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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.

Case IPR2020-00988 (U.S. Patent 10,407,458) Case IPR2020-01065 (U.S. Patent 10,407,459) Case IPR2020-01177 (U.S. Patent 10,435,742) Case IPR2020-01125 (U.S. Patent 10,457,984)<sup>1</sup>

### PATENT OWNER'S RESPONSE

<sup>1</sup> An identical Paper is being entered into each listed proceeding.

DOCKET

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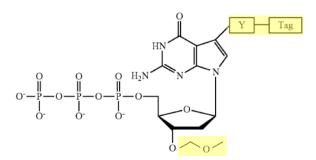
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## Case IPR2020-00988, -01065, -01125, -01177 U.S. Patent Nos. 10,407,458; 10,407,459; 10,435,742; 10,457,984

### I. <u>INTRODUCTION</u>

In the present proceedings, the claims of the patents-at-issue are narrowly tailored to a small genus of modified nucleotides. Illumina's Grounds 1 and 2 allege that a single embodiment of the genus is invalid for obviousness, specifically, the "MOM embodiment." The MOM embodiment is a nucleotide modified to have a MOM capping group attached to the 3' oxygen of the nucleotide sugar and a linker/label attached to the nucleotide base:



Ex. 1001 at claim 1 (relevant modifications highlighted).

Notably, the claims of the patents-at-issue do not cover the allyl embodiment that was previously the focus of the Allyl Claim IPRs.<sup>2</sup> In the Allyl Claim IPRs, two

<sup>2</sup> Columbia's SBS patents with the allyl embodiment are U.S. Patent Nos. 9,718,852; 9,719,139; 9,708,358; 9,725,480; and 9,868,985. They were challenged in IPR2018-00291, IPR2018-00318, IPR2018-00322, IPR2018-00385, and IPR2018-00797, respectively (collectively, "the Allyl Claim IPRs"). Case IPR2020-00988, -01065, -01125, -01177 U.S. Patent Nos. 10,407,458; 10,407,459; 10,435,742; 10,457,984 findings led a 2-1 majority to opine that the allyl embodiment would have been obvious to a POSA:

- 1. Metzker provided experimental data demonstrating some polymerase incorporation of the allyl capping group; and
- 2. Tsien prominently disclosed using the allyl capping group for Sequencing by Synthesis ("SBS").

Here, no prior art demonstrated that the MOM capping group could be incorporated by any polymerase and no prior art suggested the use of the MOM capping group for SBS. Indeed, it is undisputed that the Columbia inventors were the first to disclose using the MOM capping group for SBS, an insight they arrived at after discovering the particular chemical and structural features that dictate whether a capping group could be useful for SBS, and which the MOM capping group satisfies.

Just last week, in a European proceeding involving a corresponding European patent, Illumina admitted that a POSA would not have reasonably expected that the MOM embodiment could be successfully used in SBS, concluding that "[i]t was not plausible at the effective date [of October 6, 2000] that [Columbia's SBS] invention could be put into practice with MOM as a protective group based on the common general knowledge in the prior art." As detailed herein, that admission is one of Illumina's central positions in the European proceeding, where Illumina alleges invalidity of Columbia's European patent based on the contention that a POSA would *not* have been able to use the MOM capping group to practice SBS as of the

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