Board correctly based conception and reduction to practice on the possession of the isolated DNA segment that was shown to have the desired properties. When the subject matter is a DNA segment, conception requires possession and appreciation of the DNA segment that is claimed. *See Invitrogen Corp. v. Clontech Labs., Inc.*, 429 F.3d 1052, 1063-64 (Fed. Cir. 2005) ("[C]onception requires that the inventor appreciate that which he has invented. . . . The priority determination requires evidence that the inventor actually first made the invention, and that he understood his creation to have the features that comprise the inventive subject matter at bar."). The Board found that Pfizer had successfully searched for and isolated the IL-13bc DNA segment, and possessed and appreciated the isolated IL-13bc DNA before the Sanofi benefit date.

Discussing the consequences of Pfizer's flawed sequence analysis that was corrected after the Sanofi priority date, the Board stated that "[f]or proteins and polynucleotide species, a sequence is the gold standard for identifying species with precision . . . . It does not, however, thereby follow that a sequence is the only way to identify the composition precisely." Bd. Op. at 15. Upon selecting, isolating and characterizing clone 11 Pfizer was "able to define [the IL-13bc] so as to distinguish it from other materials, and to define how to obtain it." *Amgen*, 927 F.2d at 1206. The Board's findings are supported by substantial evidence.

On these findings, the Board held that Pfizer had conceived and reduced to practice the isolated polynucleotide of Count 3 before the Sanofi benefit date. We conclude

that the Board applied the correct law. The award of priority to Pfizer is affirmed.

AFFIRMED