



Section 112(a) – Beyond *Amgen v. Sanofi*

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USPTO BCP Customer Partnership Meeting

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Regents of the University of Minnesota v. Gilead Sciences, Inc., 61 F.4th 1350 (Fed. Cir. 2023)

Background – Nucleotide Analogs

- University of Minnesota (Carston R. Wagner) obtained U.S. Patent No. 8,815,830 ('830 patent), which describes a class of nucleotide analogs that are believed to act as antiviral and anticancer agents.
- Gilead markets a nucleotide analog known as sofosbuvir in its Sovaldi[®], Harvoni[®], Epclusa[®], and Vosevi[®] products for the treatment of hepatitis C virus (HCV) infections.

Procedural Background

- University of Minnesota sued Gilead for infringement of '830 patent – No. 16-cv-2915 (D. Minn.)
 - Transferred to N.D. Cal. – 16-cv-2915, Dkt. 241 (D. Minn.)
- Gilead filed four petitions for IPR against '830 patent – IPR2017-01712; *also* IPR2017-01753, IPR2017-02004, IPR2017-02005
- District court action stayed pending resolution of IPR proceedings – No. 17-cv-6056, Dkt. 308 (N.D. Cal)

Gilead's IPR Contentions

- Challenged claims of '830 patent are not entitled to an effective filing date earlier than the actual filing date of the '830 patent
- Therefore, the challenged claims were anticipated by U.S. Publication No. 2010/0016251 (“Sofia”)
 - Sofia corresponds to U.S. Patent No. 7,964,580, which is listed in the Orange Book for Gilead's sofosbuvir products
 - No dispute that Sofia teaches all limitations of challenged claims

'830 Patent Priority Timeline

Description	Date
U.S. Provisional App. 60/634,677 ("P1")	Dec. 9, 2004
Int. App. PCT/US2005/044442 ("NP2")	Dec. 8, 2005
U.S. Patent App. 11/721,325 ("NP3")	June 8, 2007
Sofia Publication	Jan. 21, 2010
U.S. Patent App. 13/753,252 ("NP4")	Jan. 29, 2013

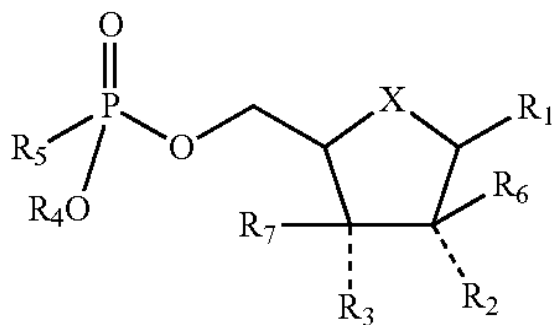
- '830 patent issued from application filed on March 28, 2014

PTAB Decision – Challenged Claims Invalid

- Challenged claims were not entitled to a priority date earlier than their own filing date of March 28, 2014
 - NP4 was filed after Sofia was published
 - NP3 has the same disclosure as NP2
 - NP2 and P1 (“NP2-P1”) did not contain written description for challenged claims – no *ipsis verbis* support or sufficient blaze marks
- Absent an earlier priority date, challenged claims were anticipated by Sofia

U.S. Patent No. 8,815,830, Claim 1

1. A compound of formula I:



wherein:

R_1 is guanine, cytosine, thymine, 3-deazaadenine, or uracil, optionally substituted by 1, 2, or 3 U; wherein each U is independently halo, hydroxy, (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, (C_1-C_6) alkoxy, (C_3-C_6) cycloalkyloxy, (C_1-C_6) alkanoyl, (C_1-C_6) alkanoyloxy, trifluoroethyl, hydroxy (C_1-C_6) alkyl, $-(CH_2)_{1-4}P(=O)(OR_w)_2$, aryl, aryl (C_1-C_6) alkyl, or NR_xR_y ;

R_2 is halo;

R_6 and R_7 are independently H or (C_1-C_6) alkyl;

I

R_3 is hydroxy;

R_4 is hydrogen, (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, aryl, aryl (C_1-C_6) alkyl, or 2-cyanoethyl;

R_5 is an amino acid;

X is oxy, thio, or methylene;

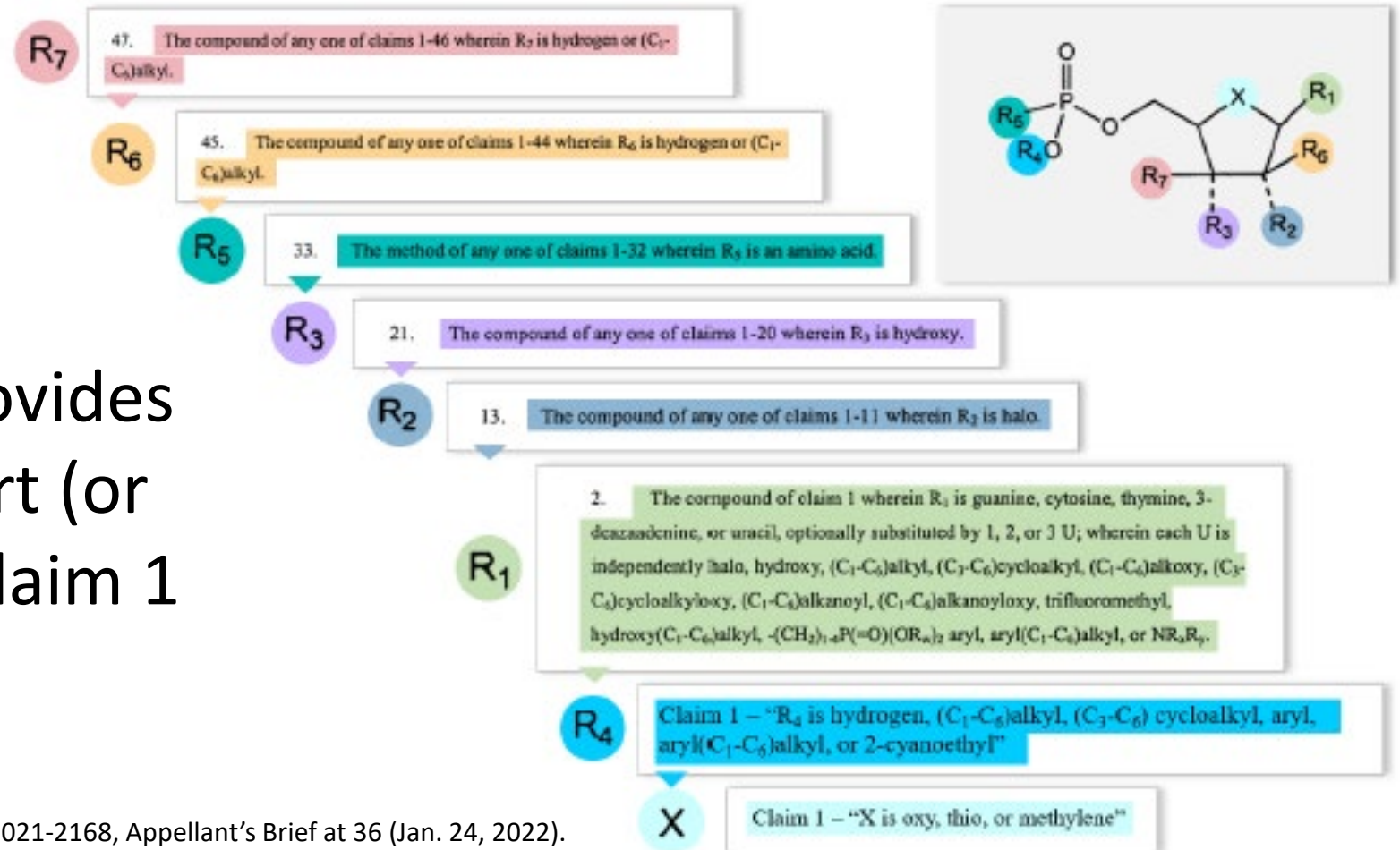
each R_w is independently hydrogen or (C_1-C_6) alkyl;

R_x and R_y are each independently hydrogen, (C_1-C_6) alkyl, (C_3-C_6) cycloalkyl, phenyl, benzyl, phenethyl, or (C_1-C_6) alkanoyl; or R_x and R_y together with the nitrogen to which they are attached are pyrrolidino, piperidino or morpholino;

(followed by several “wherein” clauses)

Minnesota Argument on Appeal

- Claim 47 of P1 provides *ipsis verbis* support (or blaze marks) for claim 1 of '830 patent



Regents of the Univ. of Minn. v. Gilead Scis., Inc. No. 2021-2168, Appellant's Brief at 36 (Jan. 24, 2022).

CAFC – No *Ipsis Verbis* Support

- “Following this maze-like path, each step providing multiple alternative paths, is not a written description of what might have been described if each of the optional steps had been set forth as the only option.”
- “[A]ll those optional choices do not define the intended result that is claim 1 of the ‘830 patent.”
- Cited *Fujikawa* for proposition that “laundry list” disclosure does not provide support for every species in genus.

Regents of the Univ. of Minn. v. Gilead Scis., Inc., 61 F.4th 1350, 1357 (Fed. Cir. 2023).

CAFC – No Blaze Marks

- “But again, similar to *Fujikawa*, even if P1 claim 47 ‘blaze[s] a trail through the forest’ that runs close to the later-claimed tree, the priority applications ‘do[] not direct one to the proposed tree in particular, and do[] not teach the point at which one should leave the trail to find it.’”

Regents of the Univ. of Minn. v. Gilead Scis., Inc., 61 F.4th 1350, 1358 (Fed. Cir. 2023).

United Therapeutics Corporation v. Liquidia Technologies, Inc., 74 F.4th 1360 (Fed. Cir. 2023)

Background – UTC and Liquidia Products

- United Therapeutics holds NDA for Tyvaso[®] (treprostinil) inhalation solution for treatment of pulmonary arterial hypertension (PAH) and pulmonary hypertension associated with interstitial lung disease (PH-ILD) to improve exercise ability.
- Liquidia Products filed NDA under §505(b)(2) of the FDCA seeking approval of Yutrepia (treprostinil) for dry inhalation.

U.S. Patent No. 10,716,793 ('793 patent)

- Listed in Orange Book for Tyvaso®
- Single independent claim:

1. A method of treating pulmonary hypertension comprising administering by inhalation to a human suffering from pulmonary hypertension a therapeutically effective single event dose of a formulation comprising treprostinil or a pharmaceutically acceptable salt thereof with an inhalation device, wherein the therapeutically effective single event dose comprises from 15 micrograms to 90 micrograms of treprostinil or a pharmaceutically acceptable salt thereof delivered in 1 to 3 breaths.

Pulmonary Hypertension

- Five subgroups – may require group-specific treatment
 - Group 1: Pulmonary arterial hypertension (PAH)
 - Group 2: Pulmonary venous hypertension, i.e., pulmonary hypertension related to left-heart disease
 - Group 3: Pulmonary hypertension associated with disorders damaging to the lungs
 - Group 4: Pulmonary hypertension caused by chronic thrombotic or embolic disease
 - Group 5: Miscellaneous pulmonary hypertension

District Court Proceedings

- United Therapeutics sued Liquidia Products for infringement of ‘793 patent and U.S. Patent No. 9,593,066
- District court held:
 - Administration of Yutrepia will directly infringe ‘793 patent
 - Liquidia Products will induce infringement of the ‘793 patent
 - Claims of ‘793 patent are not invalid for lack of enablement or written description
 - Construed “treating pulmonary hypertension” to encompass all five groups and not to require safety and efficacy

Construction of “Treating Pulmonary Hypertension”

- **Liquidia Products:** “treating pulmonary hypertension” should have been construed to require a showing of safety and efficacy (plain and ordinary meaning).
- **CAFC:** No additional safety and efficacy limitations
 - District court construed “therapeutically effective single event dose” = “dose given in single treatment session that causes *improvement in patient’s hemodynamics*” – not challenged on appeal
 - In this context, no basis for importing additional limitations

United Therapeutics Corp. v. Liquidia Techs., Inc., 74 F.4th 1360, 1368-69 (Fed. Cir. 2023).

Enablement – Liquidia’s Argument

- District court erred in finding that the claims are enabled
 - Specification provides no guidance or examples of treating Group 2 pulmonary hypertension patients
 - Even if claims are not construed to require safety, claims are not enabled because any changes in hemodynamics would provide no benefit to Group 2 patients
 - Therefore, claims are not enabled over the full scope of the claimed invention

United Therapeutics Corp. v. Liquidia Techs., Inc., 74 F.4th 1360, 1369 (Fed. Cir. 2023).

Enablement – CAFC Holding

- “[T]he claims are adequately enabled as they were construed by the district court.”
 - “The Court properly relied on . . . record evidence to conclude that a skilled artisan would understand that the claimed administration of treprostinil would . . . improve hemodynamics . . . independent of the type (*i.e.*, group) of pulmonary hypertension patient.”
 - “That was all that the claims require under the district court’s construction [which simply required improvement in hemodynamics].”
 - Failure of a study due to increased patient mortality is FDA issue.

United Therapeutics Corp. v. Liquidia Techs., Inc., 74 F.4th 1360, 1370 (Fed. Cir. 2023).

Written Description – Liquidia’s Argument

- District court erred in finding that the claims are supported by adequate written description
 - ‘793 patent never describes treating Group 2 pulmonary hypertension patients with treprostinil
 - Even if claims are not construed to require safety, claims lack written description because vasodilation is not effective in treating Group 2 patients
 - Therefore, skilled artisan would conclude that inventors were not in possession of a method of treating Group 2 patients with treprostinil

United Therapeutics Corp. v. Liquidia Techs., Inc., 74 F.4th 1360, 1369-70 (Fed. Cir. 2023).

Written Description – CAFC Holding

- “[T]he district court did not clearly err in finding that the claims of the ‘793 patent are supported by an adequate written description.”
 - “[T]he ‘793 patent claims require ‘treating pulmonary hypertension comprising administering . . . ‘therapeutically effective single event dose of a formulation containing treprostinil,’ and the specification describes that.”
 - “In other words, the specification shows possession for the claimed invention under the district court’s construction.”

United Therapeutics Corp. v. Liquidia Techs., Inc., 74 F.4th 1360, 1369-71 (Fed. Cir. 2023).

CAFC – General Comments

- “Liquidia essentially asks us to treat Group 2 PH as a claimed species within a larger genus (*i.e.*, all five groups of pulmonary hypertension).”
- “It would be incorrect to fractionate a disease or condition that a method of treatment claim is directed to, and to require a separate disclosure in the specification for each individual variant of the condition . . . in order to satisfy the enablement and written description provisions of 35 U.S.C. § 112, unless those variants are specified in the claims.”

United Therapeutics Corp. v. Liquidia Techs., Inc., 74 F.4th 1360, 1371 (Fed. Cir. 2023).

CAFC – General Comments (cont’d)

- “[F]or any given method of treatment claim, there may be a subset of patients who would not benefit from or should not take the claimed treatment. That does not mean that such claims are not sufficiently enabled or supported by written description.”
- “A subset of unresponsive patients is not analogous to unsupported species in a generic claim to chemical compounds.”

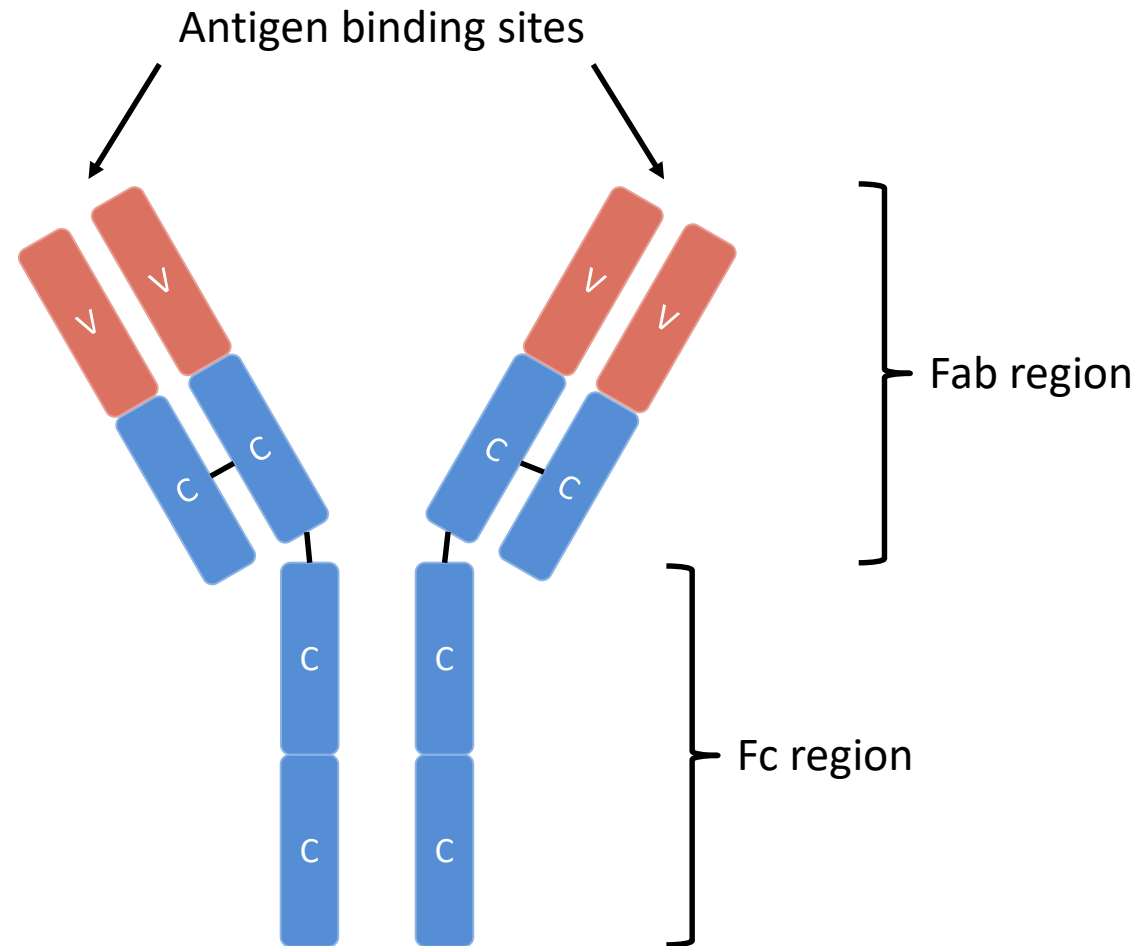
United Therapeutics Corp. v. Liquidia Techs., Inc., 74 F.4th 1360, 1371 (Fed. Cir. 2023).

Ex parte Chamberlain, Appeal 2022-001944, Application No. 16/803,690 (2023)

U.S. Patent Application No. 16/803,690

- **Title:** Fc variants with altered binding to FcRn
- **Inventors:** Chamberlain et al.
- **Applicant/Assignee:** Xencor, Inc.
- **Priority Claim:** 2008
- **Summary of the Invention:** “The present application is directed to Fc variants of a parent polypeptide [i.e., antibody] including at least one modification in the Fc region of the polypeptide.”

Background on Antibody Structure



Pending Claims

8. In a method of ***treating a patient by administering an anti-C5 antibody*** with an Fc domain, the improvement comprising said Fc domain comprising amino acid substitutions M428L/N434S as compared to a human Fc polypeptide, . . . wherein said anti-C5 antibody with said amino acid substitutions has increased in vivo half-life as compared to said antibody without said substitutions.

9. A method of ***treating a patient by administering an anti-C5 antibody*** comprising:

a) means for binding human C5 protein; and

b) an Fc domain comprising amino acid substitutions M428L/N434S as compared to a human Fc polypeptide, . . . wherein said anti-C5 antibody with said amino acid substitutions has increased in vivo half-life as compared to said antibody without said substitutions.

Final Office Action

- Rejection of claims 8 and 9 for lack of written description
 - Claims are broadly drawn to anti-C5 antibodies with Fc domain
 - Specification discloses only one specific anti-C5 antibody (5G1.1) and does not disclose structure
 - Jepson and means-plus-function claim format do not change written description requirement
- Rejection of claims 8 and 9 for obviousness type double patenting

PTAB Appeal Briefing

- Appellant challenged written description and obviousness type double patenting rejections
- Examiner withdrew written description rejections, but maintained obviousness type double patenting rejections

PTAB Holdings on Appeal

- New grounds of rejection
 - Lack of written description (claims 8 and 9)
 - Indefiniteness (claim 9)
- Affirmed 1 of 2 obviousness type double patenting rejections (claims 8 and 9)

Construction of “Anti-C5 Antibody”

- “We interpret ‘anti-C5 antibody’ to be an antibody that binds to the C5 complement protein in the normal way that antibodies bind to their cognate antigens (through the variable region of the antibody . . .).”
 - No limitation on structure of variable region
 - No limitation on epitopes of C5 to which antibody binds
 - No limitation on function or mechanism of action

Decision on Appeal at 6, *Ex parte Chamberlain*, Appeal 2022-001944 (PTAB Jan. 10, 2023).

Written Description Rejection

- “[T]he claims are directed to a broad and complex genus of anti-C5 antibodies.”
- Limited disclosure in Specification:
 - “The only anti-C5 antibody species disclosed in the Specification is ‘5G1.1.’”
 - “There is no correlation disclosed in the Specification between the function of the antibody to bind to C5 and treat the patient and to a structure of the antibody.”
- “We find that the disclosure of this single antibody species is insufficient to provide a description of the broadly claimed genus of antibodies which are used to treat a patient for an unspecified disease or condition.”

Decision on Appeal at 8-12, *Ex parte Chamberlain*, Appeal 2022-001944 (PTAB Jan. 10, 2023).

Appellant Counterargument (Claim 8)

- **Appellant:** Anti-C5 antibodies for treatment of patients were ***conventional and well-known*** (submitted list of antibodies)
- **PTAB:** Prior art antibodies do not provide written description
 - Based on the claim language, analysis focused on the four anti-C5 antibodies that had been used in the prior art ***to treat a patient***, not antibodies that were used only *in vitro* or in prophetic examples.
 - Even if more prior art antibodies are considered, Appellant has not explained how list provides a written description of the claimed broad genus – no identified ***structure-function relationship***.

Decision on Appeal at 12-18, *Ex parte Chamberlain*, Appeal 2022-001944 (PTAB Jan. 10, 2023).

Appellant Counterargument (Claim 8)

- **Appellant Counterargument:** When a claim is recited in the *Jepson claim format*, a written description of the claimed genus of anti-C5 antibodies can be established by reference to the prior art over which the improvement is claimed.
- **PTAB:** Putting claim in Jepson form does not change analysis
 - “It is the entirety of the claim that must be described, not just the improvement.”

Decision on Appeal at 19-27, *Ex parte Chamberlain*, Appeal 2022-001944 (PTAB Jan. 10, 2023).

Appellant Counterargument (Claim 9)

- **Appellant:** Claim recites “means for binding human C5 protein” and should be evaluated under section 112(f).
- **PTAB:**
 - Agreed that §112(f) applies because claim does not denote specific structure.
 - “As discussed for claim 8, there is inadequate disclosure of the antibody structure that binds to the C5 protein.”
 - “[E]ven if only one structure is required to meet section 112(f), the inquiry for compliance with section 112(a) does not end there.”

Decision on Appeal at 28-30, *Ex parte Chamberlain*, Appeal 2022-001944 (PTAB Jan. 10, 2023); Decision on Rehearing at 14, *id.* (June 1, 2023).

Subsequent Proceedings

- Appellant's Request for Rehearing was denied on June 1, 2023.
- Appellant appealed to Federal Circuit.
 - Appeal was docketed on June 21, 2023 (CAFC Appeal No. 2023-2048).
 - USPTO served certified list pursuant to Fed. Cir. R. 17(c) on July 31, 2023.
 - Appellant's principal brief is due September 29, 2023.