IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF VIRGINIA
_____ DIVISION

Takeda Pharmaceuticals America, Inc., Takeda Pharmaceuticals U.S.A., Inc., and Millennium Pharmaceuticals, Inc.,

Plaintiffs,

v.

UCB Biopharma SPRL, Celltech R&D Limited, and UCB Celltech,

Defendants.

Civil Action No. 3:18cv78

CONFIDENTIAL – FILED UNDER SEAL

COMPLAINT

Plaintiffs Takeda Pharmaceuticals America, Inc., Takeda Pharmaceuticals U.S.A., Inc., and Millennium Pharmaceuticals, Inc. (collectively, "Plaintiffs") for their Complaint against Defendants UCB Biopharma SPRL, Celltech R&D Limited, and UCB Celltech (collectively, "Defendants") respectfully allege the following:

NATURE OF THE ACTION

1. This is an action for a declaratory judgment of invalidity of U.S. Patent No. 7,566,771 ("the '771 patent") under 28 U.S.C. §§ 2201 and 2202. A true and correct copy of the '771 patent is attached hereto as Exhibit A.

THE PARTIES

2. Takeda Pharmaceuticals America, Inc. is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at One Takeda Parkway, Deerfield, Illinois 60015.

3. Takeda Pharmaceuticals U.S.A., Inc. is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at One Takeda Parkway, Deerfield, Illinois 60015.

4. Millennium Pharmaceuticals, Inc. ("Millennium") is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at 40 Lansdowne Street, Cambridge, Massachusetts 02139. Millennium Pharmaceuticals, Inc. is a wholly-owned subsidiary of Takeda Pharmaceuticals U.S.A., Inc.

5. On information and belief, UCB Biopharma SPRL ("UCB Bio") is a corporation organized and existing under the laws of Belgium, with its principal place of business at Allée de la Recherche 60, 1070 Brussels, Belgium.

6. On information and belief, Celltech R&D Limited ("Celltech") is a corporation organized and existing under the laws of the United Kingdom, with its principal place of business at 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom.

7. On information and belief, UCB Celltech is a corporation organized and existing under the laws of the Belgium, with a place of business at 208 Bath Road, Slough, Berkshire, SL1 3WE, United Kingdom.

JURISDICTION AND VENUE

8. This action arises under the Patent Laws of the United States of America, 35 U.S.C. § 100 *et seq.*

9. This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

10. On information and belief, each of the Defendants has an interest in the '771 patent.

11. This Court has personal jurisdiction over UCB Bio pursuant to 35 U.S.C. § 293, as UCB Bio is the "owner" of the '771 patent, does not reside in the United States, and has not filed in the United States Patent & Trademark Office ("USPTO") a written designation stating the name and address of a person residing within the United States on whom may be served process or notice of proceedings affecting the '771 patent or rights thereunder.

12. On information and belief, as the "owner" of a patent granted by the USPTO and enjoying rights thereunder, UCB Bio has purposely availed itself of the benefits and protections that patent registration in this country affords. *See Nat'l Patent Dev. Corp. v. T.J. Smith & Nephew Ltd.*, 877 F.2d 1003, 1009 (D.C. Cir. 1989); *see also* 35 U.S.C. § 293.

13. It is fair and reasonable to require UCB Bio to respond in this Court in this District to matters concerning the '771 patent, given that this is the District where the '771 patent is registered. *See id.* at 1009–10.

14. This Court's exercise of personal jurisdiction over UCB Bio comports with due process at least because UCB Bio owns a patent registered with the United States Patent Office and because UCB Bio has sought and has enjoyed the privileges of patent ownership. *See Amazon Web Servs., Inc. v. Global Equity Mgmt., S.A.*, No. 3:16-cv-619, 2017 WL 4052381, at *6–7 (E.D. Va. Sept. 13, 2017).

15. This Court further has personal jurisdiction over UCB Bio due to, *inter alia*, the purposeful availment of the jurisdiction of this judicial district by UCB, Inc., another subsidiary of the ultimate parent of UCB Bio. In 2014, UCB, Inc. filed a civil action in this Court seeking a declaratory judgment of invalidity of another entity's patent. *See UCB, Inc. v. Yeda Research & Dev. Co.*, No. 1:14-cv-1038-LMB-TCB, D.I. 1 at 1 (E.D. Va. Aug. 13, 2014).

16. This Court has personal jurisdiction over Celltech pursuant to 35 U.S.C. § 293, as Celltech is listed as the assignee of the '771 patent based on assignment records maintained at the USPTO, does not reside in the United States, and has not filed in the USPTO a written designation stating the name and address of a person residing within the United States on whom may be served process or notice of proceedings affecting the '771 patent or rights thereunder.

17. As the listed assignee of the '771 patent, Celltech has purposely availed itself of the benefits and protections that patent registration in this country affords. *See Nat'l Patent Dev. Corp.*, 877 F.2d at 1009; *see also* 35 U.S.C. § 293.

18. It is fair and reasonable to require Celltech to respond in this Court in this District to matters concerning the '771 patent, given that this is the District where the '771 patent is registered. *See id.* at 1009–10.

19. This Court's exercise of personal jurisdiction over Celltech comports with due process at least because Celltech is the "registered proprietor" of a patent registered with the United States Patent Office and because Celltech has sought and has enjoyed the privileges of patent ownership. *See Amazon Web Servs.*, 2017 WL 4052381, at *6–7.

20. This Court further has personal jurisdiction over Celltech due to, *inter alia*, the purposeful availment of the jurisdiction of this judicial district by UCB, Inc., another subsidiary of the ultimate parent of Celltech. In 2014, UCB Inc., filed a civil action in this Court seeking a declaratory judgment of invalidity of another entity's patent. *See Yeda Research*, D.I. 1 at 1.

21. On information and belief, this Court has personal jurisdiction over UCB Celltech pursuant to 35 U.S.C. § 293, [redacted] does not reside in the United States, and has not filed in the USPTO a written designation stating the name and address of a person residing within the United States on whom may be served process or notice of proceedings affecting the '771 patent or rights thereunder.

22. On information and belief, as an entity with an ownership interest in the '771 patent, UCB Celltech has purposely availed itself of the benefits and protections that patent registration in this country affords. *See Nat'l Patent Dev. Corp.*, 877 F.2d at 1009; *see also* 35 U.S.C. § 293.

23. It is fair and reasonable to require UCB Celltech to respond in this Court in this District to matters concerning the '771 patent, given that this is the District where the '771 patent is registered. *See id.* at 1009–10.

24. On information and belief, this Court's exercise of personal jurisdiction over UCB Celltech comports with due process at least because UCB Celltech has an ownership interest in a patent registered with the United States Patent Office and because UCB Celltech has enjoyed the privileges of patent ownership. *See Amazon Web Servs.*, 2017 WL 4052381, at *6–7.

25. This Court further has personal jurisdiction over UCB Celltech due to, *inter alia*, the purposeful availment of the jurisdiction of this judicial district by UCB, Inc., another subsidiary of the ultimate parent of UCB Celltech. In 2014, UCB Inc., filed a civil action in this Court seeking a declaratory judgment of invalidity of another entity's patent. *See Yeda Research*, D.I. 1 at 1.

26. This Court's exercise of personal jurisdiction thus meets both the statutory requirement of 35 U.S.C. § 293 and the constitutional requirement of due process.

27. Venue is proper in this judicial district pursuant to 28 U.S.C. §§ 1391(b) and 1400. On information and belief, each of the Defendants is subject to personal jurisdiction in this judicial district, and thus resides in this judicial district under 28 U.S.C. § 1391(b).

INTRODUCTION

28. This action concerns a patent on humanized antibodies, which are synthetic molecules made by combining portions of an antibody from a non-human animal, such as a mouse, and a naturally occurring human antibody.

29. The mouse antibody is called the "donor" antibody because it contributes parts to the resulting humanized antibody that give the humanized antibody the ability to bind to a pre-

defined target antigen. The parts it contributes are called amino acid residues, which are the building blocks of all proteins, whether human, mouse, or otherwise, and which are ordered in a particular sequence in the donor antibody.

30. The naturally occurring human antibody is called the "acceptor" antibody because it receives these "donor residues" from, e.g., the mouse "donor" antibody. One or more amino acid residues from the mouse donor antibody are incorporated into the human acceptor antibody sequence, thereby yielding the humanized antibody.

31. Humanized antibodies are preferred over mouse antibodies for use in human therapy because mouse antibodies can trigger an unwanted immune reaction in a human patient.

32. Celltech's initial attempt to secure patents to humanized antibodies began on December 21, 1989, when it filed a British patent application (number 8928874 ("the GB874 application")), naming John Adair and others as inventors. Over the next 30 years, Celltech and entities related to Celltech pursued a campaign to secure patents on their so-called "humanized" antibodies and methods for making them (i.e., the "Adair patents").

33. On November 30, 1999, Celltech secured U.S. Patent No. 5,994,510 ("the '510 patent") with claims to, *inter alia*, a humanized antibody molecule with specificity for the human protein tumor necrosis factor-α and having a particular amino acid sequence that resulted from its humanization method. Defendants enjoyed their patent rights under the '510 patent until the '510 patent expired at the end of its full term on November 30, 2016.

34. Nearly a decade after it secured the '510 patent, Celltech secured U.S. Patent No. 7,566,771 ("the '771 patent"), with claims to a humanized antibody of any specificity – including to the human tumor necrosis factor-α protein – as long as the antibody had "donor" residues in specified positions of the heavy chain of the antibody.

35. The '771 patent will not expire until July 28, 2026, almost ten years after the '510 patent expired.

36. Patents provide their owners a fixed term of exclusive rights, and once they expire, the public is entitled to use the patented invention without further restriction.

37. The doctrine of obviousness-type double patenting exists to prevent undermining this rule. It provides that a later-expiring patent is invalid if it encompasses a claimed invention in an expired patent, or of its claims are obvious over the claims of the expired patent.

38. UCB Bio, and Celltech before it, have aggressively asserted the Adair patents, including the '771 patent, both in the United States and the United Kingdom. In particular, UCB Bio and Celltech have advanced a broad reading of the term "donor" residue that causes their claims to capture not only humanized antibodies in which particular amino acid residues have been donated to the human "acceptor" sequence from a non-human sequence, but also those where no donation occurs at all. Under their interpretation of the term "donor" residue, residues in the human "acceptor" sequence that happen to match residues in the non-human sequence are also considered "donor" residues.

39. Under Defendants' reading of the term "donor" residue, however, every claim of the '771 patent encompasses the antibody defined in claim 3 of their expired '510 patent. Under the well-established law of obviousness-type double patenting, a broader claim is invalid if it entirely encompasses within its scope – and is thus anticipated by – an invention defined by an expired patent claim. When the '771 patent claims are read as Defendants contend, they are invalid for obviousness-type double patenting.

40. Plaintiffs seek a declaration from this Court holding the '771 patent claims invalid, *inter alia*, for obviousness-type double patenting. The scope of the '771 patent claims

and their invalidity for obviousness-type double patenting over one or more claims of the '510 patent are ripe for adjudication by this Court. Efficient resolution of these issues is aided here because UCB Bio and Celltech have taken positions regarding the scope of the claims of the '771 patent and its sister patent in prior court proceedings, both in the U.S. and in the U.K., under which the claims of the '771 patent are invalid for obviousness-type double patenting.

41. Plaintiffs also seek a declaration that the '771 patent is invalid for other deficiencies under the Patent Laws, including that its claims are not supported by an adequate written description, are not enabled and are indefinite, and that they are anticipated and/or obvious over prior work of other inventors and the prior art.

THE '771 PATENT

42. The individuals named as inventors on the face of the '771 patent are John Robert Adair, Diljeet Singh Athwal, and John Spencer Emtage.

43. At the time it was granted, the '771 patent was assigned to Celltech. Celltech is currently listed as the assignee on the face of the '771 patent and in assignment records maintained by the USPTO.

44. On information and belief, UCB Bio has represented to the United States District Court for the District of Delaware that UCB Bio "is the lawful owner of and holds all rights, title, and interest in the '771 patent." *UCB Biopharma SPRL v. MedImmune, LLC*, No. 1:16-cv-11770-UNA, D.I. 1 ¶ 8 (D. Del. Dec. 12, 2016).

45. On information and belief, UCB Celltech has represented that UCB Celltech is the owner of certain patent rights in the '771 patent and has acted in a manner consistent with ownership of the '771 patent as set forth below.

46. The '771 patent, entitled "Humanised Antibodies," was granted on July 28, 2009 by the USPTO from U.S. Patent Application No. 08/485,686 ("the '686 application"), filed June 7, 1995.[1]

47. The '686 application claims the benefit of U.S. Patent Application No. 08/303,569 ("the '569 application"), filed on September 7, 1994 and issued as U.S. Patent No. 5,859,205 ("the '205 patent"), which itself claims the benefit of U.S. Patent Application 07/743,329 ("the '329 application"), filed on September 17, 1991. The '329 application claims foreign priority to the GB874 application, filed on December 21, 1989.

48. The '771 patent is one of a number of patents derived from the GB874 Application, including, *inter alia*, the '205 Patent, U.S. Patent No. 6,632,927 ("the '927 patent"), attached hereto as Exhibit B, U.S. Patent No. 7,262,050, U.S. Patent No. 7,244,832, U.S. Patent No. 7,244,615, and U.S. Patent No. 7,241,877 (collectively, "the Adair patents"). Each of the Adair patents, with the exception of the '771 patent, has expired.

49. The substantive disclosure of the Adair patents (including the '927 patent) is the same as the disclosure of the '771 patent, but each patent has different claims.

50. The '771 patent granted from an application filed on June 7, 1995. As such, its term is governed by 35 U.S.C. § 154(c)(1), which provides:

> The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act[2] shall be the greater of the 20-year term as provided in subsection (a), or 17 years from grant, subject to any terminal disclaimers.

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1 "Humanised" is the English (United Kingdom) spelling of the word "humanized."

2 The date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act is June 8, 1995.

51. Because the date that is 17 years from the grant date of the '771 patent (i.e., July 28, 2026) is later than the date that is 20 years from the filing date of the first-filed non-provisional U.S. patent application to which the '771 patent claims priority (i.e., September 17, 2011), the term of the '771 patent is 17 years from grant under 35 U.S.C. § 154(c)(1).

52. On information and belief, the '771 patent is not subject to any terminal disclaimers that would cause its term to expire earlier than July 28, 2026.

53. On information and belief, the '771 patent will expire on July 28, 2026.

[redacted]

54. [redacted]

55. [redacted]

56. [redacted]

57. [redacted]

58. [redacted]

59. [redacted]

60. [redacted]

61. [redacted]

62. [redacted]

63. [redacted]

[redacted]

64. An actual and justiciable controversy exists between Plaintiffs and Defendants. *See, e.g., MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118, 137 (2007) (holding that MedImmune "was not required, insofar as Article III is concerned, to break or terminate its 1997 license agreement before seeking a declaratory judgment in federal court that the underlying patent is invalid, unenforceable, or not infringed"); *id.* at 128 ("There is no dispute that these standards would have been satisfied if petitioner had taken the final step of refusing to make royalty payments under the 1997 license agreement."); *Adenta GmbH v. OrthoArm, Inc.*, 501 F.3d 1364, 1370 (Fed. Cir. 2007).

PLAINTIFFS' ENTYVIO® (VEDOLIZUMAB) PRODUCT

65. Plaintiffs' ENTYVIO® product is an FDA-approved biological product for the treatment of adult ulcerative colitis and adult Crohn's disease.

66. ENTYVIO® was first approved by the FDA in 2014. Following FDA approval, ENTYVIO® was marketed and sold in the United States, prescribed by physicians, and taken by patients to treat adult ulcerative colitis and adult Crohn's disease.

67. Plaintiffs expended substantial revenues researching, developing, launching, and commercializing ENTYVIO®.

68. Millennium manufactures the ENTYVIO® product in the United States. Takeda Pharmaceuticals America, Inc. and Takeda Pharmaceuticals U.S.A., Inc. market and sell the ENTYVIO® product in the United States.

69. The active ingredient in ENTYVIO® is vedolizumab, a humanized monoclonal antibody.

70. The vedolizumab humanized antibody is the subject of Millennium's own patents, including, *inter alia*, U.S. Patent No. 7,147,851 and related patents.

ANTIBODY HUMANIZATION

71. Antibody humanization is a process whereby a non-human antibody (e.g., often from a mouse) is used to design and produce a new synthetic antibody made of both non-human and human antibody parts that is more suitable for use in humans.

72. Celltech made a number of representations to the United States District Court for the District of Columbia, all of which it believed to be true and correct, regarding "humanized" antibodies in a prior litigation involving the '927 patent, a patent which has the same disclosure as the '771 patent. *See MedImmune Inc. v. Celltech R&D Ltd.*, No. 04-cv-143, D.I. 50 at 2–10 (D.D.C. Feb. 10, 2005) ("*MedImmune I*").

73. In *MedImmune I*, Celltech made representations to the court in that case regarding an overview of antibodies and techniques used to prepare "humanized" antibodies.

74. In *MedImmune I*, Celltech represented to the court:

> Antibodies are proteins produced by the immune systems of animals in response to the exposure of the animal to foreign matter, such as bacteria or viruses (collectively referred to as "antigens"). Antibodies recognize and bind to antigens, thereby marking them for other components of the immune system to destroy. This makes antibodies suitable for targeting and destroying or inhibiting the growth of harmful agents such as bacteria, viruses, and cancer cells.

Id. at 3–4.

75. In *MedImmune I*, Celltech also represented to the court:

> Antibodies are composed of multiple protein "chains," which are in turn composed of "amino acids" (also referred to as "amino acid

residues") linked together by chemical bonds. There are twenty naturally-occurring amino acids, which are usually identified in scientific documents using either a three-letter or a one-letter abbreviation for their full name. For example, both "A" and "Ala" are abbreviations of the amino acid called "alanine," and both "V" and "Val" are abbreviations of the amino acid called "valine."

Id. at 2.

76. In *MedImmune I*, Celltech further represented to the court:

The most common human antibody, IgG ("Immunoglobulin G"), can be visualized in a simplified, two-dimensional form as shaped like the letter "Y," as indicated in Figure 1 below. It consists of four protein chains: two identical long "heavy" chains and two identical short "light" chains, which together make up the "arms" and the "tail" of the "Y." The light chain is made up of a variable region and a constant region. The heavy chain is also made up of a variable region and a constant region. The variable region of one light chain combines with the variable region of one heavy chain to form an antigen-binding site, as indicated in the figure.

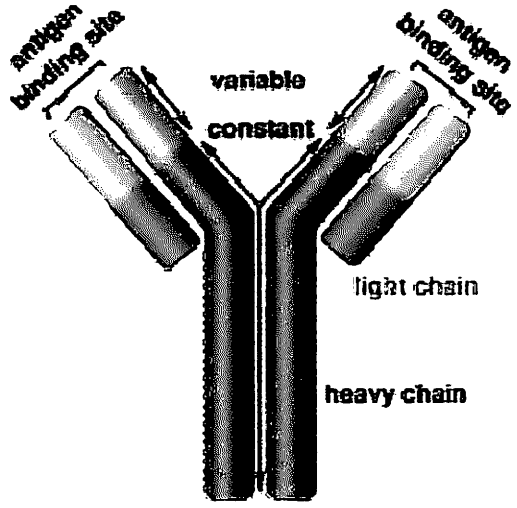


Figure 1

Id. at 3 (internal citation omitted).

77. In *MedImmune I*, Celltech also represented to the court:

The main points of interaction between the variable region and an antigen are sets of loops protruding out from the arms of the "Y," referred to as complementarity-determining regions or "CDRs."

> Each arm of the "Y" generally contains six CDRs: three on the heavy chain and three on the light chain. The amino acids in the CDRs fold together and form precise three-dimensional structures that interact with the structure of an antigen to bind the antibody to the antigen.

Id. at 3–4.

78. Celltech stated that the amino acid sequences in the variable regions of the heavy and light chains that surround the six CDRs are called "framework" regions. In *MedImmune I*, Celltech represented to the court:

> In addition, the variable regions include stretches of amino acids called "framework regions," which are not included within the CDRs. Thus, the variable region of an antibody contains both CDRs and framework regions. The amino acids of the framework regions hold the antibody together and determine the position of the CDRs relative to each other. The precise three-dimensional orientation of the CDRs is critical to the structure of the binding site, and is therefore important for antigen binding.

Id. at 4.

79. Celltech also stated that mouse ("murine") monoclonal antibodies have limitations that made them unsuitable for use in human therapy. *MedImmune I*, D.I. 50 at 7. In *MedImmune I*, Celltech represented to the court:

> For example, when murine monoclonal antibodies are administered to a human patient, the patient's immune system may respond adversely to the foreign monoclonal antibody. This Human Anti-Mouse Antibody (HAMA) response limits the therapeutic usefulness of murine monoclonal antibodies. In addition, while many non-human monoclonal antibodies are capable of interacting with the human immune system via their constant regions, human-derived constant regions are more efficient for this purpose.

Id. at 7 (internal citation omitted).

80. In *MedImmune I*, Celltech then described initial techniques to make, through genetic engineering, "chimeric" antibodies, which are synthetic antibodies that combine the

variable region of a non-human antibody with the constant region of a human antibody. *Id.* at 8.

Celltech represented to the Court:

> The first developmental step toward humanization was the production of "chimeric antibodies," which are made by attaching the variable region of an animal-derived (usually mouse-derived) antibody to the constant region of a human-derived antibody.

Id.

81. In *MedImmune I*, Celltech stated these chimeric antibodies had certain limitations. Celltech represented to the court:

> However, when chimeric antibodies were used therapeutically in humans, some patients still generated a HAMA response. As a result, more sophisticated humanization techniques were developed throughout the 1980s, with an aim towards reducing the number of murine residues in the antibody. Dr. Greg Winter, at the Medical Research Council Laboratory in Cambridge, England, realized that the most critical portions of the animal-derived variable region that needed to be retained in a humanized antibody in order to retain binding ability were the six CDRs. He therefore devised a method for designing and producing antibodies having CDRs that corresponded to the CDRs from an animal-derived monoclonal antibody. Using this method — referred to as "CDR-grafting" — humanized antibodies could be engineered to mimic the binding properties of the original animal-derived monoclonal antibody, with the improvement of being less immunogenic when injected into humans. Such CDR-grafted humanized antibodies are less likely to generate a HAMA response than chimeric antibodies, due to the lower proportion of non-human amino acid sequences. Dr. Winter presented this technique for humanization of monoclonal antibodies in a paper published in Nature in 1986.

Id. at 8–9 (internal citations and footnotes omitted).

82. In *MedImmune I*, Celltech also stated that other scientists had discovered by 1988 that CDR-grafting alone could result in a humanized antibody with unsatisfactory binding properties. Celltech represented to the court:

> However, scientists later discovered that transfer of the CDRs alone was often not sufficient to provide satisfactory antigen binding in a humanized antibody. Specifically, an article by

> Riechmann *et al.* (*Nature* (1988)) discussed that it may be necessary for additional *framework* residues of the humanized antibody product — *i.e.*, residues not within the CDRs — to correspond to the amino acid residues found in the non-human antibody.

MedImmune I, D.I. 50 at 9 (original emphasis).

83. In *MedImmune I*, Celltech, again citing prior work by other scientists, represented to the court: "These results indicated that in order to obtain effective binding activity in a humanized antibody, at some positions within the variable region but outside the CDR regions, residues should be identical to the corresponding murine residues." *Id.* at 10.

84. Claim 1 of the '927 patent reads as follows:

> An antibody molecule having affinity for a predetermined antigen and comprising a composite heavy chain and a complementary light chain, said composite heavy chain having a variable domain including complementarity determining regions (CDRs) and framework regions, wherein said framework regions of said variable domain comprise predominantly human acceptor antibody heavy chain framework region residues, the remaining heavy chain framework region residues corresponding to the equivalent residues in a donor antibody having affinity for said predetermined antigen, wherein, according to the Kabat numbering system, in said composite heavy chain: said CDRs comprise donor residues at residues 31 to 35, 50 to 58, and 95 to 102; and said framework regions comprise donor residues at amino acid residues 6, 24, 48, 49, 71, 73, and 78.

85. In *MedImmune I*, Celltech represented the humanization methods described in the common disclosure of the '927 and '771 patents to the court as follows:

> The first step of the protocol is to determine the amino acid sequence that codes for the heavy and light chain variable regions of the donor antibody. Acceptor human heavy and light chains with known amino acid sequences are chosen, and the humanized antibody is then designed starting from that basis.
>
> Next, donor residues are chosen for use in the CDRs.
>
> Once donor residues have been selected for the CDRs, the protocol sets forth an exemplary list of framework candidate residues to

> consider changing in the design if they do not already correspond to the donor residue.

Id. at 11–12 (internal citations omitted)

86. In *MedImmune I*, Celltech also represented to the court:

> The patent specifically explains that in some cases the human and non-human amino acid residues may be identical at a particular position, in which case no change is required. In other words, if a particular amino acid residue of interest is, for example, alanine in both the donor and acceptor sequences, it need not be "changed" in the design because it already corresponds to the donor sequence.

Id. at 12.

87. On information and belief, Defendants believe the quoted representations in paragraphs 74–86, made by Celltech to the District Court for the District of Columbia in *MedImmune I*, to be true and correct.

"DONOR" RESIDUE

88. Like the claims of its sibling '927 patent, the claims of the '771 patent define humanized antibodies having non-human, "donor" amino acid residues in the CDRs and in certain additional framework positions within the heavy chain variable region of a human "acceptor" sequence.

89. The term "donor" is used in conjunction with the term "residue" in each of the claims of the '771 patent.

90. The term "donor residue" appears in all of the claims of the '927 patent.

91. A residue at any particular position in a humanized heavy chain amino acid sequence may, by chance or design, be the same as the amino acid located at that position in both a non-human "donor" heavy chain and a human "acceptor" heavy chain.

92. Alternatively, a residue at any particular position in humanized heavy chain amino acid sequence may, by chance or design, differ from the amino acid located at that position in either the non-human "donor" or a human "acceptor" heavy chain sequence.

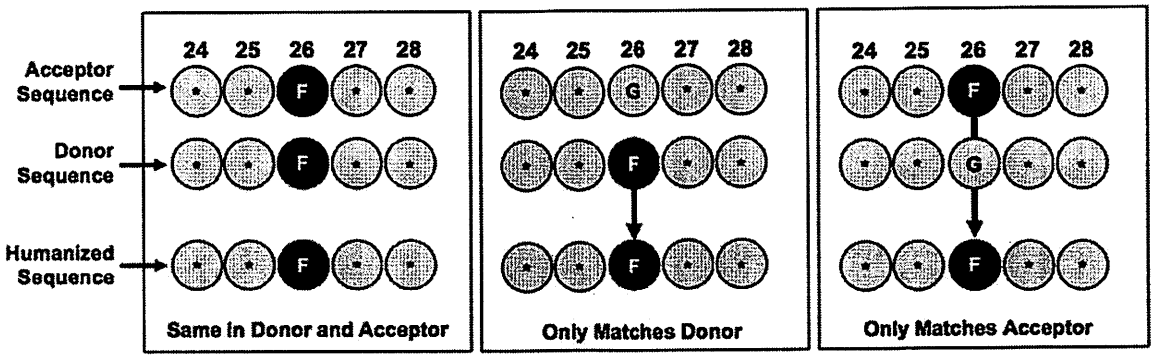
93. As illustrated in the picture below, this yields three relationships that are relevant to the '771 patent claims between each residue in the humanized heavy chain, relative to the amino acid in that position in the "donor" and "acceptor" sequences:

(i) the amino acid in the humanized heavy chain matches the amino acid residues in both the non-human "donor" sequence and the human "acceptor" sequence, such that the "same" residue appears in all three heavy chains;

(ii) the amino acid in the humanized heavy chain matches only the amino acid residue in the non-human "donor" sequence; or

(iii) the amino acid in the humanized heavy chain matches only the amino acid residue in the human "acceptor" sequence.

A fourth relationship, in which a residue in the humanized heavy chain is different than the residue at that position in both the "donor" and "acceptor" sequences, is not presented here.



94. In its 2004–2005 litigation against MedImmune, Inc., Celltech made a number of representations to the United States District Court for the District of Columbia regarding the meaning of the term "donor residue," which it believed to be true and correct. *See, e.g.*,

MedImmune I, D.I. 50 at 25–31. A true and correct copy of D.I. 50 (Celltech's Opening Claim Construction Brief) is attached hereto as Exhibit C.

95. In *MedImmune I*, Celltech made the following representation in its opening claim construction brief regarding the construction of the term "donor residue" in the '927 patent claims, which it believed to be true and correct:

> The term "donor residue" means an amino acid residue of a humanized antibody that matches the residue found at the corresponding position in the sequence of the non-human antibody used to provide the sequence of the CDRs.

Id. at 25 (Feb. 10, 2005).

96. On information and belief, Defendants believe the construction set forth in paragraph 95, represented by Celltech to the District Court for the District of Columbia in *MedImmune I*, to be true and correct.

97. Celltech's opponent in *MedImmune I*, MedImmune, Inc., contended that the term "donor residue" must be interpreted as follows:

> A residue that has the donor antibody as its source. It does not refer to an unchanged acceptor residue in the framework of a CDR-grafted antibody.

MedImmune I, D.I. 51 at 15 (Feb. 10, 2005). *See also id.* ("Where the donor antibody and the acceptor antibody match at a given framework position in CDR-grated antibody, that residue is an acceptor residue. It is not a donor residue.").

98. On information and belief, Defendants believe the construction of "donor residue" proposed by MedImmune, Inc. in *MedImmune I* and set forth above in paragraph 97 is incorrect.

99. In *MedImmune I*, Celltech contended the specification of the '927 patent supported its proposed construction of "donor residue." Celltech represented to the court:

> Celltech's construction is compelled by the specification of the patent. Although a definition of the term "donor' is not explicitly

> set forth in the specification, its meaning is clear from an analysis of the specification, particularly the examples.

MedImmune I, D.I. 50 at 25 (Feb. 10, 2005); *see also id.* at 28 ("Celltech's definition is also supported by the examples provided in the '927 patent."); *id.* at 29 ("Thus, Example 1 clearly demonstrates that common residues may be considered donor residues.").

100. On information and belief, Defendants believe the representations quoted above in paragraph 99, made by Celltech to the District Court for the District of Columbia in *MedImmune I*, to be true and correct.

101. In *MedImmune I*, Celltech also represented to the court that its "proposed construction of the term 'donor residue' is fully consistent with all of the embodiments disclosed in the specification." *Id.* at 30 (internal footnote omitted).

102. In *MedImmune I*, Celltech represented to the court:

> The prosecution history of the '927 patent confirms that Celltech's proposed construction of the term "donor residue" is correct.

Id.

103. In *MedImmune I*, Celltech also represented to the court that its construction of "donor residue" was supported by, *inter alia*, the following statements it made to the USPTO during prosecution history of the '927 patent:

> In some cases, a residue which is selected for changing according to the protocol described in the application may not need to be changed. It may be that, fortuitously, it is the same in the donor and acceptor chains. This does not mean that, if the residues had been different, it would not have been changed. It merely means that, in effect, the change had already been made.

Id. at 30–31.

104. In *MedImmune I*, Celltech also represented to the court:

> Thus, the applicants made it clear that a common residue need not be changed in the acceptor framework *because that residue is*

> *already a donor residue*. The prosecution history thus explicitly confirms that Celltech's proposed construction is correct . . . .

MedImmune I, D.I. 50 at 31.

105. In *MedImmune I*, Celltech further represented to the court:

> In other words, a residue is a donor residue if it matches the equivalent residue in the donor sequence. It is irrelevant whether or not the donor residue also matches the residue to be found at that position in the human sequence used to provide the framework sequence.

Id. at 25.

106. In *MedImmune I*, Celltech also represented to the court:

> The patent plainly indicates that if a particular residue is common to both the donor and acceptor antibodies, no change is required *because the residue is already donor*.

Id. (original emphasis) (internal citation omitted).

107. In *MedImmune I*, Celltech also represented to the court:

> If an acceptor framework that is highly homologous with the donor sequence is chosen, then fewer residues will have to be "changed" to match the donor sequence because they will already match. Thus, the patent does not require that a residue be "changed" to match the donor sequence to be a "donor" residue. Rather, the patent specifically contemplates more "convenient" situations where such a change is not required.

Id. at 26 (internal citations omitted).

108. In *MedImmune I*, Celltech also represented to the court:

> If the residue does *not* match the donor antibody, a donor residue (that is, a residue matching that found at that position in the donor sequence) is used at that position. The residue at the relevant position in the acceptor sequence could, however, fortuitously match the donor antibody, such that no change is necessary. The fact that a particular residue happens to match the non-human residue does not mean, as MedImmune contends, that the residue at the identified position is not a donor residue.

Id. at 27–28 (internal citations omitted) (original emphasis).

109. On information and belief, Defendants believe the representations in paragraphs 101–108, made by Celltech to the District Court for the District of Columbia in *MedImmune I*, to be true and correct.

110. A Markman hearing was held in *MedImmune I* on May 18, 2005. *See MedImmune I*, D.I. 75 at 1 (June 9, 2005). The court in *MedImmune I* did not issue a claim construction decision.

111. MedImmune, Inc. and Celltech stipulated to dismissal of *MedImmune I* with prejudice on June 27, 2005. *MedImmune I*, D.I. 76 at 1 (June 27, 2005).

112. UCB Bio and Celltech have taken a similar position on the meaning of "donor" residue in pending litigation in the United Kingdom regarding the '771 patent as Celltech took in *MedImmune I*. *Chugai Pharm. Co., Ltd v. UCB Pharma S.A.*, No. HP-2016-000063, Amended Statement of Case ¶ 3 (EWHC (Ch) Aug. 31, 2017) ("*Chugai*"), a true and correct copy of which is attached hereto as Exhibit D.

113. UCB Bio and Celltech represented to the Patents Court in the Chancery Division of the High Court of Justice in the United Kingdom:

> When properly construed in accordance with the principles described above, the term "non-human donor" in the claims of the 771 Patent means a residue in the humanised antibody that is present in the non-human donor antibody sequence at the relevant position, whether or not the same residue is present in the human acceptor antibody at the same position.

Id.

114. On information and belief, Defendants believe the quoted representation in paragraph 113, made by UCB Bio and Celltech to the Patents Court in the Chancery Division of the High Court of Justice in the United Kingdom, to be true and correct.

115. UCB Bio also recently filed a patent infringement suit against MedImmune, LLC with respect to MedImmune, LLC's humanized antibody Synagis® (palivizumab). *See UCB Biopharma SPRL v. MedImmune, LLC*, No. 1:16-cv-01177, D.I. 1 (D. Del. Dec. 12, 2016) ("*MedImmune II*").

116. In *MedImmune II*, UCB Bio alleged MedImmune infringed at least claim 1 of the '771 patent by making, using, and selling Synagis® (palivizumab).

117. In *MedImmune II*, UCB Bio represented to the United States District Court for the District of Delaware:

> As a humanized antibody, palivizumab includes non-human amino acid residues grafted into the human heavy chain variable region; these non-human amino acid residues derive from, *i.e.*, correspond to, the murine monoclonal antibody, Mab 1129.

MedImmune II, D.I. 1 ¶ 10.

118. In *MedImmune II*, UCB Bio also represented to the court:

> Synagis® comprises a humanized antibody with affinity for RSV antigen, in the composite heavy chain of which, according to the Kabat numbering system, at least residues 26-35, 50-58, and 95-102 in the complimentary determining regions (CDRs), and at least residues 48, 49, 71, 73, 76, 78, 88, and 91 in the framework regions, are non-human donor residues.

Id. ¶ 19.

119. On information and belief, UCB Bio asserted that palivizumab infringed one or more claims of the '771 patent in its complaint in *MedImmune II* based on substantially the same construction of "donor residue" that Celltech represented to the court in *MedImmune I*.

120. On information and belief, UCB Bio asserted that palivizumab infringed one or more claims of the '771 patent in its complaint in *MedImmune II* based on substantially the same construction of "non-human donor" residue that UCB Bio represented to the court in *Chugai*.

THE '510 PATENT

121. On information and belief, UCB Bio owns other patents naming the '771 patent inventors that issued from applications claiming priority to the original GB874 application, including U.S. Patent No. 5,994,510 ("the '510 patent"). The '510 patent is attached hereto as Exhibit D.

122. The individuals named as inventors on the face of the '510 patent are John Robert Adair, Diljeet Singh Athwal, John Spencer Emtage, and Mark William Bodmer.

123. All of the individuals named as inventors on the face of the '771 patent are named as inventors on the face of the '510 patent.

124. At the time it was granted, the '510 patent was assigned to Celltech Therapeutics Limited, which is listed as the assignee on the face of the '510 patent.

125. On information and belief, Celltech is a successor in interest of Celltech Therapeutics Limited. *See MedImmune II*, D.I. 1 ¶¶ 14, 16.

126. On information and belief, UCB Bio is the current owner of all right, title, and interest in and to the '510 patent.

127. On information and belief, the owner of the '771 patent is the same as the owner of the '510 patent.

128. The '510 patent was granted on November 30, 1999 from U.S. Patent Application No. 08/456,418, filed June 1, 1995, which is a continuation of U.S. Patent Application No. 08/373,882, filed January 17, 1995, which is a continuation of U.S. Patent Application No. 07/920,378, filed December 20, 1991, which claims priority to PCT/GB91/02300, filed Dec. 20, 1991, which claims foreign priority to U.K. Patent Application No. 9109645, filed May 3, 1991

and to PCT/GB90/02017, filed December 21, 1990, which itself claims foreign priority to the same GB874 Application as the '771 patent.

129. The '510 patent has expired.

130. Like the '771 patent, the '510 patent claims humanized antibodies having non-human "donor" residues at specified positions in a composite heavy chain.

131. The '510 patent discloses a humanized antibody designated "CDP571" having heavy and light chains, and in which the heavy chain comprises the composite heavy chain variable region amino acid sequence listed in SEQ ID NO:6 and the light chain comprises the variable region sequence listed in SEQ ID NO:3.

132. The '510 patent indicates that the CDP571 humanized antibody was made by the process described in Example 2 of the '510 patent. Example 2 of the '510 patent is titled "Further CDR-Grafting of Murine anti-human TNFα Antibodies CB0010 and 101.4." '510 patent at 15:63–16:20.

133. The '510 patent indicates the "2hEug" composite heavy chain combines elements of the mouse "donor" amino acid sequence "htnf1" and the human heavy chain" acceptor" sequence "Eu." *See* '510 patent at 16:39–42.

134. The '510 patent indicates the amino acid sequence of the "2hEug" heavy chain of the "CDP571" humanized antibody contains the heavy chain variable region sequence listed in "SEQ ID: NO.6" in the patent disclosure. '510 patent at 16:39–42.

135. Figure 1 of the '510 patent lists, *inter alia*, the amino acid sequences of:

- the variable region of the "2hEug" "humanized" heavy chain;

- the variable region of the "htnf1" mouse heavy chain, which was the "donor" sequence used to prepare the variable region of the "2hEug" humanized heavy chain; and
- the variable region of the "Eu" human heavy chain, which was the "acceptor" sequence used to prepare the variable region of the "2hEug" humanized heavy chain.

See '510 patent at 16:39–42 ("The specific combination of grafted light chain (gEU) (SEQ. ID NO: 3) and grafted heavy chain (2hEUg) (SEQ. ID NO: 6), as shown in FIG. 1, provides the antibody known as CDP571."); *id.* at 12:64–13:1 ("FIG. 1 shows amino acid sequences for the variable domains of the heavy and light chains for the human acceptor antibody EU (1EU), the murine MAb CB0010 (htnf1) and humanised CDR grafted light (gEU) and heavy (2hEUg) chains.")

136. Claim 3 of the '510 patent defines a humanized antibody that comprises, *inter alia*, a heavy chain having a variable region comprising the amino acid sequence of SEQ ID: NO. 6, stating:

> An antibody molecule which has specificity for human TNFα comprising a heavy chain having a variable domain comprising the amino acid sequence of SEQ ID: NO. 6 and a light chain having a variable domain comprising the amino acid sequence of SEQ ID: NO. 3.

'510 patent at 40:14–18 (claim 3).

137. Claim 3 encompasses the humanized antibody designated "CDP571" in the '510 patent disclosure.

138. In the early 2000s, Celltech completed clinical trials with its CDP571 humanized antibody for the treatment of Crohn's disease, but these trials failed to meet their primary

endpoints. Celltech's CDP571 humanized antibody proved ineffective for the treatment of Crohn's disease, and was not developed into an approved therapeutic.

139. Figure 1 of the '510 patent contains an alignment of the "2hEug" humanized heavy chain sequence in the CDP571 antibody to the "Eu" human heavy chain "acceptor" sequence and the "htnf1" murine heavy chain "donor" sequence. The alignment shows the amino acid residues in the heavy chain variable regions of the three sequences. The portion of Figure 1 showing an alignment of the heavy chain amino acid sequences is reproduced below:

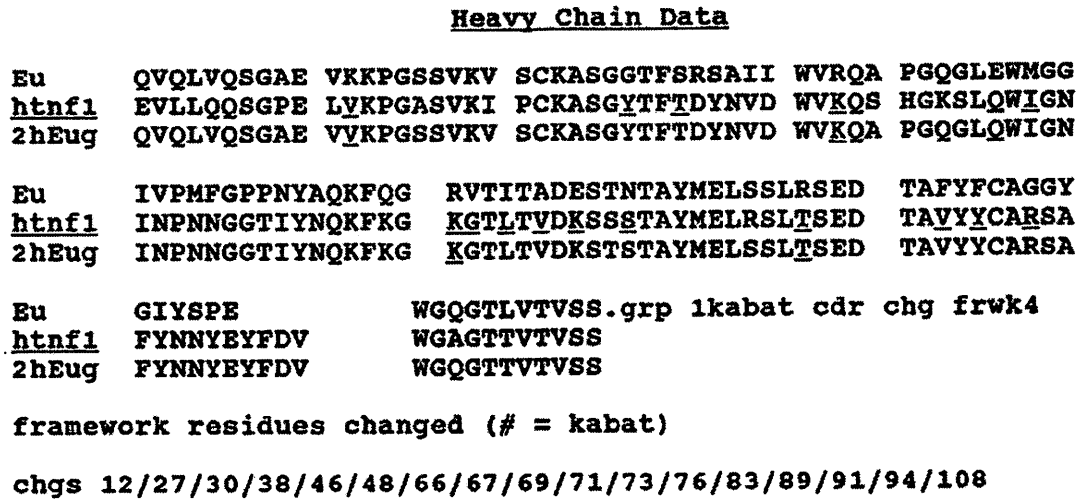


Fig. 1

140. On information and belief, in the bottom set of sequences, Figure 1 aligns residues 101–102 ("PE") of the Eu human sequence with residues 100A–100B ("YE") in the htnf1 mouse and 2hEug humanized sequences. On information and belief, for the purposes of the '771 patent claims, residues 101–102 ("PE") are to be aligned over residues 101–102 ("DV") of the htnf1 mouse and 2hEug humanized sequences.

141. According to Figure 1, the last two lines of Figure 1 list the "Eu" human heavy chain framework residues that differ from the "htnf1" mouse residues and were changed to match the mouse "donor" residue in the 2hEug humanized heavy chain.

142. According to Figure 1, the 2hEug humanized heavy chain contains mouse "donor" residues at positions 12, 27, 30, 38, 46, 48, 66, 67, 69, 71, 73, 76, 83, 89, 91, 94, and 108 (using the Kabat numbering system). At each of these positions, the residue in the 2hEug humanized heavy chain variable region matches only the mouse "donor" residue in the "htnf1" heavy chain – it does not the match the corresponding residue in the human "acceptor" "Eu" sequence.

143. As Figure 1 shows, the amino acids at positions 26 to 35, 50 to 58, and 95 to 102 in the 2hEug humanized heavy chain either:

(i) match only the "htnf1" mouse "donor" amino acid residue at that position, or

(ii) are the same as the amino acids in those positions in both the "htnf1" mouse "donor" and the "Eu" human acceptor heavy chain sequences.

144. Figure 1 shows that the amino acids at positions 2, 6, 23, 24, 49, 72, 78, 88, and 110 of the "2hEug" humanized heavy chain are the same as the amino acids at those positions in both the "htnf1" mouse "donor" and the "Eu" human "acceptor" heavy chains.

145. On information and belief, the tables below show, for each residue specified by the '771 patent claims, the result of a comparison of the amino acid residues in the variable region of the "2hEug" humanized heavy chain (i.e., SEQ ID NO. 6) to the amino acid residues at the same positions in the heavy chain variable regions of the "htnf1" mouse "donor" and the "Eu" human "acceptor" sequences. On information and belief, the tables below indicate underneath each residue whether the amino acid residue in the humanized heavy chain is the

"same" as both the mouse and human residues ("S"), matches only the "mouse" residue ("M") or matches only the "human" residue ("H").

	FR1				CDR1										FR2		CDR2									
	2	6	23	24	26	27	28	29	30	31	32	33	34	35	48	49	50	51	52	52A	53	54	55	56	57	58
SEQ 6	V	Q	K	A	G	Y	T	F	T	D	Y	N	V	D	I	G	N	I	N	P	N	N	G	G	T	I
M/S/H	S	S	S	S	S	M	S	S	M	M	M	M	M	M	M	S	M	S	M	S	M	M	S	M	M	M

	FR2								CDR3													FR4	
	71	72	73	75	76	78	88	91	95	96	97	98	99	100	100A	100B	100C	100D	101	102		108	110
SEQ 6	V	D	K	T	S	A	A	Y	S	A	F	Y	N	N	Y	E	Y	F	D	V		T	T
M/S/H	M	S	M	H	M	S	S	M	M	M	M	M	M	M	M	M	M	M	M	M		M	S

CLAIMS FOR RELIEF

COUNT 1: PATENT INVALIDITY

146. Plaintiffs incorporate by reference the allegations set forth in paragraphs 1–145 above, as if fully set forth herein.

147. Each and every claim of the '771 patent is invalid for obviousness-type double patenting over one or more claims of the expired '510 patent.

148. Obviousness-type double patenting is a judicially-created doctrine designed to "prevent claims in separate applications or patents that do not recite the 'same' invention, but nonetheless claim inventions so alike that granting both exclusive rights would effectively extend the life of patent protection." *Perricone v. Medicis Pharm. Corp.*, 432 F.3d 1368, 1373 (Fed. Cir. 2005) (citation omitted).

149. Obviousness-type double patenting prohibits the issuance of claims in a second, later-expiring patent that are "not patentably distinct from the claims of the first patent." *In re Longi*, 759 F.2d 887, 892 (Fed. Cir. 1985).

150. A later-expiring patent claim "is not patentably distinct from an earlier patent claim if the later claim is obvious over, or anticipated by, the earlier claim." *Eli Lilly & Co. v. Barr Labs.*, Inc., 251 F.3d 955, 968 (Fed. Cir. 2001).

151. A later-expiring patent claims is anticipated by an earlier-expiring patent claim if its scope fully encompasses and includes within it the subject matter defined by the earlier-expiring patent claim. For example, an earlier expiring claim to a "species" will anticipate a later-expiring claim to a "genus" that includes that "species." *See, e.g., In re Hubbell*, 709 F.3d 1140, 1146 (Fed. Cir. 2013); *In re Van Ornum*, 686 F.2d 937, 938 (C.C.P.A. 1982)

152. The doctrine of obviousness-type double patenting is intended "to prevent unjustified time-wise extension of the right to exclude granted by a patent no matter how the extension is brought about." *In re Van Ornum*, 686 F.2d at 938.

153. Obviousness-type double patenting "is designed to prevent an inventor from securing a second, later expiring patent for the same invention." *AbbVie Inc. v. Mathilda & Terence Kennedy Inst. of Rheumatology Tr.*, 764 F.3d 1366, 1373 (Fed. Cir. 2014).

154. The '771 patent will expire more than nine years after than the term of the '510 patent expired.

155. Defendants cannot terminally disclaim the term of the '771 patent that extends beyond the term of the '510 patent because the '510 patent has already expired.

156. John Robert Adair, Diljeet Singh Athwal, and John Spencer Emtage are named as inventors on the face of both the '771 patent and the '510 patent. Consequently, the '771 patent and the '510 patent have three common inventors. *See In re Hubbell*, 709 F.3d at 1148 ("It is undisputed that this overlap in inventorship is precisely the type of relationship that would give rise to double patenting under the MPEP.").

157. On information and belief, UCB Bio owns both the '771 patent and the '510 patent. Consequently, on information and belief, the '771 patent and the '510 patent have common ownership.

158. The '771 patent is not entitled to the safe harbor of 35 U.S.C. § 121 because the purported invention of the '686 application from which the '771 patent granted is neither a patent issuing on an application with respect to which a requirement for restriction under section 121 has been made nor a divisional application filed as the result of a restriction requirement.

159. The '771 patent is not entitled to the two-way test for obviousness-type double patenting at least because: (i) the claims of the '771 patent and the claims of the '510 patent could have been pursued in the same application, *see In re Berg*, 140 F.3d 1428, 1432 (Fed. Cir. 1998)), and (ii) the USPTO was not solely responsible for the delay in the issuance of the '771 patent relative to the '510 patent. *See In re Hubbell*, 703 F.3d at 1149 ("[T]he two-way test is appropriate only in the 'unusual circumstance where 'the PTO is solely responsible for the delay in causing the second-filed application to issue prior to the first.'") (quoting *In re Berg*, 140 F.3d at 1437).

160. Under the one-way test for obviousness-type double patenting, each of the claims of the '771 patent encompasses the antibody molecule defined by at least claim 3 of the '510 patent, and is thus anticipated by at least claim 3.

161. Each of the claims of the '771 patent recites a "humanised antibody molecule having affinity for an antigen and comprising a composite heavy chain and a complementary light chain . . ." or a "humanised antibody molecule having affinity for a predetermined antigen and comprising a composite heavy chain and a complementary light chain . . . ."

162. Claim 3 of the '510 patent defines an "antibody molecule which has specificity for human TNFα comprising a heavy chain having a variable domain comprising the amino acid sequence of SEQ ID: NO. 6 and a light chain having a variable domain comprising the amino acid sequence of SEQ ID: NO. 3." '510 Patent at 40:14–18 (claim 3).

163. As used in claim 3 of the '510 patent, "TNFα" is an "antigen" or a "predetermined antigen" within the meaning of each of the claims of the '771 patent.

164. As used in claim 3 of the '510 patent, the phrase "having specificity for" means "having affinity for" the specified antigen (i.e., TNFα) within the meaning of each of the claims of the '771 patent.

165. The amino acid sequence represented by SEQ ID: NO. 6 is a "humanised" heavy chain of an antibody molecule.

166. The amino acid sequence represented by SEQ ID: NO. 3 is a "humanised" light chain of an antibody molecule.

167. An antibody molecule comprised of the heavy chain defined in SEQ ID: NO. 6 and the light chain defined in SEQ ID: NO. 3 is a "humanised antibody . . . comprising a composite heavy chain and a complementary light chain . . ." within the meaning of each claim of the '771 patent.

168. The antibody molecule defined in Claim 3 of the '510 patent comprises a heavy chain with the amino acid sequence specified in SEQ ID: NO. 6, which is a "composite heavy chain having a variable domain including complementarity determining regions (CDRs) . . ." within the meaning of each claim of the '771 patent.

169. The antibody molecule defined in Claim 3 of the '510 patent thus satisfies the following common requirements of each of claims 1 to 19 of the '771 patent:

> A humanised antibody having affinity for an antigen / a predetermined antigen and comprising a composite heavy chain and a complementary light chain, said composite heavy chain having a variable domain including complementarity determining regions (CDRs), ...

170. Claim 1 of the '771 patent additionally specifies that "at least residues 26 to 35, 50 to 58, and 95 to 102 in the CDRs and at least residues 48, 49, 71, 73, 76, 78, 88, and 91 in the framework regions are non-human donor . . . ."

171. On information and belief, under Defendants' interpretation of "donor" residue, at least residues 26 to 35, 50 to 58, and 95 to 102 in the CDRs and residues 48, 49, 71, 73, 76, 88, 88, and 91 in the framework regions of the humanized heavy chain defined by claim 3 of the '510 patent are "donor" residues.

172. Under Defendants' own interpretation of "donor" residue, Claim 1 of the '771 patent is invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

173. Claim 2 of the '771 patent specifies that "said CDRs are non-human donor at residues 31 to 35, 50 to 58, and 95 to 102; and said framework regions are non-human donor at: a) residue 6; b) one or more of residues 23 and 24 c) one or more of residues 48 and 49; d) one or more of residues 71 and 73; e) one or more of residues 75, 76, and 78; and f) one or more of residues 88 and 91 . . . ."

174. On information and belief, under Defendants' interpretation of "donor" residue, at least residues 31 to 35, 50 to 58, 95 to 102, 6, 23, 24, 48, 49, 71, 73, 76, 78, 88, and 91 in the framework regions of the humanized heavy chain defined by claim 3 of the '510 patent are "donor" residues.

175. Under Defendants' own interpretation of "donor" residue, Claim 2 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

176. Claim 3 of the '771 patent depends from claim 2 and specifies that "residue 2 of said composite heavy chain is donor."

177. On information and belief, under Defendants' interpretation of "donor" residue, residue 2 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

178. Under Defendants' own interpretation of "donor" residue, Claim 3 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

179. Claim 4 of the '771 patent depends from claim 2 and specifies that "residue 72 of said composite heavy chain is donor."

180. On information and belief, under Defendants' interpretation of "donor" residue, residue 72 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

181. Under Defendants' own interpretation of "donor" residue, Claim 4 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

182. Claim 5 of the '771 patent depends from claim 2 and specifies that "residue 108 of said composite heavy chain is donor."

183. On information and belief, under Defendants' interpretation of "donor" residue, residue 108 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

184. Under Defendants' own interpretation of "donor" residue, Claim 5 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

185. Claim 6 of the '771 patent depends from claim 2 and specifies that "residue 110 of said composite heavy chain is donor."

186. On information and belief, under Defendants' interpretation of "donor" residue, residue 110 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

187. Under Defendants' own interpretation of "donor" residue, Claim 6 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

188. Claim 7 of the '771 patent specifies that "at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 72, 73, and 78 in the framework regions are non-human donor . . . ."

189. On information and belief, under Defendants' interpretation of "donor" residue, at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 72, 73, and 78 in the framework regions in the humanized heavy chain defined by claim 3 of the '510 patent are "donor."

190. Under Defendants' own interpretation of "donor" residue, Claim 7 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

191. Claim 8 of the '771 patent specifies that "at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 78, and 108 in the framework regions are non-human donor . . . ."

192. On information and belief, under Defendants' interpretation of "donor" residue, at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 78, and 108 in the framework regions in the humanized heavy chain defined by claim 3 of the '510 patent are "donor" residues.

193. Under Defendants' own interpretation of "donor" residue, Claim 8 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

194. Claim 9 of the '771 patent specifies that "at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 78, and 110 in the framework regions are non-human donor . . . ."

195. On information and belief, under Defendants' interpretation of "donor" residue, at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 78, and 110 in the framework regions in the humanized heavy chain defined by claim 3 of the '510 patent are "donor" residues.

196. Under Defendants' own interpretation of "donor" residue, Claim 9 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

197. Claim 10 of the '771 patent specifies that "at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 76, 78, 88, and 91 in the framework regions are non-human donor . . . ."

198. On information and belief, under Defendants' interpretation of "donor" residue, at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 76, 78, 88, and 91 in the framework regions in the humanized heavy chain defined by claim 3 of the '510 patent are "donor" residues.

199. Under Defendants' own interpretation of "donor" residue, Claim 10 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

200. Claim 11 of the '771 patent depends from claim 10 and specifies that "residue 2 of said composite heavy chain is donor."

201. On information and belief, under Defendants' interpretation of "donor" residue, residue 2 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

202. Under Defendants' own interpretation of "donor" residue, Claim 11 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

203. Claim 12 of the '771 patent depends from claim 10 and specifies that "residue 72 of said composite heavy chain is donor."

204. On information and belief, under Defendants' interpretation of "donor" residue, residue 72 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

205. Under Defendants' own interpretation of "donor" residue, Claim 12 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

206. Claim 13 of the '771 patent depends from claim 10 and specifies that "residue 108 of said composite heavy chain is donor."

207. On information and belief, under Defendants' interpretation of "donor" residue, residue 108 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

208. Under Defendants' own interpretation of "donor" residue, Claim 13 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

209. Claim 14 of the '771 patent depends from claim 10 and specifies that "residue 110 of said composite heavy chain is donor."

210. On information and belief, under Defendants' interpretation of "donor" residue, residue 110 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

211. Under Defendants' own interpretation of "donor" residue, Claim 14 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

212. Claim 15 of the '771 patent specifies that "at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 76, and 78 in the framework regions are non-human donor . . . ."

213. On information and belief, under Defendants' interpretation of "donor" residue, at least residues 31 to 35, 50 to 58 and 95 to 102 in the CDRs, and at least residues 6, 24, 48, 49, 71, 73, 76, and 78 in the framework regions in the humanized heavy chain defined by claim 3 of the '510 patent are "donor" residues.

214. Under Defendants' own interpretation of "donor" residue, Claim 15 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

215. Claim 16 of the '771 patent depends from claim 15 and specifies that "residue 2 of said composite heavy chain is donor."

216. On information and belief, under Defendants' interpretation of "donor" residue, residue 2 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

217. Under Defendants' own interpretation of "donor" residue, Claim 16 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

218. Claim 17 of the '771 patent depends from claim 15 and specifies that "residue 72 of said composite heavy chain is donor."

219. On information and belief, under Defendants' interpretation of "donor" residue, residue 72 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

220. Under Defendants' own interpretation of "donor" residue, Claim 17 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

221. Claim 18 of the '771 patent depends from claim 15 and specifies that "residue 108 of said composite heavy chain is donor."

222. On information and belief, under Defendants' interpretation of "donor" residue, residue 108 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

223. Under Defendants' own interpretation of "donor" residue, Claim 18 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

224. Claim 19 of the '771 patent depends from claim 15 and specifies that "residue 110 of said composite heavy chain is donor."

225. On information and belief, under Defendants' interpretation of "donor" residue, residue 110 in the humanized heavy chain defined by claim 3 of the '510 patent is a "donor" residue.

226. Under Defendants' own interpretation of "donor" residue, Claim 19 of the '771 patent is thus invalid for obviousness-type double patenting because it is anticipated by and/or obvious from the antibody molecule defined by claim 3 of the '510 patent.

227. Under Defendants' interpretation of "donor" residue, each and every claim of the '771 patent is anticipated by and/or obvious over at least claim 3 of the '510 patent under the one-way test for obviousness-type double patenting.

228. Under Defendants' interpretation of "donor" residue, each and every claim of the '771 patent is also invalid for obviousness-type double patenting over at least claim 1 of the '510 patent.

229. Claim 1 of the '510 patent specifies: "An antibody mol[e]cule which has specificity for human TNFα comprising a heavy chain and a light chain, said heavy chain having a variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID: NO. 6, SEQ ID: NO. 12, SEQ ID: NO. 16, and SEQ ID: NO. 20."

230. For the same reasons as set forth above in paragraphs 146–224, claim 1 of the '510 patent discloses humanized antibodies encompassed by each of the claims of the '771 patent.

231. On information and belief, under Defendants' interpretation of "donor" residue, claim 1 of the '510 patent discloses additional humanized antibodies, having the heavy chain variable region sequence set forth in SEQ ID NO: 12, that meet all of the limitations of each of the '771 patent claims.

232. Under Defendants' own interpretation of "donor" residue, each and every claim of the '771 patent is anticipated by and/or obvious over at least claim 1 of the '510 patent under the one-way test for obviousness-type double patenting.

233. Each of the claims of the '771 patent is therefore invalid for obviousness-type double patenting. *See, e.g.*, *In re Hubbell*, 709 F.3d at 1146; *In re Van Ornum*, 686 F.2d at 938.

234. Under Defendants' interpretation of "donor" residue, each and every claim of the '771 patent is also invalid for nonstatutory double patenting over at least claim 3 of the '510 patent based on equitable principles at least because the invention claimed in the '771 patent is not patentably distinct from the invention claimed in the '510 patent and because the term of the '771 patent would otherwise extend nearly ten years after the expiration of the term of the '510 patent.

235. One or more claims of the '771 patent are also invalid for failure to comply with one or more of the requirements for patentability set forth in Title 35 of the U.S. Patent Code, including 35 U.S.C. §§ 101, 102, 103, and/or 112.

236. One or more claims of the '771 patent are invalid under 35 U.S.C. § 101 for claiming patent ineligible subject matter.

237. One or more claims of the '771 patent are invalid under 35 U.S.C. § 102 as anticipated by, *inter alia*, U.S. Patent No. 5,585,089 to Queen et al. ("the Queen '089 patent").

238. The Queen '089 patent was filed on June 7, 1995 and claims priority to an application filed on Dec. 28, 1988.

239. Claim 1 of the '771 patent is invalid as anticipated by the Queen '089 patent because, *inter alia*, one or more humanized antibodies disclosed in the Queen '089 patent meet each of the limitations of claim 1 of the '771 patent under Defendants' interpretation of "donor" residue.

240. One or more claims of the '771 patent are invalid under 35 U.S.C. §§ 102(f) and/or 102(g)(2). On information and belief, the named inventors of the '771 patent did not themselves invent the subject matter patented in the '771 patent. On information and belief, the invention claimed in the '771 patent was made in this country by another inventor or inventors who had not abandoned, suppressed, or concealed it, including, *inter alia*, Cary Queen, Harold Selick, Lutz Riechmann, Michael Clark, Herman Waldmann, and/or Greg Winter.

241. One or more claims of the '771 patent are invalid under 35 U.S.C. § 103 as obvious over, *inter alia*, U.S. Patent No. 5,585,089 to Queen et al., U.S. Patent No. 5,530,101 to Queen et al. (filed Dec. 19, 1990 and claiming priority to an application filed Dec. 28, 1988), and/or Riechmann et al., "Reshaping human antibodies for therapy," Nature 332(6162):323–27

(1988) (published on or before March 1988), alone and/or in combination, in view of the general knowledge of a person of ordinary skill in the art. A person of ordinary skill in the art would have been motivated to combine these references because, *inter alia*, each is similarly directed to the making of humanized antibodies from non-human antibody sources, and would have had a reasonable expectation of success in making a humanized antibody meeting each of the limitations of the claims of the '771 patent based on, *inter alia*, the guidance in the prior art.

242. Each of the claims of the '771 patent are invalid under 35 U.S.C. § 112 because, *inter alia*, the purported invention is not adequately described by the disclosure of the '771 patent, because the '771 patent does not enable the full scope of the claims.

243. Claim 1 recites a broad range of potentially millions of different humanized antibodies comprising at least the non-human, "donor" residues in claim 1 and excluding only those with a fully chimeric heavy chain having a "donor" variable domain and a human constant domain.

244. Claim 1 of the '771 patent is invalid for lack of written description because, *inter alia*, the specification does not contain a sufficient number of representative examples of the broad genus of humanized antibodies having the non-human, "donor" residues specified in claim 1. Thus, the specification does not provide written description support for the broad genus of humanized antibodies encompassed by claim 1.

245. Claim 1 of the '771 patent is also invalid for lack of enablement because, *inter alia*, the specification does not provide examples of humanized antibodies across the broad range of humanized antibodies comprising at least the non-human, "donor" residues in claim 1 and excluding only a fully chimeric heavy chain with a "donor variable domain and a human constant domain" and does teach how to make such antibodies without undue experimentation.

Thus, claim 1 of the '771 patent is not enabled over the entire claimed range of humanized antibodies.

246. Claims 2–19 of the '771 patent are invalid for lack of written description and lack of enablement for the same reasons as set forth above in paragraphs 243–245.

247. Based on the foregoing, each claim of the '771 patent is invalid.

248. Plaintiffs are entitled to a declaratory judgment that the claims of the '771 patent are invalid.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs request that judgment be entered in favor of Plaintiffs and against UCB Bio:

(a) Declaring the claims of the '771 patent invalid;

(b) Awarding Plaintiffs their costs and attorneys' fees; and

(c) Awarding Plaintiffs such other relief as the nature of the case may admit or require, and any such other relief as may be deemed just and proper by this Court.

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Respectfully submitted,

By: _____

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