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5 Attorneys for Plaintiffs
6 JUNO THERAPEUTICS, INC.,
MEMORIAL SLOAN KETTERING
7 CANCER CENTER, and SLOAN
KETTERING INSTITUTE FOR
8 CANCER RESEARCH

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

Juno Therapeutics, Inc., Memorial Sloan)
Kettring Cancer Center, and Sloan)
14 Kettring Institute for Cancer Research,,)
15 Plaintiffs,)
16 v.)
17 Kite Pharma, Inc.,)
18 Defendant.)

CASE NO.: 2:17-CV-07639
**COMPLAINT FOR PATENT
INFRINGEMENT**
DEMAND FOR JURY TRIAL

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

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

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

26 **NATURE OF THE ACTION**

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

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

3 **THE PARTIES**

4 2. Juno is a corporation organized and existing under the laws of the State
5 of Delaware with its principal place of business at 400 Dexter Avenue North, Suite
6 1200, Seattle, Washington, 98109.

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

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

15 **JURISDICTION**

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

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

25 **VENUE**

26 7. Venue is proper in this District under 28 U.S.C. §§ 1391(b) and (c), and
27 1400(b), because Kite has committed acts of infringement in this District and has a
28 regular and established place of business in this District.

BACKGROUND

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

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

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

16 11. Michel Sadelain, Renier Brentjens, and John Maher are the inventors of
17 the '190 Patent. By operation of law and as a result of written assignment
18 agreements, Sloan Kettering obtained the entire right, title and interest to and in the
19 '190 Patent.

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

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

3 13. The claimed nucleic acid polymer encodes a chimeric TCR with a
4 binding element that specifically interacts with a selected target, a costimulatory
5 signaling region that comprises the amino acid sequence encoded by SEQ ID NO:6
6 in the patent, and a human CD3 ζ intracellular domain. SEQ ID NO:6 of the '190
7 Patent is derived from the CD28 costimulatory protein.

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

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

17 16. On August 13, 2015, Kite filed an IPR petition, seeking cancellation of
18 all claims (claims 1-13) of the '190 Patent. Under 35 U.S.C. § 311(a), "a person who
19 is not the owner of a patent may file with the Office a petition to institute an inter
20 partes review of the patent." Kite sought to invalidate all claims of the '190 patent as
21 obvious under 35 U.S.C. § 103. *See* 35 U.S.C. § 311(b). A copy of Kite's petition is
22 attached as Exhibit 2. On December 16, 2016, the Board issued a Final Written
23 Decision, concluding that "Kite has not shown by a preponderance of the evidence
24 that claims 1-13 of the '190 patent are unpatentable under 35 U.S.C. § 103." Exhibit
25 3 (Final Written Decision) at 29.

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

1 partes review.” 35 U.S.C. 315(e).

2 KITE’S INFRINGEMENT

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

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

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

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

1 Exhibit 6 (Kochenderfer 2009) at 690.

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

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

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

18 24. For example, Kite has publically stated that "KTE-C19 utilizes the
19 same anti-CD19 CAR construct investigated" by its scientific collaborators. Exhibit
20 8 (ASH Abstract); *see also* Exhibit 9 (Ghobadi) ("KTE-C19 utilizes the same
21 construct as used by" Kite's scientific collaborators). Kite's KTE-C19 therapy
22 therefore utilizes nucleic acid polymers encoding chimeric TCRs within the scope of
23 the '190 Patent claims. A schematic of Kite's KTE-C19 construct from one of Kite's
24 publications appears below:

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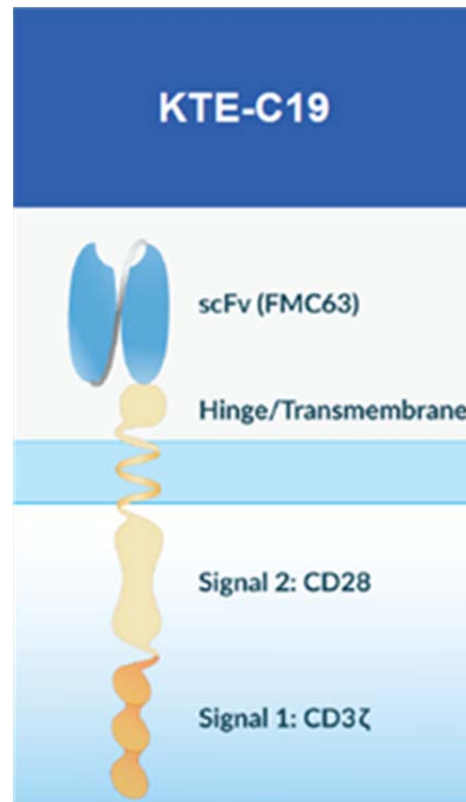


Exhibit 9 (Ghobadi) at 4.

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

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

16 Exhibit 11 (RAC Filing). The “complete nucleotide sequence” attached as Appendix
17 2 to Kite’s RAC filing encodes the identical amino acid sequence that is encoded by
18 SEQ ID NO:6, as recited by the claims of the ’190 Patent. *See* Exhibit 10 (KTE-C19
19 DNA Sequence). The nucleotide sequence also demonstrates that other elements of
20 claim 1 of the ’190 Patent, including a binding element that specifically interacts
21 with a selected target, and a zeta chain portion comprising the intracellular domain
22 of human CD3 ζ chain, are also present in Kite’s retroviral vector. *See* Exhibit 11
23 (RAC Filing) (“The retroviral vector utilizes . . . FMC63 light chain variable region
24 (FMC63 VL), linker peptide, FMC63 heavy chain variable region (FMC63 VH), . . .
25 and TCR-zeta (cytoplasmic region).”).

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

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

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

9 **COUNT 1:**

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

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

13 30. On information and belief, Kite infringes at least claims 1-3, 5, 7-9, and
14 11 of the '190 Patent pursuant to 35 U.S.C. § 271(a), literally or under the doctrine
15 of equivalents, by making, using, selling, offering to sell, and/or importing within
16 the United States, without authority, chimeric antigen receptor products that
17 comprise the claimed nucleic acid polymers, including, but not limited to, the
18 Yescarta product.

19 31. On information and belief, Kite infringes the '190 Patent in violation of
20 35 U.S.C. § 271(b) by actively inducing potential infringement of the '190 Patent,
21 literally and/or under the doctrine of equivalents, with knowledge of the '190 Patent
22 and knowledge that induces infringement of the '190 Patent, by, among other things,
23 actively and knowingly aiding and abetting, assisting and encouraging others,
24 including without limitation, partner institutions, other collaborators and end users
25 of Kite's products, to directly infringe the '190 Patent with respect to the making,
26 using, offering for sale, and/or importing within this judicial District and elsewhere
27 in the United States, without license or authority, chimeric antigen receptor products
28 that comprise the claimed nucleic acid polymers, including, but not limited to, the

1 Yescarta product.

2 32. On information and belief, Kite infringes the '190 Patent in violation of
3 35 U.S.C. § 271(c) by contributing to potential infringement of the '190 Patent,
4 literally and/or under the doctrine of equivalents, by, among other things, offering to
5 sell and/or importing within this judicial district and elsewhere in the United States,
6 without license and authority, chimeric antigen receptor products that comprise the
7 claimed nucleic acid polymers, including, but not limited to, the Yescarta product,
8 with knowledge of the '190 Patent and knowing that such products and/or
9 components are especially made or especially adapted for use in the infringement of
10 the '190 Patent, are a material part of the invention, and are not staple articles or
11 commodities of commerce suitable for substantial non-infringing use.

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

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

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

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

25 36. Kite's Yescarta product meets every limitation of several claims of the
26 '190 Patent, including without limitation claim 1. For example, vectors used with
27 Kite's Yescarta therapy incorporate a nucleic acid polymer encoding a chimeric
28 TCR with an anti-CD19 binding domain, a costimulatory region derived from

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

3 37. Kite has had knowledge of the '190 Patent at least as early as August
4 13, 2015, when it filed a petition for *inter partes* review against the '190 Patent in
5 the United States Patent and Trademark Office, before the Patent Trial and Appeal
6 Board. A copy of Kite's petition is attached as Exhibit 2. In addition, Kite has had
7 knowledge of and notice of the '190 Patent and its infringement since at least, and
8 through, the filing and service of the Complaint.

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

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

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

19 **JURY TRIAL DEMANDED**

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

22 **PRAYER FOR RELIEF**

23 WHEREFORE, Plaintiffs pray for relief as follows:

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

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

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

1 D. An order permanently enjoining Kite from further infringement of the
2 '190 Patent;

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

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

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

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DATED: October 18, 2017

Respectfully submitted,

IRELL & MANELLA LLP

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