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JUNO THERAPEUTICS, INC., MEMORIAL SLOAN KETTERING CANCER CENTER, and SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH

UNITED STATES DISTRICT COURT

CENTRAL DISTRICT OF CALIFORNIA

Juno Therapeutics, Inc., Memorial Sloan Kettering Cancer Center, and Sloan Kettering Institute for Cancer Research,, Plaintiffs, v. Kite Pharma, Inc., Defendant.	CASE NO.: 2:17-CV-07639 **COMPLAINT FOR PATENT INFRINGEMENT** **DEMAND FOR JURY TRIAL**

This litigation represents the second phase of a patent dispute that Defendant Kite Pharma, Inc. (together with its successors, "Kite") itself initiated against Plaintiffs Sloan Kettering Institute for Cancer Research ("Sloan Kettering") and Juno Therapeutics, Inc. ("Juno"). Through its scientific collaborators, Kite copied and is now commercializing a cancer immunotherapy that utilizes a chimeric T cell receptor ("chimeric TCR") invented, and patented, by prominent scientists at Sloan Kettering. The Sloan Kettering inventors' work issued as U.S. Patent No. 7,446,190 (the "'190 Patent"), which is exclusively licensed to Juno.

Knowing that it infringes the '190 Patent, Kite challenged the validity of all claims of the '190 Patent in an *inter partes* review ("IPR") in the United States Patent and Trademark Office ("PTO" or "Office") before the Patent Trial and Appeal Board ("PTAB" or "Board"). The PTAB instituted the IPR and then upheld all claims of the '190 Patent in a Final Written Decision issued December 16, 2016. The PTAB concluded that Kite did not even show "by a preponderance of the evidence"—the lower standard applicable to validity challenges in an IPR—that any claim of the '190 Patent was unpatentable.

Kite recently received marketing approval from the Food and Drug Administration ("FDA") for its Yescarta™ product (axicabtagene ciloleucel) ("axi-cel" or "Yescarta," also known as "KTE-C19") on October 18, 2017. Plaintiffs accordingly bring suit against Kite for infringement based on Kite's making, using, offering to sell, and selling of its chimeric antigen receptor products that comprise the claimed nucleic acid polymers of the '190 Patent. 35 U.S.C. § 271(a). Plaintiffs hereby allege for their Complaint against Defendant Kite, on personal knowledge as to their own actions and on information and belief as to the actions of others, as follows:

NATURE OF THE ACTION

1. This is an action for infringement of U.S. Patent No. 7,446,190 arising under the patent laws of the United States, 35 U.S.C. §§ 1 et seq. The action arises

out of the infringement of one or more claims of the '190 patent as a result of Kite's activities relating to its Yescarta product.

THE PARTIES

2. Juno is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at 400 Dexter Avenue North, Suite 1200, Seattle, Washington, 98109.

3. Sloan Kettering is a research affiliate of Memorial Sloan Kettering Cancer Center ("MSKCC"), which is a corporation organized and existing under the laws of the State of New York with its principal place of business at 1275 York Avenue, New York, New York, 10065.

4. Plaintiffs are informed and believe, and thereon allege, that Kite is a wholly owned subsidiary of Gilead Sciences, Inc., organized and existing under the laws of the State of Delaware with its principal place of business at 2225 Colorado Avenue, Santa Monica, California, 90404.

JURISDICTION

5. This action arises under the patent laws of the United States of America, 35 U.S.C. § 1 et seq. Accordingly, this Court has subject-matter jurisdiction under 28 U.S.C. § 1331 and 28 U.S.C. § 1338(a).

6. This Court has personal jurisdiction over defendant Kite because Kite has committed acts of infringement within this District. Moreover, Kite has substantial contacts with the forum as a consequence of conducting business in California and having a principal place of business in Santa Monica, California. Upon information and belief, Kite manufactures, uses, sells and/or offers to sell in, and/or imports into, the United States products relating to its Yescarta therapy.

VENUE

7. Venue is proper in this District under 28 U.S.C. §§ 1391(b) and (c), and 1400(b), because Kite has committed acts of infringement in this District and has a regular and established place of business in this District.

BACKGROUND

8. Juno is a biopharmaceutical company focused on re-engaging the body's own immune system to revolutionize the treatment of cancer. Juno was launched in collaboration with several of the world's leading cancer research institutes, including Memorial Sloan Kettering Cancer Center, the Fred Hutchinson Cancer Research Center, and Seattle Children's Research Institute. Juno is currently developing cell-based cancer immunotherapies based on chimeric antigen receptor technologies to genetically engineer T cells to recognize and kill cancer cells.

9. Memorial Sloan Kettering Cancer Center is one of the world's preeminent cancer treatment and research institutions. Located in New York City, it was founded in 1884. Since its founding, MSKCC has been at the cutting-edge of cancer research and treatment.

10. On November 4, 2008, the United States Patent and Trademark Office duly and legally issued the '190 Patent, entitled "Nucleic Acids Encoding Chimeric T Cell Receptors." A copy of the '190 Patent is attached as Exhibit 1.

11. Michel Sadelain, Renier Brentjens, and John Maher are the inventors of the '190 Patent. By operation of law and as a result of written assignment agreements, Sloan Kettering obtained the entire right, title and interest to and in the '190 Patent.

12. The '190 Patent claims nucleic acid polymers encoding a chimeric T cell receptor ("chimeric TCR") designed to redirect T cells to recognize and attack target cells, such as tumor cells, based on expression of a target antigen. Chimeric TCRs, also referred to as "chimeric antigen receptors" in some later publications, generally combine an extracellular binding domain with at least one intracellular signaling domain that can induce immune cell activation, in a way that does not exist in nature. By combining the signaling domain with a new binding domain, these chimeric TCRs are designed to "redirect" T cell activation in response to binding of a target (such as an antigen) that would normally not trigger cell

activation. If the cells are activated in this manner, they can attack and kill cells bearing the target.

13. The claimed nucleic acid polymer encodes a chimeric TCR with a binding element that specifically interacts with a selected target, a costimulatory signaling region that comprises the amino acid sequence encoded by SEQ ID NO:6 in the patent, and a human CD3ζ intracellular domain. SEQ ID NO:6 of the '190 Patent is derived from the CD28 costimulatory protein.

14. The '190 Patent describes work by the named inventors demonstrating, for the first time, chimeric TCR-expressing cells that could undergo multiple rounds of expansion and continue to specifically kill tumor cells, even after withdrawal and re-exposure to the target antigen. This groundbreaking result paved the way for success of the claimed chimeric TCR in clinical trials, including clinical trials conducted by Kite.

15. Pursuant to a license agreement Juno entered into with Memorial Sloan Kettering Cancer Center, Juno obtained an exclusive license to the '190 Patent for all therapeutic and diagnostic uses.

16. On August 13, 2015, Kite filed an IPR petition, seeking cancellation of all claims (claims 1-13) of the '190 Patent. Under 35 U.S.C. § 311(a), "a person who is not the owner of a patent may file with the Office a petition to institute an inter partes review of the patent." Kite sought to invalidate all claims of the '190 patent as obvious under 35 U.S.C. § 103. *See* 35 U.S.C. § 311(b). A copy of Kite's petition is attached as Exhibit 2. On December 16, 2016, the Board issued a Final Written Decision, concluding that "Kite has not shown by a preponderance of the evidence that claims 1-13 of the '190 patent are unpatentable under 35 U.S.C. § 103." Exhibit 3 (Final Written Decision) at 29.

17. Because the IPR resulted in a Final Written Decision finding the claims not unpatentable, Kite is estopped from asserting that the claims are invalid "on any ground that the petitioner raised or reasonably could have raised during the inter

partes review." 35 U.S.C. 315(e).

KITE'S INFRINGEMENT

18. Kite's Yescarta product involves a "therapy in which a patient's T cells are engineered to express a chimeric antigen receptor (CAR) to target the antigen CD19, a protein expressed on the cell surface of B-cell lymphomas and leukemias, and redirect the T cells to kill cancer cells." Exhibit 4 (Kite 12/13/2016 Press Release).

19. On information and belief, Kite entered into a Cooperative Research and Development Agreement with a team of scientists headed by Dr. Steven Rosenberg (collectively, Kite's "scientific collaborators") "to develop multiple engineered autologous cell therapy product candidates for the treatment of advanced hematological and solid malignancies." Exhibit 5 (Kite Website).

20. Kite's scientific collaborators have publically described the construct encoding their chimeric TCR, which is substantively identical to the Yescarta construct, as encoding:

> an anti-CD19 scFv that was derived from the FMC63 mouse hybridoma, a portion of the human CD28 molecule, and the intracellular component of the human TCR-ζ molecule. The exact sequence of the CD28 molecule included in the FMC63-28Z CAR corresponds to Genbank identifier NM_006139. The sequence includes all amino acids starting with the amino acid sequence IEVMYPPY and continuing all the way to the carboxy-terminus of the protein . . . To form the MSGV-FMC63-28Z retroviral vector, the XhoI and NotI-digested fragment encoding the FMC63 scFv was ligated into a second XhoI and NotI-digested fragment that encoded the MSGV retroviral backbone as well as part of the extracellular portion of human CD28, the entire transmembrane and cytoplasmic portion of human CD28, and the cytoplasmic portion of the human TCR-ζ molecule.

Exhibit 6 (Kochenderfer 2009) at 690.

21. Importantly, this publication cited to the '190 Patent inventors' own published work ("Maher publication"), describing embodiments of the '190 Patent claims. *Id*. (citing Exhibit 7 (Maher publication)).

22. On information and belief, on May 14, 2015, one of Kite's scientific collaborators, Dr. Rosenberg, gave a speech at the 2015 American Society of Gene & Cell Therapy Conference. During the speech, Dr. Rosenberg acknowledged the groundbreaking work by Dr. Michel Sadelain, an inventor of the '190 Patent, stating, "Well, it's a great pleasure to be here this morning, and especially to be introduced by Michel Sadelain, whose pioneering work with CD19 formed the basis for virtually all of the CD19 CAR work that is now being performed around the world."

23. On information and belief, Kite's scientific collaborators copied their anti-CD19 receptor construct, including the specific region of CD28 recited in the claims of the '190 Patent (as encoded by SEQ ID NO:6), from the chimeric T cell receptor construct described by the Maher publication, published by the inventors of the '190 Patent.

24. For example, Kite has publically stated that "KTE-C19 utilizes the same anti-CD19 CAR construct investigated" by its scientific collaborators. Exhibit 8 (ASH Abstract); *see also* Exhibit 9 (Ghobadi) ("KTE-C19 utilizes the same construct as used by" Kite's scientific collaborators). Kite's KTE-C19 therapy therefore utilizes nucleic acid polymers encoding chimeric TCRs within the scope of the '190 Patent claims. A schematic of Kite's KTE-C19 construct from one of Kite's publications appears below:

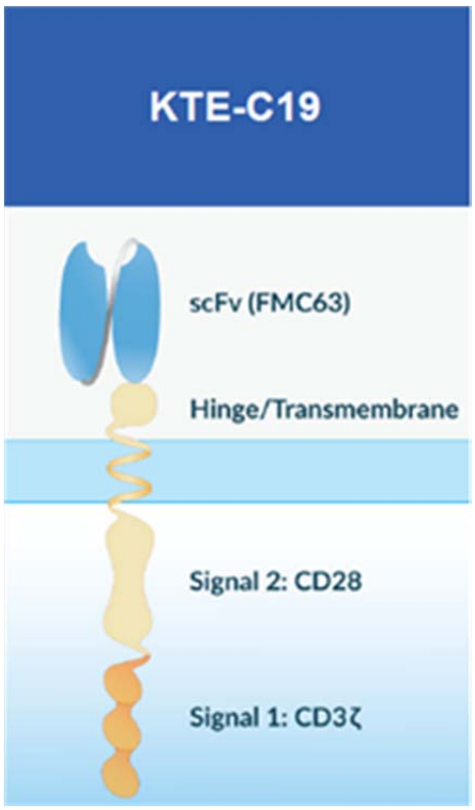

Exhibit 9 (Ghobadi) at 4.

25. On information and belief, through its scientific advisors, Kite copied the chimeric T cell receptor construct utilized in its Yescarta therapy from the work of the '190 Patent inventors.

26. Indeed, the DNA sequence of Kite's retroviral vector demonstrates that Kite's anti-CD19 chimeric TCR falls within the scope of the '190 Patent claims. In a document Kite filed with the Recombinant DNA Advisory Committee ("RAC"), a federal committee that reviews clinical trial protocols that are either directly funded by the National Institutes of Health ("NIH") or conducted at institutions that receive NIH funding, Kite provided the DNA sequence of KTE-C19's anti-CD19 chimeric TCR vector. Exhibit 10 (KTE-C19 DNA Sequence). The RAC filing described the retroviral vector used as

> encoding a chimeric antigen receptor directed against the B cell antigen, CD19 . . . The retroviral vector utilizes the MSGV1 (murine stem cell virus-based splice-gag vector 1) retroviral vector backbone

> and consists of 7026 bps including the 5' long terminal repeat (LTR) from the murine stem cell virus (promoter), packaging signal including the splicing donor (SD) and splicing acceptor sites, FMC63-based (anti-CD19 FMC63-28) CAR protein containing a signal peptide (human GM-CSF receptor), FMC63 light chain variable region (FMC63 VL), linker peptide, FMC63 heavy chain variable region (FMC63 VH), CD28 (hinge, transmembrane and cytoplasmic region), and TCR-zeta (cytoplasmic region), followed by the murine stem cell virus 3'LTR. This particular vector was provided by Dr. Steven A. Rosenberg from the Surgery Branch/NCI and is the same vector used in an ongoing RAC-approved clinical trial of which Dr. Stephen A. Rosenberg is the Principal Investigator (OBA/RAC submission 0809-940). . . . [T]he complete nucleotide sequence as determined by the standard nucleotide sequencing protocol is shown in Appendix 2 of this application.

Exhibit 11 (RAC Filing). The "complete nucleotide sequence" attached as Appendix 2 to Kite's RAC filing encodes the identical amino acid sequence that is encoded by SEQ ID NO:6, as recited by the claims of the '190 Patent. *See* Exhibit 10 (KTE-C19 DNA Sequence). The nucleotide sequence also demonstrates that other elements of claim 1 of the '190 Patent, including a binding element that specifically interacts with a selected target, and a zeta chain portion comprising the intracellular domain of human CD3ζ chain, are also present in Kite's retroviral vector. *See* Exhibit 11 (RAC Filing) ("The retroviral vector utilizes . . . FMC63 light chain variable region (FMC63 VL), linker peptide, FMC63 heavy chain variable region (FMC63 VH), . . . and TCR-zeta (cytoplasmic region).").

27. During the IPR Kite initiated against the '190 Patent, Sloan Kettering's expert, Prof. Thomas Brocker, the Director of the Institute for Immunology at the Ludwig-Maximilians University in Munich, Germany, compared the chimeric TCR

used by Kite's scientific collaborators to the claims of the '190 Patent, demonstrating that Kite's collaborators' chimeric TCR construct, and thus, Kite's own KTE-C19 product, falls within the scope of at least claims 1-3 and 5 of the '190 Patent. Exhibit 12 (Brocker Declaration), ¶ 224. The NCI chimeric TCR analyzed by Prof. Brocker contains the same nucleotide sequence as KTE-C19's chimeric TCR. *See* Exhibit 11 (RAC Filing).

28. On October 18, 2017, Kite received approval for the FDA to market and sell Yescarta (axicabtagene ciloleucel) in the United States.

COUNT 1:

INFRINGEMENT OF THE '190 PATENT UNDER 35 U.S.C. § 271(a)

29. Plaintiffs re-allege and incorporate by reference the allegations contained in paragraphs 1-28 above.

30. On information and belief, Kite infringes at least claims 1-3, 5, 7-9, and 11 of the '190 Patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine of equivalents, by making, using, selling, offering to sell, and/or importing within the United States, without authority, chimeric antigen receptor products that comprise the claimed nucleic acid polymers, including, but not limited to, the Yescarta product.

31. On information and belief, Kite infringes the '190 Patent in violation of 35 U.S.C. § 271(b) by actively inducing potential infringement of the '190 Patent, literally and/or under the doctrine of equivalents, with knowledge of the '190 Patent and knowledge that induces infringement of the '190 Patent, by, among other things, actively and knowingly aiding and abetting, assisting and encouraging others, including without limitation, partner institutions, other collaborators and end users of Kite's products, to directly infringe the '190 Patent with respect to the making, using, offering for sale, and/or importing within this judicial District and elsewhere in the United States, without license or authority, chimeric antigen receptor products that comprise the claimed nucleic acid polymers, including, but not limited to, the

Yescarta product.

32. On information and belief, Kite infringes the '190 Patent in violation of 35 U.S.C. § 271(c) by contributing to potential infringement of the '190 Patent, literally and/or under the doctrine of equivalents, by, among other things, offering to sell and/or importing within this judicial district and elsewhere in the United States, without license and authority, chimeric antigen receptor products that comprise the claimed nucleic acid polymers, including, but not limited to, the Yescarta product, with knowledge of the '190 Patent and knowing that such products and/or components are especially made or especially adapted for use in the infringement of the '190 Patent, are a material part of the invention, and are not staple articles or commodities of commerce suitable for substantial non-infringing use.

33. On information and belief, Kite infringes the '190 Patent, literally and/or under the doctrine of equivalents, in violation of 35 U.S.C. § 271(f)(1), by, among other things, supplying or causing to be supplied in or from the United States, without license or authority, products or components of products that are combined and/or used outside the United States in a manner that falls within the scope of one or more claims of the '190 Patent. For example, Kite supplies or causes to be supplied in or from the United States all or a substantial portion of the components of its Yescarta product, where such components are uncombined in whole or in part, in such manner as to actively induce the combination of such components outside of the United States in a manner that would infringe the '190 Patent. Such products or components include without limitation chimeric antigen receptor products that comprise the claimed nucleic acid polymers including, but not limited to, the Yescarta product. Plaintiffs are informed and believe, and thereon allege, that Kite will export such products or components of products to destinations where Kite expects to commercialize its Yescarta product, including without limitation, Europe.

34. On information and belief, Kite infringes the '190 Patent, literally

and/or under the doctrine of equivalents, in violation of 35 U.S.C. § 271(f)(2), by, among other things, supplying or causing to be supplied in or from the United States, without license or authority, products or components of products that are combined and/or used outside the United States in a manner that falls within the scope of one or more claims of the '190 Patent. For example, Kite supplies or causes to be supplied in or from the United States components of its Yescarta product that are made or especially adapted for infringing the '190 Patent and are not a staple article or commodity of commerce suitable for substantial non-infringing use, where such components are uncombined in whole or in part, knowing that such component is so made or adapted and intending that such component be combined outside of the United States in a manner that would infringe the '190 Patent. Such products or components include without limitation chimeric antigen receptor products that comprise the claimed nucleic acid polymers including, but not limited to, the Yescarta product. Plaintiffs are informed and believe, and thereon allege, that Kite does and/or will export such products or components of products to destinations where Kite expects to commercialize its Yescarta product, including without limitation, Europe.

35. Attached as Exhibit 13 to this complaint is a chart that provides examples of Kite's infringement with respect to exemplary claims of the '190 Patent. This chart is not a complete identification of all of Kite's infringing products and does not list each claim of the '190 Patent infringed by Kite. Exhibit 13 is hereby incorporated by reference in its entirety. Plaintiffs will provide their list of asserted claims and infringement contentions in accordance with the Court's schedule.

36. Kite's Yescarta product meets every limitation of several claims of the '190 Patent, including without limitation claim 1. For example, vectors used with Kite's Yescarta therapy incorporate a nucleic acid polymer encoding a chimeric TCR with an anti-CD19 binding domain, a costimulatory region derived from

CD28, which comprises the amino acid sequence encoded by SEQ ID NO:6, and an intracellular human CD3ζ signaling region.

37. Kite has had knowledge of the '190 Patent at least as early as August 13, 2015, when it filed a petition for *inter partes* review against the '190 Patent in the United States Patent and Trademark Office, before the Patent Trial and Appeal Board. A copy of Kite's petition is attached as Exhibit 2. In addition, Kite has had knowledge of and notice of the '190 Patent and its infringement since at least, and through, the filing and service of the Complaint.

38. Kite's infringement of the '190 Patent injures Juno in its business and property rights.

39. Kite's infringement of the '190 Patent causes and will continue to cause irreparable harm to Juno unless and until Kite's infringing activities are enjoined by this Court.

40. On information and belief, Kite's infringement of the '190 Patent is deliberate and willful. Kite has actual knowledge of the '190 Patent, based on its filing of a petition for an *inter partes* review. Despite this actual knowledge, Kite continues to infringe the '190 Patent despite an objectively high likelihood that its actions constitute infringement.

JURY TRIAL DEMANDED

41. Pursuant to Federal Rule of Civil Procedure 38(b) and Local Rule 38-1 of this Court, Plaintiffs demand a trial by jury of all issues so triable.

PRAYER FOR RELIEF

WHEREFORE, Plaintiffs pray for relief as follows:

A. Judgment in their favor on all claims for relief;

B. Judgment that Kite has infringed (whether literally or under the doctrine of equivalents) one or more claims of the '190 Patent;

C. A determination that Kite's infringement has been willful and deliberate;

D. An order permanently enjoining Kite from further infringement of the '190 Patent;

E. An award to Plaintiffs of their costs and reasonable expenses to the fullest extent permitted by law;

F. A declaration that this case is exceptional pursuant to 35 U.S.C. § 285, and an award of attorneys' fees and costs; and

G. An award of such other and further relief as the Court may deem just and proper.

DATED: October 18, 2017

Respectfully submitted,

IRELL & MANELLA LLP

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