

MAIWALD · Eisenstraße 3 · 80335 München

Europäisches Patentamt

80298 München

Maiwald Patentanwalts- und
Rechtsanwalts-gesellschaft mbH

München
Düsseldorf

Eisenstraße 3
80335 München
T +49 89 7472660
F +49 89 776424
H www.maiwald.eu

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Patentee: The Trustees of Columbia University in the City of New York
Opponent: ILLUMINA INC.

Our Ref.: I09472EPOP/DJB

Dr. Dirk Bühler
Partner
buehler@maiwald.eu

Dr. Eva Dörner
Partner
doerner@maiwald.eu

This is in response to the summons to attend oral proceedings pursuant to Rule 115(1) EPC.

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Columbia Ex. 2076
Illumina, Inc. v. The Trustees
of Columbia University in the
City of New York
IPR2020-00988, -01065,
-01177, -01125, -01323



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A. Requests

- ¹ We maintain the request to revoke EP 3 034 627 B1 in its entirety on the basis of Articles 100 (a), 100 (b) and 100 (c) EPC.
- ² Our request for oral proceedings is maintained as well.

B. Further cited documents

- ³ In addition to the documents on file, we herewith file the following documents in order to address the issues raised in the preliminary opinion in connection with the question of insufficiency of disclosure:

- D26:** R. E. Ireland et al., J. Org. Chem., 1986, vol. 51, no. 5, pp. 635-648
- D27:** A. Kamal et al., Tetrahedron Letters, 1999, vol. 40, pp. 371-372
- D28:** H. Ruparel et al., PNAS, 2005, vol. 102, no. 17, pp. 5932-5937
- D29:** WO 2004/018497 A2
- D30:** A. F. Gardner et al., Nucleic Acids Research, 2002, vol. 30, no. 2, pp. 605-613
- D31:** F. Guibé, Tetrahedron, 1998, vol. 54, pp. 2967-3042
- D32:** S. S. Flack, Tetrahedron Letters, 1995, vol. 36, no. 19, pp. 3409-3412
- D33:** J. Ju et al., PNAS, 2006, vol. 103, no. 52, pp. 19635-19640
- D34:** J. Guo et al., PNAS, 2008, vol. 105, no. 27, pp. 9145-9150
- D35:** Declaration by F. Romesberg dated July 1, 2020
- D36:** Declaration by J. Ju dated May 26, 2017
- D37:** Declaration by J. Kuriyan dated June 1, 2020
- D38:** K. Davies, The \$ 1,000 Genome”, 2010, Free Press, New York, Chapter 5
- D39:** T. W. Greene, P. G. M. Wuts, Protective Groups in Organic Synthesis, Third Edition, Chapter II, 1999, John Wiley & Sons, Inc.

- D40:** Declaration by S. M. Menchen dated June 1, 2020
- D41:** S. Lemaire-Audoire et al., Tetrahedron Letters, 1994, vol. 35, no. 47, pp. 8783-8786
- D42:** S. Lemaire-Audoire et al., Journal of Molecular Catalysis A: Chemical 116, 1997, pp. 247-258
- D43:** V. M. Swamy, Synlett, 1997, pp. 513-514
- D44:** C.-H. Lee et al., Proc. Natl. Acad. Sci. USA, 1981, vol. 78, no. 5, pp. 2838-2842
- D45:** L. Levine et al., Biochemistry, 1963, vol. 2, no. 1, pp. 168-175
- D46:** E. J. Corey et al., Tetrahedron Letters, 1975, no. 38, pp. 3269-3270
- D47:** E. J. Corey et al., Tetrahedron Letters, 1975, no. 31, pp. 2643-2646
- D48:** Grant application by Dr. Romesberg and Dr. Ju issued in May 2006
- D49:** EP 1 530 578 B1
- D50:** Submission of September 23, 2016 by Patentee during prosecution
- D51:** Thesis by Q. Meng, Columbia University, 2006
- D52:** Declaration by S. Peisayovich dated 23 March 2021
- D53:** Patentee's response in IPR proceedings dated September 9, 2020
- D54:** WO 98/53300 A2
- D55:** Bentley et al., Nature, 2008, vol. 456, no. 6, pp. 53-59
- ⁴ D26 and D27 are named in paragraph [0007] of the contested patent as evidence of cleavage conditions for MOM and allyl which allegedly are compatible with SBS requirements. They are thus both known to the Patentee and relied upon by the Patentee for their sufficiency of disclosure arguments.
- ⁵ D40 is introduced as evidence that the **cleavage conditions set forth in the contested patent for allyl (i.e., D27) are not suitable** for SBS. D40

is an expert declaration that has been submitted by the Patentee in the context of IPR proceedings relating to US patent 9,868,985, claiming priority to the same patent application as the opposed patent, and is thus known to the Patentee.

- ⁶ D28 is evidence that extensive research efforts were required after the relevant date of the contested patent **to identify a polymerase**, namely a mutant 9°N polymerase, **and cleavage conditions** which would allow allyl to be used as a 3'-OH protective group for SBS. It is co-authored by Dr. Ju and is thus known to the Patentee. These research efforts were necessary because the polymerase and cleavage conditions in the contested patent were not functional.
- ⁷ D29 and D30 are introduced as evidence that the only polymerase which D28 discloses to be functional with allyl, namely a particular mutant 9°N polymerase, was **developed after** the relevant date of the contested patent. D51 and D48 is further evidence which shows that polymerases other than the 9°N polymerase which were known at relevant date of the contested patent were **not suitable for effective SBS when using allyl** as a 3'-OH protective group. D51 is a PhD thesis from the group of Dr. Ju at Columbia. D48 is a grant application by Dr. Romesberg and was supported by Dr. Ju. Further, both were previously cited in US proceedings in which Columbia is participating. These documents are thus known to the Patentee.
- ⁸ D31 and D32 are both references which D28 refers to when explaining why the **cleavage conditions** disclosed in these documents were not suitable for allyl. D41 and D42 are introduced as evidence that the cleavage conditions which were used in D28 for allyl required extensive research activities and were not part of the common general knowledge. These cleavage conditions differ from those mentioned in the patent, i.e., D27 (Kamal).
- ⁹ D33 is another post-published publication by the group of Dr. Ju and thus known to the Patentee. It is introduced as evidence that the photocleavable linker as shown in the various figures of EP'627 had to be replaced by an allyl linker in order to implement efficient SBS. D50 is a submission by the Patentee during examination of the contested patent which comments on D33.
- ¹⁰ D34 is another post-published publication by the group of Dr. Ju. It shows that, based on the findings of D28 (Ruparel) and D33 (Ju), only after switching to azidomethyl as a 3'-OH protective group SBS beyond 20 nucleotides became possible.

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