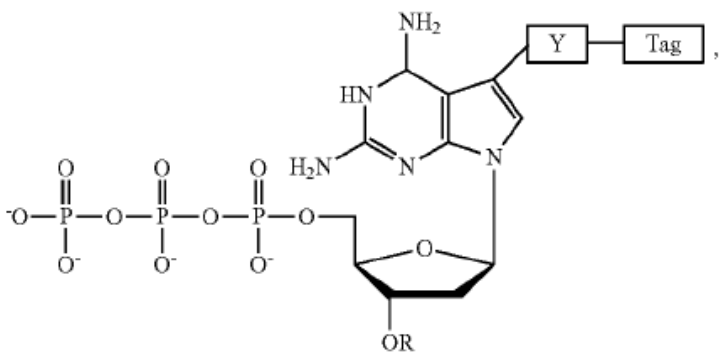
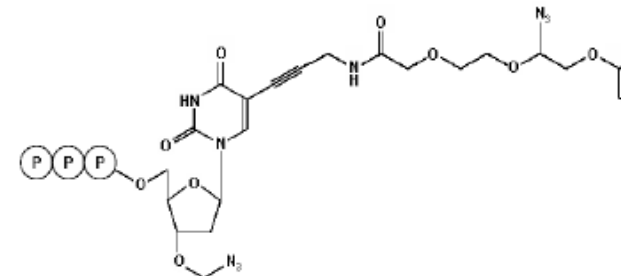
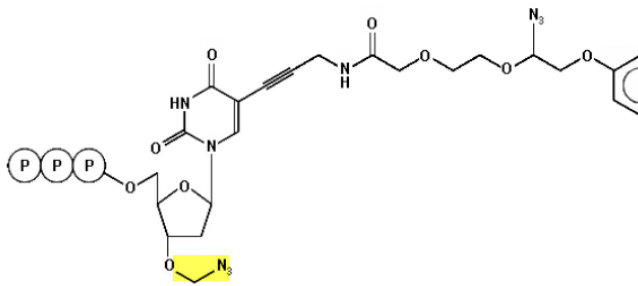


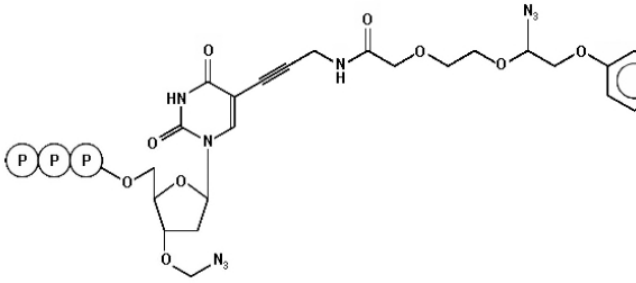
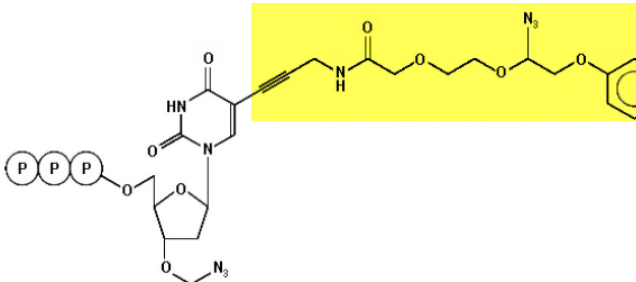
EXHIBIT 7

Columbia Ex
Illumina, Inc
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IPR2020-01

EXHIBIT 7

<p align="center">U.S. Pat. No. 10,407,458</p>	<p align="center">Infringement by Illumina’s nucleoside analogues in the 4-Channel Accused</p> <p align="center">Bentley <i>et al.</i>, Nature, Vol. 456:53-59 (2008) (“Bentley”)</p> <p align="center">Supplementary Information to Bentley (2008)</p> <p align="center">Milton <i>et al.</i>, WO 2004018497 A2 (2004) (“Milton”)</p>
<p>1. An guanine deoxyribonucleotide analogue having the structure:</p> 	<p>Illumina’s sequencing chemistry uses guanine deoxyribonucleotide analogues.</p> <p>“To ensure base-by-base nucleotide incorporation in our sequencing-by-synthesis chemistry, we used a set of four reversible terminators, 3’-O-azido deoxynucleoside triphosphates (A, C, G and T), each with a different removable fluorophore (Supplementary Fig. 1).</p>  <p>Ex. 5 at 14, Fig. 1a. Although only the structure for a guanine deoxyribonucleotide analogue is provided, Bentley in his patent and G nucleotides have the same general structure. Bentley’s patent also states that On information and belief, Illumina uses a guanine deoxyribonucleotide analogue with a linker attached to the 7-deaza position of the guanine base, as shown in the claimed structure. Ex. 12 at 74, component</p>

	linker attached to the 7-deaza position of a guanine).
wherein R (a) represents a small, chemically cleavable, chemical group capping the oxygen at the 3' position of the deoxyribose of the deoxyribonucleotide analogue, (b) does not interfere with recognition of the analogue as a substrate by a DNA polymerase, (c) is stable during a DNA polymerase reaction, (d) does not contain a ketone group, and (e) is not a $-\text{CH}_2\text{CH}=\text{CH}_2$ group;	<p>As shown in Fig. 1a of Supplementary Information to Ex. 5 at 14, Illumina uses an azidomethyl group (CH_2N_3) at position R (highlighted in yellow). The azidomethyl group is a small chemically cleavable group that does not contain a ketone group, and is not a $-\text{CH}_2\text{CH}=\text{CH}_2$ group.</p> <p><i>a</i></p>  <p>Ex. 5 at 14, Fig. 1a. Illumina uses these modified nucleotides for sequencing. Ex. 4 at 53 (“We sequenced DNA templates in 100 cycles of polymerase-directed single base extension.”) states that Illumina uses these nucleotides successfully in a polymerase reaction. “To accomplish DNA sequencing, it follows that the azidomethyl group does not interfere with recognition of the analogue as a substrate by a DNA polymerase and is stable during a DNA polymerase reaction.”</p>
wherein OR is not a methoxy group or an ester group;	Illumina uses an azidomethyl group to cap the 3'-OH of the deoxyribose to form an OR moiety. This OR moiety is not a methoxy group.
wherein the covalent bond between the 3'-oxygen and R is stable during a DNA polymerase reaction;	As Illumina uses nucleotides with an azidomethyl group for sequencing, base-by-base nucleotide incorporation in a stepwise manner, it follows that the bond between the 3'-oxygen and R is stable during a DNA polymerase reaction.

	<p>polymerase reaction. Ex. 4 at 53.</p>
<p>wherein tag represents a detectable fluorescent moiety;</p>	<p>As shown in Fig. 1a below, Illumina’s modified nucleotide includes a fluorescent moiety tag (highlighted below).</p> <p><i>a</i></p>  <p>Ex. 5 at 14, Fig. 1a.</p>
<p>wherein Y represents a chemically cleavable, chemical linker which (a) does not interfere with recognition of the analogue as a substrate by a DNA polymerase and (b) is stable during a DNA polymerase reaction; and</p>	<p>As shown in Fig. 1a below, Illumina’s modified nucleotide includes a chemically cleavable linker (highlighted below).</p> <p><i>a</i></p>  <p>Ex. 5 at 14, Fig. 1a. Illumina has indicated that this linker is cleavable using tris(2-carboxyethyl)phosphine (TCEP).</p> <p>As Illumina “sequenced” DNA templates by repeated polymerase-directed single base extension” using nucleotides, it follows that this linker (a) does not interfere</p>

	<p>the analogue as a substrate by a DNA polymerase and a DNA polymerase reaction. Ex. 4 at 53 (emphasis added) Figure S13 (showing “Illumina sequence reads” identified resulting from incorporation by a DNA polymerase of a deoxyribonucleotide analogue having a label attached to a cleavable, chemical linker); Ex. 12 at 74, compound 2</p>
<p>wherein the guanine deoxyribonucleotide analogue:</p> <ul style="list-style-type: none"> i) is recognized as a substrate by a DNA polymerase, ii) is incorporated at the end of a growing strand of DNA during a DNA polymerase reaction, iii) produces a 3'-OH group on the deoxyribose upon cleavage of R, iv) no longer includes a tag on the base upon cleavage of Y, and v) is capable of forming hydrogen bonds with cytosine or a cytosine nucleotide analogue. 	<p>As discussed above, as Illumina “<i>sequenced</i> DNA templates” cycles of polymerase-directed single base extension” nucleotide analogues, including guanine deoxyribonucleotide analogues, that these nucleotide analogues are recognized as a substrate by a DNA polymerase, are incorporated at the end of a growing strand of DNA during a DNA polymerase reaction, and are capable of forming hydrogen bonds with cytosine or a cytosine nucleotide analogue.</p> <p>Illumina also discloses using tris(2-carboxyethyl)phosphonium salts to remove the fluorescent dye [<i>i.e.</i> tag] and side arm from the base and simultaneously regenerate a 3' hydroxyl group for the next cycle of nucleotide addition (Supplementary Figure S53). Thus, Illumina’s sequencing chemistry results in a deoxyribonucleotide that produces a 3'-OH group on the deoxyribose upon cleavage of R and no longer includes a tag on the base upon cleavage of Y.</p>
<p>2. An guanine deoxyribonucleotide analogue having the structure:</p>	<p>Illumina’s sequencing chemistry uses guanine deoxyribonucleotide analogues.</p> <p>“To ensure base-by-base nucleotide incorporation in a sequencing reaction, we used a set of four reversible terminators, 3'-O-azido deoxynucleoside triphosphates (A, C, G and T), each with a different removable fluorophore (Supplementary Fig.</p>

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