UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DAIICHI SANKYO, INC. AND
ASTRAZENECA PHARMACEUTICALS, LP
Petitioners

v.

SEAGEN INC.
Patent Owner

U.S. Patent No. 10,808,039

PETITION FOR POST-GRANT REVIEW
OF U.S. PATENT NO. 10,808,039

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Regulations

Other Authority

PETITIONER'S EXHIBIT LIST

No.	Reference	Referred To As
1001	U.S. Patent No. 10,808,039	'039 Patent
1002	Declaration of John M. Lambert, Ph.D.	Lambert Decl.
1003	Curriculum Vitae of John M. Lambert, Ph.D.	Lambert CV
1004	Press Release, Daiichi Sankyo, Daiichi Sankyo Announces Two Lancet Oncology Publications of Phase 1 Dose Expansion Results of [Fam-] Trastuzumab Deruxtecan in HER2 Positive Metastatic Breast and Gastric Cancer (Apr. 29, 2019)	DS's April 29, 2019 Press Release
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1006	October 19, 2020 Complaint	E.D. Tex. Complaint
1007	File History of European Patent Application No. 18,180,055	EP '055 Pat. Hist.
1008	European Patent Office Search Report (February 21, 2020) (Excerpt from File History of European Patent Application No. 20,151,269, excerpted from the '039 Pat. Hist.)	EP '269 Application Search Report
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	Antibody-Drug Conjugate, in Tumors with Human Epidermal Growth Factor Receptor 2 Heterogeneity, 107 CANCER SCI. 1039 (June 22, 2016)	
1010	As-filed Disclosure of U.S. Provisional Patent Application No. 60/518,534 (Excerpt from File History of International Patent Application No. PCT/US04/038392)	’534 Provisional
1011	As-filed Disclosure of U.S. Provisional Patent Application No. 60/557,116 (Excerpt from File History of U.S. Provisional Patent Application No. 60/557,116)	’116 Provisional
1012	As-filed Disclosure of U.S. Provisional Patent Application No. 60/598,899 (Excerpt from File History of U.S. Provisional Patent Application No. 60/598,899)	’899 Provisional
1013	As-filed Disclosure of U.S. Provisional Patent Application No. 60/622,455 (Excerpt from File History of U.S. Provisional Patent Application No. 60/622,455)	’455 Provisional
1014	As-filed Disclosure of U.S. Patent Application No. 10/983,340 (Excerpt from File History of U.S. Patent Application No. 10/983,340)	’340 Application
1015	As-filed Disclosure of U.S. Patent Application No. 11/833,954 (Excerpt from File History of U.S. Patent Application No. 11/833,954)	’954 Application
1016	As-filed Disclosure of U.S. Patent Application No. 13/098,391	’391 Application

	(Excerpt from File History of U.S. Patent Application No. 13/098,391)	
1017	As-filed Disclosure of U.S. Patent Application No. 14/194,106 (Excerpt from File History of U.S. Patent Application No. 14/194,106)	’106 Application
1018	As-filed Disclosure of U.S. Patent Application No. 15/188,843 (Excerpt from File History of U.S. Patent Application No. 15/188,843)	’843 Application
1019	As-filed Disclosure of U.S. Patent Application No. 15/811,190 (Excerpt from File History of U.S. Patent Application No. 15/811,190)	’190 Application
1020	Certified File History of U.S. Application No. 16/507,839 through July 20, 2020	’039 Pat. Hist.
1021	Nicolas Joubert et al., *Antibody-Drug Conjugates: The Last Decade*, 13(9) PHARMACEUTICALS 245 (2020)	Joubert
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1026	John M. Lambert & Ravi V.J. Chari, *Ado-trastuzumab Emtansine (T-DM1): An Antibody-Drug Conjugate (ADC) for HER2-Positive Breast Cancer*, 57(16) J. MED. CHEM. 6949 (2014)	Lambert & Chari
1027	Applicant Arguments/Remarks Made in an Amendment (October 14, 2010) (Excerpt from File History of U.S. Patent Application No. 12/016,978)	'978 Application Applicant Argument
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1072	RESERVED	

1073	US Patent No. 7,498,298	’298 Patent
1074	US Patent No. 7,994,135	’135 Patent
1075	US Patent No. 8,703,714	’714 Patent
1076	US Patent No. 10,414,826	’826 Patent

I. INTRODUCTION

Daiichi Sankyo, Inc. ("Daiichi Sankyo US") and AstraZeneca Pharmaceuticals, LP ("AstraZeneca US") (collectively, "Petitioners") request post-grant review of Claims 1–5, 9, and 10 of U.S. Patent No. 10,808,039 ("the '039 Patent") (Ex. 1001), assigned to Seagen Inc. ("Patent Owner" or "PO," formerly known as "Seattle Genetics, Inc."). 35 U.S.C. § 321.

The '039 Patent discloses antibody-drug conjugate ("ADC") compounds that share one signature feature: a dolastatin/auristatin-type drug moiety. This is plain from the '039 Patent's specification and the 10 applications to which it asserts priority, which date back to November 2003. In July 2019, after more than 15 years of prosecuting this patent family, PO abruptly dropped from the claims this signature feature and substituted an entirely new one with no basis in the specification: a tetrapeptide unit consisting of glycine and/or phenylalanine residues.

PO's pivot was no coincidence, conspicuously occurring just after public disclosures of (i) promising clinical data for DS-8201, a revolutionary cancer therapy discovered and patented by Daiichi Sankyo scientists many years before PO filed the July 2019, application that issued as the '039 Patent, and (ii) a $6.9 *billion* collaboration between Petitioners' overseas parent companies (Daiichi Sankyo Company, Limited ("Daiichi Sankyo Japan") and AstraZeneca UK

Limited ("AstraZeneca UK")) for the commercialization of DS-8201. (*See, e.g.*, Ex. 1004; Ex. 1005.) The '039 Patent thus reflects PO's transparent attempt to ensnare DS-8201, which has that newly claimed tetrapeptide but lacks PO's original signature, the dolastatin/auristatin-type drug moiety. Indeed, PO rushed to file a lawsuit in the United States District Court for the Eastern District of Texas alleging that DS-8201 falls within the claim scope of the '039 Patent. (Ex. 1006.)

PO's transparent effort to claim in a continuation application compositions that it did not invent mandates cancelation under 37 C.F.R. § 42.204(b). The challenged claims fail to meet several statutory requirements that prevent patent applicants from claiming later what they did not invent:

First, the challenged claims lack written description. 35 U.S.C. § 112(a). (*See infra* § VI.B; Ex. 1002 ¶¶ 99–117.) Specifically, Claims 1–5, 9, and 10 represent an impermissible attempt to claim technology that PO's scientists did not invent at any point in time, much less by the pre-2019 filing dates to which PO alleges priority. This is evident from the '039 Patent's specification and is consistent with on-point criticism that PO faced in its related prosecution efforts before the EPO. (*See, e.g.*, Ex. 1008 at 5 (recognizing PO's application to be "trying to lay claim on Daiichi S[ankyo]'s . . . very promising chemotherapeutic drug, by mixing and matching features not disclosed in combination in the original application"); Ex. 1007 at 497–503 (deeming PO's application to be withdrawn

after criticizing its "radical[] shift . . . away from what is on file").)[1]

Second, the '039 Patent does not enable the person of ordinary skill in the art ("POSA") to make and use the full scope of ADCs recited in Claims 1–5, 9, and 10 without undue experimentation. 35 U.S.C. § 112(a). (*See infra* § VI.C; *see, e.g.*, Ex. 1002 ¶¶ 122–57.) To the contrary, its disclosures are directed to ADCs that have a drug moiety that is a dolastatin/auristatin derivative. The '039 Patent also does not enable the POSA to make and use the full scope of claimed ADCs or to identify those ADCs that meet the claims' functional limitation. (*See, e.g.*, Ex. 1002 ¶¶ 128–33, 147–54.)

Third, Claims 1–5, 9, and 10 do not set forth what the '039 Patent's named inventors regarded as their inventions. 35 U.S.C. § 112(b). (*See infra* § VI.D; *see, e.g.*, Ex. 1002 ¶¶ 118–21.)

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[1] While prosecuting the '039 Patent, PO did not disclose to the PTO this application's existence or ultimate withdrawal after the EPO's criticisms and rejection of PO's efforts to obtain claims where "D is no longer limited to an auristatin/dolastatin analog." (Ex. 1007 at 499.)

Fourth, because Claims 1–5, 9, and 10 are not entitled to any priority date before the filing of the July 2019 application that first proposed them, they are anticipated by Daiichi Sankyo's earlier public disclosures of its drug, DS-8201, in, for example, Daiichi Sankyo's 2016 Cancer Science Publication (Ex. 1009 ("*DS Cancer Sci Article*")).[2] 35 U.S.C. § 102(a). (*See infra* § VI.E.)

II. STANDING AND GROUNDS

Petitioners certify that the '039 Patent is available for Post-Grant Review ("PGR") and Petitioners are not barred or estopped from requesting PGR of the '039 Patent on the grounds identified herein.

As established herein, the '039 Patent is eligible for PGR because it has at least one claim that is not entitled to any pre-AIA filing date. (*See infra* § VI.A–C.)

Petitioners respectfully request review of Claims 1–5, 9, and 10 ("challenged claims") of the '039 Patent, and cancellation of these claims as unpatentable.

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[2] This reference is prior art to the '039 Patent, which is not entitled to the benefit of any filing dates earlier than the July 10, 2019, filing date of U.S. Patent Application 16/507,839 ("the '839 Application"). (*See infra* § VI–VI.C.)

The challenged claims should be canceled as unpatentable on the following grounds:

Ground 1: Claims 1–5, 9, and 10 are unpatentable under AIA 35 U.S.C. § 112(a) as failing to satisfy the written description requirement.

Ground 2: Claims 1–5, 9, and 10 are unpatentable under AIA 35 U.S.C. § 112(a) as failing to satisfy the enablement requirement.

Ground 3: Claims 1–5, 9, and 10 are unpatentable under AIA 35 U.S.C. § 112(b) as failing to set forth subject matter that the named inventors regarded as the invention.

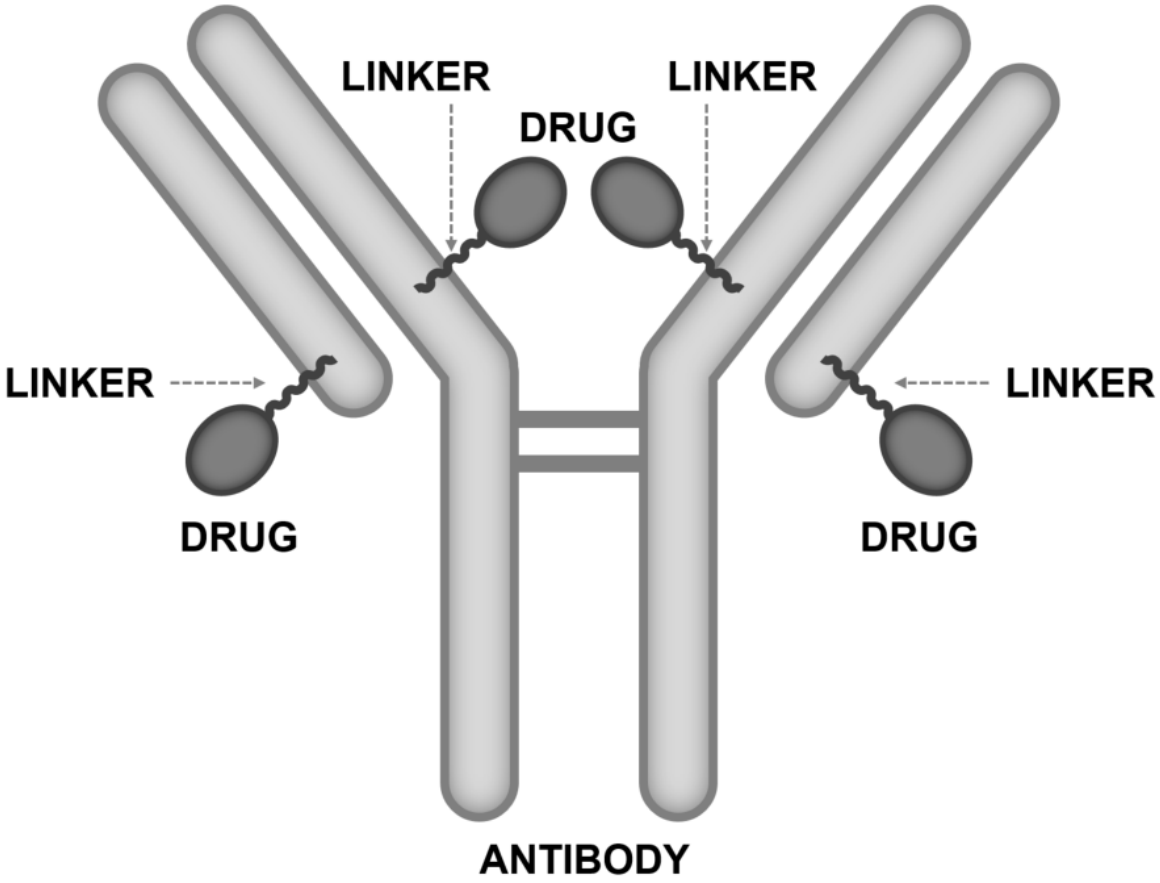
Ground 4: Claims 1–5, 9, and 10 are unpatentable under AIA 35 U.S.C. § 102(a)(1) as being anticipated by a scientific journal article by Daiichi Sankyo authors Yusuke Ogitani et al., "Bystander Killing Effect of DS-8201a, a Novel Anti-Human Epidermal Growth Factor Receptor 2 Antibody-Drug Conjugate, in Tumors with Human Epidermal Growth Factor Receptor 2 Heterogeneity," Cancer Science, (June 22, 2016) ("*DS Cancer Sci Article*"). (Ex. 1009.) *DS Cancer Sci Article* was published electronically on June 22, 2016, and in print in July 2016. (Ex. 1009.)

III. BACKGROUND OF THE ’039 PATENT

A. The Technology at Issue

ADCs are a type of therapeutic that uses antibodies to selectively deliver drugs to specific targets, such as cells that express a specific tumor-associated antigen. (*See, e.g.*, Ex. 1002 ¶¶ 31–32.[3]) In general terms, the antibody component of an ADC is connected (i.e., “conjugated”) to a “linker” that is attached to a drug:

[3] Petitioners’ Declarant, John M. Lambert, Ph.D., is an independent biotechnology consultant who has several decades of experience with antibodies and ADCs. (*See, e.g.*, Ex. 1002 ¶¶ 9–19; Ex. 1003.)



(Ex. 1002 ¶ 31.)

When designing ADCs, there are a host of complex factors to consider. (*See, e.g.*, Ex. 1002 ¶¶ 35–37.) Some of these factors relate to selection of a particular ADC component (e.g., linker susceptibility to enzymes and drug potency upon release). (*See, e.g.*, Ex. 1002 ¶¶ 38–51.) Others relate to how those components can be chemically bound to one another and how interactions among them can affect or impart properties on each ADC as a whole in physiological

environments (which may vary depending on the type of patient to which the ADC is administered). (*See, e.g.*, Ex. 1002 ¶¶ 35–40, 44–51.)

For instance, the POSA would have understood that some ADCs lack the requisite stability in a patient to survive the extracellular environment prior to cellular internalization. (*See, e.g.*, Ex. 1002 ¶¶ 45–51.) In other instances, ADCs may be capable of surviving the extracellular environment, but their components render them hydrophobic and lead to extracellular aggregation that prevents cellular internalization. (*See, e.g.*, Ex. 1002 ¶¶ 49, 51.) Other times, ADCs may be both stable and available for internalization, but they are not cleavable. (*See, e.g.*, Ex. 1002 ¶ 45.) ADC design is thus extremely difficult and involves much research, experimentation, and discovery. (*See, e.g.*, Ex. 1002 ¶¶ 35–40, 44–51.) ADC components cannot simply be mixed and matched, including because components can interact with each other and result in unpredictable properties. (*See, e.g.*, Ex. 1002 ¶¶ 35–37, 51, 141.)

The history of ADC development is illustrative. Prior to the 2003 filing of the first provisional application to which the ’039 Patent seeks to claim priority, only one ADC was FDA-approved, and many ADCs had failed clinical trials. (Ex. 1002 ¶ 41.) Even today, after several decades of dedicated ADC work, only 10 ADCs have received FDA approval. (Ex. 1002 ¶¶ 35 n.4, 41.) Of these 10 ADCs, four utilize a dolastatin/auristatin derivative. (Ex. 1002 ¶ 41.) As described

below, however, dolastatin/auristatin derivatives are just one type of ADC drug moiety. (*See, e.g.*, Ex. 1002 ¶¶ 7, 41–43.)

B. Real-World Developments Preceding the '039 Patent

The '039 Patent issued from the '839 Application, a July 10, 2019-filed utility application that asserts priority to (i) four provisional applications filed between November 2003 and October 2004[4] and (ii) six utility applications filed between November 2004 and November 2017.[5] Consistent with their disclosures, each of these priority applications, and all resulting patents, expressly limit all of

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[4] *See* As-filed Disclosures of U.S. Provisional Patent Application Nos. 60/518,534 (Ex. 1010); 60/557,116 (Ex. 1011); 60/598,899 (Ex. 1012) and 60/622,455 (Ex. 1013). Because the '116 and '899 Provisional Applications do not share at least one common inventor with the '039 Patent, it cannot be afforded their priority dates. *See, e.g., New Railhead Mfg., LLC v. Vermeer Mfg. Co.*, 298 F.3d 1290, 1294 (Fed. Cir. 2002).

[5] *See* As-filed Disclosures of U.S. Patent Application Nos. 10/983,340 (Ex. 1014); 11/833,954 (Ex. 1015); 13/098,391 (Ex. 1016); 14/194,106 (Ex. 1017); 15/188,843 (Ex. 1018); and 15/811,190 (Ex. 1019).

their claims to dolastatin/auristatin derivatives. (Exs. 1010–19, 1073–76; *see, e.g.*, Ex. 1002 ¶¶ 93, 95–98.)

In 2019, public disclosures of (i) promising clinical data concerning Daiichi Sankyo's novel ADC trastuzumab deruxtecan, which is known as DS-8201 and sold under the tradename "Enhertu®," and (ii) a $6.9 billion collaboration between Daiichi Sankyo Japan and AstraZeneca UK, (Ex. 1005; Ex. 1004), caused Seagen to abandon its consistent approach. Following these disclosures, in July 2019, PO filed the '839 Application, shifting strategy dramatically and proposing claims that purportedly sought to capture ADCs with drug moieties beyond dolastatin/auristatin derivatives. (Ex. 1020; Ex. 1002 ¶¶ 7–8, 93–98.) PO's motives did not escape the notice of objective observers, such as the EPO examiner tasked with providing a preliminary search report on such claims:

> ***It is quite manifest that Applicants are trying to lay claim on Daiichi Seyaku's [sic] Tz-exatecan (D4)***, a very promising chemotherapeutic drug, by mixing and matching features not disclosed in combination in the original application.

(Ex. 1008 at 5.)

PO's new approach coincided with a meritless arbitration claim, based on a long-expired contract that seeks patent rights and ownership of ADC technology that Daiichi Sankyo scientists invented, including the patent rights to Daiichi

Sankyo's novel drug, DS-8201. PO's arbitration claim is pending. (*See infra* § VIII.B–C.)

C. Disclosure of the '039 Patent

The '039 Patent, which issued from the '839 Application, relates to dolastatin/auristatin derivatives, including monomethyl auristatin E ("MMAE") and monomethyl auristatin F ("MMAF"). (Ex. 1001 at Abstract; Ex. 1002 ¶¶ 56, 61–64, 67–68, 67 n.8, 72, 94–97, 101–05, 109, 112–13, 118–20, 135, 139–40.) The '039 Patent notes a "clear need in the art for dolastatin/auristatin derivatives having significantly lower toxicity, yet useful therapeutic efficiency," touting its disclosed dolastatin/auristatin derivatives as an important advancement over what was known in the art.[6] (Ex. 1001 at 4:22–29; *see, e.g.*, Ex. 1002 ¶¶ 64, 102.)

[6] It is axiomatic that "incorporation by reference does not convert . . . incorporated [material] into the invention of the host patent." *Modine Mfg. Co. v. U.S. Int'l Trade Comm'n*, 75 F.3d 1545, 1553 (Fed. Cir. 1996), *abrogated on other grounds by Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 234 F.3d 558 (Fed. Cir. 2000); *Ex parte Michelle Fisher*, 2020 WL 3076451 at *8 (P.T.A.B. June 2,

Unsurprisingly, all of the claims in the applications to which the '039 Patent claims priority are narrowly directed to these dolastatin/auristatin derivatives. (*See, e.g.*, Ex. 1015 at Claims; Ex. 1016 at Claims; Ex. 1017 at Claims; Ex. 1018 at Claims; Ex. 1019 at Claims; Ex. 1002 ¶¶ 6, 61, 64, 67–68, 93–98.) Four of these patent applications gave rise to patents, and their issued claims are expressly limited to dolastatin/auristatin derivatives. (*See* Exs. 1073–1076 at Claims.)

The specification's focus on dolastatin/auristatin derivatives is emphasized throughout the '039 Patent disclosure. (*See, e.g.*, Ex. 1002 ¶¶ 61–64, 67–68, 72, 97, 101–07, 109, 112–13, 118–20, 135, 139–40.) For example, both the title and abstract focus on "monomethylvaline compounds" and "[a]uristatin peptides," which fall within the auristatin drug category. (Ex. 1001 at Cover; *see, e.g.*, Ex. 1002 ¶¶ 56, 67, 97, 101.) In disclosing the invention, the specification states that the "drug moiety (D) of the antibody drug conjugates (ADC) are of the dolastatin/auristatin type . . . ." (Ex. 1001 at 71:19–30; *see, e.g.*, Ex. 1002 ¶¶ 67, 95, 106, 126–27, 139.) Indeed, the only drug moiety used in the specification's

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2020) (affirming written description rejection because the POSA would not have recognized allegedly incorporated disclosures to be part of the instant invention).

examples and figures are dolastatin/auristatin derivatives. (*See, e.g.*, Ex. 1001 at Figs. 1–19, Examples 2–16; Ex. 1002 ¶¶ 67–68, 72, 97, 102–05, 109, 112–13, 118–20, 135, 140.)

Although the specification, examples, and figures of the '039 Patent are expressly limited to dolastatin/auristatin derivatives, Claims 1–5, 9, and 10 of the '039 Patent do not recite that limitation. (Ex. 1001 at 4:22–29, 71:19–30, Figs. 1–19, Examples 2–16; *see, e.g.*, Ex. 1002 ¶¶ 23, 63–64, 67–68, 72, 97, 101–07, 109, 112–13, 118–20, 135, 139–40.) Indeed, "dolastatin" and "auristatin" and their structures are entirely absent from Claims 1–5, 9, and 10. (Ex. 1001 at Claims; *see, e.g.*, Ex. 1002 ¶¶ 127, 139.) PO has clearly asserted that the challenged claims are not limited to dolastatin/auristatin derivatives (*see* Ex. 1006 at 8–9), and extend far beyond the subject matter the inventors disclosed in the specification and previously claimed in a decade and a half of patent prosecution based on that specification. (*See, e.g.*, Ex. 1002 ¶¶ 7–8, 23, 56–57, 79–80, 93, 100, 118–20.)

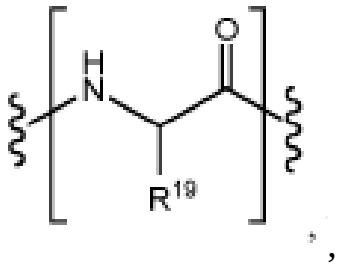
D. Prosecution History

In the 15 years preceding PO's filing of the '039 Patent, its prosecution efforts focused solely on dolastatin/auristatin derivatives. (*See infra* § VI.B.) That focus was not limited to the ADC context—some of the claims in this family recite dolastatin/auristatin derivatives in isolation (i.e., not attached to an ADC linker). (*See, e.g.*, Ex. 1073 at Claims.) Only after four provisional applications, six utility

applications, four issued patents, and—most importantly—public reporting in 2019 of Daiichi Sankyo's clinical success and $6.9 billion commercial collaboration, did PO attempt to lay claim to ADCs not limited to these drug moieties. (*See infra* § III.C; Ex. 1005.)

PO's shift toward Daiichi Sankyo's DS-8201 is reflected in the as-filed claims of its '839 Application, which are directed toward purportedly novel ADCs having, among other things, "drug moiet[ies]" that are not expressly limited to dolastatin/auristatin derivatives, or to any specific drug moiety structures at all, and, in *dependent* claims, tetrapeptides having only glycine and/or phenylalanine residues ("gly/phe-only tetrapeptides"). (Ex. 1020 at 458–59 (*see, e.g.*, Claims 1 and 5).) PO submitted with the '839 Application a letter that purported to identify "support" in PO's pre-existing specification. (*Id*. at 125–27.) As explained below, the "[s]upport" identified in this letter is deficient. (*See infra* § VI.A.)

Following a restriction requirement (which resulted in PO's election of claims drawn to ADCs, as opposed to methods for treating cancer) and in response to rejections for anticipation and obviousness, PO submitted an amendment. (Ex. 1020 at 454–61.) Among other changes, PO amended its sole independent claim to require a tetrapeptide unit wherein each amino acid unit in the tetrapeptide independently has the structure depicted below:



wherein the "R^{19}" side chain attached to each amino acid is either a hydrogen atom or a benzyl group (meaning each amino acid ("residue") is either a glycine ("gly") or a phenylalanine ("phe")). (Ex. 1001 at Claims; *see, e.g.*, Ex. 1020 at 768–72; Ex. 1002 ¶ 60.) For brevity, this limitation will be referred to herein as the "Gly/Phe-Only Tetrapeptide Limitation."

Despite PO's "Gly/Phe-Only Tetrapeptide Limitation," the Examiner again rejected PO's claims, this time for obviousness[7] over a combination of two prior art references that disclosed (1) ADCs having a gly-phe-leu[8]-gly tetrapeptide (*see* Ex. 1023 at 855 ("Dubowchik") and (2) polymeric carrier conjugates ("PCCs") having gly/phe-only tetrapeptides (*see* Ex. 1024 at 1931 ("Nogusa")). (Ex. 1020 at

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[7] PO faced rejections under 35 U.S.C. § 112, but they were based on indefiniteness of claims depending from withdrawn claims. (*See* Ex. 1020 at 897.)

[8] "Leu," is an abbreviation for the amino acid leucine, whose side chain is neither a hydrogen nor a benzyl group. (Ex. 1002 ¶ 74.)

897–902.) Responding to this rejection, PO argued that ADCs, unlike Nogusa's PCCs, must be capable of entering a cell to undergo intracellular cleavage. (*See id.* at 932 ("[The ADC] must be capable of entering a cell expressing a cell-surface receptor specific for the antibody such that the drug moiety in the [ADC] is intracellularly cleaved (as recited in Claim 1 as amended)").) Following the aforementioned rejection, PO again amended its sole independent claim to recite a functional limitation (previously found only in the dependent claims) requiring that "the drug moiety is intracellularly cleaved in a patient from the antibody of the antibody-drug conjugate or an intracellular metabolite of the antibody-drug conjugate." (*Id.* at 926, 929.) For brevity, this limitation is referred to herein as the "Intracellular Cleavage Limitation."

IV. CLAIM CONSTRUCTION

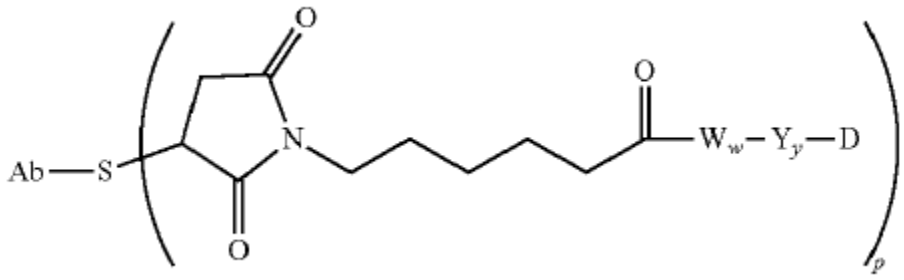
The applicable claim construction standard is articulated in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*). 37 C.F.R. § 42.200(b). When applying this standard, the Board "do[es] not apply a rule of construction with an aim to preserve the validity of the claims." *Groupon, Inc. v. Kroy IP Holdings, LLC*, IPR2019-00061, Paper 12 at 14 (P.T.A.B. Apr. 19, 2019). It need only construe terms "that are in controversy, and only to the extent necessary to resolve the controversy." *Vivid Techs., Inc. v. Am. Sci. & Eng'g, Inc.*, 200 F.3d 795, 803 (Fed. Cir. 1999); *see also Hybrigenics SA v. Forma Therapeutics, Inc.*,

PGR2018-00098, Paper 10 at 10–11, 18, 48 (P.T.A.B. Mar. 20, 2019).

Pursuant to 37 C.F.R. § 42.204(b)(3), Petitioners identify for use in this PGR the apparent claim construction for "drug moiety" that is urged by PO in related infringement litigation ("the Texas Litigation," *see infra* § VIII.B).[9] *See 10X Genomics, Inc. v. Bio-Rad Lab'ys, Inc.*, IPR2020-00088, Paper 8 at 15–18 (P.T.A.B. Apr. 27, 2020); *Western Digital Corp., v. SPEX Techs. Inc.*, IPR2018-00084, Paper 14 at 11–12 (P.T.A.B. Apr. 25, 2018).

This claim term first appears in independent Claim 1, which recites a genus of ADCs having particular biochemical properties and a particular "formula," depicted below:

[9] An alternative interpretation of "drug moiety" would limit that term, on the basis of definitional language in the specification, to dolastatin/auristatin derivatives. This Petition is based on the claim construction urged by PO in the Texas Litigation. (*See* Ex. 1006.)



Claim 1 further recites that "D" is "a drug moiety." (Ex. 1001 at 331:35–45, 66.)

PO's construction of "drug moiety" lacks structural limitation and is broad enough to encompass all drug moieties, and not just dolastatin/auristatin derivatives. (Ex. 1006 at 9.) Indeed, in the Texas Litigation, PO interpreted independent Claim 1 to cover Enhertu®, alleging "the drug that is conjugated to the antibody with the linker is the camptothecin derivative DXd, which acts as a topoisomerase inhibitor." (Ex. 1006 at 9.) In asserting it is met by Enhertu®, PO did not impose any structural limitation of any sort on the claim term "drug moiety," interpreting it to encompass any substance that exerts a physiological effect, such as topoisomerase inhibition. Moreover, in prosecuting a European counterpart to the '039 Patent, PO tellingly did not dispute the EPO's interpretation

of "drug moiety" to mean "any drug."[10] (Ex. 1007 at 499–502.)

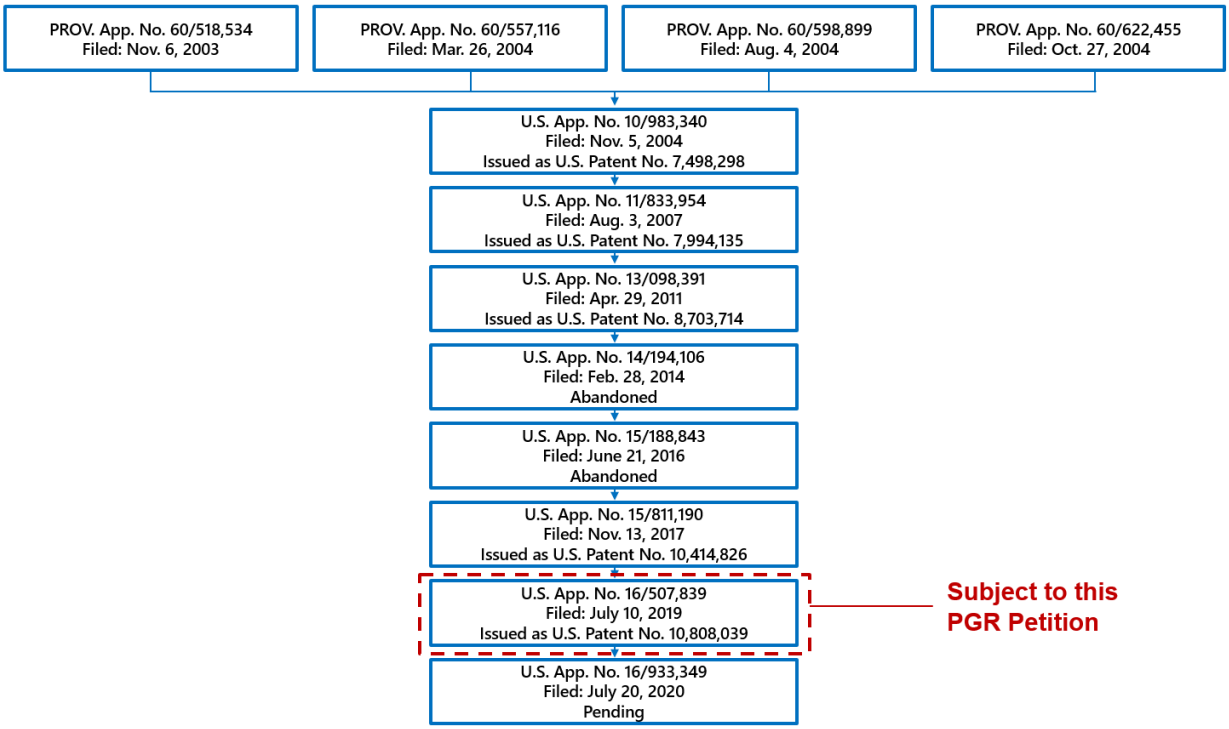
V. LEVEL OF ORDINARY SKILL IN THE ART

According to Dr. Lambert, the POSA in the field of the '039 Patent would have had either (1) a Ph.D. in biochemistry or a similar field, or (2) a master's degree in biochemistry or a similar field with at least two to three years of experience with ADC design. (Ex. 1002 ¶ 20.) More education can supplement practical experience, and vice-versa. (*Id.*) This high level of skill in the ADC field is applicable as of the filing of the provisional applications through to July 2019, the '039 Patent's effective filing date, as described below.

VI. THE CHALLENGED CLAIMS ARE UNPATENTABLE

The '039 Patent issued from an application filed on July 10, 2019, and is eligible for PGR. It claims priority to a series of applications filed prior to the effective date of the America Invents Act. The relationship of '039 Patent to those applications, as well as patents issued therefrom, is shown in the purported priority chain below:

[10] The EPO itself recognized that PO was "trying to lay claim on" Enhertu®. (Ex. 1008 at 5.)



Because these priority applications fail to support Claims 1–5, 9, and 10 under 35 U.S.C. § 112, *PowerOasis, Inc. v. T–Mobile USA, Inc.*, 522 F.3d 1299, 1306 (Fed. Cir. 2008), these challenged claim are all eligible for PGR. *See, e.g.*, *Eli Lilly & Co. v. Genentech, Inc.*, PGR2019-00043, Paper 11 at 11 (P.T.A.B. Oct. 7, 2019) (collecting cases); *U.S. Endodontics v. Gold Standard Instruments, LLC*, PGR2015-00019, Paper 54 at 11–12 (P.T.A.B. Dec. 28, 2016); *Schul Int'l Co. v. Emseal Joint Sys., Ltd.*, PGR2017-00053, Paper 10 at 12–13 (P.T.A.B. Apr. 9, 2018); *Inguran, LLC v. Premium Genetics (UK) Ltd.*, PGR2015-00017, Paper 8 at 17–18 (P.T.A.B. Dec. 22, 2015).

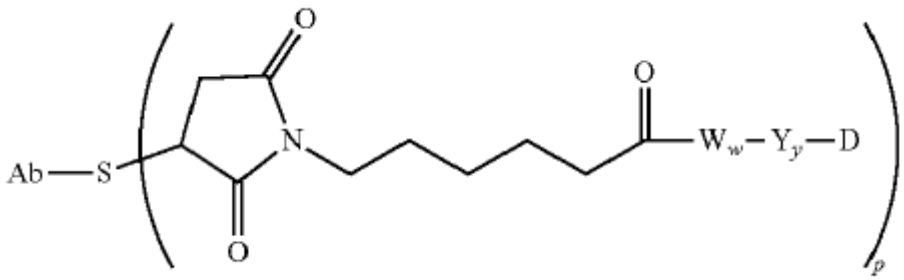
The claims lack priority support for at least three reasons. First, PO's priority applications lack written description support for the Gly/Phe-Only Tetrapeptide Limitation of Claims 1–5, 9, and 10, which first appeared in the July 10, 2019, application that issued as the '039 Patent. (*See infra* § VI.A.) Second, PO's priority applications lack written description support for the full scope of claimed ADCs, particularly the virtually limitless genus of ADCs having drug moieties other than dolastatin/auristatin derivatives. The '039 Patent itself shares this lack of written description, as explained in Ground 1. (*See infra* § VI.B.) Third, PO's priority applications fail to enable the full scope of claimed ADCs, including ADCs having drug moieties other than dolastatin/auristatin derivatives. The '039 Patent itself is similarly deficient, as explained in Ground 2. (*See infra* § VI.C.)

The dearth of priority support for Claims 1–5, 9, and 10 illustrates PO's Enhertu®-inspired claiming strategy, which itself is sufficient to render the claims unpatentable for failing to set forth what the named inventors regarded as their inventions, as explained in Ground 3. (*See infra* § VI.D.) Moreover, because the claims have an effective filing date of July 10, 2019 (for any of the three reasons outlined above), pre-existing public disclosures of Enhertu® are prior art. For example, a 2016 scientific journal article by Daiichi Sankyo authors (Ex. 1009) qualifies as § 102(a)(1) prior art and anticipates Claims 1–5, 9, and 10, as

explained in Ground 4. (*See infra* § VI.E.)

A. PO's Priority Applications Do Not Support ADCs Having a Gly/Phe-Only Tetrapeptide

Independent Claim 1 of the '039 Patent recites the following formula for the ADCs of the claim:



(Ex. 1001 at 331:35–45.) Claim 1 further requires that "W_w" is a "tetrapeptide" in which each of the four amino acids has (i) a backbone that is not N-methylated and (ii) a side chain that is either "hydrogen or benzyl," i.e., the amino acids must be glycine or phenylalanine. (*See, e.g.*, Ex. 1002 ¶ 58; Ex. 1020 at 769, 773 ("Claim 1 recites the W_w unit to be a ***tetrapeptide, with each amino acid being independently glycine or phenylalanine***.") (emphasis in original).) Because phenylalanine has two possible stereoisomers and glycine has one, the genus of tetrapeptides recited in Claims 1–5, 9, and 10 encompasses 3^4 (i.e., 81) different

species.[11] (*See, e.g.*, Ex. 1002 ¶¶ 81–83, 83 n.13.) PO's priority applications identify none of them.

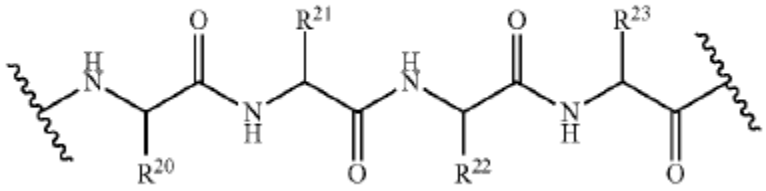
In fact, PO's priority applications identify no linkers having amino acid units—of any length—that are entirely composed of glycine and/or phenylalanine residues. Instead, they prophetically disclose linkers having amino acid units that are a "dipeptide, tripeptide, tetrapeptide, pentapeptide, hexapeptide, heptapeptide, octapeptide, nonapeptide, decapeptide, undecapeptide or dodecapeptide unit." (*See, e.g.*, Ex. 1010 at 23; Ex. 1011 at 23; Ex. 1012 at 73; Ex. 1013 at 67; Ex. 1014 at 85; Ex. 1015 at 87; Ex. 1016 at 87; Ex. 1017 at 86; Ex. 1018 at 86; Ex. 1019 at 86; Ex. 1002 ¶ 84.) They further disclose that each residue within an amino acid unit "independently" has a backbone that is, optionally, N-methylated. (Ex. 1001 at 65:53–64 (N-methylated backbone at right); *see, e.g.*, Ex. 1002 ¶ 90.)

[11] The '039 Patent's specification states that the amino acids in a linker may independently be L-amino acids or D-amino acids. (*See, e.g.*, Ex. 1001 at 67:66–67; *see also, e.g.*, Ex. 1001 at 137:15–28 (embodiments having only L-amino acids, only D-amino acids, and combinations thereof); Ex. 1002 ¶ 66.)

These disclosures are not limited by the identity of the particular amino acids, let alone to glycine and phenylalanine in particular. On the contrary, the priority applications allow for each non-N-methylated residue of an amino acid unit to "independently" be any of 83 potential options. (*See* Ex. 1002 ¶ 82 (explaining that the 39 side chains identified in specification provide 83 potential options, because 35 of those residues may exist in either of two stereoisomers, three of them may exist in any of four stereoisomers, and glycine may exist in only one stereoisomer); *see, e.g.*, Ex. 1010 at 23–24; Ex. 1011 at 23–24; Ex. 1012 at 73–74; Ex. 1013 at 67–68; Ex. 1014 at 85; Ex. 1015 at 87; Ex. 1016 at 87; Ex. 1017 at 86; Ex. 1018 at 86; Ex. 1019 at 86.)

Consequently, the priority applications reference 83^4 (i.e., over 47 million) different species of tetrapeptide amino acid units having the (non-N-methylated) backbone recited in Claims 1–5, 9, and 10. (Ex. 1002 ¶ 83.) Yet the priority applications actually identify just two of those—and neither meets the side-chain limitations recited in Claims 1–5, 9, and 10 (i.e., that each R group is independently hydrogen or benzyl):

(IX)



wherein R^{20}, R^{21}, R^{22} and R^{23} are as follows:

R^{20}	R^{21}	R^{22}	R^{23}
H	benzyl	isobutyl	H; and
methyl	isobutyl	methyl	isobutyl.

(Ex. 1001 at 67:35–50; *see, e.g.*, Ex. 1002 ¶¶ 86, 88.) Nor do the priority applications identify tetrapeptides as useful for conjugates in which the ligand is an *antibody*. (Ex. 1001 at 65:45–50 (linking drug units to *ligand* units), 63:16–38 (same); *see, e.g.*, Ex. 1002 ¶ 87.)

The priority applications exemplify ADCs that either (i) lack an amino acid unit or (ii) have a dipeptide that is either valine-citrulline or phenylalanine-lysine. (*See, e.g.*, Ex. 1002 ¶¶ 72, 83.) Consistent with the rest of the specification, the priority applications' examples do *not* include any ADC having a tetrapeptide, let alone any of the 81 species of tetrapeptides that fall within the scope of Claims 1–5, 9, and 10. (*See, e.g.*, Ex. 1002 ¶ 83.) This failure to identify the specifically claimed genus of tetrapeptides—or even a single member of the claimed subgenus—dooms PO's claim of priority.

The Federal Circuit's "blaze marks" case law forecloses PO's effort to claim, on the basis of the specification's sweeping reference to over 47 million non-N-methylated tetrapeptides, a narrower subgenus of 81 tetrapeptides wherein each side chain is independently hydrogen or benzyl. "One cannot disclose a forest in the original application, and then later pick a tree out of the forest and say here is my invention." *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326 (Fed. Cir. 2000). Yet that is what PO did here, where the only blaze marks to any subgenus in the application point *away* from the later-claimed genus.

The Federal Circuit has held repeatedly that such after-the-invention claiming of subgenuses is improper. *See, e.g.*, *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1164 (Fed. Cir. 2019); *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570 (Fed. Cir. 1996). This black-letter rule dates back to the Court of Patent and Customs Appeals, which explained that supporting a claimed genus requires a "guide indicating or directing that this particular selection should be made rather than any of the many others which could also be made." *In re Ruschig*, 379 F.2d 990, 995 (C.C.P.A. 1967).

For example, the application in *Fujikawa* disclosed a molecule with, among other features, a substituent labeled "R," for which "R" could be any of several options, including "most preferably methyl or isopropyl." 93 F.3d at 1570. The court analyzed whether the application adequately described a count to molecules

in which "R" was "cyclopropyl," and held that it did not. *See id.* at 1571. The court reached that conclusion despite the fact that the application "lists cyclopropyl as one possible moiety for R in his disclosure of the genus." *Id.* It reasoned that "just because a moiety is listed as one possible choice for one position does not mean there is *ipsis verbis* support for every species of sub-genus that chooses that moiety." *Id.* The court rejected the notion that "a 'laundry list' disclosure of every possible moiety for every possible position would constitute a written description of every species in the genus." *Id.* PO's disclosure of 83 different non-N-methylated amino acids that could be used in a peptide linker is no different from *Fujikawa*'s "laundry list," and it similarly cannot as a matter of law be interpreted to describe "every possible moiety for every possible position." *Id.*

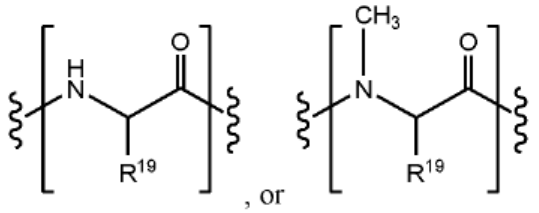
PO's effort to claim a gly/phe-only tetrapeptides here is particularly egregious because, as in *Idenix*, 941 F.3d at 1165, the priority applications *do* disclose a particular subgenus, just not the claimed subgenus. Formula IX encompasses two tetrapeptide sequences, but neither falls within the scope of tetrapeptides recited in Claims 1–5, 9, and 10. Therefore the priority applications do not "'reasonably lead' those skilled in the art" to the claimed genus. *Fujikawa*, 93 F.3d at 1571.

The first and only disclosure of the claimed subgenus of gly/phe-only tetrapeptides appears in the new claims submitted with the July 10, 2019,

application (Ex. 1020 at 397–98 (*e.g.*, Claim 5); *see, e.g.*, Ex. 1002 ¶¶ 75, 80), filed just a few months after the announcement of a Daiichi Sankyo Japan and AstraZeneca UK collaboration to bring Enhertu® (with its gly-gly-phe-gly linker) to market. (*See* Ex. 1020 at 1; Ex. 1005.) Those claims introduced new matter that appears nowhere in the specification, in a transparent attempt to cover a competitor's invention—precisely the type of overreach that the written description requirement proscribes. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1353–54 (Fed. Cir. 2010) (en banc).

Notwithstanding the clear absence of any description of a tetrapeptide containing only glycine and phenylalanine, PO advised the Examiner that it "believes no new matter is added" in connection with its new July 2019 claims. (Ex. 1020 at 457.) Claim 2 required that the recited ADCs' linker be comprised of glycine or phenylalanine. (*Id.* at 458–59.) Claim 5 required that this linker be a tetrapeptide. (*Id.* at 459.) The only support identified by PO for these claims respectively was "page 92, lines 2-5" and "page 92, line 1" of the specification. (*Id.* at 126.) Those lines, reproduced below, were plucked out selectively from the much larger disclosure of a genus of linkers discussed above:

W_w- is a dipeptide, tripeptide, tetrapeptide, pentapeptide, hexapeptide, heptapeptide, octapeptide, nonapeptide, decapeptide, undecapeptide or dodecapeptide unit. Each -W- unit independently has the formula denoted below in the square brackets, and w is an integer ranging from 0 to 12:



, or

wherein R^{19} is hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, benzyl, *p*-

(*Id.* at 246 (Specification page 92).)

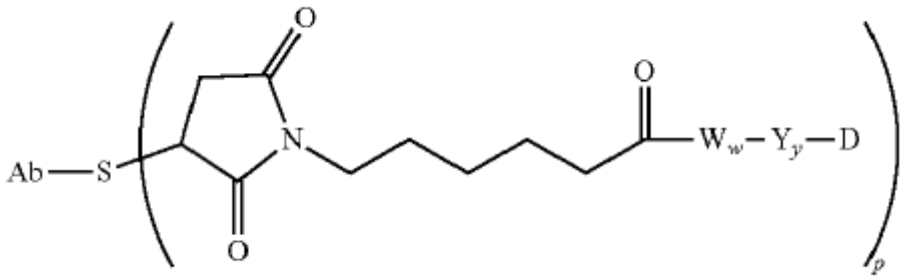
PO's prosecution argument was deficient for several reasons. First, contrary to the expurgated passage PO cited, the specification's actual disclosure of amino acid side chains is not limited to a single line reciting only "hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, [and] benzyl" as potential options for R^{19}. (*See*, *e.g.*, Ex. 1002 ¶ 66.) Rather, the disclosure encompasses dozens more side chain options, and PO's effort to erase—without explanation or basis—the vast majority of them is precisely the sort of picking and choosing the Federal Circuit consistently has proscribed. *See Idenix*, 941 F.3d at 1160–61. The PO did not—and cannot—explain how the POSA would have recognized the now-claimed subgenus from among this substantially larger genus absent the post-factum (and still legally inadequate) blaze marks it first attempted to provide in 2019.

Second, PO never pointed out to the Examiner that the specification's only disclosure of any subgenus of tetrapeptides, in Formula IX, points *away* from the claimed subgenus. (*See, e.g.*, Ex. 1002 ¶¶ 75, 86.)

Third, even setting aside the clear absence of support for the claimed Gly/Phe-Only Tetrapeptide Limitation, PO's methodology of identifying support on a limitation-by-limitation basis was rejected by the Federal Circuit. *See Novozymes A/S v. DuPont Nutrition Biosciences APS*, 723 F.3d 1336, 1349 (Fed. Cir. 2013). Claims must be described "as an integrated whole rather than as a collection of independent limitations." *Id.* The pertinent question is not simply whether the priority applications say "tetrapeptide" anywhere, or include glycine or phenylalanine on a list. The pertinent inquiry requires that the priority applications describe—as an integrated whole—the claimed subgenus of ADCs that feature a tetrapeptide consisting of only glycine or phenylalanine. *Id*. They unambiguously do not. Because the priority applications, and the specification, fail to describe the claimed subgenus, the '039 Patent's claims have an effective filing date of July 10, 2019, and are eligible for PGR.

B. Ground 1: The '039 Patent Does Not Describe ADCs Having Drug Moieties That Are Not Dolastatin/Auristatin Derivatives

Independent Claim 1 recites a genus of ADCs with the following formula:



Pursuant to PO's claim construction, applied here, the drug moiety (i.e., "D") is broad enough to encompass all drug moieties, and not just dolastatin/auristatin derivatives. (*See supra* § IV.) While dependent Claims 2–5, 9, and 10 further limit the structure of the antibody, the spacer, or the drug-antibody ratio of the ADCs of Claim 1, none of the claims further limit D, the drug moiety. The claimed genus of ADCs further requires a "tetrapeptide" comprised of glycine and phenylalanine amino acids, as discussed above in § VI.A.

To satisfy the written description requirement with respect to such a genus of ADCs with any drug as the drug moiety and the recited tetrapeptide, the specification must disclose either "a representative number of species falling within the scope of the genus" or "structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Ariad*, 598 F.3d at 1350.

The '039 Patent does not describe the full scope of this claimed genus, because its disclosure is limited to ADCs containing drugs known as

dolastatin/auristatins, and none of which comprise the claimed tetrapeptide. (*See, e.g.*, Ex. 1002 ¶¶ 100–14.) Accordingly, the '039 Patent describes *zero* species falling within the genus. And the '039 Patent's disclosure of dolastatin/auristatin-containing ADCs does nothing to illuminate the "common structural features" of ADCs comprising drug moieties of any structure, as opposed to derivatives of the dolastatin/auristatin structure.

Because the '039 Patent satisfies neither of *Ariad*'s requirements for describing a genus of compounds, the challenged claims lack written description support, making the '039 patent eligible for PGR and requiring that Claims 1–5, 9, and 10 be canceled.[12]

1. The '039 Patent Discloses Zero Species Within the Claimed Genus

The '039 Patent plainly focuses on ADCs containing auristatins, compounds derived from a class of natural compounds known as dolastatins isolated from a

[12] PO's priority applications fail to satisfy *Ariad* for at least the same reasons as the '039 Patent itself. (*See generally* Exs. 1010–1019; *see also, e.g.*, Ex. 1002 ¶¶ 94, 96, 98.) Accordingly, the '039 Patent is not entitled to the benefit of any effective filing date earlier than the July 10, 2019, filing date of the '839 Application.

marine mollusk. (Ex. 1001 at 3:51–67; *see, e.g.*, Ex. 1002 ¶¶ 63, 100–14.) The specification conveys consistently that the drug moieties of the invention are dolastatin/auristatin and certain chemical derivatives thereof. The patent's abstract refers to "auristatin peptides" and the "resulting ligand drug conjugates." (Ex. 1001 at Abstract.) And in the background of the invention, the patent states that there is "a clear need in the art for dolastatin/auristatin derivatives having significantly lower toxicity, yet useful therapeutic efficiency [*sic*]." (*Id*. at 4:22–29; *see, e.g.*, Ex. 1002 ¶ 102.)

There are no examples in the patent of any ADC with a drug that is not a dolastatin/auristatin derivative. (*See, e.g.*, Ex. 1002 ¶¶ 102–05.) Every single working example in the patent involves an ADC with a dolastatin/auristatin derivative as its drug moiety, a very narrow subset of the claimed drug moieties. (*See, e.g.*, *id.* ¶¶ 105–06.) And because not a single one of those exemplified compounds features the tetrapeptide required by Claims 1–5, 9, and 10, the '039 Patent discloses *zero* examples of an ADC falling within the claimed genus. (*See, e.g.*, *id.* ¶¶ 100–08.) Zero examples cannot satisfy the requirement to disclose a "representative number" of species within the claimed genus. *Univ. of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 927 (Fed. Cir. 2004); *In re Alonso*, 545 F.3d 1015, 1021–22 (Fed. Cir. 2008).

Even if the Board somehow were to credit the patent's disclosure of various

ADCs despite their lacking the claimed tetrapeptide (and thereby falling outside the claim)—and as a legal matter, it cannot, *see Ariad*, 598 F.3d at 1350—each of those examples contains a dolastatin/auristatin derivative. (*See, e.g.*, Ex. 1002 ¶¶ 102–06.) There is not a single example of an ADC made with a "drug moiety" other than dolastatin/auristatin. (*See, e,g., id.* ¶¶ 100, 102–06.) And, glaringly, there is no example of an ADC made using camptothecin derivatives like exatecan, as in Enhertu®. The absence of even one, let alone a "representative" number of species of the claimed genus, precludes PO from satisfying the written description requirement under this prong of *Ariad*. 598 F.3d at 1350.

The Federal Circuit's precedent on describing a genus by identifying a representative number of species emphasizes the importance of ascertaining "how large a genus is involved and what species of the genus are described in the patent." *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1299–1300 (Fed. Cir. 2014). The *AbbVie* court explained the law by "analogizing the genus to a plot of land." *Id.* at 1300. "[I]f the disclosed species only abide in a corner of the genus, one has not described the genus sufficiently to show that the inventor invented, or had possession of, the genus." *Id.* That was the case in *AbbVie*: although the patent disclosed *hundreds* of species within the scope of the claimed genus, they were all structurally related and "not representative of the full variety or scope of the genus." *Id.* The '039 Patent's

disclosed species all contain auristatin derivatives, a very narrow corner of the genus that covers all drug moieties of any kind. (*See, e.g.*, Ex. 1002 ¶¶ 95–96, 100–10.) The absence of any examples of an ADC that includes any other types of drug, let alone examples within the scope of the claim, forecloses any possibility of satisfying the *en banc* Federal Circuit's standard. *See Ariad*, 598 F.3d at 1349–50.

2. The '039 Patent Discloses No Common Structural Features of the "Drug Moieties" Within the Claimed Genus

If a patent does not describe representative number of species of a claimed genus, it must disclose "structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." *Ariad*, 598 F.3d at 1350. The '039 Patent plainly fails this prong of *Ariad*, as it does not identify any common structural features of the "drug moiety" that would permit the POSA to visualize the claimed genus' members by its structure, rather than by its function as a drug. (*See, e.g.*, Ex. 1002 ¶¶ 108–13.)

As an initial matter, SGI's newly added claim limitation of a "drug moiety" is not a structural limitation. Instead, it is a functional limitation to anything that can be considered a "drug." A "drug" performs a pharmacological function but does not specify any particular structural feature that accomplishes that function. (*See, e.g.*, Ex. 1002 ¶ 110.) Claims with such functional limitations are particularly likely to raise written description problems, because they "simply claim a desired

result, and may do so without describing species that achieve that result." *Ariad*, 598 F.3d at 1349. Uncoupled from any description of the structural features shared by the genus' species, such claims uniformly have been rejected as deficient. *Id.* at 1350; *Alonso*, 545 F.3d at 1021–22; *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1125 (Fed. Cir. 2008).

a) The Dolastatin/Auristatin Structures Are Not "Common Structural Features"

The '039 Patent discusses at length the use of dolastatin/auristatins as the "drug moiety" in the patent's ADCs. Section 9.4, entitled "The Drug Unit (Moiety)," begins: "the drug moiety (D) of the antibody drug conjugates (ADC) are of the dolastatin/auristatin type . . . which have been shown to interfere with microtubule dynamics[.]" (Ex. 1001 at 71:20–30.) This section discloses as "one embodiment" ADCs with drug moieties according to formulas D_E (which includes auristatin E derivatives) or D_F (which includes auristatin F derivatives). (*Id*. at 71:39–74:10; *see, e.g.*, Ex. 1002 ¶ 109.) It then provides 11 "illustrative Drug units (-D)." (Ex. 1001 at 74:11; *see, e.g.*, Ex. 1002 ¶ 109.) The first is monomethyl auristatin E, the second is monomethyl auristatin F, and the other nine are derivatives of monomethyl auristatin F. (Ex. 1001 at 74:12–77:16; *see, e.g.*, Ex. 1002 ¶¶ 67, 109.)

These disclosures make clear that structures like dolastatin and auristatin are within the scope of the claims' "drug moiety." The question is whether the patent discloses any structural features that these molecules have in common with the overwhelming majority of the members of the claimed genus, which are *not* "of the dolastatin/auristatin type."

The answer is no. The '039 Patent nowhere identifies any "drug moiety" that is not a dolastatin/auristatin derivative.[13] (*See, e.g.*, Ex. 1002 ¶¶ 100–10.) The '039 Patent therefore nowhere compares the dolastatin/auristatin structures to any other "drug moieties," nor does it identify what particular structural features of the dolastatin/auristatins, if any, would be shared with other "drug moieties" within the scope of the claim. (*See, e.g.*, *id.* ¶¶ 108, 110, 113.) The structural similarity apparent from the '039 Patent's eleven "illustrative" drug moieties—that they are

[13] The '039 Patent does include tables of various therapeutic compounds. (Ex. 1001 at 162:10 (Table 4), 165:42 (Table 6), 168:34 (Table 8).) These compounds are identified as agents to be administered as part of multi-drug therapy *with* the patent's ADCs, not *as* the drug moieties of the patent's ADCs. (*Id*. at 31:39–33:31, 161:60–163:28; *see, e.g.*, Ex. 1002 ¶ 107.)

all structural derivatives of dolastatin/auristatin—underscores the specification's failure to disclose structural features common to a genus that is not limited to drug moieties of the dolastatin/auristatin type. (*See, e.g., id.* ¶¶ 67, 109–10.)

The patent's limited and deficient disclosure is emphasized by the final paragraph Section 9.4 "The Drug Unit (Moiety)." It explains how certain groups can be "attached to the Drug Unit at R^{11}." (Ex. 1001 at 77:18–20.) The POSA would understand R^{11} to refer to a substituent in a diagram of "the Drug Unit." But the only such diagram containing an R^{11} group appears in the formulas Ib and D_F, both auristatin derivative formulas. (*See, e.g.*, Ex. 1002 ¶ 109.) The patent nowhere identifies any other "drug moiety" structures, nor where "R^{11}" would be on such structures, confirming that it lacks the requisite disclosure of ADC compounds with a drug moiety other than a dolastatin/auristatin derivative, let alone structural features common to those other drug moieties. (*See, e.g.*, Ex. 1002 ¶ 109.)

b) A Nitrogen Atom That Attaches the Drug to the Linker Is Not a "Common Structural Feature"

The '039 Patent states that "D is a Drug unit (moiety) having a nitrogen atom that can form a bond with the Spacer unit when y=1 or 2[.]" (Ex. 1001 at 71:31–32; *see also id.* at 146:10, 40–41, 45–46 (discussing synthesis of drug-linker compounds wherein a reactive site at the terminus of the spacer unit "is reactive to

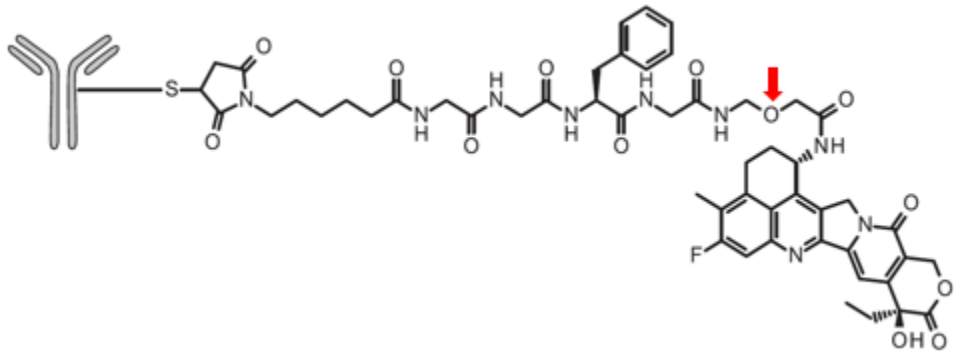
a nitrogen atom of the Drug"); *id*. at 150:46–49 (referencing Figure 33, which purports to show methods of forming drug-linkers by reacting linkers to "an amino group of a Drug Compound of Formula (Ib)"[14]).)

To the extent that a nitrogen atom may be a structural feature common to the "drug" in each of these disclosures, the POSA would have understood that countless organic compounds—many of which are inert and thus are not drugs—and virtually all pharmaceutical agents, comprise a nitrogen atom. (*See, e.g.*, Ex. 1002 ¶ 111.) Accordingly, a nitrogen atom is not a common structural feature that would permit the POSA to "visualize or recognize the members of the genus" under *Ariad*. (*See, e.g., id.*) Were such a ubiquitous feature sufficient to describe a claimed genus, the Federal Circuit's jurisprudence regarding description of biological genuses effectively would become a dead letter, and every case applying it to invalidate claims for lack of written description would have been decided differently. *See, e.g.*, *Alonso*, 545 F.3d at 1022 (finding claims to genus not described, even though all species of the genus were comprised of amino acids that

[14] Formula Ib is a disclosure of dolastatin/auristatin derivatives. (*See, e.g.*, Ex. 1002 ¶ 119.)

contain nitrogen atoms).

Even if a single nitrogen atom of a "drug moiety" that is bound to an adjacent spacer could suffice as a common structural feature under *Ariad*, which it cannot, PO has taken the position that the scope of the challenged claims is not so limited. For example, in the Texas Litigation, PO alleges that Enhertu®, depicted below, has a spacer (which PO purports to be a self-immolative moiety), bound to a drug moiety (which PO purports to be the camptothecin derivative DXd) via an *oxygen* atom, not a *nitrogen* atom.



(*See* Ex. 1006 at 8–9; Ex. 1009 at 1041 (red arrow added).)

A single nitrogen atom connecting a drug moiety to the rest of an ADC cannot constitute common "structural features" to permit the POSA to visualize the members of the genus and thereby satisfy the *en banc* Federal Circuit's governing standard. But even if it could, PO has not construed its claim even to be limited to ADCs with this feature.

c) The Patent's Synthetic Methods Do Not Disclose Any "Common Structural Features"

The '039 Patent includes a Section 9.6.1 entitled "Drug Moiety Synthesis." (Ex. 1001 at 143:17–146:2.) The section suggests how to synthesize "peptide-based Drugs" generically, and then more specifically explains how to make dolastatin/auristatin derivatives by combining various peptides. (*Id.*; *see, e.g.*, Ex. 1002 ¶¶ 112–13.) These disclosures, like those addressed above, provide no structural information for ADCs with drug moieties—like the vast majority of the members of the genus—that are not auristatin/dolastatin derivatives. Nor does the paragraph labeled "General Procedure D: Drug Synthesis." Rather, it explains how to combine a dipeptide intermediate and a tripeptide intermediate, a reaction that is useful to synthesize certain auristatin/dolastatin derivatives but not a scheme that can be generalized to make all drugs of the genus. (Ex. 1001 at 145:25–42; *see, e.g.*, Ex. 1002 ¶¶ 112–13.)

The final paragraph of this section states that "the above methods are useful for making Drugs that can be used in the present invention." (Ex. 1001 at 146:1–2.) But as explained by Dr. Lambert, the disclosure of the patent's Section 9.6.1 is limited to explaining the synthesis of peptide drugs, and specifically auristatin/dolastatins. (*See, e.g.*, Ex. 1002 ¶¶ 112–13.) It does not offer any guidance regarding how to make, for example, camptothecin derivatives like the

moiety found in Enhertu®. (*See, e.g.*, *id.* ¶¶ 100–13.) And most importantly for purposes of the governing standard, whatever it discloses regarding synthesis, this "Drug Moiety Synthesis" section, like the section entitled "Drug Unit (Moiety)," discloses no structural feature common to the full scope of the claimed genus or sufficient structure to permit the POSA to recognize members of the genus. Disclosure of a method of finding or making members of the claimed genus—a disclosure that, in any event, is lacking here—cannot substitute for the requisite structural description of the genus's members. *See Alonso*, 545 F.3d at 1020, 1022.

* * *

These disclosures of the '039 Patent directed to the "drug moiety" portion of the claimed ADCs would not have permitted the POSA to recognize *any* structural feature common to the genus of ADCs that encompass *any* drug. Without the disclosure of a single common feature, it would have been impossible for the POSA to "visualize" the members of the genus, *Ariad*, 598 F.3d at 1350, based on the patent's disclosure. (*See, e.g.*, Ex. 1002 ¶¶ 108, 114.)

Dr. Lambert's interpretation of the '039 Patent's disclosure is consistent with that of the European Patent Office. (*See, e.g.*, *id.* ¶ 115.) In examining claims similar to those challenged here, the EPO remarked, "[t]he Application as originally filed and published consistently referred to dolastatin/auristatin, and the

need to find safe derivatives and conjugates thereof . . . . The application does not clearly and unambiguously teach that D can be any drug . . . . " (Ex. 1008 at 4.) And in examining a related application, the EPO noted, "[w]hat was shown [in the original application] was an antibody-drug combination wherein the drug was auristatin or dolastatin," and noting of the drug moiety "other than auri- or dolastatin: *no basis*." (*Id.* at 5 (emphasis added).)

The Patent Office here erred in allowing the challenged claims. Because the '039 Patent does not describe the claimed genus of ADCs containing any drug moiety, Claims 1–5, 9, and 10 are eligible for PGR and should be canceled.

C. Ground 2: The '039 Patent Does Not Enable the Claimed ADCs

The specification must teach the POSA to make and use the claimed invention without "undue experimentation." *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). As the Supreme Court has explained, "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." *Brenner v. Manson*, 383 U.S. 519, 536 (1966). The '039 patent does not reflect the "successful conclusion" of PO's purported invention of the claimed subject matter. In fact, it does not disclose even one ADC within the scope of its claims. (*See, e.g.*, Ex. 1002 ¶¶ 99–117, 123.) The '039 Patent instead reflects, at best, an unguided suggestion to try to synthesize claimed compounds

that are structurally disparate and functionally unpredictable. The '039 Patent fails to enable the POSA to make the full scope of the claimed genus of ADCs and identify which compounds will be "intracellularly cleaved" as the challenged claims require. Accordingly, the specification and priority applications do not satisfy the requirements of 35 U.S.C. § 112(a), rendering the '039 Patent both PGR eligible and unpatentable.

1. The Claimed ADCs are Complex and Unpredictable

ADCs are "one of the most complex drug platforms in the oncology armamentarium." (Ex. 1025 at 2168; *see, e.g.*, Ex. 1002 ¶¶ 35–37, 124.) Complex chemical interactions among ADC components affect its structure and properties. (*See, e.g.*, Ex. 1002 ¶¶ 35–37, 127, 130, 141.) Given this complexity, one review article remarked that, as of 2016, it was not surprising that "we have only two commercially available agents despite over one hundred clinical trials evaluating this platform." (Ex. 1025 at 2168.) Dr. Lambert has been working on ADCs since the field's inception in the 1980s. (*See, e.g.*, Ex. 1002 ¶¶ 12–14.) As he explains, ADCs are intricate molecules that involve problems of medicinal chemistry, synthetic chemistry, immunology, pharmacokinetics and distribution, and

metabolism, to name a few. (*See, e.g.*, *id.* ¶ 124.) Describing the "nature of the invention"[15] as "complex" is an understatement. (*See, e.g.*, *id.*)

Work with such complex molecules typically involves multi-disciplinary teams at specialized, research-focused enterprises. Dr. Lambert worked for decades at ImmunoGen, one of a small number of companies that specialized in designing ADCs. Over the years, several of the world's largest pharmaceutical companies, including Amgen, Bayer, Novartis, Roche, and Sanofi, partnered with ImmunoGen to access the expertise of Dr. Lambert and his colleagues. (Ex. 1002 ¶¶ 14, 14 n.2, 44.) The relative skill[16] of these teams working in the nascent and unpredictable ADC field is quite high, as befits the staggering complexity involved in making these molecules. (*See, e.g.*, *id.* ¶¶ 125–26.)

Claim 1 embraces a vast genus of ADCs. (*See, e.g.*, *id.* ¶¶ 127–29.) It is not limited to any particular drug or structural class of drugs. (*See, e.g.*, *id.* ¶ 127.) While the claim does limit one aspect of the *linker* that attaches the drug to the

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[15] *Wands*, 858 F.2d at 737 (factor 4).

[16] *Wands*, 858 F.2d at 737 (factor 6).

antibody—for example, the linker must comprise a tetrapeptide consisting of glycine or phenylalanine (*see supra* § VI.A)—the structural limitations of the claim still encompasses an astronomical number of structurally and functionally disparate compounds.[17] (*See, e.g.*, *id.* ¶¶ 127–29.) Moreover, in addition to these structural requirements, the claim includes the functional limitation requiring that the ADC's drug moiety be "intracellularly cleaved in a patient from the antibody of the antibody-drug conjugate or an intracellular metabolite of the antibody-drug conjugate." (*See, e.g.*, *id.* ¶ 128.) Whether a composition meets this functional limitation of the challenged claims cannot be ascertained without testing and undue experimentation. (*See infra* § VI.C.3; *see, e.g.*, *id.* ¶¶ 8, 46–51, 122, 154.)

Compared to the breadth of the challenged claims, the '039 Patent's disclosure offers scarce guidance[18] and extremely limited working examples.[19] (*See, e.g.*, Ex. 1002 ¶¶ 129–38.) As explained above, the patent provides no disclosure of which of the innumerable linkers it discloses generically can be

[17] *Wands*, 858 F.2d at 737 (factor 8).

[18] *Wands*, 858 F.2d at 737 (factor 2).

[19] *Wands*, 858 F.2d at 737 (factor 3).

combined with which drug moieties other than the narrowly described auristatin derivatives. (*See supra* § VI.B; Ex. 1002 ¶¶ 111, 145.) With respect to making the claimed ADCs, the'039 Patent does not provide generally applicable guidance, and its examples do not involve any drug moieties other than dolastatin/auristatin derivatives. (*See, e.g.*, Ex. 1001 at 130:38–141:58 (testing performed only with MMAE and MMAF drug moieties); Ex. 1002 ¶¶ 129–30, 134–35.) As described in § VI.C.2 below, the hard experimental work of finding methods to make ADCs using other drug moieties has been left to the field. With respect to determining whether an ADC is intracellularly cleaved as the claims require, the '039 Patent offers nothing—not even an assay for testing this limitation or a working example, as discussed further in § VI.C.3. (*See, e.g.*, Ex. 1002 ¶¶ 131–33, 136–37.)

These issues as to which the '039 Patent offers insufficient guidance—including how to identify and make the claimed ADCs and how to determine whether an ADC satisfies the Intracellular Cleavage Limitation—raise complex issues of chemistry and biology. With respect to these topics, the quantity of

experimentation, the existing state of the art, and predictability of the art[20] is addressed in detail below.

2. The POSA Cannot Make the Full Scope of Claimed ADCs Without Undue Experimentation

Claim 1 recites a structure in which the drug moiety "D" is covalently attached to either Y_y, a "Spacer unit," or, when y is zero, W_w, a tetrapeptide. But simply drawing a bond between two atoms does not mean that such a bond can actually be formed or that the bound molecule will be stable and functional. Attaching a drug moiety to the linker unit in the claimed ADCs would require the drug moiety to have a functional group capable of forming such a bond with a spacer or a gly/phe-only tetrapeptide. (*See, e.g.*, Ex. 1002 ¶¶ 39, 142.) The '039 Patent does not enable the POSA to make this vast genus of ADCs it claims. (*See, e.g.*, *id.* ¶¶ 122–57.)

Extensive research is necessary to determine how to attach a linker to a drug moiety in a manner that retains its activity. (*See, e.g.*, *id.* ¶¶ 39, 44, 125, 130, 142.) Dr. Lambert undertook such a project while at ImmunoGen. (*See, e.g.*, *id.* ¶¶ 44, 63; Ex. 1026 at 6951–52.) Endeavoring to make an anti-HER2 ADC, he and his

[20] *Wands*, 858 F.2d at 737 (factors 1, 5, and 7).

colleagues considered as a potential drug moiety maytansine, a natural product that was known to inhibit tubulin polymerization. (*See, e.g.*, Ex 1002 ¶¶ 44, 63; Ex. 1026 at 6950–51.) Because maytansine itself "lacked a suitable functional group" for attachment to an ADC linker, Dr. Lambert and his team of scientists conducted years of painstaking research creating "maytansinoids." (Ex. 1026 at 6951; *see, e.g.*, Ex. 1002 ¶¶ 44, 63.) These maytansine derivatives have functional groups that allow for attachment to linkers without sacrificing drug activity. (Ex. 1026 at 6952.)

The '039 Patent's exemplified ADCs all incorporate auristatins. (Ex. 1002 ¶¶ 134–35, 139–40.) These compounds are derivatives of the natural product dolastatin 10, which, like maytansine, lacks a suitable functional group for attachment to a linker. (*See, e.g.*, *id.* ¶ 63.) Even a derivative of dolastatin 10, auristatin PE, was believed by PO to be "unsuitable for attachment" because it contained a "dimethylamine terminus" (i.e., a tertiary amine). (Ex. 1027 at 15; *see, e.g.*, Ex. 1002 ¶¶ 143–44.) By contrast, all of the auristatins disclosed in the '039 Patent's specification incorporate a primary or secondary amine as a functional group for attachment to the ADC linker. (*See, e.g.*, Ex. 1002 ¶ 144; Ex. 1001 at 6:49–7:2, 71:31–37.)

The '039 Patent provides no examples or specific disclosure for attaching any drug moiety other than dolastatin/auristatin derivatives—a small corner of the

vast genus of drug moieties covered by the challenged claims—to linkers of the claimed ADCs. (*See, e.g.*, Ex. 1002 ¶¶ 61, 97, 129–30, 134–35, 139–40, 145.) Nor does the patent disclose a general rubric for attaching any drug moiety to linkers of the claimed ADCs, because no such rubric exists. (*See, e.g.*, *id.* ¶ 145.) In the years since PO filed its priority applications, researchers around the world still have labored to develop attachment techniques, and when a new reaction suitable for attaching a moiety is discovered, it typically is treated as an innovative advance, rather than routine chemistry. (*See, e.g.*, *id.* ¶ 146.)

By way of example, a 2016 publication co-authored by some of PO's named inventors pressed the "strong need to expand ADC linker technology to encompass a broad array of anticancer drugs." (Ex. 1028 at 7951.) Regarding alcohol-containing drug moieties in particular, the authors explained how, over the years, they had "installed" amines into drugs "when possible," but lamented that "introducing an amine functional group may not always be synthetically feasible, and it may have a detrimental impact on the pharmacology of the resulting drug analogue." (*Id*. at 7948.) The authors then trumpeted their present work as "validat[ing]" their purportedly "novel" construct for use with "alcohol-containing drugs within ADCs." (*Id*. at 7948–49.)

PO's published patent application on that purported advancement, filed a decade after the earliest utility patent application to which the '039 Patent claims

priority, reinforces the ’039 Patent’s lack of enablement. (*See generally* Ex. 1029.) Among other things, the published application confirms that “[c]ertain drug classes thought to be lacking appropriate conjugation handles have been considered *unsuitable* for use as ADCs” and that, “[a]lthough it *may* be possible to modify such a drug to include a conjugation handle, such a modification can negatively interfere with the drug’s activity profile.” (*Id.* at [0003] (emphases added).) Having surveyed the art’s prior efforts to make ADCs using alcohol-containing drugs, PO’s researchers concluded, approximately a decade after the’039 Patent specification was first filed: “a need exists for new linker technologies that can be used to attach drugs heretofore believed to be unsuitable for use as ADCs.” (*Id.* at [0005].) Such admissions belie the notion that PO’s earlier-filed specification of the ’039 Patent would have enabled the POSA to make the claimed ADCs, at least with respect to alcohol-containing drug moieties and the numerous other classes of drug moieties the specification fails to address. (*See*, *e.g.*, Ex. 1002 ¶ 146.)

As another example regarding types of drug moieties lacking enabling disclosure in the ’039 Patent, another 2016 publication co-authored by some of PO’s named inventors purported to have developed a “novel” strategy to “*expand* the scope of antibody–drug conjugate (ADC) payloads to include tertiary amines, a functional group commonly present in biologically active compounds.” (Ex. 1030 at OF1 (emphasis added); Ex. 1002 ¶ 146.) In particular, the paper stated that the

"commonly present" tertiary amine functional group "has not been utilized as a linker element in previously described ADCs." (Ex. 1030 at OF1.) Instead, analogs with secondary amines were generated (as with auristatin) or other functional groups in the molecule used. (*Id.*) But the paper recounted how these strategies for attachment did not work generally, explaining how efforts to introduce functional groups into a class of drugs known as tubulysins had failed. (*Id*. at OF1–OF2; Ex. 1002 ¶ 146.) The authors closed by touting their present work as "a new and viable strategy for arming antibodies," positing that it "should apply to an array of drugs" and noting their plan to "expand [it] to include new tertiary amine containing compounds." (Ex. 1030 at OF7.)

Had the '039 Patent's specification enabled the POSA to make ADCs using drugs containing tertiary amines without undue experimentation, this quaternary ammonium strategy would not have "expanded" (to use PO's own words) the repertoire of drugs that could be used in ADCs. That named inventors of the '039 Patent had to develop a new synthetic "strategy" to make such ADCs is powerful evidence that the '039 Patent does not enable Claim 1. *ALZA Corp. v. Andrx Pharms., LLC*, 603 F.3d 935, 942 (Fed. Cir. 2010).

These classes of drugs—alcohol-containing drugs and tertiary amine-containing drugs—are just two of many examples of drug moieties that could not be incorporated into ADCs using the '039 Patent's disclosure without undue

experimentation. (*See, e.g.*, Ex. 1002 ¶¶ 144, 146.) Each required the application of different medicinal chemistry techniques to attach them to an ADC linker. As Dr. Lambert explains, and the contemporaneous literature reflects, different classes of drug moieties pose distinct challenges with respect to attachment to ADC linkers. (*See, e.g.*, Ex. 1002 ¶¶ 145–46.) Section 112(a) requires that a patent's disclosure enable the POSA to make the *full* scope of the claimed invention. *Idenix*, 941 F.3d at 1154. A disclosure that fails to do so, such as by failing to provide reaction conditions needed to produce the claimed molecules, cannot satisfy the enablement requirement. *See Genentech, Inc. v. Novo Nordisk, A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). That principle applies with special force to circumstances where, as here, different reactions and conditions are required for the various classes of drug moieties used in the claims, and finding those reactions requires extensive experimentation and ingenuity. (Ex. 1002 ¶¶ 139–46.)

Here, the '039 Patent provides several columns of disclosure concerning synthesis of "Compounds of the Invention" and a table identifying "exemplary" ADCs that PO says it prepared, all of which incorporate dolastatin/auristatin derivatives by coupling the dolastatin/auristatin derivatives' primary or secondary amine to a linker. (Ex. 1001 at 141:60–154:14.) Dr. Lambert has examined these disclosures and concluded that they do not enable the synthesis of ADCs other than by coupling to a drug's primary or secondary amine. (*See, e.g.*, Ex. 1002 ¶¶ 112,

135, 145.) That the '039 Patent provides eleven figures depicting synthesis schemes and over a dozen columns of text to teach how to make a small fraction of conjugates—those containing dolastatin/auristatin derivatives—starkly illustrates what the '039 Patent is lacking: any disclosure of how to make an ADC using a drug moiety *other than* dolastatin/auristatin derivatives. (*See, e.g.*, *id.* ¶¶ 72, 109, 123, 129–30, 135.) As the Federal Circuit explained in *Genentech*, "Patent draftsmen are not loath to provide actual or constructive examples, with details, concerning how to make what they wish to claim." 108 F.3d at 1367. Like the inventors in *Genentech*, PO's named inventors "knew how to enable that which they had invented." *Id.* That they did not provide any guidance for how to make ADCs like, for example, those using alcohol-containing drugs moieties or tertiary amine-containing drug moieties, further shows Claim 1's lack of enablement.

Claims 2–5 and 9–10 are similarly not enabled by the '039 Patent. Claims 2–3 further limit the spacer Y included in the ADC, Claims 4–5 further limit the drug-to-antibody ratio of the ADC, and Claims 9–10 further limit the antibody included in the ADC. None of these dependent limitations restrict the scope of drug moieties encompassed within the claimed genus of ADCs, and thus they do not mitigate the enablement problems shown herein with respect to Claim 1. (*See, e.g.*, Ex. 1002 ¶¶ 156–57.)

One consequence of Claims 1–5, 9, and 10 not being enabled by the '039 Patent's specification is that they cannot claim priority to any of the various previously-filed applications, giving these claims an effective filing date of July 10, 2019. This makes the '039 Patent eligible for PGR. This lack of enablement also is a reason why Claims 1–5 and 9–10 should be canceled.

Nor can PO rely on the art developed between the initial application filing and the 2019 priority date (including the literature addressed above) to assert that it enables the POSA to practice the claims without undue experimentation. This argument was addressed and rejected squarely in *Genentech*. That a specification "need not disclose what is well known in the art" is "merely a rule of supplementation, not a substitute for a basic enabling disclosure." *Genentech*, 108 F.3d at 1366. Thus, the "omission of minor details" will not undermine enablement, but "when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out," the patent does not enable the claims, and this lack of enablement "cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art." *Id.* The information missing from the '039 Patent—any guidance on making an ADC with a drug moiety other than a dolastatin/auristatin derivative—is precisely the type of "basic enabling disclosure" that a patent must disclose in its specification. In any event, though the literature discussed above reflects scientists' breakthroughs in

synthesizing ADCs using certain particular classes of drug moieties, the claim's scope as interpreted by PO is far broader and includes ADCs with numerous drug moieties that the literature does not assist in synthesizing. (Ex. 1002 ¶¶ 145–46.)

3. Identifying ADCs Susceptible to Intracellular Cleavage Requires Undue Experimentation

Claim 1 is limited to those ADCs for which the "drug moiety is intracellularly cleaved in a patient from the antibody of the antibody-drug conjugate or an intracellular metabolite of the antibody-drug conjugate." This functional limitation requires that "the covalent attachment, e.g., the linker, between the drug moiety (D) and the antibody (Ab) is broken, resulting in the free drug dissociated from the antibody inside the cell." (Ex. 1001 at 29:52–55.) And this release of free drug inside a cell must occur *in a patient*. Accordingly, enabling Claim 1 requires not just a teaching of how to make the ADCs (the problem discussed in § VI.C.2 above), but also of how to identify the ADCs that possess the required functional characteristic of being cleaved intracellularly in a patient. *See, e.g.*, *Idenix*, 941 F.3d at 1159 (holding that, because claims included an efficacy limitation, enablement required identification of which compounds were efficacious).

Given the complex and unpredictable nature of the nascent field of designing ADCs with desirable properties, the design of each unidentified ADCs throughout

the scope of the unfathomably large claimed genus would have been a distinct research project requiring substantial skill and experimentation. (Ex. 1002 ¶¶ 145–46, 154.) To design ADCs throughout the scope of the claim would have required undue experimentation, in view of the complexity of the technology and the paucity of guidance provided by the '039 Patent. (*See Idenix*, 941 F.3d at 1159, *see also* Ex. 1002 ¶ 154.)

But the design of the vast scope of unidentified ADCs within the claim scope is just the beginning of the improper research plan the '039 Patent provides in the absence of the requisite enabling disclosure. The ADCs need not only be designed—they must be synthesized, itself a challenging task that requires undue experimentation. (*See supra* § VI.C.2.) And even after they are designed and synthesized, the claims require that its ADCs possess the functional property of intracellular cleavage.

The '039 Patent does not teach how to identify which ADCs will be intracellularly cleaved as claimed and which ADCs will not. Such cleavage is a biologically complex phenomenon. (*See e.g.*, Ex. 1002 ¶¶ 147–51.) The Intracellular Cleavage Limitation requires that the ADCs be internalized to cells that the cells express a protease that can cleave the ADC, and that cleavage occurs as the claims require (i.e., in a manner that releases the free drug, *see* Ex. 1001 at Claim 1, 29:48–57). But, as Dr. Lambert explains, the '039 Patent does not

disclose *any* assay for identifying ADCs that would meet this cleavage requirement. (*See, e.g.*, Ex. 1002 ¶¶ 133, 150–51, 153.)

The '039 Patent offers instead, at most, the prophetic and general observation that ADCs with "useful" linkers "can be designed and optimized in their selectivity for enzymatic cleavage by a particular enzyme, for example, a tumor-associated protease." (Ex. 1001 at 67:56–60.) But the '039 Patent does not teach which combinations of antibodies, linkers, drugs, and drug-antibody ratios will produce ADCs capable of internalization. (*See, e.g.*, Ex. 1002 ¶¶ 148, 150.) It does not identify relationships between particular linkers and particular intracellular proteases that could cleave those linkers. (*See, e.g.*, *id.* ¶¶ 148, 151.) And it does not teach the POSA how to ensure that such cleavage releases free drug instead of, for example, a fragment comprising the drug and a portion of the linker. (*See, e.g.*, *id.* ¶¶ 148, 151.)

These are exceptionally complex problems, as Dr. Lambert explains from personal experience. He is an author of a 2016 paper (Ex. 1031) that characterized the properties of an ADC having a gly-gly-gly amino acid unit. Attempting to discern whether and how a single ADC with this tripeptide was cleaved—even *in vitro*—was a painstaking process taking months of work. (*See, e.g.*, *id.* ¶¶ 50, 152.) Dr. Lambert and his team developed various methods that involved treating a tumor cell line with a saturating level of the ADC, washing the cells to remove any

ADC that had not internalized, and incubating the cells for the right amount of time for proteolytic processing to have occurred, but not long enough to allow the potential activity of internalized drug moieties to thwart the assay (e.g., by causing cell death). (*See, e.g.*, *id.* ¶¶ 50, 152; Ex. 1031 at 1315.) Dr. Lambert and his team then used HPLC methods to characterize any resulting ADC fragments. (*See, e.g.*, Ex. 1002 ¶¶ 50, 152; Ex. 1031 at 1315.)

Dr. Lambert's results underscore the unpredictability of these complex biological processes. For one tumor cell line (COLO 205), the primary intracellular catabolite was DM-CX2, a fragment in which a glycine from the triglycyl linker remained covalently attached to the drug and spacer, reflecting a cleavage event outside the scope of the Intracellular Cleavage Limitation. The secondary intracellular catabolite was DM-CX-Lysine, a fragment in which the linker was not cleaved at all. (*See, e.g.*, Ex. 1002 ¶ 152; Ex. 1031 at 1315–16.) But in another tumor cell line (Calu-3), the detected catabolites were DM-CX2 and DM-CX1, a fragment comprised of only the drug and spacer. (*See, e.g.*, Ex. 1002 ¶ 152; Ex. 1031 at 1315–16.) These results show how even a thorough, painstaking, and challenging *in vitro* exploration of ADC cleavage can produce different results depending on the cell line used. (*See, e.g.*, Ex. 1002 ¶¶ 133, 152.)

Because "intracellular cleavage" depends on the extent to which particular cells express particular proteases and the extent to which those proteases prefer to

cleave (or not) at different positions in a linker (*see, e.g.*, *id.* ¶¶ 151–54), it may be impossible to determine whether an ADC will release free drug intracellularly in a single *in vitro* experiment (*see, e.g.*, *id.* ¶¶ 151–54). And, of course, the claimed functional limitation is directed not to *in vitro* cleavage, but to intracellular cleavage *in a patient*. Dr. Lambert, an expert with four decades of experience in this field, is aware of no assay that could be used to screen ADCs for *in vivo*, intracellular cleavage in a patient. (*See, e.g.*, *id.* ¶¶ 12–14, 153–54.)

Dr. Lambert's opinions are consistent with the 2016 industry white paper published by the International Consortium for Innovation and Quality in Pharmaceutical Development's working group on ADC absorption, distribution, metabolism, and excretion issues. (Ex. 1032.) This white paper, co-authored by a PO-affiliated author, stated that "current ADCs are not completely stable in the circulation" and that such instability can occur where the drug is "cleaved by extracellular proteases, especially in the proximity of the tumor." (*Id.* at 621.) For example, the clinical observation that Adcetris (an ADC using the valine-citrulline linker most frequently exemplified in the patent) is efficacious against tumors that do *not* express the antigen to which Adcetris binds (and thus might internalize) has led to the hypothesis that Adcetris may, in actual patients, release its drug extracellularly. (Ex. 1033 at 216–17; *see, e.g.*, Ex. 1002 ¶ 77.)

The industry white paper does identify some *in vitro* assays pertinent to ADC stability, confirming their insufficiency to assess achievement of the claims' functional Intracellular Cleavage Limitation. (Ex. 1032 at 621.) Affirming Dr. Lambert's observation of differential ADC catabolism by different cell lines, the white paper warns that "selection of the appropriate cell line would depend on the target expression" and thus any such assays "cannot be standardized and used across multiple programs." (*Id.*) And none of these *in vitro* assays illuminate whether an ADC is cleaved *in vivo* by extracellular or intracellular processes. (Ex. 1002 ¶ 133.) The white paper concludes by emphasizing that, as of 2016, "ADC technology is still evolving" and "there needs to be a continuous re-evaluation of ADME approaches as it matures over the next several years." (Ex. 1032 at 622.)

Given these exemplary difficulties involved in identifying which ADCs release free drug *in vivo* as a result of intracellular cleavage, Claim 1 cannot be enabled. In *Wyeth & Cordis Corp. v. Abbott Lab'ys*, the Federal Circuit held claims not enabled where the specification disclosed "only a starting point for further iterative research in an unpredictable and poorly understood field." 720 F.3d 1380, 1386 (Fed. Cir. 2013). Here, the '039 Patent does not even provide a starting point for identifying the ADCs that meet the Intracellular Cleavage

Limitation, let alone the requisite disclosure to reach the finish line without undue experimentation.

Wyeth continued: "Even putting the challenges of synthesis aside, one of ordinary skill would need to assay each of at least tens of thousands of candidates" and it would take "weeks to complete each of these assays." *Id.* Here, the claimed genus is orders of magnitude larger, and the necessary assay does not even exist. (*See, e.g.*, Ex. 1002 ¶¶ 150, 153–54.) Practicing the claimed invention by designing, synthesizing, and assessing the cleavage of the claimed ADCs is a far more challenging task than the Federal Circuit confronted in *Wyeth*.

The Federal Circuit in *Idenix* reaffirmed these principles articulated in *Wyeth*, explaining that "even if routine," screening thousands of compounds to identify those that might satisfy a claim's requirements constitutes undue experimentation. 941 F.3d at 1163. The Board cannot conclude otherwise here, where the claims are far broader and the testing is anything but routine. The scope of the genus and the effort required to test for the '039 Patent's claimed functional property, if the POSA even could devise such an assay, make Claim 1 unpatentable for lack of enablement just as were the claims in *Wyeth* and *Idenix*. Accordingly, the '039 Patent is eligible for PGR and Claim 1 should be canceled. Dependent Claims 2–5, 9, and 10 likewise should be canceled because they do not in any way address the undue experimentation required to determine whether an ADC meets

the Intracellular Cleavage Limitation included in those claims. (*See, e.g.*, Ex. 1002 ¶¶ 156–57.)

D. Ground 3: Claims 1–5, 9, and 10 Do Not Set Forth Subject Matter That the Named Inventors Regarded as their Invention

The claims of a patent must set forth "the subject matter which the inventor or a joint inventor regards as the invention." 35 U.S.C. § 112(b).[21] Accordingly, a patent claim is invalid "[w]here it would be apparent to one of skill in the art, based on the specification, that the invention set forth [therein] is not what the patentee regarded as his invention." *Allen Eng'g*, 299 F.3d at 1349. As explained below, the '039 Patent fails to satisfy this requirement with respect to Claims 1–5, 9, and 10. (*See also* Ex. 1002 ¶¶ 118–21.)

That the named inventors regarded their inventions as necessarily comprising dolastatin/auristatin derivatives is plain from (i) the '039 Patent's specification, (ii) expert testimony regarding the understandings of the POSA, and

[21] This requirement of 35 U.S.C. § 112(b) (previously § 112 ¶ 2) is separate from its definiteness requirement. *See, e.g.*, *Allen Eng'g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1348–49 (Fed. Cir. 2002).

(iii) PO's related prosecution efforts. (*See, e.g., supra* § III.) Even on its face, the '039 Patent is directed to "[a]uristatin peptides" and ligand-drug conjugates thereof. (Ex. 1001 at Abstract.) Each of the three categories of "compounds of the invention" described in the specification include dolastatin/auristatin drug moieties. (*See, e.g., id.* at 44:57–59 (regarding "Drug-Linker-Ligand Conjugates having Formula Ia," wherein the drug moiety is a dolastatin/auristatin derivative of structural Formula D_E or D_F), 51:48–60 (regarding "Drug Compounds of Formula (Ib)," which have a dolastatin/auristatin structure), 57:20–22 (regarding "antibody-drug conjugate compounds (ADC) having Formula Ic," wherein the drug moiety is a dolastatin/auristatin derivative of structural Formula D_E or D_F).) Expert testimony submitted herewith confirms that the POSA would have recognized these basic facts. (*See, e.g.*, Ex. 1002 ¶¶ 118–20.)

The dolastatin/auristatin-focused nature of PO's purported inventions is further apparent from the fact that one of the patents that issued from an application to which the '039 Patent claims priority (and with which the '039 Patent shares its specification) contains claims that are directed to dolastatin/auristatin derivatives outside the context of ADCs. (Ex. 1073 at Claims.) In fact, the EPO described European counterparts to the '039 Patent as "consistently referr[ing] to dolastatin/auristatin, and the need to find safe

derivatives and conjugates thereof[.]" (*See, e.g.*, Ex. 1008 at 4 (excerpt from'039 Pat. Hist.); *see also* Ex. 1001 at 4:25–29.)

Despite that clear focus on dolastatin/auristatin derivatives, PO has taken the position that Claims 1–5, 9, and 10 cover ADCs *not* having them. (*See supra* § IV, *infra* § VI.E.) The EPO has noted the possibility of such an interpretation in criticizing the claims of PO's related applications. (*See, e.g.*, Ex. 1008 at 4 (noting that the drug moiety is "no longer limited to an auristatin/dolastatin analog"), 5 ("Applicants [i.e., PO] are trying to lay claim on Daiichi S[ankyo]'s . . . very promising chemotherapeutic drug, by mixing and matching features not disclosed in combination in the original application").) Such claims—unmoored from the purportedly novel teachings of a patent and divorced from need that its inventions purportedly meet—are precisely what the "regards as the invention" requirement of 35 U.S.C. § 112(b) seeks to prevent. The Board should cancel the challenged claims for at least this reason.

E. Ground 4: Claims 1–5, 9, and 10 Are Anticipated

PO asserted the '039 Patent against Daiichi Sankyo Japan in the U.S. District Court for the Eastern District of Texas, alleging that Enhertu® (DS-8201) falls within the scope of the claims of the '039 Patent. (*See* Ex. 1006 ¶ 4.) Assuming, *arguendo*, that DS-8201 falls within the scope of the '039 Patent's claims as SGI argues in that district court action, those claims would be anticipated

under the "century-old axiom of patent law [that] holds that a product 'which would literally infringe if later in time anticipates if earlier.'"[22] *Upsher-Smith Lab'ys, Inc. v. Pamlab, LLC*, 412 F.3d 1319, 1322 (Fed. Cir. 2005). As shown above, the '039 Patent is not entitled to the benefit of any effective filing date earlier than the July 10, 2019, filing date of the '839 Application, which is years *after* Daiichi Sankyo began publicly disclosing—and PO verifiably was aware of—DS-8201. (*See supra* § VI–VI.C.)

For example, in 2015, Daiichi Sankyo scientist Dr. Yuki Abe publicly disclosed the chemical structure and preclinical use of DS-8201 with skilled

[22] This ground for unpatentability is based on PO's proposed construction of the claim term "drug moiety," as urged in its Complaint in the Texas Litigation and applied herein with respect to 35 U.S.C. § 112, which is broad enough to encompass all drug moieties and not just dolastatin/auristatin derivatives. (*See supra* § IV.) No further construction of claim terms is necessary given PO's arguments in the Texas Litigation that Daiichi Sankyo's DS-8201 falls within the claims of the '039 Patent.

artisans at the Antibody Engineering & Therapeutics Conference, an annual meeting of the Antibody Society held in San Diego, California.[23] (Ex. 1034; Ex. 1035 at 10 (Track C at 4:45), 22 (ND2).) In fact, Dr. Lambert attended this presentation and "was intrigued" by Daiichi Sankyo's success designing "an ADC with eight drug-linkers conjugated to eight cysteine residues on a single antibody and pharmacokinetic properties conducive to therapeutic benefit." (Ex. 1002 at ¶ 5.) This disclosure apparently caught the eye of PO's representatives, as PO contacted Daiichi Sankyo just weeks after the conference to both (i) note that PO's "research team" took an interest in DS-8201 and (ii) inquire about whether this technology was "available for partnering." (Ex. 1036 at 2.) Daiichi Sankyo declined PO's invitation to pursue a partnership concerning Daiichi Sankyo's DS-8201 technology. (*Id.*)

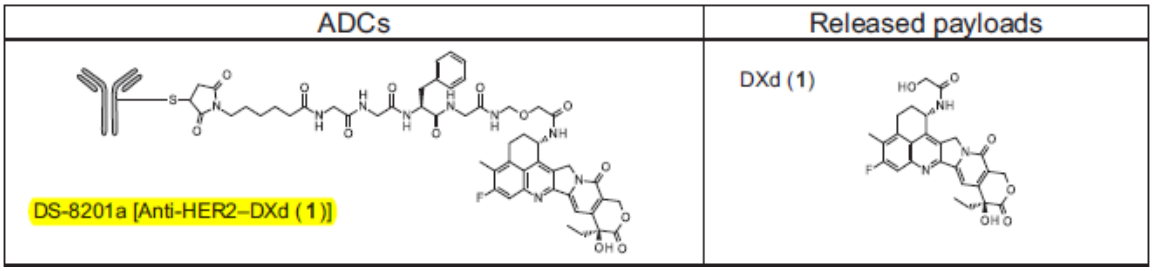
Daiichi Sankyo continued to pursue and publicize its ADC DS-8201 after that 2015 conference. For example, Daiichi Sankyo authors Yusuke Ogitani et al. submitted a scientific journal article regarding DS-8201 titled "Bystander killing

[23] The structure disclosed by Dr. Abe was the same as the structure disclosed in *DS Cancer Sci Article*. (*Compare* Ex. 1034, *with* Ex. 1009.)

effect of DS-8201a, a novel anti-human epidermal growth factor receptor 2 antibody-drug conjugate, in tumors with human epidermal growth factor receptor 2 heterogeneity" in Cancer Science. This article published electronically on June 22, 2016, and in print in July 2016. (Ex. 1009.) Therefore it qualifies as prior art to the '039 Patent under 35 U.S.C. § 102(a)(1).

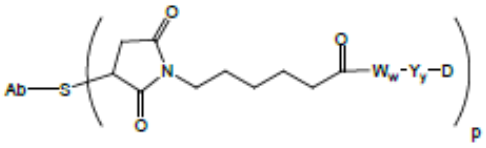
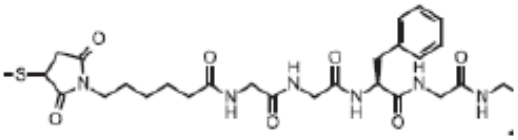
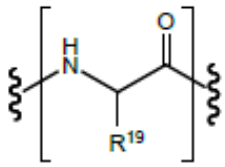
1. Claims 1–4

Based on PO's infringement allegations regarding the '039 Patent, *DS Cancer Sci Article* anticipates Claims 1–4. For example, the below excerpt shows that *DS Cancer Sci Article* discloses the structure of DS-8201, an ADC also known as DS-8201a (Ex. 1002 ¶ 159 n.24):



(Ex. 1009 at 1041 (emphasis added).)

PO's infringement allegations replicate the structure of DS-8201 and assert that it meets each limitation of at least Claims 1–4 of the '039 Patent:

Claim 4	DS-8201
1. An antibody-drug conjugate having the formula:  or a pharmaceutically acceptable salt thereof, wherein:	DS-8201 is an antibody-drug conjugate. In DS-8201, the payload drug is conjugated to the antibody using a linker that has the claimed formula, including a stretcher unit mc, an amino acid unit W_w with the tetrapeptide motif GGFG, and an aminomethylene spacer unit Y_y: 
Ab is an antibody,	In DS-8201, the antibody to which drugs are conjugated is trastuzumab.
S is sulfur,	In DS-8201, the linker's stretcher unit mc bonds to sulfur atoms on cysteine residues of the antibody.
each -W_w- unit is a tetrapeptide; wherein each –W– unit is independently an Amino Acid unit having the formula denoted below in the square bracket:  , wherein R^{19} is hydrogen or benzyl,	In DS-8201, the linker has an amino acid unit with the tetrapeptide motif GGFG. Glycine, or G, corresponds with the claimed amino acid formula wherein R^{19} is hydrogen. Phenylalanine, or F, corresponds with the claimed amino acid formula wherein R^{19} is benzyl.
Y is a Spacer unit,	In DS-8201, the linker has an aminomethylene spacer unit.

y is 0, 1 or 2,	In DS-8201, there is one spacer, so y is 1.
D is a drug moiety, and	In DS-8201, the drug that is conjugated to the antibody with the linker is the camptothecin derivative DXd, which acts as a topoisomerase inhibitor.
p ranges from 1 to about 20, and	In DS-8201, the value of p, which represents drug loading in terms of the drug-to-antibody ratio or "DAR", is about 7.7.
wherein the S is a sulfur atom on a cysteine residue of the antibody, and	In DS-8201, the linker's stretcher unit mc bonds to sulfur atoms on cysteine residues of the antibody.
wherein the drug moiety is intracellularly cleaved in a patient from the antibody of the antibody-drug conjugate or an intracellular metabolite of the antibody-drug conjugate.	DS-8201's linker is cleaved within the cell by proteases to release the camptothecin derivative drug DXd.
2. The antibody-drug conjugate of claim 1, wherein Y is a self-immolative spacer.	In DS-8201, the linker's aminomethylene spacer unit is self-immolative.
3. The antibody-drug conjugate of claim 2, wherein y is 1.	In DS-8201, there is one spacer, so y is 1.
4. The antibody-drug conjugate of claim 3, wherein p is about 3 to about 8.	In DS-8201, the value of p, which represents drug loading in terms of the drug-to-antibody ration or "DAR", is about 7.7.

(*See* Ex. 1006 at 8–9.) Though this chart is directed to dependent Claim 4, it incorporates all the limitations of Claims 1–3 from which it depends. In addition, a

disclosure that falls within the scope of a narrower claim would necessarily fall within the scope of a broader claim from which that narrower claim depends. As such, anticipation of Claim 4 establishes anticipation of Claims 1–3 as well.

2. Claim 5

Claim 5 depends directly from Claim 4 and further requires that "p is about 8." (Ex. 1001 at Claim 5.) Based on PO's own infringement allegations, and the maxim of that which infringes if later anticipates if earlier, Claim 5 is anticipated by *DS Cancer Sci Article*. PO's Complaint states that "the claims that depend from claim 4[] are exemplary on the issue of infringement." (Ex. 1006 at 7; *see also* Ex. 1006 at 9 ("[i]n DS-8201, the value of p . . . is about 7.7").) The *DS Cancer Sci Article* states that the "DAR is approximately 7 to 8." (Ex. 1009 at 1040.) Dr. Lambert confirms that DS-8201 comprises an ADC with "eight linker-drug structures conjugated to an antibody" and that "DS-8201a as disclosed in Exhibit 1009 has a 'p' value of 'about 8.'" (Ex. 1002 ¶¶ 162–63.) Accordingly, *DS Cancer Sci Article* anticipates Claims 5.

3. Claims 9–10

Claim 9 depends from any of Claims 1–5 and recites the further limitation "wherein the antibody is a monoclonal antibody." (Ex. 1001 at Claim 9.) Claim 10 depends from Claim 9 and recites the additional limitation "wherein the antibody is a humanized monoclonal antibody." (*Id.* at Claim 10.) As reflected in

DS Cancer Sci Article, the drug linker of DS-8201 is conjugated to the HER2-targeting antibody trastuzumab. (Ex. 1009 at 1039, 1040.) PO acknowledged this in its Complaint. (Ex. 1006 at 8 ("the antibody to which drugs are conjugated is trastuzumab").) The POSA at the relevant time would have understood trastuzumab to be a humanized monoclonal antibody. (Ex. 1037 at 164; Ex. 1002 ¶¶ 159–61.) Dr. Lambert confirms that "DS-8201a, an ADC disclosed in Exhibit 1009, contains a 'monoclonal antibody' and a 'humanized antibody.'" (Ex. 1002 ¶¶ 159–61.) Accordingly, *DS Cancer Sci Article* anticipates Claims 9 and 10.

VII. DISCRETIONARY DENIAL IS NOT APPROPRIATE HERE

A. The Office Has Not Already Considered Petitioners' Arguments

The Board has consistently "held that a reference that 'was neither applied against the claims nor discussed by the Examiner' does not weigh in favor of exercising . . . discretion under § 325(d)." *Fasteners for Retail, Inc. v. RTC Indus., Inc.*, IPR2019-00994, Paper 9 at 7–11 (P.T.A.B. Nov. 5, 2019); *Hobbico, Inc. v. Traxxas, L.P.*, IPR2018-00010, Paper 8 at 19 (P.T.A.B. Apr. 18, 2018) (citation in an IDS and consideration without comment are insufficient to indicate the substantive consideration of a reference).

The sole reference asserted in the grounds for unpatentability raised herein, *DS Cancer Sci Article* (Ex. 1009), was *not* of record during prosecution of the

'039 Patent. Accordingly, the reference asserted herein was neither applied against Claims 1–5, 9, and 10 nor discussed by the Examiner during prosecution of the '039 Patent,[24] and the arguments presented herein are not the same or substantially the same as those considered during prosecution. *See* IPR2019-00994, Paper 9 at 7–11.

As for Grounds 1, 2, and 3, the Office did not have the benefit of considering the unpatentability arguments as presented here (in the asserted grounds supported by expert testimony). The file history does not indicate that the Examiner considered these grounds. Thus, discretionary denial under 35 U.S.C. § 325(d) should not be exercised here. *See, e.g.*, *Paragon 28, Inc. v. Wright Med.*

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[24] Because the '839 Application purported to be entitled to multiple filing dates prior to public disclosures of DS-8201 (*see, e.g.*, Exs. 1009 (2016), 1034 (2015)), any potentially equivalent disclosures of DS-8201 would have been presented to the Office as non-prior art. And examiners need not verify entitlement to priority under 35 U.S.C. § 112(a) "unless the filing date of the earlier nonprovisional application is *relied upon* in a proceeding before the Office." MPEP § 201.08 (emphasis added).

Tech., Inc., IPR2019-00896, Paper 16 at 30 (P.T.A.B. Oct. 14, 2019); *Apple Inc. v. Omni Medsci, Inc.*, IPR2020-00029, Paper 7 at 52–55 (P.T.A.B. Apr. 22, 2020).

Thus, the proposed grounds are not cumulative to warrant discretionary denial.

B. Institution is Appropriate Under *Fintiv*

PO asserted the '039 Patent in the Texas Litigation against only Daiichi Sankyo Japan (Ex. 1006), and not the Petitioners, who cannot be sued for infringement in Texas. Petitioners and Daiichi Sankyo Japan then filed an action in Delaware seeking declaratory judgment of non-infringement of the '039 Patent ("the Delaware-1524 Litigation"). (*See infra* § VIII.B; Ex. 1038.) These litigations remain in their infancy.[25] This Petition was filed before a responsive pleading is due in the Texas Litigation. Accordingly, as explained below, the Board should institute a trial and not exercise its discretion to deny this Petition under *NHK Spring Co., Ltd. v. Intri-Plex Techs., Inc.*, IPR2018-00752, Paper 8

[25] A separate litigation in Delaware ("the Delaware-2087 Litigation") remains stayed pending the Arbitration, neither of which will include invalidity defenses or counterclaims. (*See infra* § VIII.B.)

(P.T.A.B. Sept. 12, 2018). The six *Fintiv* factors collectively favor institution. *See Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 11 (P.T.A.B. Mar. 20, 2020) (precedential).

The first *Fintiv* factor weighs in favor of institution.[26] Even absent evidence that a stay will be granted, this factor is neutral and does not support discretionary denial. *See, e.g.*, *Apple Inc. v. Fintiv, Inc.*, IPR2020-00019, Paper 15 at 12 (P.T.A.B. May 13, 2020) (informative); *Sand Revolution II, LLC v. Cont'l Intermodal Grp.–Trucking LLC*, IPR2019-01393, Paper 24 at 7 (P.T.A.B. June 16, 2020) (informative). Though the Board has recognized generally that courts "have the discretion to order stays after the Board has decided to institute trial on an asserted patent" and they often do just that,[27] a post-institution stay is especially

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[26] The first factor is "whether the court granted a stay or evidence exists that one may be granted if a proceeding is instituted." *Fintiv*, IPR2020-00019, Paper 11 at 6.

[27] *Precision Planting, LLC v. Deere & Co.*, IPR2019-01044, Paper 17 at 14 (P.T.A.B. Dec. 2, 2019) (citing *NFC Tech. LLC v. HTC Am., Inc.*, No. 2:13-cv-

likely here. In the most analogous circumstances, with respect to the progress of the litigation at the time of the institution decision—before claim construction or substantive rulings have issued—the very judges who are presiding over the Texas Litigation and the Delaware-1524 Litigation repeatedly have granted stays following institution. *See, e.g.*, *Uniloc USA, Inc. v. Avaya Inc.*, No. 6:15-cv-1168-JRG, 2017 WL 2882725 (E.D. Tex. Apr. 19, 2017) (Gilstrap, J.); *Image Processing Techs., LLC v. Samsung Elecs. Co.*, No. 2:16-cv-505-JRG, 2017 WL 7051628 (E.D. Tex. Oct. 25, 2017) (Gilstrap, J.); *Customedia Techs., LLC v. DISH Network Corp.*, No. 2:16-cv-129-JRG, 2017 WL 3836123 (E.D. Tex. Aug. 9, 2017) (Gilstrap, J.); *Intell. Ventures II LLC v. BITCO Gen. Ins. Corp.*, No. 6:15-cv-59-JRG, 2016 WL 4394485 (E.D. Tex. May 12, 2016) (Gilstrap, J.); *454 Life Scis. Corp. v. Ion Torrent Sys., Inc.*, No. 1:15-595-LPS, 2016 WL 6594083 (D. Del. Nov. 7, 2016) (Stark, J.).

In *Uniloc*, for instance, the defendants filed an IPR petition five months after service of the complaint, and the institution decision issued around the close of fact

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1058, 2015 WL 1069111, at *6 (E.D. Tex. Mar. 11, 2015) (Bryson, J., sitting by designation).

discovery—later in the litigation than it would issue here. 2017 WL 2882725 at *1–2. Judge Gilstrap granted a stay because the "bulk of the expenses that the parties would incur in pretrial work and trial preparation [were] still in the future" and the IPR proceeding could be "entirely case dispositive." *Id.* at *2–3; *see also Intell. Ventures II*, 2016 WL 4394485, at *3 (stayed following institution where the defendants filed IPR petitions seven and sixth months after service of the original and amended complaints, respectively). A stay is even more likely here, where Petitioners filed not long after service of the complaint, before a responsive pleading was filed in the Texas Litigation, and where fact discovery and claim construction will not have concluded by the time of the institution decision.

Judge Stark's decision in *Ethicon LLC v. Intuitive Surgical, Inc*., No. 17-871-LPS, 2019 WL 1276029 (D. Del. Mar. 20, 2019), is also informative. There, by the time the Board instituted proceedings, the court had already issued its claim construction order, fact discovery was complete, expert discovery was nearly concluded, and trial was just seven months away. *Id.* at *2. Notwithstanding the advanced stage of the case, Judge Stark granted the defendants' motion for a stay, in large part because the IPR would simplify the issues for trial. *Id.*

By the time the Board renders an institution decision on this Petition, the Texas Litigation and the Delaware-1524 Litigation will be less advanced, and farther from trial, than the litigations in *Uniloc* or *Ethicon*. Following institution,

Judges Gilstrap and Stark therefore are likely to stay the litigations at issue pending resolution of this potentially case dispositive petition, thereby favoring institution. *Cf. Medtronic, Inc. v. Teleflex Innovations S.A.R.L.*, IPR2020-00134, Paper 20 at 9–10 (P.T.A.B. June 26, 2020); *Google LLC v. Agis Software Dev., LLC*, IPR2020-00872, Paper 16 at 7–8 (P.T.A.B. Nov. 25, 2020) (analyzing presiding judge's consideration of motions to stay).

Accordingly, the primary concern that animates discretionary denials—that the proceedings before the PTAB and district courts will produce inefficient and inconsistent results, *see Fintiv*, IPR2020-00019, Paper 11 at 6—does not apply here.

The second *Fintiv* factor also supports institution.[28] There are no trial dates scheduled in any of the related matters before the U.S. District Courts. Even if one or both courts were to set a trial date, any motions regarding venue and Rule 12, and any attendant appeals, are unlikely to have been adjudicated by the time of

[28] The second factor is "proximity of the court's trial date to the Board's projected statutory deadline for a final written decision." *Fintiv*, IPR2020-00019, Paper 11 at 6.

institution, rendering any trial date far less certain than usual. *See Precision Planting*, IPR2019-01044, Paper 17 at 14 (U.S. District Courts will often "extend or accelerate deadlines and modify case schedules for myriad reasons."); *see also Sands Revolution II*, IPR2019-01393, Paper 24 at 8–10. That uncertainty is especially pronounced now, given that the Eastern District of Texas recently suspended jury trials for five months following the trial-related COVID infection of multiple attorneys, court staff, and jurors. *Infernal Tech., LLC v. Sony Interactive Entm't LLC*, No. 2:19-cv-00248-JRG (Dkt. No. 261) (E.D. Tex. Nov. 20, 2020).

The Board "continues to be fully operational and meeting all statutory deadlines for final written decisions." *Juniper Networks, Inc. v. Packet Intel. LLC*, IPR2020-00339, Paper 21 at 18 (P.T.A.B. Sept 10, 2020) (citation omitted) (internal quotation marks removed). Even without subsequent adjustment, any trial date set by a district court will be, at the earliest, in close proximity to the statutory deadline for a final written decision in these proceedings, militating against discretionary denial. *See, e.g., SMIC, Ams. v. Innovative Foundry Techs., LLC*, IPR2020-00786, Paper 10 at 20–21 (P.T.A.B. Oct. 5, 2020); *Apple Inc. v. Parus Holdings, Inc.*, IPR2020-00687, Paper 9 at 14–15 (P.T.A.B. Sept. 23, 2020) (about a two month difference, institution granted); *Juniper Networks, Inc.*, IPR2020-00339, Paper 21 at 15–16.

The third *Fintiv* factor, "investment in the parallel proceeding by the court and the parties," favors institution, given the infancy of the district court litigations and the lack of significant resource investment by the courts and the parties in those cases. *Fintiv*, IPR2020-00019, Paper 11 at 6.

As to the fourth *Fintiv* factor, "overlap between issues raised in the petition and in the parallel proceeding," *id.*, such overlap exists in virtually every PGR with parallel district court litigation. As explained with respect to the first and second *Fintiv* factors, however, the Board's expertise in addressing patentability issues prior to the district courts reaching them at trial provides for the possibility of simplifying issues for trial in those litigations or eliminating the need for trial altogether. *See, e.g. Juniper Networks*, IPR2020-00339, Paper 21 at 17–18; *MED-EL Elektromedizinische Geräte Ges.m.b.H v. Sonova AG*, IPR2020-00176, Paper 13 at 15 (P.T.A.B. June 3, 2020) ("[O]verlap may inure to the district court's benefit, however, by simplifying issues for trial should we reach our determination on the challenges raised in the Petition before trial.").

In addition, neither of the Petitioners are parties to the Texas Litigation, and, consistent with the law regarding venue, neither could have been sued in the Texas

Litigation. This fact weighs strongly in favor of institution pursuant to the fifth *Fintiv* factor.[29]

PGR was created to provide an "alternative to litigation" of a patent asserted in district court. 77 Fed. Reg. 48,612 (Aug. 14, 2012). Relying on such litigation to deny PGR institution frustrates that purpose. Even as applied to real party-in-interest Daiichi Sankyo Japan, the discretionary denial of this quickly filed PGR would render illusory the congressionally mandated right to challenge newly issued patents, specifically including patents already involved in district court infringement actions. *See* 35 U.S.C. § 325(a)(3). But the opportunity of petitioners like AstraZeneca US to seek cancellation through PGR of a patent that threatens their business cannot be abrogated on the basis of a lawsuit in which it was not—and legally could not have been—named as a Defendant. That result contravenes both Congressional intent and basic principles of fairness, especially given the demonstrated willingness of the two district courts at issue to stay

[29] The fifth factor is "whether the petitioner and the defendant in the parallel proceeding are the same party." *Fintiv*, IPR2020-00019, Paper 11 at 6.

litigation following institution and defer to the Board's determination on unpatentability.

Finally, other circumstances (*Fintiv* factor six[30]), including that Petitioners diligently sought review within approximately two months of PO's infringement allegations (and long before expiry of the nine-month statutory window) and the manifest unpatentability of the challenged claims, favor institution. *See* 35 U.S.C. § 321(c). The Supreme Court recently underscored the significant public interest against "leaving bad patents enforceable," *Thryv, Inc. v. Click-To-Call Techs., LP*, 140 S. Ct. 1367, 1374 (2020), and the evidence and arguments set forth herein establish that Claims 1–5, 9, and 10 of the '039 Patent are unpatentable. (*See supra* § VI.)

VIII. MANDATORY NOTICES UNDER 37 C.F.R. § 42.8

A. Real Parties-in-Interest

Real parties-in-interest include Petitioners Daiichi Sankyo, Inc. and AstraZeneca Pharmaceuticals, LP, as well as Daiichi Sankyo Company, Limited and AstraZeneca UK Limited.

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[30] The sixth factor is "other circumstances that impact the Board's exercise of discretion, including the merits." *Fintiv*, IPR2020-00019, Paper 11 at 6.

B. Related Matters

The ’039 Patent is implicated in the following co-pending matters:

- *Daiichi Sankyo Co., Ltd. v. Seattle Genetics, Inc.*, No. 1:19-cv-02087-LPS (D. Del.) (“the Delaware-2087 Litigation”)
- *Seattle Genetics, Inc. v. Daiichi Sankyo Co., Ltd.*, American Arbitration Association Case No. 01-19-0004-0115 (Brown, Arb.) (“the Arbitration”)
- *Seagen Inc. v. Daiichi Sankyo Co., Ltd.*, No. 2:20-cv-00337 (E.D. Tex.) (“the Texas Litigation”)
- *Daiichi Sankyo, Inc*. et al. *v. Seattle Genetics, Inc.*, No. 1:20-cv-01524-LPS (D. Del.) (“the Delaware-1524 Litigation”)

C. Counsel and Service Information

Petitioners designate lead and back-up counsel as noted below. Powers of attorney pursuant to 37 C.F.R. § 42.10(b) accompany this Petition.

Lead Counsel	Back-Up Counsel
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Please address all correspondence to counsel at the addresses above. Petitioners consent to electronic service by email at: Daiichi_Sankyo-Seagen-PGR-PH@paulhastings.com, and Enhertu@wc.com.

D. Time for Filing Under 37 C.F.R. § 42.202

The '039 Patent issued on October 20, 2020, and this Petition is being timely filed no later than the date that is nine months after the date of the grant of the '039 Patent.

E. Payment of Fees Under 37 C.F.R. § 42.15(a)

The PTO is authorized to charge all fees due at any time during this proceeding, including filing fees, to Deposit Account No. 50-2613.

IX. CONCLUSION

For the reasons presented above, Petitioners request institution of PGR for Claims 1–5, 9, and 10 of the '039 Patent, and a finding that the claims are unpatentable based on the above grounds.

Respectfully submitted,

Dated: December 23, 2020 By: /Preston K. Ratliff II /
Preston K. Ratliff II (Reg. No. 43,034)
Counsel for Petitioners

CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that the foregoing Petition for Post-Grant Review of U.S. Patent No. 10,808,039 contains, as measured by the word processing system used to prepare this paper, 16624 words. This word count does not include the items excluded by 37 C.F.R. § 42.24 as not counting towards the word limit.

Respectfully submitted,

Dated: December 23, 2020

By: /Preston K. Ratliff II /
Preston K. Ratliff II (Reg. No. 43,034)
Counsel for Petitioners

CERTIFICATE OF SERVICE

I hereby certify that on December 23, 2020, I caused a true and correct copy of the foregoing Petition for Post-Grant Review of U.S. Patent No. 10,808,039 and supporting exhibits to be served via express mail on the PO at the following correspondence address of record as listed on PAIR:

Fish & Richardson P.C.
PO Box 1022
Minneapolis, MN 55440-1022

Respectfully submitted,

Dated: December 23, 2020 By: /Preston K. Ratliff II /
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