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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.

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

Patent Owner.

IPR2020-01177
Patent 10,435,742

**PETITIONER ILLUMINA'S REPLY TO
PATENT OWNER'S PRELIMINARY RESPONSE**

The Board should reject Columbia’s procedural challenges under 35 U.S.C. §§ 314(a) and 315(d) and irrelevant commentary regarding claim construction.

I. The Board’s §314(a) *Fintiv* Factors Favor Institution

A. *Fintiv* Factor #6 (Compelling circumstances and the merits)

The Board has extensive experience with the subject matter in this third-wave of IPRs. A Final Written Decision (“FWD”) here would mark nearly a decade of Board adjudication between identical parties, patent specifications, and Tsien and Dower prior art. The claims at issue are identical to those previously adjudicated, with a single negative limitation added. Pet.: 1-4. The Board is well-situated to adjudicate this matter.

On the merits, Columbia’s POPR concedes that the prior art meets all claim limitations. Columbia merely raises a similar grab-bag of arguments on motivation and expectation-of-success that the Board adjudicated against Columbia in past IPRs. Columbia’s retreat to those arguments demonstrates the Petition’s strength.

B. *Fintiv* Factors #1, 2, 3 and 5 (Likelihood of stay; Proximity of trial to FWD; Investment in parallel proceeding; Identity of parties)

The district court tentatively scheduled a 5-day jury trial that would conclude three weeks before the statutory deadline for a FWD in closely related IPR2020-00988. Ex. 1154: 18. The district court case, however, has already required seven extensions. *See* Exs. 1146-1153. The parties recently extended document production by nearly two months. Ex. 1152. This extension is evidence of the parties’ limited

investment in the case so far. To date, Columbia has produced just 10 documents that are non-duplicative with prior litigations. No fact witness depositions have been scheduled. Expert discovery on the merits has not yet commenced.

Additional district court delays are likely. Columbia extended claim construction briefing by filing a motion for reconsideration of the *Markman* Order. Ex. 1159. This motion, coupled with the two-month document production delay, could have a cascading effect to delay the remaining schedule. Ex. 1154: 19-20. Further, COVID-19 has caused countless Delaware jury trials to be continued and a backlog of trials because “it is anticipated that the Court will conduct no more than one jury trial at a time and will give priority to criminal trials.” Ex. 1155 ¶¶1, 5. District court uncertainty abounds, yet the Board has adhered to the 1-year statutory deadline for issuing FWDs. Illumina’s request to have unpatentability tried in this forum, which continues to provide date-certainty, should be given due consideration.

Illumina filed this IPR approximately nine months after the district court complaint. This time period spanned early lockdown phases of COVID-19, during which Illumina diligently evaluated the prosecution history, prior art, and substantial body of prior litigation between the parties, interacted with its expert witness, and drafted a meritorious IPR petition. Columbia argues that the timing of this IPR filing was delayed for tactical advantage in the pending Federal Circuit appeal. POPR: 58. Not true. While Columbia cited a single portion of this IPR Petition in its Federal

Circuit appeal (Ex. 1164: 3-4), it did so in a disingenuous attempt to confuse the Federal Circuit; it misleadingly conflated concepts of 3' protecting group cleavage efficiency and nucleotide polymerase incorporation efficiency. Ex. 1165: 4-6; Ex. 1166: 3-4. Illumina gains no advantage from the timing of this IPR, as this patent expired last month. Columbia's quibble with timing is the product of its own choice to assert unpatentable claims against Illumina in disjointed, multi-wave attacks over the past decade, causing inevitable overlap of any number of dates.

C. *Fintiv* Factor #4 (Overlap of issues)

Illumina's district court invalidity contentions include multiple preliminary invalidity grounds. A few of those grounds overlap with this IPR, while most do not. Ex. 2004: 5-11. Whether the IPR grounds will overlap with those actually litigated in district court remains uncertain given the early stages of the Delaware action.

II. The Board Should Reject Columbia's §325(d) Arguments

Columbia seeks to evade Hovinen's demonstration of efficient polymerase incorporation of a substituted 3'-*O*-MOM group under §325(d). POPR: 60. Columbia relies on the false premise that the POSA would myopically limit their prior art considerations to one type of nucleotide sequencing, SBS, and exclude other related sequencing techniques. *Id.* This premise is untenable. Columbia's witness agrees with Illumina that the POSA was broadly "researching DNA polymerases, and/or addressing DNA sequencing techniques" and Columbia "does not dispute"

these interests. Ex. 2048 ¶21; Pet.: 13; POPR: 6; Ex. 1024: 42. Columbia concedes that Hovinen was researching polymerase incorporation of substituted 3'-O-MOM nucleotides. Ex. 2048 ¶57. Under the POSA's agreed-upon interests, Hovinen (even if viewed as a Sanger reference) provides significant motivation. Indeed, Tsien, Dower, and Metzker demonstrate that the POSA routinely looked to Sanger sequencing methods (such as Prober) to improve SBS given that both are polymerase-based sequencing methods. *See* Ex. 1030: 14:53-56 (“analogous”), 25:4-12; Ex. 1031: 29:10-14; Ex. 1039: 4262 (“analogous”), 4266 (SBS nucleotides “tested in a Sanger-type DNA sequencing scheme”); Ex. 1029: 20-22; Ex. 1092: 38-39 (Dr. Ju's lab admitting Sanger and SBS are integrable). Columbia's argument that a POSA would not pursue Hovinen's substituted 3'-O-MOM nucleotides for SBS is belied by its own prior art Exhibit 2021 (“Kwiatkowski”), which is an SBS reference. Ex. 2021: 7:32-8:6 (citing Tsien); 3:18-37, 1:1-7; POPR: 46-47. Kwiatkowski demonstrated that substituted 3'-O-MOM nucleotides are efficiently incorporated by a polymerase. Ex. 2021: 17:11-18:29, Fig. 4 (compound 16).

Columbia also seeks to avoid Hiatt's disclosure of 3'-O-MOM nucleotides for polymerase incorporation under §325(d) because the Board previously stated that Hiatt “presents an immense number of possibilities for the blocking group.” POPR: 60-61. Hiatt was filed in 1994, six years before the priority date of Columbia's patent. Columbia's POPR seeks to anchor the POSA's understanding of Hiatt to

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