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On behalf of **Illumina, Inc.**

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ILLUMINA, INC.
Petitioner

v.

**THE TRUSTEES OF COLUMBIA UNIVERSITY
IN THE CITY OF NEW YORK**
Patent Owner

IPR2018-00291	Patent 9,718,852
IPR2018-00318	Patent 9,719,139
IPR2018-00322	Patent 9,708,358
IPR2018-00385	Patent 9,725,480
IPR2018-00797	Patent 9,868,985*

ILLUMINA'S SUPPLEMENTAL BRIEF REGARDING ESTOPPEL

*This identical paper is being filed in each of these five IPRs.

TABLE OF CONTENTS

	Page No.
1. Question 1: Collateral estoppel applies to these IPRs	1
2. Question 2: Columbia is estopped from relitigating the previously decided <i>issues</i>	1
3. Question 3: A patentable distinction under 37 C.F.R. § 42.73(d)(3)(i) is not necessarily a material difference for these purposes	2
4. Question 4: Columbia has made it unnecessary for the Board to reweigh obviousness for the claims as a whole in these IPRs.....	4
a. The existence of different claim elements in a subsequent patent does not avoid estoppel if the new elements are not materially different	4
b. In these IPRs, Columbia has not identified a new claim element that materially alters the question of patentability	5
c. Columbia confuses “issues” with “arguments”	9
5. Question 5: Estoppel applies to all issues raised in these IPRs.....	10
a. Collateral estoppel applies that Tsien (alone or in view of Prober) renders obvious nucleotide analogues for SBS, including cleavability and incorporation of 3'-O-allyl.....	10
b. Collateral estoppel applies that Tsien (alone or in view of Prober) renders obvious nucleotide analogues in SBS, including the claimed label attachment means and locations	13
c. Prior conclusions of obviousness were based on the specific 3'-O-allyl (2-propenyl) blocking group	15
d. Columbia is estopped from relitigating patentability over Dower	15

TABLE OF AUTHORITIES

Page No.

<i>Aqua Products, Inc. v. Matal</i> 872 F.3d 1290 (Fed. Cir. 2017) (en banc)	12
<i>B & B Hardware v. Hargis Indus., Inc.</i> , 135 S. Ct. 1293 (2015).....	1, 2, 5
<i>Bourns, Inc. v. United States</i> , 537 F.2d 486 (Ct. Cl. 1976) (per curiam)	4, 5, 8, 9
<i>MaxLinear, Inc. v. CF Crespe LLC</i> , 880 F.3d 1373 (Fed. Cir. 2018)	1, 5
<i>MaxLinear, Inc. v. Cresta Tech. Corp.</i> , IPR2015-00592, Paper 78 (P.T.A.B. 2018).....	5
<i>Nestle USA, Inc. v. Steuben Foods, Inc.</i> , 884 F.3d 1350 (Fed. Cir. 2018)	1
<i>Ohio Willow Wood Co. v. Alps S., LLC</i> , 735 F.3d 1333 (Fed. Cir. 2013)	1, 4, 9
<i>Roche Palo Alto LLC v. Apotex, Inc.</i> , 531 F.3d 1372 (Fed. Cir. 2008)	13
<i>Westwood Chem. Inc. v. U.S.</i> , 525 F.2d 1367 (Ct. Cl. 1975).....	9

OTHER AUTHORITIES

37 C.F.R. § 42.73	2, 3, 4, 13
77 Fed. Reg. 48612 (Aug. 14, 2012)	13

Pursuant to the Board's Order (Paper 61),¹ Petitioner Illumina, Inc. ("Illumina") addresses the estoppel issues as requested by the Board.

1. Question 1: Collateral estoppel applies to these IPRs

"[T]he general rule [of collateral estoppel] is that when an issue of fact or law is actually litigated and determined by a valid and final judgment, and the determination is essential to the judgment, the determination is conclusive in a subsequent action between the parties, whether on the same or a different claim." *B & B Hardware v. Hargis Indus., Inc.*, 135 S. Ct. 1293, 1303 (2015); Paper 61 at 3-4. Collateral estoppel applies in IPR proceedings at the PTAB. *See, e.g., MaxLinear, Inc. v. CF Crespe LLC*, 880 F.3d 1373, 1376 (Fed. Cir. 2018); *Nestle USA, Inc. v. Steuben Foods, Inc.*, 884 F.3d 1350, 1351 (Fed. Cir. 2018).

The Board previously held all challenged claims of Columbia's U.S. Pat. Nos. 7,713,698, 7,790,869, and 8,088,575 unpatentable; and the Federal Circuit affirmed. Pet. at 1. These decisions are binding as a matter of collateral estoppel, and Columbia cannot argue otherwise. *See MaxLinear*, 880 F.3d at 1376.

2. Question 2: Columbia is estopped from relitigating the previously decided issues

Collateral estoppel in IPRs "is not limited 'to patent claims that are identical. Rather, it is the identity of the *issues* that were litigated that determines whether collateral estoppel should apply.'" *Nestle*, 884 F.3d at 1352 (quoting *Ohio Willow*

¹ Citations to papers and exhibits are from IPR2018-00291 except where indicated.

Wood Co. v. Alps S., LLC, 735 F.3d 1333, 1342 (Fed. Cir. 2013) (emphasis in original). Thus, although the instant proceedings are based on different claims, Columbia is collaterally estopped from relitigating the *issues* decided in the prior proceedings. The specific issues where estoppel applies are discussed below.

3. Question 3: A patentable distinction under 37 C.F.R. § 42.73(d)(3)(i) is not necessarily a material difference for these purposes

Patent Owner Estoppel under Rule 42.73(d)(3) is different from the common law doctrine of collateral estoppel in *B & B Hardware*. But both doctrines lead to the same result in these IPRs; both Patent Owner Estoppel and collateral estoppel dictate that the instant claims should be cancelled.

Patent Owner Estoppel applies when there is an adverse judgment, and the adverse judgment precludes a patent applicant or owner “from taking action inconsistent with the adverse judgment.” 37 C.F.R. § 42.73(d)(3). Subsection (i) of this rule provides one example of a precluded action—obtaining “a claim that is not patentably distinct from a finally refused or canceled claim.” *Id.* Patent Owner Estoppel is distinct from common law collateral estoppel, and a patentable distinction under 37 C.F.R. § 42.73(d)(3)(i) is therefore not necessarily a material difference when applying *B & B Hardware*.

Columbia violated Rule 42.73(d)(3) while prosecuting the claims at issue. The Examiner found the claims were “not patentably distinct” (Ex. 1009 at 100) from claims previously held unpatentable. *Id.* at 102; Pet. at 4-7. Columbia was

bound by Rule 42.73(d)(3) to refrain from obtaining these claims unless it convinced the Examiner to withdraw this finding. Instead, Columbia evaded the Examiner's finding with a terminal disclaimer. The Examiner's patentably indistinct finding was not addressed during prosecution and remains intact today.

During prosecution, Columbia's sole argument for nonobviousness was that it invented a nucleotide with a "small" 3'-O-group. Ex. 1009 at 22-24. The Board, however, previously held Claim 31 of the '869 patent unpatentable, which recited "wherein the cleavable chemical group capping the 3' OH group is a small chemical moiety." Ex. 1005 at 11; Ex. 1010 at 34:48-50. The same is true of cancelled Claim 1 of the '575 patent. Ex. 1007 at 11, 13, 16-17; Pet. at 61, 65; Ex. 1054 at 33:40-44. Columbia ignored the C.F.R. by premising patentability on a limitation (a "small" 3'-O-group) that is indistinct from the cancelled claims.

Columbia continued to violate Rule 42.73(d)(3) in these IPRs by arguing for patentability based on subject matter ("small") and two other issues already previously-held unpatentable by the Board—Tsien and Dower disclosing (1) polymerase incorporation and (2) cleavage conditions. *See infra*, Section 4.b.

Rule 42.73(d)(3) provides an appropriate mechanism for the Board to police Columbia's actions. Columbia is prosecuting ***an additional 10 pending applications*** that share the same specification with the previously cancelled patents. Paper 60 at 1. Should any of those issue, it is likely that the Parties will

be back before the Board yet again, potentially on these same issues. Failure to apply and enforce Rule 42.73(d)(3) against Columbia would render this rule meaningless, especially in view of Columbia's demonstrated history of evading Examiner findings of patentable indistinctness to prosecute and obtain patents that are indistinct from the finally refused claims of the previous IPRs.

4. Question 4: Columbia has made it unnecessary for the Board to reweigh obviousness for the claims as a whole in these IPRs

Common law estoppel applies to preclude Columbia's patents in these IPRs. Columbia did not argue that any of its "narrowed" claim elements convey patentability, so it is unnecessary for the Board to consider those elements when considering estoppel.

a. The existence of different claim elements in a subsequent patent does not avoid estoppel if the new elements are not materially different

The Federal Circuit has explained that, where the differences between the unadjudicated and adjudicated claims do not materially alter the question of validity, collateral estoppel applies:

In Ohio Willow Wood Co. v. Alps South, LLC, 735 F.3d 1333, 1342 (Fed. Cir. 2013), we pointed out that "precedent does not limit collateral estoppel to patent claims that are identical.... If the differences between the unadjudicated patent claims and adjudicated patent claims do not materially alter the question of invalidity, collateral estoppel applies." *See also Soverain*, 778 F.3d at 1315; *Bourns, Inc. v.*

United States, 537 F.2d 486, 493 (Ct. Cl. 1976) (per curiam).

MaxLinear, 880 F.3d at 1377 (ellipses in original, emphasis added). “[T]he Federal Circuit’s citation of *Bourns* is of particular relevance.” *MaxLinear, Inc. v. Cresta Tech. Corp.*, IPR2015-00592, Paper 78 at 4 (P.T.A.B. 2018). In *Bourns*, the court explained the practicalities of applying estoppel as follows:

Where, as here, the distinguishing features of the adjudicated and unadjudicated claims appear to be the same, and neither the text of the patent nor the plaintiffs here attribute any importance or significance to the additional elements included in the unadjudicated claims, it is difficult to justify a further trial merely because of the presence of those elements in the claims.

Bourns, 537 F.2d at 494. The court recognized that “several differently worded claims may present identical issues.” *Id.* at 492. Trivial variations in subject matter do not create different issues, “[o]therwise, a party could escape the preclusive effect of an adverse judgment simply by adding an immaterial feature.” *B & B Hardware*, 135 S. Ct. at 1308. “Where the differences revealed by a comparison of the claims do not vary the relevant issues bearing on obviousness, collateral estoppel should apply.” *Bourns*, 537 F.2d at 493.

b. In these IPRs, Columbia has not identified a new claim element that materially alters the question of patentability

Columbia has filed over 175 pages of responses in this IPR. As Illumina previously stated, none of these pages argue that any of these “narrower” elements

Columbia added to the claims convey new patentability to its claims. Reply at 27-28; Ex. 1139 at 60-65. The *issues* related to patentability rely on the same claim elements previously adjudicated to be in or obvious over Tsien and Dower.

Columbia used underlining to identify allegedly new features in the present claims on pages 63-64 of its Patent Owner Response (“POR”). But the only two claim elements actually *argued* by Columbia as bearing on obviousness in this proceeding are “R(a) represents a small, chemically cleavable, chemical group capping the oxygen at the 3’ position” and “(b) does not interfere with recognition of the analogue as a substrate by a DNA polymerase.” Reply at 27-28.

Columbia underlined “small” as an allegedly unlitigated issue, but the presence of a small, chemically cleavable capping group that does not interfere with a polymerase in the art at issue in these IPRs was litigated previously. For example, Claim 1 of the ’575 patent recited “a small removable chemical moiety capping the 3’-OH group of the sugar of the nucleotide analogue, wherein said small cleavable chemical group does not interfere with the recognition of the nucleotide analogue by polymerase as a substrate.” Ex. 1054 at 33:40-44 (emphases added). Dependent Claim 2 recited “removing the chemical moiety capping the 3’-OH.” *Id.* at 34:31-35. The Board found “[t]he evidence as outlined above persuades us that Illumina has met its burden of proof by a preponderance of evidence” for Tsien and Dower. Ex. 1007 at 13, 17. The Board held both claims

unpatentable over Tsien and Dower. *Id.* at 13, 17. To do so, it was essential for the Board to determine that Tsien and Dower met these limitations. Thus, estoppel attaches to the issues of smallness, incorporation and cleavability.

Independent Claim 12 of the '869 patent recited “a cleavable chemical group capping the 3' OH group” that was cleaved by “a chemical means.” Ex. 1010 at 33:40-50; *see also id.* at 33:51-54 (dependent Claim 13, which required “chemical” cleavage). Dependent Claim 28 recited “wherein said cleavable chemical group does not interfere with the recognition of the nucleotide by a polymerase.” *Id.* at 34:40-42. Dependent Claim 31 recited “wherein the cleavable chemical group capping the 3'OH group is a *small chemical moiety*.” *Id.* at 34:48-50 (emphasis added). The Board found “Illumina identified specific disclosure in Tsien where each limitation is found” and held these claims unpatentable. Ex. 1005 at 11. In reaching this holding, it was essential for the Board to determine that Tsien met these limitations. Thus, collateral estoppel applies on the issues of smallness, incorporation and cleavability.

The remaining “features” of the present claims underlined by Columbia at pages 63-64 of its POR were routine in the prior art. For example, the “adenine” analogue recited in the preamble (underlined in POR at 63), is common and pervasive throughout the disclosures of both Tsien and Dower. *See* Pet. at 12-14, 17-20, 56-57. The same is true for thymine, cytosine, and guanine analogues. *See*

IPR2018-00318 Pet. at 13-14, 19-20, 56-57; IPR2018-00322 Pet. at 14, 17-20, 56-57; IPR2018-00385 Pet. at 15, 18-23, 56-59. These analogues were ubiquitous, and it is insulting to the knowledge of a POSA to suggest otherwise.

Columbia also underlined limitation R(c)—that the 3'-capping group “is stable during a DNA polymerase reaction.” POR at 63-64. Columbia further underlined “the covalent bond between the 3'-oxygen and R is stable during a DNA polymerase reaction.” POR at 64. The Petition showed that Tsien and Dower disclose these features, and Columbia did not dispute them. Pet. at 14, 25-26, 28-30, 61-62, 64-65. Indeed, the Petition identified disclosures for all underlined features, and Columbia chose not to dispute any of it. Reply at 28.

Columbia may be “technically correct that the claims are each directed to different combinations, but when analyzed realistically, the substance of the adjudicated and unadjudicated claims must be viewed as the same and the issues relevant to their validity are the same.” *Bourns*, 537 F.2d at 497. Applying even the slightest scrutiny reveals that “the differences between the adjudicated and unadjudicated claims relate only to things known in the art and, hence, the differences between the prior art and the claims at issue are the same.” *Bourns*, 537 F.2d at 493 (citation omitted). The additional elements recited in Columbia’s unadjudicated claims “do not distinguish the claimed combination as a whole from the prior art.” *Id.* Thus, they do not provide an adequate basis “on which to

withhold application of the estoppel.” *Id.* at 497.

Columbia had a full and fair opportunity to argue that any of the underlined features provides a patentable distinction. Its silence on these features indicates they were in the prior art. *See Bourns*, 537 F.2d at 493-94 (“Most significantly, plaintiffs do not contest this, offering not one word that suggests that either of those features contributed in any way to any of the stated objects of the patent, or that they are in any way important to the combination set forth in the claims in which they appear.”); *see also Ohio Willow Wood*, 735 F.3d at 1343. The current proceedings have been “relitigation of the same issues already decided adversely to the patentee and [are] a transparent attempt to overturn the prior obviousness determination. That is improper and collateral estoppel is applicable under such circumstances.” *Bourns*, 537 F.2d at 495; *see also Westwood Chem. Inc. v. U.S.*, 525 F.2d 1367, 1380 (Ct. Cl. 1975).

c. Columbia confuses “issues” with “arguments”

In its Sur-reply, Columbia argued that Illumina failed to identify any argument made in these IPRs that were made in a prior IPR. Sur-reply at 31. That is untrue. Reply at 27; Ex. 1127 at 11-12; Ex. 1128 at 3; Ex. 1139 at 68-71. But even if it was true, it would have been immaterial. Binding precedent is clear that the proper collateral estoppel analysis is whether any added/different claim element materially alters the question of patentability. The Board previously

decided the *issue* of patentability on the exact same claim elements that Columbia has argued in these proceedings. Columbia's assertion that it is making *new arguments* against the *same issues* is irrelevant to estoppel.

5. Question 5: Estoppel applies to all issues raised in these IPRs

Columbia's entire defense in these proceedings relates to the issues of "smallness," incorporation, and cleavability. As discussed above, each of these issues was previously decided against Columbia, and Columbia is collaterally estopped from now relitigating those same issues.

a. Collateral estoppel applies that Tsien (alone or in view of Prober) renders obvious nucleotide analogues for SBS, including cleavability and incorporation of 3'-O-allyl

The Board previously determined that Tsien and Dower "describe SBS methods which use base-label nucleotides and nucleotides containing a removable chemical moiety at the 3'-OH position." Ex. 1005 at 5. The Board found that Columbia did not identify disclosures that disparage Tsien's disclosures "or that would have led one of ordinary skill in the art to conclude that they were unsuitable for the SBS purpose described by Tsien." *Id.* at 25.

"Columbia raise[d] the issue of whether there would have been a reasonable expectation of success that a nucleotide analogue with a label on the base and a capping group on the 3'-OH would be incorporated into a DNA." Ex. 1006 at 24. Columbia litigated whether Metzker provided evidence of unpredictability in

incorporation. *Id.* at 25. The Board found “Metzker describes testing 3’-OH modified terminators for their ability to be substrates for polymerases” and “shows the routines of testing” for incorporation. *Id.* After considering Columbia’s arguments, the Board determined “the preponderance of the evidence establishes that there was a reasonable expectation of success, and Columbia has not directed us to sufficient evidence to establish that it was unpredictable to have used the claimed nucleotide as a polymerase substrate for DNA sequencing.” *Id.* at 26.

In addition, Claim 2 of the ’698 patent recited “removing the chemical moiety capping the 3’-OH group of the sugar of the incorporated nucleotide analogue, thereby permitting the incorporation of a further nucleotide analogue so as to create a growing annealed nucleic acid primer extension strand.” Ex. 2003 at 35:24-28 (emphases added). This claim recited both cleavage and incorporation. Columbia’s expert raised the issue of whether sufficient cleavage conditions were known. Ex. 1098 at 112:8-24; Ex. 1034 ¶¶31, 39; Ex. 1047 at 6, 9; Ex. 1139 at 71. The Board held this claim obvious over identical art. Ex. 1006 at 9-14. Thus, the issues of expectation of success of cleavage and incorporation were determined, and collateral estoppel precludes Columbia from relitigating these issues.

In IPR2012-00007, Columbia essentially abandoned its original independent claims and focused its arguments on the amended claims. Ex. 1047 at 13-25; IPR2012-00007, Paper 136 at 53-54 (P.T.A.B. 2014). The substitute claims were

essentially the original dependent claims. Ex. 1137 at 4-7. Columbia's Motion to Amend included Proposed Substitute Claim 40, which contained a single limitation: "wherein said cleavable chemical group comprises $-\text{CH}_2\text{CH}=\text{CH}_2$ " (which is the allyl (2-propenyl) group). Ex. 1137, Appx. A at 4; Reply at 28.

Substitute Claim 40 depended from independent proposed Substitute Claim 34, which recited a "base that is attached to a detectable label through a cleavable linker," "the base is a deazapurine," and a "cleavable chemical group capping the 3' OH group" that is cleaved by "a chemical means." Ex. 1137, Appx A at 3-4; Reply at 28. The Parties litigated the efficient incorporation and cleavage of the 3'-O-allyl group. *See* Ex. 1128 at 3 ("Tsien discloses an allyl 3' blocking group, which would not interfere."); Ex. 1127 at 11-12 (same); Ex. 1098 at 112:8-24 (Columbia's expert raising the same allyl cleavage argument re-raised here).

The Board "considered the amended claim language and found that the amended claims remain unpatentable" and denied Columbia's motion. Ex. 1005 at 47. The Federal Circuit affirmed this denial because Columbia did "not establish patentability over the prior art" and explaining, at that time "motions to amend may properly be denied where the patentee has failed to establish patentability over the prior art of record." Ex. 1008 at 32.²

² The motion to amend burden was changed by *Aqua Products*, but "there is no 'change of law' or fairness exception to prevent application of claim preclusion."

In denying Columbia's motion on Claim 40, an essential element of the Board's judgment included a determination that the sole limitation, **the 3'-O-allyl group**, did not provide a patentable feature over Tsien. Thus, collateral estoppel precludes Columbia from relitigating patentability of the 3'-O-allyl capping group.

In addition, the "allyl" disclosure of Tsien was cited to meet the "incorporated" and "does not interfere" elements of Proposed Substitute Claims 43 and 49. Ex. 1127 at 11-12. These elements corresponded to original claims 22 and 28. Ex. 1137, Appx. A at 5-6. This provides further reasons for estoppel to apply.

In addition, Patent Owner Estoppel under 37 C.F.R. § 42.73(d)(3)(i) precludes Columbia from relitigating the patentability of the 3'-O-allyl group. This Rule "provides estoppel against claims that are patentably indistinct from those claims that were lost, and claim amendments that were presented and denied, during a trial." USPTO Response to Comment 213, 77 Fed. Reg. 48612, 48649 (emphasis added). Columbia presented the 3'-O-allyl blocking group as an amendment during trial, and the Board denied the amendment. Thus, Patent Owner Estoppel precludes Columbia from relitigating the 3'-O-allyl group.

b. Collateral estoppel applies that Tsien (alone or in view of Prober) renders obvious nucleotide analogues in SBS, including the claimed label attachment means and locations

The Board previously found that "the disclosure in three publications of a

Roche Palo Alto LLC v. Apotex, Inc., 531 F.3d 1372, 1380 (Fed. Cir. 2008).

label on the nucleotide base and of a removable 3'-OH group (e.g., Tsien, Dower, and Stemple III) shows a recognition within the prior art that such nucleotides were useful and effective in SBS methods.” Ex. 1005 at 6. The Board determined that unpatentable Claim 15 was “directed to a nucleotide analogue comprising the following features: (1) a base that is attached to a detectable label; (2) through a cleavable linker; (3) a deoxyribose comprising a cleavable chemical group capping the 3'-OH group; and 4) a deaza-substituted base.” *Id.* at 19-20. The Board made detailed findings about Tsien’s disclosures of features (1), (2) and (3). *Id.* at 20-23. With respect to feature (4), the Board found “there is generic disclosure in Tsien of labeling the base moiety, including a specific reference to Prober I, the latter describing C-7 deaza-labeled purine bases.” *Id.* at 29. The Board found that Prober discloses a linker attached “to the 7 position in the 7-deazapurines.” *Id.* at 23-24, 26-29. The Federal Circuit affirmed that “the express invitation to incorporate a 3'-blocked dNTP having a fluorescent base label using the method disclosed in Prober provides a motivation to combine Tsien with the 7-deazapurine of Prober.” Ex. 1008 at 21.

In the previous IPRs, “Columbia raise[d] the issue of whether there would have been a reasonable expectation of success that a nucleotide analogue with a label on the base and a capping group on the 3'-OH would be incorporated into a DNA.” Ex. 1005 at 33. The Board held Columbia’s claims unpatentable because

“[a] preponderance of the evidence supports an affirmative answer.” *Id.* Columbia is therefore collaterally estopped from relitigating this issue.

c. Prior conclusions of obviousness were based on the specific 3'-O-allyl (2-propenyl) blocking group

As discussed above in Section 5.a, Columbia moved to amend its claims to include the 3'-O-allyl (2-propenyl) group, the Parties litigated the patentability of this group, and the Board denied Columbia's Motion to Amend. Columbia is estopped from relitigating patentability based on the 3'-O-allyl blocking group.

d. Columbia is estopped from relitigating patentability over Dower

The Board previously found Dower “describes nucleotides with a label attached to the base and a small removable chemical moiety capping the 3'-OH group of the sugar of the nucleotide analogue, the two structural features of the nucleotide utilized in the claimed method of ‘determining the identity of a nucleotide analogue incorporated into a nucleic acid primer extension strand.’” Ex. 1007 at 10. The Board held Claim 1 of the '575 patent unpatentable over Dower. *Id.* at 9-13. Claim 1 also recited “wherein said small cleavable chemical group does not interfere with the recognition of the nucleotide analogue by polymerase.” *Id.* at 8. The Board previously decided unpatentability of the small, incorporation, and cleavage issues based on Dower. Estoppel applies.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of the foregoing **ILLUMINA'S SUPPLEMENTAL BRIEF REGARDING ESTOPPEL** is being served on March 26, 2019, via e-mail to counsel for the Trustees of Columbia University, at the email addresses below:

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