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On behalf of: Patent Owner Illumina Cambridge Ltd.

By:

Lead Counsel: Robert A. Lawler REINHART BOERNER VAN DEUREN S.C. Tel.: 608-229-2217 Email: rlawler@reinhardtllaw.com	Backup Counsel: Brenton R. Babcock William R. Zimmerman (<i>pro hac vice</i>) Jonathan E. Bachand Sheila N. Swaroop KNOBBE, MARTENS, OLSON & BEAR, LLP Tel.: (949) 760-0404 Email: BoxIllumina@knobbe.com Derek C. Walter (<i>pro hac vice</i>) WEIL, GOTSHAL & MANGES, LLP Tel.: (650) 802-3000 Email: derek.walter@weil.com
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

INTELLIGENT BIO-SYSTEMS, INC.

Petitioner,

v.

ILLUMINA CAMBRIDGE LTD.

Patent Owner.

Case IPR2013-00517

U.S. Patent 7,566,537

**ILLUMINA'S MOTION FOR OBSERVATIONS ON THE
CROSS-EXAMINATION TESTIMONY OF
BRUCE BRANCHAUD, PH.D. AND MICHAEL METZKER, PH.D.**

Columbia Exhibit 2033
Illumina, Inc. v. The Trustees of Columbia
University in the City of New York
IPR2018-00322

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Zavgorodny's lack of data fails to provide an expectation of success

1. In Ex. 2155 at 290:9-12, Dr. Branchaud agreed that a one sentence statement with no references or data is insufficient for drawing conclusions. Zavgorodny only provides one sentence about azidomethyl cleavage, without any references or data. IBS' obviousness position rests on this single sentence; precisely the type of sentence that Dr. Branchaud testified is insufficient to support such a position.

2. In Ex. 2154 at 106:5-110:9, Dr. Metzker testified that he would require data before he could rely on Canard's single sentence statement that azides and carbonyl groups have strikingly similar electrophilicities and reactivities with nucleophiles in polymerases. He also admitted that Zavgorodny's azidomethyl disclosure is a single sentence, unsupported by data. *Id.*, 114:23-115:14. Applying Dr. Metzker's requirement for data to Zavgorodny renders Zavgorodny's single sentence azidomethyl disclosure unreliable and insufficient to provide an expectation that Zavgorodny would be compatible with Ju/Tsien.

Tsien's "N3" did not suggest an azidomethyl or removable blocking group

3. In Ex. 2155 at 32:15-18, Dr. Branchaud admitted he was not aware of any removable 3'-OH protecting groups containing an azido moiety when Tsien published. This contradicts his statement that Tsien's reference to "N3" could refer to a removable 3'-OH protecting group. Ex. 1031, ¶ 10. Dr. Branchaud's new testimony (Ex. 1031, ¶ 10) also contradicts his prior testimony, in which he

interpreted Tsien's "N3" statement to be non-removable from a 3'-carbon. Ex. 2081, 100:1-101:6. Dr. Branchaud's cross-examination confirms that Tsien was not referring to a removable 3'-OH protecting group containing an azido moiety.

4. In Ex. 2155 at 42:4-43:3, Dr. Branchaud conceded that Tsien's "blocking groups" refer to both irreversible and reversible blocking groups. But Dr. Branchaud's declaration replaces Tsien's "blocking group" terminology with his own "protecting group" terminology. Ex. 1031, ¶ 10. Protecting groups can be removed to expose a 3'-OH group, but irreversible blocking groups cannot. Ex. 2155, 42:4-43:3. Dr. Branchaud testified that several of Tsien's groups are not removable (*i.e.*, not protecting groups). Ex. 2081, 100:1-101:6; Ex. 2155, 45:7-46:23; Ex. 2083, 118:13-119:13. This supports that Tsien's "N3" group was an irreversible blocking group that could not be removed to expose a 3'-OH group.

Azido protecting groups would not be expected to work with Ju or Tsien

5. In Ex. 2155 at 157:13-158:2, Dr. Branchaud testified that the reaction of a phosphine with an azide on a nucleotide produces an amine that cleaves phosphate ester linkages in DNA. Ex. 1035, pp. 85-86. He also confirmed that Zavgorodny's cleavage conditions produce an amine. Ex. 2155, 246:19-247:15. Thus Zavgorodny's cleavage conditions would have been expected to be incompatible with the DNA in Ju and Tsien's methods.

6. In Ex. 2154 at 236:6-23, Dr. Metzker confirmed that 3'-O-azidomethyl

groups cause steric clashes within the active site of DNA polymerases. Ex. 2147, p. 7412, Fig. 4; Ex. 1025, 70:7-73:3. Thus Zavgorodny's 3'-O-azidomethyl group would have been expected to be incompatible with Ju's and Tsien's methods due to steric clashes within DNA polymerases. This is also consistent with Dr. Romesberg's testimony that shape matters more than size for polymerases, and azido groups have a very rigid shape. Ex. 1025, 70:1-71:25.

7. In Ex. 2154 at 81:8-13, Dr. Metzker testified that it was not known that ether bonds were hard to cleave under DNA compatible conditions. But the art did teach this. Ex. 2043, p. 4; Ex. 1002, 3:9-14.

8. IBS incorrectly asserts that "Ju *states* that ether linkages are preferred 3'-OH protecting groups . . ." Paper 54, p. 3 (emphasis added). Dr. Metzker correctly testified that Ju makes no such statement. Ex. 2154, 75:17-76:4.

Zavgorodny's conditions were not expected to be compatible with Ju/Tsien

9. In Ex. 2155 at 224:10-228:16, Dr. Branchaud testified that he did not offer any opinion on 3'-protecting group cleavage efficiency required for Ju and Tsien's methods. Dr. Metzker is also silent on this issue. Ex. 2154, 197:23-198:4. Thus, IBS did not rebut Illumina's evidence that Zavgorodny's expected efficiency would fail to be compatible with the requirements of Ju /Tsien. *See, e.g.*, Ex. 2011, ¶¶ 32-33, 37, 44-53.

10. In Ex. 2155 at 177:12-179:11, Dr. Branchaud recognized that there are

examples of Staudinger reactions with side products in which the efficiency is less than quantitative. Ex. 2151, p. 6270. This is consistent with Loubinoux's data that reduction of azides by phosphines was less efficient than other methods. Ex. 2011, ¶ 44. Moreover, the reduction of azides on nucleotides was known to produce more side-products than the reduction of azides on nucleosides. Ex. 2155, 197:3-198:20; Ex. 2152, p. 16001. This contradicts Dr. Branchaud's opinion (Ex. 1031, ¶¶ 15-17) that optimization of Zavgorodny would result in compatibility with Ju/Tsien.

11. In Ex. 2155 at 169:17-171:5, Dr. Branchaud testified that contaminants can reduce reaction efficiency. Ex. 1033, p. 34. Triphenylphosphine can contain contaminants up to 1%. Ex. 2155, 173:4-174:14; Ex. 2150, p. 1337. Dr. Metzker stated that 0.5% contaminants is problematic for sequencing. Ex. 2147, p. 7408. Thus, the expected contaminants in Zavgorodny's triphenylphosphine would be expected to be incompatible with Ju and Tsien.

12. In Ex. 2155 at 160:9-161:11, 216:16-18, and 238:3-16¹, Dr. Branchaud testified that none of the references he identified provided azide reduction efficiency for a nucleotide. Dr. Branchaud agreed that Ex. 2152 reports that the

¹ While Dr. Branchaud refers to a Staudinger reaction to make a nucleotide in Ex. 1041, he later clarified that this is not a Staudinger reaction relevant to this IPR, but rather an Arbusov rearrangement. Ex. 2155, 243:5-244:24 & 323:8-21.

reduction of an azide to an amine on a nucleoside (AZT) was 80% efficient, whereas with the nucleotide (AZTMP) it was 19.6% efficient. Ex. 2155, 197:20-199:16 & 159:8-14; Ex. 2152, p. 16001; Ex. 2011, ¶¶ 42, 51, & 53. But Ju and Tsien require nucleotide compounds. Ex. 1002, 21:3-16; Ex. 1008, pp. 28-32. This indicates that Zavgorodny's nucleoside cleavage conditions would not have been expected to meet the requirements of nucleotides in Ju/Tsien. Ex. 2011, ¶¶ 42, 51, & 53.

13. In Ex. 2155 at 247:23-249:3-14, Dr. Branchaud admitted that a phenol holds on to substituents less tightly than a nucleotide 3'-OH. This is relevant to Dr. Branchaud's testimony on the relative hydrolysis of phenolic and nucleotide -O-CH₂-NH₂ groups. Ex. 1031, ¶ 24. This admission indicates that hydrolysis of a phenolic -O-CH₂-NH₂ group would not provide an expectation of the efficiency of hydrolysis for a -O-CH₂-NH₂ group attached to a nucleotide for use in Ju or Tsien.

14. In Ex. 2155 at 290:9-12, Dr. Branchaud testified that documents lacking substantiating data are unsuitable for drawing conclusions. Dr. Branchaud could not identify any experimental data in Ex. 1035 to support cleavage of azido groups by TCEP. Ex. 2155, 155:2-11. Likewise, Dr. Branchaud conceded that Ex. 1038 did not provide any data supporting its one-line suggestion that the Staudinger reaction could be quantitative. Ex. 2155, 212:4-10. The only data in Ex. 1038 demonstrates that the Staudinger reaction proceeds with non-quantitative

efficiency. Ex. 1038, p. 3. This undermines Dr. Branchaud's reliance on Exs. 1035 and 1038 in paragraphs 18 and 21 of his second declaration (Ex. 1031).

It would not be routine to optimize Zavgorodny to meet Ju or Tsien's methods

15. Dr. Branchaud and Dr. Metzker testified that numerous conditions need to be systematically tested and varied to optimize Zavgorodny's cleavage conditions. Ex. 2155, 53:23-56:5, 59:4-64:6, 83:13-84:19, 93:5-95:19; Ex. 2154, 247:13-249:5; Ex. 1033, p. 34. These conditions include researching at least 10 different parameters: (1) reaction time (Ex. 2155, 91:24-92:17); (2) temperature (*id.*, 97:14-98:9); (3) effect of various solvents (*id.*, 105:21-107:2, 109:5-111:13); (4) molar ratios of reactants (*id.*, 112:23-114:18); (5) pH (*id.*, 116:10-22); (6) pressure (*id.*, 127:7-129:4); (7) testing different phosphine reagents (*id.*, 144:6-145:4); (8) additives (*id.*, 83:13-84:19); (9) catalysts (*id.*, 55:13-56:5); and (10) screening thousands of polymerases (*id.*, 59:4-64:6). Dr. Branchaud repeatedly testified that researching the optimal conditions is an empirical process that is unpredictable.² Ex. 2155, 94:13-20, 95:15-16, 102:9-16, 107:13-108:21, 110:21-111:2, 115:9-21, 128:19-22, 138:21-24. Even if one tested just 4 different conditions for the 10

² Despite conceding that nucleotide cleavage is an empirical and unpredictable process, neither Dr. Branchaud nor Dr. Metzker performed any experiments to test the veracity of their opinions. Ex. 2155, 19:9-20:3; Ex. 2154, 184:16-23.

parameters identified, over 1 million reactions are needed. Optimizing Zavgorodny for use with Ju or Tsien would require extensive experimentation.

16. In Ex. 2155 at 114:19-23, Dr. Branchaud testified that using several times the amount of phosphine relative to azide would be expected to give a better result. Ex. 1031, ¶ 25. But this is untrue, as a reference using 4.75 times phosphine only reports 61-80% efficiency. Ex. 2015, 16:1-35, 20:43-21:8.

17. In Ex. 2155 at 256:21-257:10, Dr. Branchaud conceded that doubling the concentration of phosphine does not necessarily make a Staudinger reaction go two times faster. This is relevant because his declaration stated the exact opposite. Ex. 1031, ¶ 26.

18. In Ex. 2154 at 255:10-256:1, Dr. Metzker testified that it takes “aggressive technological innovation fueled by major investment” including “hundreds of millions of dollars” to develop DNA sequencing. Ex. 2148, p. 914. Dr. Metzker further testified that making nucleotides with a 3'-O-protecting group is one of “the most demanding aspects” of DNA sequencing. Ex. 2154, 208:3-211:6; Ex. 2146, p. 1773. Dr. Metzker also testified that he could not predict whether switching phosphine reagents would provide better or worse results. Ex. 2154, 197:18-200:18; 224:11-24. This testimony undermines IBS' argument that it would be easy to modify Zavgorodny to meet Ju or Tsien's methods. Paper 54, pp. 5-6. This testimony also supports Illumina's position that there would not have been a

reasonable expectation of success for meeting the requirements of Ju's or Tsien's methods using Zavgorodny.

19. In Ex. 2155 at 78:7-13, Dr. Branchaud testified that there is always a motivation to make a reaction better. *Id.*, 76:24-77:1. This contradicts his statement that there was no motivation to try to achieve 100% isolated yields in the articles of record. Ex. 1031, ¶ 22. The optimization efforts of the authors of Exs. 2013-2017 resulted in just 50-90% efficiencies. These efficiencies are insufficient to meet the requirements of Ju's and Tsien's methods. Ex. 2011, ¶ 50.

20. In Ex. 2155, 68:1-8, Dr. Branchaud admitted that he did not think Canard ever succeeded in optimizing deprotection of the 3'-protected nucleotide. This contradicts his use of Canard as an example of optimization. Ex. 1031, ¶ 15.

21. In Ex. 2155 at 267:10-14, Dr. Branchaud testified that Illumina's notebooks (which are not prior art) provide an expectation that the Staudinger reaction would proceed quantitatively. Dr. Branchaud testified that he relied on other non-prior art references to form his opinions. *Id.*, 161:20-163:8 (relying on Faucher, Ex. 1036). This demonstrates that Dr. Branchaud's opinions are based on improper hindsight.

Dr. Metzker inaccurately opines that azides are not electrophiles

22. In Ex. 2154 at 58:6-9, Dr. Metzker testified that an azido group cannot act as an electrophile. But the evidence of record indicates that azides are indeed electrophiles. *See, e.g.*, Ex. 2109, p. 10863; Ex. 2011, ¶ 31; Ex. 2141, pp. 5, 10,

Fig. 4; Ex. 2154, 101:10-103:19; Ex. 2140, p. 3007; Ex. 1032, p. 1361. This is relevant because Ju (Ex. 1002, 3:16-20) teaches that electrophilic 3'-protecting groups are unsuitable for sequencing, and the evidence establishes that azide groups are electrophiles.

23. In Ex. 2154 at 62:16-22, 65:17-66:4 and 70:10-14, Dr. Metzker testified that he interpreted Ju's warning against electrophiles to be limited to ketone groups. Dr. Metzker's interpretation is inconsistent with Dr. Branchaud's interpretation of Ju's electrophile as any "electron-deficient group" that will react with a nucleophile. Ex. 2039, 73:7-75:1. Dr. Metzker's interpretation is also inconsistent with the plain words of Ju, where "ketone groups" are just one type of electrophile. Ex. 1002, 3:16-20. This shows that Dr. Metzker and IBS require a strained and unjustifiably narrow interpretation of Ju to avoid the natural conclusion derived from Ju and Canard: an azido group is a strikingly similar electrophile to a carbonyl group that would have been unsuitable for a 3'-O-protecting group. Ex. 2011, ¶¶ 29-31.

24. In Ex. 2154 at 98:1-10, Dr. Metzker testified that azides are more reactive to nucleophilic phosphines than carbonyls. This contradicts the implication in his declaration (Ex. 1046, ¶ 31) that carbonyls are always more reactive than azides. This also supports Canard's statement that azido groups at the 3'-position would be susceptible to nucleophilic attack. Ex. 2019, p. 10863; Paper 32, pp. 14-16.

25. In Ex. 2154 at 54:10-58:4, Dr. Metzker admitted that he selectively omitted

the time frame from Dr. Romesberg's testimony about azides being electrophiles. *See* Ex. 1046, ¶ 26. Dr. Romesberg clearly testified that in 2002 one would have considered an azido group to be an electrophile. Ex. 1025, 81:21-82:2. Dr. Metzker's selective exclusion of evidence that directly contradicts his opinion reflects the bias of a witness who has made a career being adverse to Illumina, a fact IBS failed to disclose to the Board. *See, e.g.*, Ex. 2154, 8:10-11:23.

26. In Ex. 2154 at 97:4-14, Dr. Metzker testified that the relative electrophilic nature of carbonyls and azido groups referred to in his declaration (Ex. 1046, ¶ 31) was not within the context of a polymerase reaction. But Canard's statement about the similarity of electrophilicity for carbonyls and azides was in the context of a polymerase environment (Ex. 2019, p. 10863) and polymerase environments are much different than free solvent environments. Ex. 1025, 82:13-83:17, 71:15-72:1.

27. In Ex. 2154 at 59:10-61:6, Dr. Metzker admitted that Ju did not limit its teaching to avoid electrophilic protecting groups to any specific polymerase. This contradicts Dr. Metzker's interpretation of Ju's teaching "as not applying to all polymerases." Ex. 1046, ¶ 28. This illustrates that Dr. Metzker, in hindsight, took an improperly narrow interpretation of Ju, whereas the plain statements in Ju teach away from a 3'-azidomethyl ether with any polymerase. Paper 32, pp. 14-16.

28. In Ex. 2154 at 86:22-87:4, Dr. Metzker testified that *Taq* polymerase did not exhibit catalytic editing (the ability to remove the 3'-ester protecting group) in

Canard. Ex. 1046, ¶ 28. This is inconsistent with Canard's data demonstrating that *Taq* polymerase incorporated dATP after incorporation of a 3'-esterified dNTP. Ex. 2019, p. 10861; Ex. 2154, 93:4-8, 94:4-23.

Zavgorodny's cleavage conditions would denature the DNA in Ju and Tsien

29. In Ex. 2154 at 170:8-171:3, Dr. Metzker admitted that his own publication teaches that hydrophobic solvents denature DNA. Ex. 2143, ¶ [0075]. Zavgorodny uses pyridine, a hydrophobic solvent that would denature DNA. Ex. 2011, ¶ 55.

30. In Ex. 2154 at 149:4-19 and 151:1-7, Dr. Metzker admitted that Levine (Ex. 1048) showed that pyridine was better at denaturing (requires less pyridine to denature) DNA than formamide, methanol, ethylene glycol, and dimethylformamide. Ex. 1048, p. 171, Table II. Dr. Metzker also admitted that Hanlon (Ex. 2142) reported concentrations at which various organic solvents (formamide, methanol, ethylene glycol, and dimethylformamide) met the criteria for the column labeled "Denaturation" with a footnote explaining that the temperature was 25 °C. Ex. 2154, 161:14-163:16; Ex. 2142, p. 864. In addition, Dr. Metzker confirmed that Kit (Ex. 2018) stated that many organic solvents denature DNA at 25 °C. Ex. 2154, 165:2-17; Ex. 2018, p. 62. Hanlon, Levine, and Kit each indicate that Zavgorodny's aqueous pyridine would denature DNA in Ju/Tsien.

31. Dr. Branchaud confirmed that Ex. 1045 provides several organic solvent denaturants. Ex. 2155, 286:20-287:8; Ex. 1045, 19:34-37. This supports that

Zavgorodny's organic solvent would denature the DNA in Ju and Tsien's methods.

32. In Ex. 2154 at 131:16-132:16 and 141:23-142:2, Dr. Metzker testified that Kit and Levine describe the melting temperature (T_m) of DNA, which is the temperature at which half the DNA is denatured. Dr. Metzker also testified that substantial amounts of DNA are denatured at temperatures below the T_m . *Id.*, 171:19-172:3-9. Dr. Metzker failed to account for the substantial denaturation that would occur if pyridine were used in Ju/Tsien at temperatures below the T_m .

33. In Ex. 2154 at 125:12-126:12, Dr. Metzker testified that pH, ionic strength, and DNA concentration are critical parameters for determining whether DNA will be denatured. Dr. Metzker also testified that Zavgorodny failed to provide these critical parameters. *Id.*, 185:8-186:3. Therefore, Dr. Metzker lacks the critical information he identified as necessary to support his opinion in Ex. 1046, ¶ 33.

34. In Ex. 2054 at 177:2-178:16, Dr. Metzker admitted that phenol is only soluble in water at a ratio of 1 gram per 15 mL. *See also id.*, 179:4-23. Given that the molecular weight of phenol is 94.11 g/mol, this equates to a molarity of about **0.71** for Kirby's (Ex. 1050) solution. *Id.*, 183:6-18. This is relevant because Kirby's actual phenol concentration is much less than the **5.1** molarity that Dr. Metzker erroneously relied upon. Ex. 1046, ¶ 36.

35. Dr. Metzker conceded that Kirby never teaches DNA is not denatured by phenol. Ex. 2154, 182:23-183:4. Therefore, Dr. Metzker's reliance on Kirby to

opine (Ex. 1046, ¶ 36) that pyridine would not denature DNA is unsupported.

36. In Ex. 2154 at 121:8-13, Dr. Metzker testified that Tsien's 0.1 M pyridine at 40 °C would not denature DNA. This testimony is consistent with Dr. Romesberg's testimony that small concentrations of organic solvents may not denature DNA, whereas large concentrations will. Ex. 1025, 144:5-14. But Zavgorodny requires high concentrations that would denature DNA in Ju/Tsien. Ex. 2011, ¶¶ 54-55.

IBS' single-stranded oligonucleotide manufacturing theory is incorrect

37. In Ex. 2155 at 271:8-21, Dr. Branchaud testified that he did not offer an opinion that there would be a reason to use terminal transferase in the manner described in Ex. 1031, ¶ 37, but only that it could be done. In fact, the transferase method had never been monitored by labeled nucleotides, and had been abandoned. Ex. 1045, 2:13-15; Ex. 2155, 273:18-276:8, 285:15-286:2, 291:19-292:2. Dr. Branchaud suggested that solid support attachment might solve the problems with the transferase method that resulted in its abandonment. Ex. 2155, 275:12-18. But that was not what the art taught. *Id.*, 277:5-278:14; Ex. 1045, 2:59-66. Dr. Branchaud also testified that he did not know if terminal transferase would work in the presence of pyridine. Ex. 2155, 298:22-299:1. But Zavgorodny uses substantial amounts of pyridine. Ex. 2011, ¶¶ 54-55. Thus, there was no reason to use terminal transferase with labeled nucleotides in the manner described in ¶ 37 of Dr. Branchaud's second declaration (Ex. 1031).

38. In Ex. 2155 at 303:10-14, 305:16-306:4, and 307:23-308:7, Dr. Branchaud testified that using labeled nucleotides for oligonucleotide synthesis (1) could leave scars on the nucleobases that could interfere with subsequent use of the oligonucleotides, and (2) required use of non-natural nucleobases. Dr. Branchaud further testified that the reference (Ex. 1045) cited in ¶ 38 of his declaration taught methods for monitoring nucleotide incorporation without labeled nucleotides. Ex. 2155, 291:3-292:2. This reinforces that skilled artisans would not have had a reason to use labeled nucleotides to monitor oligonucleotide manufacturing.

39. In Ex. 2155 at 280:21-282:22, Dr. Branchaud agreed that Ex. 1045 used an enzymatic method for synthesis with blocked nucleotides where the advantage was that the synthesis could be done in one pot (*i.e.*, without purification steps). This was achievable in Ex. 1045 because cleavage was done by an enzyme that was heat deactivated between cycles. *Id.*, 282:23-283:21. This method is not combinable with Zavgorodny because there is no evidence that azidomethyl groups can be cleaved by an enzyme or other heat deactivatable reagent. *Id.*, 85:13-86:18.

Secondary considerations support the nonobviousness of the claimed method

40. In Ex. 2154 at 37:10-22, 39:13-22, 41:4-42:7, 110:23-111:19, and 139:1-11, Dr. Metzker testified that he was not aware of anyone other than Illumina/Solexa making the nucleotide of the claimed method until over 17 years after Zavgorodny was published. Even then, those groups were following Illumina/Solexa's work,

and they only made the claimed subject matter after Illumina/Solexa successfully launched a commercial product using it. *Id.*; *see also*, Paper 54, pp. 14-15. This provides objective evidence that IBS' obviousness position is based on hindsight.

41. In Ex. 2154 at 40:22-41:20, Dr. Metzker testified that he selected a 3'-O-azidomethyl protected nucleotide in 2010 to serve as the benchmark for evaluating other reversible terminators. This demonstrates the industry recognition of superior properties associated with Illumina's 3'-O-azidomethyl protected and labeled nucleotides, and also supports Illumina's evidence of industry praise.

42. In Ex. 2154 at 202:2-203:6, Dr. Metzker clarified that his comment about Bentley using one phosphine and one enzyme (Ex. 1046, ¶ 49) was not a criticism. This testimony undermines IBS' reliance on Ex. 1046, ¶ 49 to argue that Bentley's results do not support Illumina's unexpected results. Paper 54, p. 13.

43. In Ex. 2154 at 35:9-37:8, Dr. Metzker testified that he credited Illumina/Solexa for the development of 3'-O-azidomethyl protected and labeled nucleotides. Ex. 2139, p. 35. This is relevant because it shows that the industry recognized Illumina, and not others, as the inventor of this nucleotide.

44. In Ex. 2155 at 309:10-310:6, Dr. Branchaud testified that he offered no opinions on praise, copying, and long-felt, unmet need. Dr. Metzker was likewise silent on these issues. This shows that IBS' only response to Drs. Romesberg's and Burgess' opinions on these issues is unsupported attorney argument.

Respectfully submitted,

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By: /Robert A. Lawler/
Robert A. Lawler, Reg. No. 62,075
Email: rlawler@reinhardtllaw.com
REINHART BOERNER VAN DEUREN S.C.

Brenton R. Babcock, Reg. No. 39,592
William R. Zimmerman (admitted *pro hac vice*)
Jonathan E. Bachand, Reg. No. 67,884
Sheila N. Swaroop, Reg. No. 53,658
KNOBBE, MARTENS, OLSON & BEAR, LLP
Email: BoxIllumina@knobbe.com

Derek C. Walter (admitted *pro hac vice*)
WEIL, GOTSHAL & MANGES, LLP
Email: derek.walter@weil.com

Attorneys for Patent Owner
Illumina Cambridge Ltd.

CERTIFICATE OF SERVICE

I hereby certify that a true and correct copy of **ILLUMINA'S MOTION FOR OBSERVATIONS ON THE CROSS-EXAMINATION TESTIMONY OF BRUCE BRANCHAUD, PH.D. AND MICHAEL METZKER, PH.D.** is being served on September 2, 2014, via email pursuant to 37 C.F.R. § 42.6(e) per agreement of the parties, to counsel for Intelligent Bio-Systems, Inc., at the addresses below:

Scott D. Marty
martys@ballardspahr.com

Marc S. Segal
segalm@ballardspahr.com

Robert R. Baron, Jr.
baron@ballardspahr.com

Daniel A. Nadel
nadeld@ballardspahr.com

BALLARD SPAHR LLP
999 Peachtree St., Suite 1000
Atlanta, GA 30309
678-420-9300

Dated: September 2, 2014

/Nicole A. Wilson/

Nicole A. Wilson, Reg. No. 66,672
Practitioner for Patent Owner
Illumina Cambridge Ltd.