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Nelson Mullins Riley & Scarborough LLP/Alexion One Post Office Square 30th Floor Boston, MA 02109-2127			ROGERS, JAMES L	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Notice of Pre-AIA or AIA Status

The present application is being examined under the pre-AIA first to invent provisions.

This Office Action vacates the Office Action mailed on 5/31/2019 and resets the time to respond. The Office Action is identical to the correspondence mailed on 5/31/2019 except that the Office Action includes a TC Director's signature.

DETAILED ACTION

1. Claims 52-59 pending and under consideration in the instant examination.
2. Applicant's IDSs filed on 8/22/2017, 3/28/2018, 4/27/2018, and 4/29/2019 are acknowledged and have been considered.

Priority

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The priority date of the instant claims of the current application is considered to be 3/15/2007, the filing date of PCT/US2007/006606.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained even though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the

various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claim 52 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hillmen et al. (N Engl J Med 2004; 350: 552-9; IDS 8/22/2017), in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017), and Bowdish et al. (US 2003/232972; IDS 4/29/2019).

Hillmen teaches a method for treating a human patient that suffers from paroxysmal nocturnal hemoglobinuria (PNH) by administering to the patient an effective amount of eculizumab (p. 552, "methods) which specifically binds to the terminal complement protein C5, inhibiting its cleavage into C5a and C5b (p. 553, 3rd ¶).

Hillmen differs from the claimed invention in the recitation that the pharmaceutical composition comprises a 300 mg single-use formulation of 30 ml of a 10 mg/ml sterile, preservative free solution as in claim 6. Instead, Hillmen teaches that patients received infusion of 600 mg of eculizumab (treatment schedule at p. 554).

Evans teaches the antibody 5G1.1, eculizumab, is effective at doses of 2.2, 3, or 5 mg per kg body weight; this corresponds to 154, 210, or 350 mg of antibody for a 70kg adult human ('245 patent, column 16 lines 10-30). Evans (the '245 patent) also teaches that eculizumab is therapeutically effective when as little as 210 mg are present (column 16 lines 10-15). Evans teaches that the antibodies are particularly advantageous in that they are highly active even when administered in low doses (col 8 lines 25-32), providing a reasonable expectation of success in treating PNH with a dose less than what was disclosed by Hillmen. The reference teaches that it is within the skill of an artisan, particularly a physician, to determine the optimal dose (column 18 lines 15-30). Evans teaches formulations of the anti-C5 antibodies may be formulated in a pharmaceutically effective carrier such saline, which is considered to be a "preservative free solution". (col 18 lines 30-45).

Neither Hillmen nor the '245 patent (Evans) teaches a 300 mg single unit dosage as recited in the claims.

Nevertheless it would have been obvious to one of ordinary skill in the art to modify the teachings of Hillmen to administer 300 mg single unit dosages. Hillmen teaches that both 600 and 900 mg dosages can be used, and since Evans patent teaches that 210 or 350 mg of antibody would be expected to be therapeutically effective, arriving at the 300 mg dosage would be routine, convenient and obvious. One of ordinary skill in the art would have a reasonable expectation of success, as Evans teaches that the antibody exerts its effect at low doses.

It is further noted, [I]t is not inventive to discover the optimum or workable ranges by routine experimentation.” In re Aller, 220 F.2d 454, 456 (CCPA 1955); see also In re Peterson, 315 F.3d 1325 (Fed. Cir. 2003). “Only if the ‘results of optimizing a variable’ are ‘unexpectedly good’ can a patent be obtained for the claimed critical range.” In re Geisler, 116 F.3d 1465, 1469 (Fed. Cir. 1997) (quoting In re Antonie, 559 F.2d 618, 620 (CCPA 1977)). “[Discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art.” In re Boesch, 617 F.2d 272, 276 (CCPA 1980).

Finally, **Wang** teaches that eculizumab is highly soluble, including at up to 30 mg per ml (paragraph 0171, Figure 10). Wang further teaches that pharmaceutically acceptable carriers include pyrogen-free water may be used in formulation of the antibody (¶71) (sterile, preservative free solution). Therefore the artisan of ordinary skill would have had a reasonable expectation of success in making a 10 mg / ml solution of the antibody sterile, preservative free solution.

The combined references still do not precisely teach that the antibody that binds C5 has a heavy chain consisting of SEQ ID NO: 2 and a light chain consisting of SEQ ID NO: 4 as currently claimed.

Bowdish teaches construction of a 5G1.1+peptide antibody (see ¶191 which references Figs. 13A and 13B) having a humanized antibody H chain with an amino acid sequence (SEQ ID NO: 67) which has 96% sequence identity to the currently claimed heavy chain SEQ ID NO: 2. (see sequence alignment below)

```
Query Match          96.0%; Score 2300.5; DB 1; Length 472;\par
  Best Local Similarity 95.4%; \par
    Matches 437; Conservative 2; Mismatches 4; Indels 15; Gaps 2;\par
\par
Qy      1 QVQLVQSGAEVKKPGASVKVSCKASGYIFSNIQWVRQAPGQGLEWMGEILPGSGSTEY 60\par
      |||||
Db      20 QVQLVQSGAEVKKPGASVKVSCKASGYIFSNIQWVRQAPGQGLEWMGEILPGSGSTEY 79\par
\par
Qy      61 TENFKDRVMTTRDTSTSTVYMESSLRSEDTAVYYCAR-----YFFGSSPNWYFD 110\par
      |||||
Db      80 TENFKDRVMTTRDTSTSTVYMESSLRSEDTAVYYCARLPIEGPTLRQWLAARAP----- 134\par
\par
Qy      111 VWGQGTTLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS 170\par
      |||||
Db      135 VWGQGTTLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTS 194\par
\par
Qy      171 GVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVRKCCVECPP 230\par
      |||||
Db      195 GVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVRKCCVECPP 254\par
\par
Qy      231 CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKT 290\par
      |||||
Db      255 CPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHNAKT 314\par
\par
Qy      291 KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVY 350\par
      |||||
Db      315 KPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVY 374\par
\par
Qy      351 TLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSR 410\par
      |||||
Db      375 TLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSR 434\par
\par
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Qy      411  LTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK 448\par
          |||
Db      435  LTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK 472\par
```

Bowdish also teaches that the 5G1.1+ peptide has a humanized antibody L chain with an amino acid sequence (SEQ ID NO: 69) which has 100% sequence identity to the currently claimed light chain SEQ ID NO: 4 (see sequence alignment below).

```
Query Match          100.0%; Score 1110; DB 4; Length 236;
Best Local Similarity 100.0%;
Matches 214; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy      1  DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWFQQKPGKAPKLLIYGATNLDGVPS 60
          |||
Db      23  DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWFQQKPGKAPKLLIYGATNLDGVPS 82

Qy      61  RFSGSGSGTDFLTITISLQPEDFATYYCQNVLTPLTFGQGTKVEIKRTVAAPSVFIFPP 120
          |||
Db      83  RFSGSGSGTDFLTITISLQPEDFATYYCQNVLTPLTFGQGTKVEIKRTVAAPSVFIFPP 142

Qy      121 SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLT 180
          |||
Db      143 SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSLSTLT 202

Qy      181 LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC 214
          |||
Db      203 LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC 236
```

Bowdish further teaches that the sequence of the above **humanized antibody H chain** SEQ ID NO: 67, which as noted supra has 96% sequence identity to the currently claimed H chain SEQ ID NO: 2, is based on Evan's eculizumab 5G1.1 antibody framework from U.S. Application Ser. No. 06/487,263, which is the USD 6,355,245 Evans Patent supra, with the exception that the CD3 region was replaced with a TPO mimetic peptide sequence (¶191). (see Fig. 13A of Bowdish which depicts the TPO H chain sequence where the CDR3 region that has been substituted with the TPO mimetic is highlighted in bold).

→ (SEQ ID NO: 67)

5G1.1 - TPO Heavy Chain (Bold denotes TPO mimetic) Amino acid sequence:

MKIYSWVILFLLSVTAGVHSQVQLVQSGAEVKKPGASVKVSCKASGYIFSNIYWIQW
VRQAPGQGLEWMGEILPGSGSTEYTENFKDRVTMTTRDTSTSTVYMELSSLRSED
TAVYYCARLPIEGPTLRQWLAARAPYWGQGLTVTVSSASTKGPSVFPLAPCSR
STSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV
PSSNFGTQTYTCNVDPKPSNTKVDKTKVERKCCVECPPCAPPVAGPSVFLFPPKP
KDTLMISRTPEVTCVVVDVSDPEVQFNWYVDGVEVHNAKTKPREEQFNSTY
RVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTKAKGQPREPQVYTLPPSQ
EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRL
TVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK.

However, Evan's '245 Patent in Fig. 19 provides the missing CD3 sequence for the 5G1.1 eculizumab antibody (see Fig. 19 from Evans, which shows framework 5G1.1

antibody with the CDR3 sequence underlined).

```
-19                                     -1 +1
atg aaa tgg agc tgg gtt att ctc ttc CTC CTG TCA GTA ACT GCA GGT GTC CAC TCC CAG
M   K   W   S   W   V   I   L   F   L   L   S   V   T   A   G   V   H   S   Q

                                     10                                     20
GTT CAG CTG CAG CAG TCT GGA GCT GAG CTG ATG AAG CCT GGG GCC TCA GTG AAG ATG TCC
V   Q   L   Q   Q   S   G   A   E   L   M   K   P   G   A   S   V   K   M   S

                                     26                                     30                                     35                                     40
TGC AAG GCT ACT GGC TAC ATA TTC AGT AAC TAC TGG ATA CAG TGG ATA AAG CAG AGG CCT
C   K   A   T   G   Y   I   F   S   N   Y   W   I   Q   W   I   K   Q   R   P
                                     CDR-H1
                                     50                                     52a                                     60
GGA CAT GGC CTT GAG TGG ATT GGT GAG ATT TTA CCT GGA AGT GGT TCT ACT GAG TAC ACT
G   H   G   L   E   W   I   G   E   I   L   P   G   S   G   S   T   E   Y   T
                                     CDR-H2
                                     65                                     70                                     80
GAG AAC TTC AAG GAC AAG GCC GCA TTC ACT GCA GAT ACA TCC TCC AAC ACA GCC TAC ATG
E   N   F   K   D   K   A   A   F   T   A   D   T   S   S   N   T   A   Y   M

                                     82a 82b 82c                                     90                                     95
CAA CTC AGC AGC CTG ACA TCA GAG GAC TCT GCC GTC TAT TAC TGT GCA AGA TAT TTC TTC
Q   L   S   S   L   T   S   E   D   S   A   V   Y   Y   C   A   R   Y   F   F

                                     100 a b c d e                                     102                                     110
GGT AGT AGC CCC AAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC
G   S   S   P   N   W   Y   F   D   V   W   G   A   G   T   T   V   T   V   S
                                     CDR-H3

TCA
S
```

FIG.19

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute Bowdish's TPO mimic amino acid sequence in Bowdish's H chain published SEQ ID NO: 67 which is 96% identical with currently claimed H chain SEQ ID NO: 2 with Evan's CDR3 5G1.1 eculizumab amino acid sequence, thereby arriving at a H chain sequence having 100% sequence identity to currently claimed H chain SEQ ID NO: 2 and to have combined that H chain sequence with Bowdish's L chain SEQ ID NO 69 that has 100% sequence identity to currently claimed L chain SEQ ID NO: 4.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because Bowdish teaches that the 5G1.1+peptide antibody H chain is based on the 5G1.1 antibody framework taught by Evans, with the exception that the

CDR3 was replaced with a TPO mimic sequence. But the substituted CDR3 was taught by Evans. One of skill in the art would accordingly look to the '245 Evans Patent for the native CDR3. Evans Fig. 19 shows the heavy chain variable region as residues 95-102. Substituting the CDR3 from Evans into the heavy chain 5G1.1+ taught by Bowdish would result in a sequence having 100% sequence identity to currently claimed SEQ ID NO: 2. Bowdish also teaches that the light chain of 5G1.1" (published SEQ ID NO: 69), which as shown supra has 100% amino acid sequence identity to currently claimed L chain SEQ ID NO:4.

Thus upon reading Bowdish, one of ordinary skill in the art would have found it obvious to substitute CDRH3 from the 5G1.1 of Evans into the H chain SEQ ID NO: 67 which is only 96% identical in sequence identity due to the missing CDR3 region as taught by Bowdish to arrive at 100% sequence identity for the H chain of currently claimed SEQ ID NO: 2 and to pair it with the L chain SEQ ID NO: 69 from Bowdish, thereby producing an antibody identical to currently claimed SEQ ID NO: 2 and 4. The motivation to do so comes directly from the two references, as Bowdish indicates that the 5G1.1 sequence is that of Evans, albeit with an altered CDR3 in the heavy chain.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. Claims 52-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillmen et al. (N Engl J Med 2004; 350: 552-9; IDS 8/22/2017), in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017), and Bowdish et al. (US 2003/232972; IDS 4/29/2019), as applied to claim 52 above, and further in view of Bell et al. (US 2005/0191298; IDS 8/22/2017).

The prior art teachings of Hillmen, Evans, Wang, and Bowdish are discussed supra.

The teachings differs with respect to the characteristics of the patient population. For example, the references differ in the recitation that the patient has received at least four transfusion in the twelve months prior to administration of the antibody (claims 53 and 57), has a platelet count greater than or equal to 100k per microliter prior to administration of the antibody (claims 54 and 58).

The teachings also differ in the recitation that the patient exhibits decreased lactate dehydrogenase levels (claim 56).

The teachings also differ in the recitation that the patient is treated with the antibody for at least 26 weeks as in claims 55 and 59.

However, Hillmen further teaches that the patients in its study had received at least four red-cell transfusions in the preceding 12 months (p. 553, last 2 lines).

Bell also teaches treating PNH using an anti-C5 antibody such as h5G1.1 mAb eculizumab (¶52). Bells teaches that PNH patients were transfusion dependent and hemolytic with a history of four or more transfusion within 12 months (¶81).

Bell further teaches that the patient for treatment has a platelet count preferably in excess of 150k per microliter (¶67).

Bell further teaches that that patients received weekly intravenous infusion of anti-C5 antibody for 64 weeks (¶82).

Bell also teaches that lactate dehydrogenase levels (LDH) are used as an objective indicator of hemolysis and that LDH levels were decreased as a result of the treatment (¶85).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have continued eculizumab treatment for PNH for a period of at least 26 weeks to a patient population having received at least four transfusion in the twelve months prior to administration of eculizumab and having a platelet count in excess of 100k per microliter prior to administration of the antibody as well as to have also used a decreased LDH as a measure of clinical outcome in a method of treating PNH as taught by Hillmen. Those of skill in the art would have had reason to do so because Hillmen itself teaches that patients for treatment of PNH by administration of eculizumab had received at least 4 transfusion in the preceding 12 months, most preferably having a platelet count in excess of 150k, and Bell teaches that in the treatment of PNH with eculizumab, LDH is a known indicator of efficacy and that treatment can continue for 64 weeks, which is a period of greater than 26 weeks. The combination of familiar elements according to known methods is obvious when it does no more than yield predictable results (see *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1739 (2007)).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper time wise extension of the “right to exclude” granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(I)(1) - 706.02(I)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

8. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claim 1 of **US Patent 9,732,149**, in view of Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 149 Patent claim the same antibody having a H chain of SEQ ID NO: 2 and L chain of SEQ ID NO: 4.

While the '149 Patent is drawn to a composition whereas the current application is drawn to administering the antibody to a patient suffering from PNH, it is clear from the specification of the '149 that the intended use for the antibody is PNH (see abstract) and that said antibody is administered as a single unit dosage form at 300 mg in 30 ml of a 10 mg/ml sterile, preservative free solution (¶ before detailed description). See *Sun Pharmaceuticals Industries, Ltd., v. Eli Lilly and Company*, Fed. Cir. 2010 for the

appropriateness of making an ODP to a product claim where one of the intended uses of the product is for the method as now claimed).

While the '149 does not specifically recite some of the limitations contained in the dependent claims such as that the patient exhibits decreased LDH levels, these limitations would have been obvious in view of Bell as is discussed supra.

9. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-3 of **US Patent 9,718,880**, in view of Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 880 Patent claim the same antibody having a H chain of SEQ ID NO: 2 and L chain of SEQ ID NO: 4, in a sterile, preservative free 300 mg single-use dosage form comprising 30 ml of a 10 mg/ml solution..

While the '880 Patent is drawn to a composition whereas the current application is drawn to administering the antibody to a patient suffering from PNH, it is clear from the specification of the '149 that the intended use for the antibody is PNH (see abstract) and that said antibody is administered as a single unit dosage form at 300 mg in 30 ml of a 10 mg/ml sterile, preservative free solution (§ before detailed description). See *Sun Pharmaceuticals Industries, Ltd., v. Eli Lilly and Company*, Fed. Cir. 2010 for the appropriateness of making an ODP to a product claim where one of the intended uses of the product is for the method as now claimed).

While the '880 does not specifically recite some of the limitations contained in the dependent claims such as that the patient exhibits decreased LDH levels, these limitations would be obvious in view of Bell as is discussed supra.

10. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-10 of **US Patent 9,725,504**, in view of Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 504 Patent claim the same method of treating PNH using an antibody having a H chain of SEQ ID NO: 2 and L chain of SEQ ID NO: 4, in a sterile, preservative free 300 mg single-use dosage form comprising 30 ml of a 10 mg/ml solution. See in particular claims 1, and 4-6 of the '504 patent.

The '504 also claims a decreased in mean levels of LDH after administration (claim 9).

11. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-17 of **US Patent 9,409,980**, in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017) and Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 980 Patent appear to claim the same anti-C5 antibody (see claim 1 of the '980). In addition, the '980 claim using the antibody to treat PNH (see claim 17).

While the '980 does not specifically recite that the antibody is a single-unit dosage form of 300 mg in 30 mL of sterile, preservative free solution or the various limitations contained in the dependent claims, those limitation would be obvious in view of Evans, Wang and Bell as is discussed supra.

12. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-15 of **US Patent 9,415,102**, in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017) and Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 102 Patent appear to claim the same anti-C5 antibody (see claims 1-2 of the '102). In addition, the '102 claims using the antibody to treat PNH (see claim 17).

While the '102 Patent is drawn to a composition whereas the current application is drawn to administering the antibody to a patient suffering from PNH, it is clear from the specification of the '102 that the intended use for the antibody is PNH (see methods of treatment in the specification) See *Sun Pharmaceuticals Industries, Ltd., v. Eli Lilly and Company*, Fed. Cir. 2010 for the appropriateness of making an ODP to a product claim where one of the intended uses of the product is for the method as now claimed).

While the '102 does not specifically recite that the antibody is a single-unit dosage form of 300 mg in 30 mL of sterile, preservative free solution or the various limitations contained in the dependent claims, those limitation would be obvious in view of Evans, Wang and Bell as is discussed supra.

13. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-14 of **US Patent 9,556,263**, in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017) and Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 256 Patent appear to claim the same eculizumab antibody (see claim 1 of the '263). In addition, the '263 claim using the antibody to treat PNH (see claim 3).

While the '263 does not specifically recite that the antibody is a single-unit dosage form of 300 mg in 30 mL of sterile, preservative free solution or the various limitations contained in the dependent claims, those limitation would be obvious in view of Evans, Wang and Bell as is discussed supra.

14. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-12 of **US Patent 9,352,035**, in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017) and Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 035 Patent appear to claim the same eculizumab antibody (see claim 1 of the '035).

While the '035 Patent is drawn to a composition whereas the current application is drawn to administering the antibody to a patient suffering from PNH, it is clear from the specification of the '035 that the intended use for the antibody is PNH (see ¶129 of the '35 which lists PNH as one of the complement associated disorders that can be treated by the composition) See *Sun Pharmaceuticals Industries, Ltd., v. Eli Lilly and Company*, Fed. Cir. 2010 for the appropriateness of making an ODP to a product claim where one of the intended uses of the product is for the method as now claimed).

While the '035 does not specifically recite that the antibody is a single-unit dosage form of 300 mg in 30 mL of sterile, preservative free solution or the various limitations contained in the dependent claims, those limitation would be obvious in view of Evans, Wang and Bell as is discussed supra.

15. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-13 of **US Patent 9,925,262**, in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017) and Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 262 Patent claim the same method of treating PNH using an eculizumab antibody. See in particular claims 1, and 4 of the '262 patent.

While the '262 does not specifically recite that the antibody is a single-unit dosage form of 300 mg in 30 mL of sterile, preservative free solution or the various limitations contained in the dependent claims, those limitation would be obvious in view of Evans, Wang and Bell as is discussed supra.

16. Claims 52-59 are rejected on the ground of nonstatutory obviousness- type double patenting as being unpatentable over claims 1-33 of **US Patent 10,239,937**, in view of Evans et al. (US 6,355,245 B1, issued 3/12/2002; IDS 8/22/2017), Wang (US 2005/0271660; IDS 8/22/2017) and Bell et al. (US 2005/0191298; IDS 8/22/2017).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both the current application and 937 Patent claim the same method of treating PNH using an eculizumab antibody. See in particular claims 1, and 11 of the '937 patent.

While the '937 does not specifically recite that the antibody is a single-unit dosage form of 300 mg in 30 mL of sterile, preservative free solution or the various limitations contained in the dependent claims, those limitation would be obvious in view of Evans, Wang and Bell as is discussed supra.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Rogers whose telephone number is (571) 270-5374. The examiner can normally be reached Monday through Friday from 8:00 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Daniel Kolker** can be reached on (571) 272-3181. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

June 6, 2019

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