United States District Court,
N.D. California.

GENENTECH, INC., a Delaware corporation, and Tercica, Inc., a Delaware corporation,
Plaintiffs.
v.
INSMED INCORPORATED, a Virginia corporation; Celtrix Pharmaceuticals, Inc., a Delaware corporation; and Insmed Therapeutic Proteins, a Colorado Corporation,
Defendants.
And Related Counterclaim,
And Related Counterclaims.

No. C 04-5429 CW

June 30, 2006.

Background: Biotechnology companies sought construction of disputed terms used in patents relating to an insulin-like human growth factor (IGF-I). Parties also filed cross-motions for summary judgment on issues of infringement and validity.

Holdings: The District Court, Wilken, J., held that:
(1) one patent was literally infringed;
(2) one patent was not invalidated by prior art;
(3) summary judgment in favor of accused infringers was precluded on issue of whether patentee satisfied adequate written description requirement with respect to one patent; and
(4) any recovery for infringing, inducing and/or contributing to infringement of patents based on activities pre-dating six years from the date of filing of the infringement action was time-barred.

Plaintiff's motion granted; defendant's motion granted in part and denied in part.

6,331,414. Infringed.

M. Patricia Thayer, Heller Ehrman White & McAuliffe LLP, San Francisco, CA, William G. Gaede, III, Andrew A. Kumamoto, Lauren J. Smith, Cooley Godward LLP, Palo Alto, CA, for Plaintiffs.

ORDER ON CLAIM CONSTRUCTION AND CROSS-MOTIONS FOR SUMMARY JUDGMENT

WILKEN**, District Judge.**

Plaintiffs and Counterdefendants Genentech, Inc. and Tercica, Inc. and Defendants and Counterclaimants

Insmed Incorporated, Celtrix Pharmaceuticals, Inc. and Insmed Therapeutic Proteins, Inc. dispute the meaning of several terms and phrases used in U.S. Patent No. 6,331,414 ('414 patent), U.S. Patent No. 5,187,151 (the '551 patent) and U.S. Patent No. 5,258,287 ('287 patent). Plaintiffs and Defendants each ask the Court to adopt their proposed construction of the disputed terms and phrases. In addition, Plaintiffs move for partial summary judgment. Defendants oppose the motion and cross-move for summary judgment. Plaintiffs oppose that motion. The matter was heard on May 19, 2003. Having considered the parties' papers, the evidence cited therein and oral argument, the Court construes the disputed terms and phrases as set forth below. The Court grants Plaintiffs' motion and grants Defendants' motion in part and denies it in part.

BACKGROUND

Plaintiffs and Defendants are biotechnology companies competing to penetrate and serve a market of 6,000 children in the United States who suffer from a rare disorder known as Severe Primary Insulin-Like Growth Factor Deficiency (Severe Primary IGFD). In humans, growth hormone (GH) stimulates the production of insulin-like growth factor (IGF-I), which then stimulates statural growth and increases whole-body, lean tissue mass. Most children who fail to grow normally can be treated with GH. Children who suffer from Severe Primary IGFD, however, do not respond to standard GH therapy because GH does not stimulate IGF-I production in their bodies. These children typically will grow if they are given an IGF-I based therapy. There are two approved products for administering IFG-I to treat children with Severe Primary IGFD: Plaintiff Tercica's Increlex product, comprising "free" IGF-I, and Defendant Insmed's IPLEX product, comprising IGF-I complexed to IGFBP-3. The Food and Drug Administration (FDA) approved Increlex on August 27, 2005; IPLEX was approved on December 12, 2005.

At issue are three patents awarded to Plaintiff Genentech: the '414 patent, "Preparation of Human IGF via Recombinant DNA Technology"; the '151 patent, "Use of Binding Protein with IGF-I as an Anabolic Growth Promoting Agent"; and the '287 patent, "DNA Encoding and Methods of Production of Insulin-like Growth Factor Binding Protein BP53." Plaintiff Genentech licensed these patents to Plaintiff Tercica. Plaintiffs claim that Defendants' IPLEX infringes the patents. Defendants assert that, not only do they not infringe the patents, the patents are invalid and unenforceable.

DISCUSSION

I. Claim Construction

A. Legal Standard

The construction of a patent is a matter of law for the Court. Markman v. Westview Instruments, Inc., 517 U.S. 370, 372, 116 S.Ct. 1384, 134 L.Ed.2d 577 (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) (en banc) (quoting Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc., 381 F.3d 1111, 1115 (Fed.Cir.2004)). Accordingly, in construing disputed terms, the Court first looks to the words of the claims. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.Cir.1996). Generally, the Court ascribes the words of a claim their ordinary and customary meaning. *Id*. The Federal Circuit instructs that "the ordinary and customary meaning of a claim term 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." Phillips, 415 F.3d at 1313. Other claims of the

patent in question can also assist in determining the meaning of a claim term. Id. at 1314. "Because claim terms are normally used consistently throughout the patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims." *Id*.

The Federal Circuit also instructs that claims "must be read in view of the specification, of which they are a part." *Id*. at 1315 (quoting Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed.Cir.1995) (en banc)). The specification must contain a description of the invention that is clear and complete enough to enable those of ordinary skill in the art to make and use it, and thus the specification is "always highly relevant" to the Court's claim construction analysis. Vitronics, 90 F.3d at 1582. "Usually, [the specification] is dispositive; it is the single best guide to the meaning of a disputed term." *Id*. In some cases, the specification may reveal that the patentee has given a special definition to a claim term that differs from its ordinary meaning; in such cases, "the inventor's lexicography controls." Phillips, 415 F.3d at 1316. The specification also may reveal the patentee's intentional disclaimer or disavowal of claim scope. "In that instance, as well, the inventor has dictated the correct claim scope, and the inventor's intention, as expressed in the specification, is regarded as dispositive." *Id*. However, claims are not limited to the preferred embodiment described in the specification. *See* SRI Int'l v. Matsushita Elec. Corp. of Am., 775 F.2d 1107, 1121 (Fed.Cir.1985) *(en banc,* plurality opinion).

In addition to reviewing the specification, the Court should consider the patent's prosecution history. Markman, 52 F.3d at 980. The prosecution history is intrinsic evidence that "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 then it would otherwise be." Phillips, 415 F.3d at 1317; *see also* Chimie v. PPG Indus., Inc., 402 F.3d 1371, 1384 (Fed.Cir.2005) ("The purpose of consulting the prosecution history in construing a claim is to exclude any interpretation that was disclaimed during prosecution.") (internal quotations omitted).

While emphasizing the importance of intrinsic evidence in claim construction, the Federal Circuit has authorized courts to rely on extrinsic evidence, which consists of "all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Phillips, 415 F.3d at 1317 (quoting Markman, 52 F.3d at 980). While extrinsic evidence may be useful to the Court, it is less significant than intrinsic evidence in determining the legally operative meaning of claim language. *Id; see also* C.R. Bard, Inc. v. U.S. Surgical Corp., 388 F.3d 858, 862 (Fed.Cir.2004). Furthermore, extrinsic evidence is unlikely to lead to a reliable interpretation of claim language unless considered in the context of the intrinsic evidence. Phillips, 415 F.3d at 1319.

B. The '414 Patent

1. Claim 1

Claim 1 provides, "A process for producing human IGF-I comprising preparing a replicable expression vector capable of expressing the DNA sequence encoding human IGF-I in a prokaryotic host cell, transforming a prokaryotic host cell culture with said vector to obtain a recombinant host cell, culturing said recombinant host cell culture under conditions permitting expression of said human IGF-I-encoding DNA sequence to produce human IGF-I, and recovering said human IGF-I."

a. Expression

[1] The parties dispute whether this claim covers both fusion and direct expression of a human IGF-I-

encoding DNA sequence. Their differing constructions of terms in this claim arises out of this dispute. Plaintiffs contend that claim 1 covers both. Defendants, however, claim that claim 1 covers only direct expression, not fusion.

Defendants' expert conceded that a person of ordinary skill in the art understands the term expression to encompass both fusion and direct expression. *See* Gaede Dec., Ex. 5 at 79:25-80:3. The Federal Circuit instructs that the ordinary meaning of a term governs absent an express disclaimer in the patent. *See, e.g.,* NTP, Inc. v. Research In Motion, Ltd., 418 F.3d 1282, 1308-9 (Fed.Cir.2005). As Plaintiffs note, here, there is no express disclaimer. Instead, the patent itself, the specification and the prosecution history demonstrate that the inventors used the ordinary meaning of the term "expression."

Although claim 1 uses the term "expression" without the adjectives direct or fusion, claims 5 and 9 expressly refer to fusion expression. FN1 The term "direct expression" is used in the specification, demonstrating that the inventors were aware of the two different types of expression and, when appropriate, specified which form of expression they were discussing.

FN1. Claim 5 provides, "A method for producing human IGF-I comprising preparing a replicable expression vector capable of expressing in prokaryotic cells a DNA sequence encoding a fusion protein comprising the amino acid sequence of mature human IGF-I and a bacterial protein, transforming prokaryotic cells with said vector, culturing said transformed cells under conditions permitting expression of said DNA sequence to produce the fusion protein, recovering the fusion protein from the culture, and cleaving the fusion protein to obtain mature human IGF-I, wherein the prokaryotic cells are capable of such expression and of processing the IGF-I."

In the prosecution history, the Examiner raised an enablement issue as to claim 1, which was then claim 5: "In addition, claims 5 and 21 encompass direct expression of IGF-I and IGF-II in prokaryotes in the absence of a fusion partner." Stipulated File History of the '414 patent, Tab 4 at 7-9. Plaintiffs note the word "encompass,"used by the Examiner, shows that the claims's scope includes but is not limited to direct expression. Defendants' argument, that the Examiner's objection was based on the difficulty of producing IGF-I or IGF-II without regard to whether the protein was expressed directly or as a fusion protein, is irrelevant in determining whether claim 1 includes both direct and fusion expression. During the prosecution, Plaintiff Genentech confirmed its belief that expression was not limited to direct expression when it wrote: "The Examiner also urges that claims 5 and 21 encompass direct expression of human IGF-I and IGF-II in prokaryotes, as well as fusion proteins and secreted proteins, with no guidance model." Id, Tab 8 at 15.

In light of the claims, the specification and the patent history, Defendants' arguments that claim 1 entails only direct expression are not convincing. Accordingly, the Court construes the term "expression" used in claim 1 as covering both fusion and direct expression.

b. Human IGF-I

[2] The parties also dispute the construction of the term "human IGF-I." Plaintiffs contend that human IGF-I means "a polypeptide that corresponds in amino acid sequence to mature human insulin-like growth factor-I (IGF-I) naturally occurring in human blood, and optionally can include an additional amino acid at the N terminal end." Defendants construe this term to mean a polypeptide having the same amino acid sequence

and disulfide bond configuration as human IGF-I isolated from human blood or serum and to exclude IGF-I fusion proteins. The Court agrees that this term excludes IGF-I fusion proteins, but it will not use the term Defendants propose. Instead, it will use the definition provided in the patent. Thus, the Court construes the term "human IGF-I" as comprising the amino acid sequence corresponding to human IGF native to human tissue; human IGF-I does not include fusion proteins. *See* col. 4:64-2.

2. Claim 9

[3] Claim 9 discloses, "A process for producing mature human IGF-I comprising culturing a recombinant prokaryotic host cell, transformed with a replicable expression vector capable of expressing in a suitable host cell a DNA sequence encoding a fusion protein comprised of human IGF-I fused at the N-terminus of the IGF-I to amino acid sequence exogenous to human IGF-I, under conditions permitting expression of the DNA sequence, and cleaving the fusion protein to release mature human IGF-I having the proper amino terminus (gly)."

The parties dispute the construction of the term "fusion protein comprised of human IGF-I fused at the N-terminus to amino acid sequence exogenous to human IGF-I." Plaintiffs contend that the terms means a non-natural protein encompassing an amino acid sequence that corresponds to the mature human IGF-I sequence linked at its N-terminus to an amino acid sequence from any other source other than the human IGF-I sequence. Defendants contend that the term means " 'a fusion protein' composed of an amino acid sequence taken from a prokaryotic cell attached to the N-terminus of a domain with the amino acid sequence of 'Human IGF-I.' " Defendants separately construe the term "a fusion protein." According to Defendants, "a fusion protein" means "a final translation product that is a single polypeptide chain composed of amino acid sequences from two or more distinct proteins." At the hearing, however, the parties agreed that the Court need not construe the term "fusion protein," nor any other term except "exogenous to human IGF-I."

Plaintiffs point out that Defendants' experts conceded that the ordinary meaning of the term "exogenous" does not convey a specific source for the amino acids, and encompasses anything outside of that which is endogenous. *See, e.g.,* Gaede Dec., Ex. 9 at 195-97. Defendants do not, however, show a clear disclaimer of the ordinary meaning through "redefining the term or by characterizing the invention in the intrinsic record using words or expressions of manifest exclusion or restriction, representing a clear disavowal of claim scope." Teleflex, Inc. v. Ficosa North Am. Corp., 299 F.3d 1313, 1327 (Fed.Cir.2002).

As Plaintiffs note, the claim language defines the fusion protein in reference to only one source, the human IGF-I amino acid sequence, and requires only that the fusion partner be an amino acid sequence not derived from that source. Unlike in claim 5, no other source limitations are recited, and the language encompasses any amino acid sequences, not just portions from proteins. Claim 5 expressly restricts the fusion partner source by reciting that it comes from a bacterial protein, a limitation not present in claim 9. During prosecution, the Examiner required Plaintiff Genentech to limit claim 5 to "bacterial protein" fusions, but did not impose such a requirement on claim 9, leaving its scope undisturbed.

The Court construes the term "exogenous to human IGF-I" to mean any other source other than the human IGF-I sequence.

3. Bioactivity

[4] Defendants assert that the human IGF-I, in claim 1, and the mature human IGF-I, in claim 9, require proper disulfide configuration. Plaintiffs contend that Defendants are reading additional limitations into

claims 1 and 9. According to Plaintiffs, human IGF-I and mature human IGF-I are defined by their primary amino acid sequence and do not require any disulfide bond configuration.

The patent does not include the phrase "disulfide bond configuration." But it does stress bioactivity, and, according to Defendants' expert, IGF-I that does not have proper disulfide bonds formed are likely to be inactive. Defendants contend that the only utility disclosed in the '414 patent for human IGF-I is its use as a therapeutic agent, and thus bioactivity is required. In discussing the present invention, the patent states, "All such products have been found to be biologically active, hence useful as intended." '414 patent, col. 1:44-53. The goal of the invention was to produce human IGF as a product of recombinant DNA technology from a host organism: "Such materials would exhibit bioactivity admitting of their use clinically in the treatment of various growth affect conditions." Id. at col. 2:226-32. In addition to the specification, Defendants point to the prosecution history, which reinforces the bioactivity requirement.

Plaintiffs point to other parts of the specification. They note that the specification teaches that the claimed IGF proteins are "defined by means of DNA, gene and deductive sequencing," not only bioactivity. Id. at col. 5:2-5. The specification further describes the invention as "directed to the preparation of polypeptides comprising the amino acid sequence of IGF." Id. at 3:56-61. The parts of the specification Plaintiffs cite, however, do not show that there is no bioactivity requirement. And Plaintiffs fail to address the portions of the specification emphasizing the need for bioactivity. Nor do Plaintiffs adequately address the prosecution history. For example, in response to an office action, Plaintiff Genentech stated that undue experimentation would not be required "to determine whether a given IGF-I or IGF-II protein, expressed directly, secreted or as a fusion protein, is biologically active and thus falls within the scope of the present claims." '414 Patent Stipulated File History, Tab. 8 at 18.

The Court construes the term "human IGF-I," in claim 1, and term "mature human IGF-I," in claim 9, to refer to bioactive material.

C. The '151 Patent

Claim 1 provides, "A method for producing an anabolic state in a mammal comprising co-administering to the mammal by subcutaneous bolus injection effective amounts of IGFBP-3 and IGF-I in a molar ratio of IGFBP-3 to IGF-I of about 0.5:1 to about 3:1 so as to produce a greater anabolic state in the mammal than that achieved using an equivalent dose of IGF-I alone, wherein growth hormone is not also administered to the mammal."

1. "produce a greater anabolic state"

[5] Plaintiffs contend that this term means "promoting a greater gain of total body weight or statural growth." According to Plaintiffs, here, Plaintiff Genentech acted as its own lexicographer; the patent's specification contains an explicit definition of producing an anabolic state, and that definition must be followed. Defendants disagree, arguing that the term should be given its common and ordinary meaning. Defendants state the term means "characterized by or promoting constructive metabolism." Defendants contend that the intrinsic evidence, including the specification, is consistent with the common and ordinary meaning of the term.

The specification provides,

As used herein, the words "producing an anabolic state" refer to promoting total body weight gain as well as

the dynamics of statural growth experienced by an individual during infancy, childhood, and adolescence as depicted by a normal growth curve, i.e., growth of linear-producing bone plate driven by chondrocytes, as well as growth of osteoblast cells, derived from a different part of the bone. Restoration of normal growth patterns would allow the patient to approach a more satisfactory growth curve. Examples of patients that are relatively resistant to GH but require treatment to induce an anabolic effect include those with Turner's Syndrome, GH-deficient children who grow poorly in response to GH treatment, children who experience a slowing or retardation in their normal growth curve about 2-3 years before their growth plate closes, so that GH administered alone would no longer increase growth of the children, so-called short normal children, and patients where the IGF-I response to GH has been blocked chemically (i.e., by glucocorticoid treatment) or by a natural condition such as in adult patients where the IGF-I response to GH is naturally reduced. In addition, the method herein is useful for treating pregnant women who are in a catabolic state and/or experience loss of bone mass, for treating women with osteoporosis, and for repairing bone.

'151 patent, col. 6:38-68.

Plaintiffs focus on the first sentence of the above paragraph; Defendants focus on the last sentence. Defendants also highlight other parts of the specification that they contend support their definition. As they note, the Field of the Invention states, "This invention relates to a method for producing an anabolic or growth promoting state in a mammal. More specifically, this invention is directed to the use of a complex of IGF-I and one or more of its binding proteins to produce an anabolic state, including enhancing whole body and bone growth." '151 patent, col. 1:7-12. The specification also states, "Efficacious results are measured by increases in body weight gain, lean body mass, bone growth, or statutory [sic] growth approximating the normal range, or by other criteria for measuring the anabolic state of a mammal, as defined herein, as are deemed appropriate by the practitioner." '151 patent, col. 8:2-7. These statements and the last sentence in the paragraph quoted above, however, do not support Defendants' definition. The patent and its history do not contain the term "constructive metabolism." The last sentence of the quoted paragraph, stating that the method described is useful for treating pregnant women and for repairing bone, is not part of the definition; it does not broaden the definition beyond what the patent explicitly states that it is. Rather, that sentence provides examples of patients and conditions that can also benefit from the method for producing an anabolic state as claimed in the patent.

Plaintiffs are correct that the specification's definition of "produce a greater anabolic state" controls. Therefore, the Court construes the term "produce a greater anabolic state" to mean promoting greater total body weight gain as well as statural growth.

2. "greater anabolic state in the mammal than achieved using an equivalent dose of IGF-I"

[6] Plaintiffs contend that this phrase means to "promote total body weight gain or statural growth that is greater than whatever total body weight gain or statural growth would be observed if the same amount of IGF-I as present in the IGF-I/IGFBP-3 mixture were administered by the same route, regimen, and schedule of administration as is used in the administration of the IGF-I/IGFBP-3 mixture." In short, Plaintiffs state that it requires "that the doses compared, i.e., complexed IGF-I/IGFBP-3 versus IGF-I alone, must contain the same quantity of IGF-I and they must be administered following the same dosing regimen." Defendants contend that this phrase means that "a greater state of constructive metabolism is produced in the mammal when an IGFI/IGFBP-3 complex is administered than when an 'equivalent dose' of 'IGF-I' is administered alone." Defendants separately define equivalent dose as a dose of IGF-I alone which has, within the measurement error, the same number of molecules of IGF-I as the dose of IGFBP-3/IGF-I complex to

which it is being compared. Plaintiffs believe that no separate construction of equivalent dose is necessary because it should be construed as part of the phrase.

Both parties rely on the specification to support their constructions. Plaintiffs point to language, under the heading "Modes for Carrying Out the Invention," stating that the "amounts administered will promote a greater anabolic state in the treated patient over the anabolic effect obtained using the same amount of IGF-I administered by the same protocol, regimen, and route, but without IGFBP being also administered." '151 patent, col. 7:20-25. As Plaintiffs note, the '151 patent does not purport to teach, or claim, benefits based on different amounts of IGF-I, different protocols, different doses, or different routes of administration. Defendants note that the language Plaintiffs quote from the specification relates to the term "effective amounts," which the parties have stipulated means "the amounts of IGF-I and IGFBP-3 co-administered produce a 'greater anabolic state in the mammal than that achieved using an equivalent dose of IGF-I alone.' " Regardless, the specification language quoted above is not to be ignored just because it concerns a different phrase. *See* ACTV, Inc. v. Walt Disney Co., 346 F.3d 1082, 1088 (Fed.Cir.2003). The specification language Plaintiffs quote concerning the "same protocol, regimen, and route" is more useful in construingthe phrase "greater anabolic state in the mammal than achieved using an equivalent dose of IGF-I" than the language to which Defendants point. For example, in their section on equivalent doses, Defendants contend that the patent refers to dose as the amount delivered per day, not per injection. Although this is true, the patent provides how many injections are to be given daily, e.g., "IGF-I delivery at 0.3 mg/kg/day (two injections of 15 g per day)." '151 patent, col. 12:4-5. The experiments described in the patent illustrate that the '151 patent compares forms of the drug, not different doses or numbers of injunctions.

Defendants' other two arguments in support of their construction are based on their expert's report and English grammar. Neither argument is persuasive. Their expert states that, when making comparisons between two different treatments, "clinicians often compare total daily dosage of a drug, without regard to whether the drug is administered in one injection per day or two injections per day" and "comparison of daily dosages is scientifically relevant." 2d Spencer Report at para. 47. This is extrinsic evidence, regarding what clinicians often compare, does not pertain to the patent at issue and is not useful. Defendants further argue that the phrase uses a past participle-the word achieved-and thus requires that a direct comparison have been made between the effect "achieved" using a complex of IGF-I and IGFBP-3 and that "achieved" using IGF-I alone. According to Defendants, Plaintiffs seek to rewrite the claim by adding the words "if" "were" and "would," to change the claim to require only a theoretical comparison of the effects of the complex and IGF-I alone that has not yet occurred and that may never occur. This argument is unavailing as well.

Based on the intrinsic evidence presented, the Court construes the phrase "greater anabolic state in the mammal than achieved using an equivalent dose of IGF-I" to mean promote total body weight gain or statural growth that is greater than whatever total body weight gain or statural growth would be observed if the same amount of IGF-I as is present in the IGF-I/IGFBP-3 mixture were administered by the same route, regimen, and schedule of administration as used in the administration of the IGF-I/IGFBP-3 mixture. The Court will not separately construe the term "equivalent dose" because it is construed as part of the above phrase.

D. The '287 Patent

Claim 1 provides, "An isolated DNA molecule comprising a sequence that hybridizes, under stringent

conditions of 50% formamide with 0.75M NaCl and 0.075M sodium citrate, at 420 C., to the portion of the DNA sequence of FIG. 3 coding for mature BP53 or the preprotein for BP53 and which encodes a BP53 protein that binds to IGF-I or IGF-II, excluding BP28, PP12, and HEP-G2."

1. "hybridizes, under stringent conditions"

[7] Plaintiffs state that the parties largely agree to the construction of this term. Defendants contend that it means "single strands of DNA from two sources form a stable double-stranded structure that remains intact during manipulation in the following conditions: Hybridizing in 50% formamide at 5XSSC at a temperature of 420 C. and washing the filters in 0.2XSSC at 600 C. These conditions are intended to exclude sequences that hybridize to the BP28 sequence." According to Plaintiffs, the difference between the parties' constructions is Defendants' attempt to add the sentence on intent.

Plaintiffs argue that the intent sentence is from the specification and should not be imported to the definition of this term. Defendants contend that the intent sentence is an affirmative limitation that Plaintiff Genentech added to claim 1 during prosecution to overcome an enablement rejection. They note that the Examiner initially rejected claim 1 for lack of enablement because the specification did "not enable all DNAs which would hybridize to the DNA of Fig. 3 under stringent conditions." '287 Patent Stipulated File History, Tab 12 at 3. But Defendants include only a portion of the Examiner's sentence. The sentence in full reads: "The specification does not enable all DNAs which would hybridize to the DNA of Fig. 3 under stringent conditions wherein the sequence is at least 10 nucleotides in length as set forth in claim 1." Id. According to Plaintiffs, Plaintiff Genentech overcame this rejection by replacing the minimum length limitation with a limitation that the DNA molecules must encode a protein with specific biological activity that is not the BP28 protein. Furthermore, as Plaintiffs note, the intrinsic evidence also contradicts Defendants' interpretation. The words of the claim and the prosecution history demonstrate that the final phrase of claim 1-excluding BP28, PP12, and HEP-G2-is meant to exclude certain proteins from the claim, not to exclude DNA sequences that hybridize to certain other DNA sequences.

The Court construes the term "hybridizes, under stringent conditions" to mean that single strands of DNA from two sources form a stable double-stranded structure that remains intact during manipulation in the following conditions: Hybridizing in 50% formamide at 5XSSC at a temperature of 42 (deg.) C. and washing the filters in 0.2XSSC at 60 (deg.) C.

II. Summary Judgment

A. Legal Standard

Summary judgment is properly granted when no genuine and disputed issues of material fact remain, and when, viewing the evidence most favorably to the non-moving party, the movant is clearly entitled to prevail as a matter of law. Fed.R.Civ.P. 56; Celotex Corp. v. Catrett, 477 U.S. 317, 322-23, 106 S.Ct. 2548, 91 L.Ed.2d 265 (1986); Eisenberg v. Ins. Co. of N. Am., 815 F.2d 1285, 1288-89 (9th Cir.1987).

The moving party bears the burden of showing that there is no material factual dispute. Therefore, the court must regard as true the opposing party's evidence, if supported by affidavits or other evidentiary material. Celotex, 477 U.S. at 324, 106 S.Ct. 2548; Eisenberg, 815 F.2d at 1289. The court must draw all reasonable inferences in favor of the party against whom summary judgment is sought. Matsushita Elec. Indus. Co. v. Zenith Radio Corp., 475 U.S. 574, 587, 106 S.Ct. 1348, 89 L.Ed.2d 538 (1986); Intel Corp. v. Hartford Accident & Indem. Co., 952 F.2d 1551, 1558 (9th Cir.1991).

Material facts which would preclude entry of summary judgment are those which, under applicable substantive law, may affect the outcome of the case. The substantive law will identify which facts are material. Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248, 106 S.Ct. 2505, 91 L.Ed.2d 202 (1986).

Where the moving party does not bear the burden of proof on an issue at trial, the moving party may discharge its burden of production by either of two methods. Nissan Fire & Marine Ins. Co., Ltd., v. Fritz Cos., Inc., 210 F.3d 1099, 1106 (9th Cir.2000).

The moving party may produce evidence negating an essential element of the nonmoving party's case, or, after suitable discovery, the moving party may show that the nonmoving party does not have enough evidence of an essential element of its claim or defense to carry its ultimate burden of persuasion at trial.

Id.

If the moving party discharges its burden by showing an absence of evidence to support an essential element of a claim or defense, it is not required to produce evidence showing the absence of a material fact on such issues, or to support its motion with evidence negating the non-moving party's claim. *Id.; see also* Lujan v. Nat'l Wildlife Fed'n, 497 U.S. 871, 885, 110 S.Ct. 3177, 111 L.Ed.2d 695 (1990); Bhan v. NME Hosps., Inc., 929 F.2d 1404, 1409 (9th Cir.1991). If the moving party shows an absence of evidence to support the non-moving party's case, the burden then shifts to the non-moving party to produce "specific evidence, through affidavits or admissible discovery material, to show that the dispute exists." Bhan, 929 F.2d at 1409.

If the moving party discharges its burden by negating an essential element of the non-moving party's claim or defense, it must produce affirmative evidence of such negation. Nissan, 210 F.3d at 1105. If the moving party produces such evidence, the burden then shifts to the non-moving party to produce specific evidence to show that a dispute of material fact exists. *Id*.

If the moving party does not meet its initial burden of production by either method, the non-moving party is under no obligation to offer any evidence in support of its opposition. *Id*. This is true even though the non-moving party bears the ultimate burden of persuasion at trial. *Id*. at 1107.

Where the moving party bears the burden of proof on an issue at trial, it must, in order to discharge its burden of showing that no genuine issue of material fact remains, make a *prima facie* showing in support of its position on that issue. UA Local 343 v. Nor-Cal Plumbing, Inc., 48 F.3d 1465, 1471 (9th Cir.1994). That is, the moving party must present evidence that, if uncontroverted at trial, would entitle it to prevail on that issue. *Id.; see also* Int'l Shortstop, Inc. v. Rally's, Inc., 939 F.2d 1257, 1264-65 (5th Cir.1991). Once it has done so, the non-moving party must set forth specific facts controverting the moving party's *prima facie* case. UA Local 343, 48 F.3d at 1471. The non-moving party's "burden of contradicting [the moving party's] evidence is not negligible." *Id*. This standard does not change merely because resolution of the relevant issue is "highly fact specific." *Id*.

B. Plaintiffs' Motion for Partial Summary Judgment

Plaintiffs move for summary judgment that Defendants' process for making IPLEX literally meets every element of claims 2 and 9 of the '414 patent. In addition, they move for summary judgment of validity as against Defendants' anticipation and obvious defenses to the '151 patent.

1. '414 patent

Plaintiffs note that Defendants' non-infringement position as to claim 2, which depends on claim 1, and claim 9 rests on Defendants' claim construction of the terms "expression" and "exogenous to human IGF-I." Indeed, Defendants do not dispute that, if the Court adopts Plaintiffs' constructions, they literally infringe claims 1, 2 and 9. The Court has adopted Plaintiffs' constructions regarding these terms and grants Plaintiffs summary judgment that Defendants literally infringe claims 1, 2 and 9 of the '414 patent.

2. '151 patent

[8] Plaintiffs contend that no reasonable jury would find that the Maack and Sommer abstracts qualify as prior art under 35 U.S.C. s. 102(a). According to Plaintiffs, the inventions asserted were reducedto practice in September, 1990, before the January, 1991 publication of the abstracts, and thus the abstracts are not prior art. Reduction to practice occurs when the inventors perform a process that satisfies all of the limitations of the claim, and determine it will work for the intended purpose. *See* Slip Track Sys., Inc. v. Metal Lite, Inc., 304 F.3d 1256, 1266 (Fed.Cir.2002).

[9] Plaintiffs provide evidence, including corroborating evidence, showing that Plaintiff Genentech's scientists reduced claims 1, 4, 5 and 7 to practice approximately four months prior to the abstracts' publication. They meet their "burden of production to present evidence of its asserted actual reduction to practice prior to the filing date of its patent application." Loral Fairchild Corp. v. Matsushita Elec., 266 F.3d 1358, 1361 (Fed.Cir.2001). They point out that Defendants bear the burden of showing by clear and convincing evidence that the Maack and Sommer abstracts are prior art. *See id*. (noting that, because of the statutory presumption of patent validity, at trial defendants would bear the burden of proving by clear and convincing evidence that a reference was published prior to plaintiff's reduction to practice). Plaintiffs note that Defendants did not submit expert testimony on reduction to practice.

Defendants respond that there are genuine issues of material fact as to whether the asserted claims of the '151 patent were reduced to practice before the Maack and Sommer abstracts were published. But Defendants provide no evidence to rebut Plaintiffs' prima facie showing that the claims were reduced to practice prior to publication of the abstracts. Instead, Defendants criticize Plaintiff's corroborating evidence. That criticism, however, is not sufficient to create an issue of fact. It is Defendants' burden to prove that the Maack and Sommer references were published prior to Plaintiff's reduction to practice. They cannot produce evidence of a triable issue of fact by relying only upon attorney argument. Thus, the Court grants Plaintiffs summary judgment that the patent is not invalidated by prior art.

C. Defendants' Motion for Summary Judgment

Defendants move for summary judgment that they do not infringe claims 1 through 4 and 9 and 10 of the '414 patent, that the asserted claims of the ' 414 patent are invalid under 35 U.S.C. s. 101 and s. 112, that they do not infringe claims 1, 4, 5, and 7 of the '151 patent, and that they are not liable for activities that occurred more than six years before the filing of this suit and/or which are covered by the safe harbor doctrine.

1. '414 patent

a. Infringement

Defendants conceded at the hearing that if the Court construes the term expression to cover both direct and fusion expression then summary judgment of no infringement cannot be granted. As explained above, the Court did construe expression to cover both direct and fusion expression, and it granted Plaintiffs summary judgment that Defendants infringe claims 1, 2 and 9 of the ' 414 patent. Thus, the Court denies Defendants summary judgment that they did not infringe claims 1 through 4 and 9 and 10 of the '414 patent.

a. Invalidity

Defendants contend that, if the Court adopts Plaintiffs' construction of "human IGF-I," in claim 1, and "mature human IGFI", in claim 9, which does not require a disulfide bond configuration or bioactivity, then the claims at issue are invalid for lack of utility. *See* 35 U.S.C. s. 101. The Court adopted the patent's definition of "human IGF-I" and construed that term, and the term mature human IGF-I, to refer to bioactive material. The claims are not invalid as a matter of law for lack of utility.

[10] Defendants further contend that, if the Court rejects their construction of the asserted claims, the claims are invalid because they do not comply with the written description requirement of 35 U.S.C. s. 112. Section 112 requires, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention." The Federal Circuit explains, "The adequate written description requirement, which is distinct from the enablement and best mode requirements, serves 'to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material.' " In re Alton, 76 F.3d 1168, 1172 (Fed.Cir.1996) (quoting In re Wertheim, 541 F.2d 257, 262 (Cust. & Pat.App.1976)). To meet the adequate written description requirement, "the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012 (Fed.Cir.1989) (citation omitted).

[11] Plaintiffs respond that there are genuine issues of fact on this issue, pointing to their experts' reports that conclude the asserted claims are not invalid under section 112. Defendants contend that Dr. Keith Backman's report, in particular, is irrelevant or inconsistent with the facts and law. That is incorrect. Dr. Backman's report demonstrates that there are disputed issues of fact, making summary judgment inappropriate. Dr. Backman concludes that the specification conveys to one of skill in the art that the inventors were in possession of the claimed invention. His report is not based solely upon his interpretation of what a person of ordinary skill would have thought was obvious based upon a combination of the '414 patent's specification and other art. Nor is it dispositive that the patent does not contain an express description of a heterologous/ heterologous fusion protein. Because there is a disputed issue of fact as to whether the patent's description clearly allows persons of ordinary skill in the art to recognize that the inventors invented what is claimed, the Court denies summary judgment.

2. '151 Patent

Defendants contend that Plaintiffs fail to meet their burden to show that they infringe claims 1, 4, 5 and 7 of the '151 patent. But, as both parties note, this contention depends upon the Court accepting Defendants' proposed construction of the claims. The Court did not adopt Defendants' construction. Rather, the Court adopted Plaintiffs' construction of the disputed terms. The Court will not summarily adjudicate that Defendants did not infringe the asserted claims of the '151 patent.

3. Defendant Celtrix's liability

Plaintiffs accuse Defendant Celtrix of infringing, inducing and/or contributing to infringement of the '151 and '287 patents. Defendants contend that all of Defendant Celtrix's activities allegedly infringing the patents fall outside the statute of limitations and fall within the safe-harbor provided by 35 U.S.C. s. 271(e)(1).

a. Statute of limitations

[12] Title 35 U.S.C. s. 286, entitled "Time limitation on damages," provides that "no recovery shall be had for any infringement committed more than six years prior to the filing of the complaint or counterclaim for infringement in the action." As Plaintiffs noted, for the first time, at the hearing, s. 286 is not a statute of limitations in the sense of barring a suit for infringement; rather, it limits recovery to damages for infringing acts committed within six years of the date of the filing of the infringement action. A.C. Aukerman Co. v. R.L. Chaides Const. Co., 960 F.2d 1020, 1030 (Fed.Cir.1992).

[13] Plaintiffs' original complaint was filed on December 23, 2004; therefore, any recovery based on activities pre-dating December 23, 1998 is time-barred. Relying on the declaration of Dr. Andreas Sommer, the Chief Scientific Officer of Insmed Incorporated, Defendants contend that, prior to December, 1998, Celtrix ceased to perform any activities that could be alleged to have infringed, or contributed to or induced infringement of Plaintiff Genentech's patents. Dr. Sommer notes that, due to financial difficulties, Celtrix closed its manufacturing facility and laid off its manufacturing employees in September, 1998; between December 28, 1998 and May 31, 2000, when Defendant Celtrix was acquired by Defendant Insmed, Defendant Celtrix did not produce any form of what was to become IPLEX.

Plaintiffs respond that Dr. Sommer's recollection is unreliable, noting that Dr. Sommer states that to "the best of his recollection" neither Defendants Celtrix nor Defendant Insmed provided Dr. Martin Zdanowicz with IPLEX after December 23, 1998. Plaintiffs point to an article by Dr. Zdanowicz, published in 2003, that states that the complex, IPLEX, was "kindly provided by Celtrix Pharmaceuticals." According to Plaintiffs, the reasonable inference is that the drug used in Dr. Zdanowicz's study, discussed in his 2003 article, probably was supplied after December, 1998. Plaintiffs contend that a jury should be able to weigh the evidence of this recent article against the credibility of Dr. Sommer's recollection. This 2003 article, however, is not enough to create a material dispute of fact, especially because Plaintiffs do not rebut Defendants' claim that Defendant Celtrix did not produce IPLEX from December, 1998, to May, 2000, when Defendant Insmed acquired Defendant Celtrix. As Defendants note, Plaintiffs did not take any discovery from Dr. Zdanowicz. Because Plaintiffs fail to provide evidence that Defendant Celtrix infringed, or induced others to infringe, after December 28, 1998, the Court grants Defendant Celtrix summary judgment that no recovery can be had against it based on Plaintiffs' allegations regarding Dr. Zdanowicz. FN2

FN2. In their moving papers, Defendants sought summary judgment that all Celtrix activities infringing the '151 and '287 patents fall outside s. 286. But in their reply, they seek summary adjudication only as to the allegations regarding Celtrix and Dr. Zdanowicz.

b. Safe-harbor

[14] Defendants contend that even if Defendant Celtrix had engaged in any activities that would infringe, induce or contribute to infringement of the patents at issue after December 23, 1998, those activities would

fall within the safe-harbor provided by 35 U.S.C. s. 271(e). Under this safe-harbor doctrine, it is not an act of infringement to make, use or sell a patented invention solely for purposes reasonably related to the development and submission of information under a federal law which regulates the manufacture, use or sale of drugs. As the Supreme Court recently instructed, "the use of patented compoundsin preclinical studies is protected under s. 271(e)(1) as long as there is a reasonable basis for believing that the experiments will produce the types of information that are relevant to an IND or NDA." Merck KGaA v. Integra Lifesciences I, Ltd., 545 U.S. 193, 125 S.Ct. 2372, 2383-84, 162 L.Ed.2d 160 (2005).

[15] Plaintiffs argue that Defendants have not met their burden of proving a section 271(e) safe harbor as an affirmative defense. They contend that Protegan, a consultant company to which Defendant Insmed supplied IGFBP-3 made by Celtrix, conducted infringing experiments for commercial activities, which are not exempted by section 271(e)(1) because they are not reasonably related to any FDA submission. But, as discussed at the hearing, any research conducted by Protegan, was for FDA purposes. Without FDA approval, Defendants could not sell their drug on the market. The Court finds that, even if the allegedly infringing experiments were conducted, in part, for commercial reasons, the experiments would produce information that would be given to the FDA in order to get FDA approval. Thus, research conducted by Protegan would be protected under the safe harbor doctrine. Accordingly, the Court grants Defendants summary judgment on this ground.

CONCLUSION

For the foregoing reasons, the Court construes the disputed terms and phrases in the foregoing manner. The Court GRANTS Plaintiffs' Motion for Partial Summary Judgment (Docket No. 412). The Court grants Plaintiffs summary judgment that Defendants infringe claims 1, 2 and 9 of the '414 patent and that the '151 patent is not invalidated by the Maack and Sommer abstracts. The Court GRANTS Defendants' Motion for Summary Judgment (Docket No. 426) IN PART and DENIES it IN PART. The Court denies Defendants summary judgment that they did not infringe claims 1 through 4 and 9 and 10 of the ' 414 patent and that the '414 patent is invalid. There are disputes of fact regarding claims 3, 4 and 10. The Court will not summarily adjudicate that Defendants did not infringe claims 1, 4, 5 and 7 of the '151 patent. The Court, however, does grant Defendants summary judgment that no recovery can be had against Defendant Celtrix based on Plaintiffs' allegations regarding Dr. Zdanowicz and that research conducted by Protegan is protected under the safe harbor doctrine. FN3

FN3. To the extent that the Court relied upon evidence to which there is an objection, the parties' objections are overruled. To the extent that the Court did not rely on such evidence, the parties' objections are overruled as moot.

IT IS SO ORDERED.

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