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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-06496 **COMPLAINT FOR PATENT INFRINGEMENT** **DEMAND FOR JURY TRIAL**

This litigation represents the second phase of a patent dispute that Defendant Kite Pharma, Inc. ("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 in the process of 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.

Now on the brink of obtaining marketing approval from the Food and Drug Administration ("FDA"), Kite's activities in preparing for commercialization of its axicabtagene ciloleucel ("KTE-C19") product constitute infringement of the '190 Patent. Plaintiffs accordingly bring suit against Kite both for infringement based on Kite's current activities, including making and using chimeric antigen receptor products that comprise the claimed nucleic acid polymers of the '190 Patent, *see* 35 U.S.C. § 271(a), and for a declaration that Kite's imminent sales and other activities relating to those products do and will constitute further infringement of the '190 Patent. Plaintiffs accordingly 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 KTE-C19 product. Plaintiffs further seek a declaration that Kite's KTE-C19 product infringes and/or will infringe (whether literally or under the doctrine of equivalents) at least claims 1-3, 5, 7-9, and 11 of the '190 Patent.

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 corporation 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. This Court has subject-matter jurisdiction under 28 U.S.C. § 1331 and 28 U.S.C. § 1338(a). The Court also has subject-matter jurisdiction under the Declaratory Judgment Act, 28 U.S.C. §§ 2201 and 2202, because an immediate and substantial controversy exists between Plaintiffs and Kite with respect to Kite's infringement of the '190 Patent based on activities relating to its KTE-C19 product.

6. This Court has personal jurisdiction over defendant Kite based on its

principal place of business in California.

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 lead product candidate, KTE-C19, 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 KTE-C19 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:

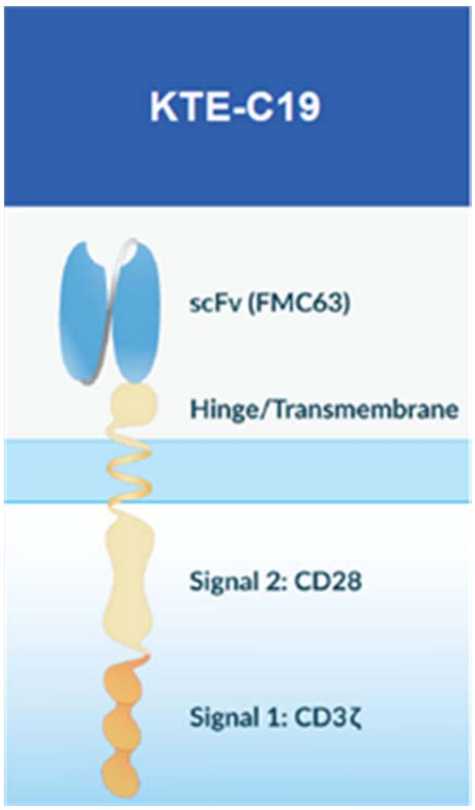

Exhibit 9 (Ghobadi) at 4.

25. On information and belief, through its scientific advisors, Kite copied the chimeric T cell receptor construct utilized in its KTE-C19 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. Kite has made systematic attempts to meet U.S. regulatory requirements for marketing approval of its KTE-C19 product. On December 4, 2016, Kite issued a press release announcing its initiation of a rolling submission of a Biologics License Application ("BLA") to the United States Food and Drug Administration ("FDA") for KTE-C19. Kite stated that "[t]he company expects to complete its BLA submission by the end of the first quarter of 2017." Exhibit 13 (Kite 12/4/2016 Press Release). True to its word, Kite announced that it had completed submission of its BLA for KTE-C19 on March 31, 2017. Exhibit 14 (Kite 3/31/2017 Press Release). In the same press release, Kite stated that "[i]f approved, Kite plans to commercially launch axicabtagene ciloleucel in 2017." *Id*.; *see also* Exhibit 15 (Kite 10/19/2016 Press Release) ("[W]e prepare to manufacture and commercialize KTE-C19 upon approval [of the FDA]").

29. On May 26, 2017, Kite announced that the FDA had "accepted for priority review the Biologics License Application (BLA) for axicabtagene ciloleucel. The submission follows positive data demonstrated with a single infusion of axicabtagene ciloleucel in the ZUMA-1 Phase 2 trial in patients with refractory aggressive non-Hodgkin lymphoma (NHL). The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of November 29, 2017." Exhibit 16 (Kite 5/26/2017 Press Release). When the FDA grants priority review, the FDA is given six months to review a drug or biologic for approval. Exhibit 17 (FDA Priority Review Webpage). Though the FDA has set a target approval date of November 29, 2017, the FDA can, and often does, announce a decision prior to the PDUFA date. Exhibit 18 (PDUFA Date Article).

30. Indeed, on August 8, 2017, during a call with analysts, Kite announced that the FDA had notified Kite that "regulators w[ould] not be organizing a panel review with outside experts for axi-cel." Exhibit 19 (Endpoints News Article). The FDA had previously organized a panel of advisors for Novartis AG's ("Novartis") chimeric antigen receptor product targeting CD19, and the panel voted to back the

biologic in a 10-0 vote. Exhibit 20 (Bloomberg Article). At the time, commentators noted that Novartis's chimeric antigen receptor treatment was "on the brink of approval" after receiving unanimous backing. *Id*. Similarly, commentators noted that, after the FDA chose to forego a similar panel for Kite's KTE-C19 product, "[t]he FDA has evidently learned all it wants at this point from outside oncology experts on CAR-T. Kite's closely-watched CAR-T drug axi cel is getting a pass on an adcomm meeting, which may signal a quick thumbs up from regulators." Exhibit 19 (Endpoints News Article). Though "Novartis had been seen as the clear front-runner in the race to get on the market first," Kite's news "blurr[ed]" the finish line, and "they may now both launch almost simultaneously." *Id*. The FDA's decision to abstain from an advisory panel followed "an FDA inspection of [Kite's] manufacturing facility and its treatment centers in the lead-up to an accelerated review and final decision." *Id*.

31. Dr. David Chang, Kite's Chief Medical Officer and Executive Vice President of Research & Development was likewise "encouraged by the recent advisory committee meeting . . . We believe it was a major milestone for the field of cell therapy and provided clarity on how the agency will view this innovative therapy as it enters the commercial space." Exhibit 21 (8/8/2017 Call Transcript).

32. Indeed, on August 30, 2017, the FDA "granted approval of Kymriah [Novartis's anti-CD19 chimeric antigen receptor gene therapy] to Novartis Pharmaceuticals Corp." for certain pediatric and young adult patients with a form of acute lymphoblastic leukemia (ALL). Exhibit 22 (FDA Kymriah Press Release). Novartis's Kymriah (tisagenlecleucel) is "the first gene therapy available in the United States, ushering in a new approach to the treatment of cancer and other serious and life-threatening diseases." *Id*. FDA Commissioner, Dr. Scott Gottlieb, also stated that "[a]t the FDA, we're committed to helping expedite the development and review of groundbreaking treatments that have the potential to be life-saving." *Id*.

33. Kite has made clear on numerous occasions that it is ready for commercialization in the event of early FDA approval. During a conference call, Kite's Chairman, President, and Chief Executive Officer, Dr. Arie Belldegrun stated that Kite was ready "for commercialization in the U.S. with all teams in place." Exhibit 21 (8/8/2017 Call Transcript). Shawn Tomasello, Kite's Chief Commercial Officer, reiterated this sentiment, stating, "I'd like to cover the following topics, the buildout and launch readiness preparations for Europe and the U.S. launch operational readiness. The headline, yes, we're ready." *Id*. In discussing U.S. launch readiness, he described that "[a]nd yes, coming soon it's a potential approval of axi-cel in the U.S. Much of this discussion we've reviewed on previous calls. However, I think it's important to reinforce a few key points. And that is point #1, yes, we will be launch-ready by September, to ensure that we're prepared for an approval at any time. Our commercial headquarters and field-based teams are fully staffed, trained and ready for launch." *Id*. He further explained that "[t]o prepare for execution at launch, we're conducting end-to-end rehearsal dry runs at each site. These activities enable us and our centers to be confident in the logistics of our workflow processes surrounding axi-cel therapy." *Id*.

34. On information and belief, this advanced stage of commercial readiness makes clear that Kite is engaging in activities that constitute present infringement of the '190 Patent. Although KTE-C19 is an individualized therapy that involves genetically reengineering a cancer patient's own immune cells, the claims of the '190 Patent do not require expressing a chimeric TCR in a patient's T cells. The '190 Patent claims a nucleic acid polymer that encodes a chimeric T cell receptor, such as Kite's vector that will be used to genetically reengineer patients' immune cells, which contains a nucleic acid polymer covered by the scope of the '190 patent. As set forth below, on information and belief, Kite is already making and using vectors containing the claimed nucleic acid polymer for commercial purposes, and not "solely for uses reasonably related to the development and submission of

information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products." 35 U.S.C. § 271(e)(1).

35. Based on Kite's public statements, including its statements that the FDA has completed inspections of Kite's manufacturing facility and its treatment centers, Exhibit 19 (Endpoints News Article), the vector used in Kite's KTE-C19 therapy (which contains Plaintiffs' claimed nucleic acid polymer) can—and must—be stockpiled to some extent prior to commercial launch. In general, infectious viral vectors containing a desired nucleic acid are produced by introducing plasmids into so-called "producer" or "packaging" cell lines. Exhibit 23 (Vector Manufacturing Article). By inserting a desired nucleic acid sequence into the appropriate host cells, gene expression by the "producer" cell can be manipulated and the cells cultured to produce infectious viral vectors containing the desired nucleic acid. The infectious viral vectors in turn may be stored and later used to transduce patient cells, causing the patient cells to express the desired sequence. Exhibit 23 (Vector Manufacturing Article). Therefore, the viral vectors that will be used as part of the KTE-C19 therapy contain a nucleic acid sequence of Plaintiffs' claimed chimeric TCR-encoding nucleic acid polymers. *See, e.g.*, Exhibits 11 (RAC Filing) and 10 (KTE-C19 DNA Sequence).

36. On information and belief, given Kite's repeated public representations that it will be commercial launch-ready by September (if not sooner), Kite has begun stockpiling the vector that will be used for the KTE-C19 therapy. According to Kite's public statements, the pre-approval inspection of Kite's facility and commercial manufacturing process has already been completed. Exhibit 21 (8/8/2017 Call Transcript) ("To date, the FDA has completed its mid-cycle review, inspection of our commercial manufacturing facility in El Segundo."). This pre-approval inspection process involves an inspection by an FDA officer of the facility and manufacturing process where the biologic will be made. *See* 21 C.F.R. 600.22(c)-(d). The inspection is conducted by "an officer of the Food and Drug

Administration having special knowledge of the methods used in the manufacture and control of products and designated for such purposes by the Commissioner of Food and Drugs, or by any officer, agent, or employee of the Department of Health and Human Services specifically designated for such purpose by the Secretary." 21 C.F.R. 600.20. Importantly, this inspection is not made "until the establishment is in operation and ***is manufacturing the complete product for which a biologics license is desired***." 21 C.F.R. 600.21 (emphasis added). As part of the inspection, the inspector "[i]nvestigate[s] as fully as he deems necessary the methods of propagation, processing, testing, storing, dispensing, recording, or other details of manufacture and distribution of each licensed product, or product for which a license has been requested, including observation of these procedures in actual operation." 21 C.F.R. 600.22(d). The inspector also "certif[ies] as to the condition of the establishment and of the manufacturing methods followed and make[s] recommendations as to action deemed appropriate with respect to any application for license or any license previously issued." 21 C.F.R. 600.22(h). If part of the biologic is manufactured by a contract manufacturer, such as the retroviral vector, then the FDA also inspects the contract manufacturer as part of the inspection process. This inspection serves to verify the data that has been submitted in the BLA against the facility, and to ensure that the facility and manufacturing process are ready to be licensed. Part of this inspection is to ensure that, upon FDA approval, the establishment is prepared to supply the market.

37. On information and belief, in part to prepare for the pre-approval inspection, Kite has manufactured in, and/or induced the manufacturing of from, this District vector lots containing the claimed nucleic acid polymers to be used commercially once approval is granted. On information and belief, these vectors were manufactured according to a validated process, and fulfill the requirements of the specification for KTE-C19 submitted to the FDA. It is common for the FDA to inspect vector lots during a facility inspection. Accordingly, on information and

belief, Kite has already manufactured or caused to be manufactured vector lots meeting the validation requirements required by the FDA. On information and belief, these vector lots are not intended for clinical trials but are segregated for commercial use once FDA approval is granted.

38. On information and belief, Kite has stockpiled, or is causing to be manufactured, enough vector lots to supply up to six or more months of patient demand at launch. On information and belief, this would approximately amount to as many as 10-20 lots of vector.

39. On information and belief, Kite's public statements regarding its own commercial readiness highlight the extent to which it has already stockpiled vectors. On a recent conference call with investors, Kite announced that it was "ready to start making the personalized [KTE-C19] therapy and start shipping almost immediately." Exhibit 19 (Endpoints News Article). Shawn Tomasello repeated this sentiment, stating that "yes, we will be launch-ready by September, to ensure that we're prepared for an approval at any time. Our commercial headquarters and field-based teams are fully staffed, trained, and ready for launch . . . Following FDA approval we expect to have at least 10 of the top centers in the United States ready for final site activation. Beyond these initial centers, we're actively working with over 30 additional sites, bringing them to our site readiness process." Exhibit 21 (8/8/2017 Call Transcript). On information and belief, Kite could not be "launch-ready by September" in the absence of stockpiling vector.

40. As a result, Kite has already made or used, or induced others to make or use, vectors that include nucleic acid polymers that fall within the scope of the claims of the '190 Patent. On information and belief, Kite's foregoing activities are, at least in part, for commercial purposes, and hence are not "solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products." 35 U.S.C. § 271(e)(1). As a result, such activities are outside

the scope of the safe harbor of § 271(e)(1) and constitute present infringement of the '190 Patent.

KITE'S COMMERCIAL READINESS

41. Kite has also taken additional, significant, concrete steps in the meaningful preparation of commercializing the KTE-C19 product. For example, on June 20, 2016, Kite opened a new commercial facility in El Segundo, California, for the manufacturing of KTE-C19. Exhibit 24 (Kite 6/20/2016 Press Release). Kite announced that the manufacturing facility "has been designed to produce chimeric antigen receptor (CAR) and T-cell receptor (TCR) product candidates for clinical trials, as well as for the potential launch and commercialization of Kite's lead CAR T-cell product candidate, KTE-C19, which is in a clinical study for the treatment of chemorefractory diffuse large B-cell lymphoma (DLBCL) and other B-cell malignancies. Kite anticipates commercial launch of KTE-C19 in 2017." *Id*. Kite also stated that "[t]he facility is estimated to have the capacity to produce up to 5,000 patient therapies per year. The plant's location, adjacent to Los Angeles International Airport, is intended to expedite receipt and shipment of engineered T-cells from and to patients across the United States and Europe." *Id*.

42. As another example, on September 29, 2016, Kite announced the addition of Christine Cassiano as its Senior Vice President of Corporate Communications and Investor Relations. Exhibit 25 (Kite 9/29/2016 Press Release). Dr. Belldegrun, stated that "Christine arrives at a key inflection point for Kite as we advance our CAR-T and TCR pipeline toward key company milestones, including our BLA submission for KTE-C19 with the FDA, and evolve Kite into a commercial organization." *Id*.

43. On October 13, 2016, Kite announced that it had appointed Chris Nowers as its Head of Europe to "oversee European commercial operations to build awareness in the region of Kite's growing pipeline portfolio of chimeric antigen receptor (CAR) and T-cell receptor (TCR) therapy product candidates and prepare

for the potential launch of the company's lead product candidate, KTE-C19." Exhibit 26 (Kite 10/13/2016 Press Release).

44. Kite also discussed its "KTE-C19 Launch Preparedness" at its "Investor Day" on October 18, 2016. Specifically, Kite "reviewed its proven clinical cell manufacturing capability, preparations to produce and deliver KTE-C19 at commercial scale following U.S. regulatory approval, and ongoing activities to automate next generation manufacturing," including an "[e]fficient and consistent manufacturing process" and "[e]stimated capacity for 4,000+ patient treatments per year and ability to expand quickly." Exhibit 15 (Kite 10/19/2016 Press Release). During its Investor Day, Kite also "discussed its ongoing activities to build scientific awareness and to commercialize KTE-C19 following U.S. regulatory approval." *Id*. These "ongoing activities" include a "Medical Science Liaison team" that is "ready for deployment in the fourth quarter of 2016," a "[p]roactive Market Access strategy and engagement with payers," and a "[c]ontrolled launch approach [that] lays groundwork for expansion, understanding of therapy, patient management, and reimbursement." *Id*.

45. On December 1, 2016, Kite announced that it had appointed Jian Irish, Ph.D. as the company's Senior Vice President of Supply Chain. Exhibit 27 (Kite 12/1/2016 Press Release). Kite stated that "Dr. Irish will work closely with both the commercial and technical operations organization to create operational strategies for supply chain design, product life cycle management, launch and commercialization as the company prepares for the potential approval of Kite's lead product candidate, KTE-C19, by the U.S. Food and Drug Administration." *Id*.

46. On December 13, 2016, Kite announced that it had entered into a "strategic partnership" with Vitruvian Networks, Inc., a cell and gene therapy software and analytics platform company, to "create a software solution to support commercial availability of T-cell therapies. Together, the parties will design and develop a platform for patients, physicians and treatment centers that enables

commercial-scale ordering, logistics, monitoring and delivery of autologous cell therapies if they are FDA-approved, including axicabtagene ciloeucel (formerly known as KTE-C19), Kite's lead investigational engineered T-cell therapy for aggressive non-Hodgkin lymphoma." Exhibit 4 (Kite 12/13/2016 Press Release).

47. In early 2017, Kite's CEO made clear that Kite is prepared to commercially launch KTE-C19 "within days" of FDA approval. For example, Kite's CEO, Dr. Arie Belldegrun, stated during a conference call with investors that:

> Beginning in late December 2014, Kite was able to dramatically accelerate development, and now we look at 27 months from an investigational new drug submission [in December 2014] to biologic license submission, lining up axi-cel [KTE-C19] to potentially become the fastest and most efficient development program to reach commercialization in oncology. If axi-cel is approved, we expect to begin processing the first commercial orders within days. We are preparing for success and are in a position of strength . . . .

Exhibit 28 (Kite Q4 2016 Earnings Call Tr.). During the same call, Kite informed investors that it is "in discussions with payors, with hospitals. We have an outstanding team of commercial experts that are ready to move on if and when approved." *Id*.

48. Since those statements, it has become increasingly clear that Kite's efforts in preparing for commercial launch have only accelerated. For example, on August 8, 2017, Kite stated during a conference call with analysts that, though it faces a November 29, 2017 PDUFA date, "it's ready to start making the personalized [KTE-C19] therapy and start shipping almost immediately." Exhibit 19 (Endpoints News Article). During the same call, Dr. Belldegrun stated that "[a]t Kite today, we await possible approval for axi-cel in the United States. We [are ready] for commercialization in the U.S. with all teams in place." Exhibit 21 (8/8/2017 Call Transcript).

49. During the call with investors, Dr. Chang recounted Kite's close collaboration with the FDA to ensure marketing approval for KTE-C19. For

example, Dr. Chang stated that "[w]e have just pas[sed] the midpoint of FDA review of our BLA. To date, the FDA has completed its mid-cycle review, inspection of our commercial manufacturing facility in El Segundo. And the [Good Clinical Practices] inspections of our clinical sites. The FDA has informed us, that they will not schedule an advisory meeting for axi-cel. Overall, we continue to work closely with [the] agency as their review process moves toward the final phase." Exhibit 21 (8/8/2017 Call Transcript).

50. On the same call, Shawn Tomasello reiterated his colleagues' comments regarding commercialization of KTE-C19: "[Y]es, we will be launch-ready by September, to ensure that we're prepared for an approval at any time. Our commercial headquarters and field-based teams are fully staffed, trained, and ready for launch . . . Following FDA approval we expect to have at least 10 of the top centers in the United States ready for final site activation. Beyond these initial centers, we're actively working with over 30 additional sites, bringing them to our site readiness process." Exhibit 21 (8/8/2017 Call Transcript). Tomasello added that "[t]o prepare for execution at launch we're conducting end-to-end dry runs at each site. These activities enable us and our centers to be confident in the logistics of our workflow processes surrounding axi-cel therapy." *Id*.

51. Tomasello also addressed insurance coverage for Kite's KTE-C19 product, stating that "[o]ur market access teams have been laying the foundation for coverage and reimbursement, meeting multiple times with all of the national payers and the majority of regional players. The teams have also held multiple meetings with CMS, centers for Medicare and Medicaid services and have also met with all 12 MACs or Medicare Administrative Contractors." *Id*.

52. Kite has also announced the initiation of a KTE-C19 clinical program in the European Union. Exhibit 29 (Kite 8/7/2017 Press Release). "Kite filed a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for axicabtagene ciloleucel in July 2017, the first CAR-T application in

Europe." *Id*.

53. Kite's systematic attempts to meet the FDA's regulatory requirements, coupled with the acts of hiring key managerial personnel, the construction of a manufacturing facility for the KTE-C19 product, and Kite's commercialization efforts demonstrate that Kite has meaningfully prepared to engage in infringing activity. As a result, an immediate and substantial controversy exists between Plaintiffs and Kite.

54. Kite has acknowledged that an actual controversy exists between Juno and Kite. In an SEC filing, Kite stated that, "[w]e are aware of a U.S. patent held by one of our competitors relating to certain CAR compositions of matter . . . If and when KTE-C19 or another of our CAR-based product candidates is approved by the FDA, that competitor may then seek to enforce its patent by filing a patent infringement lawsuit against us. On August 13, 2015, we filed a petition with the USPTO to institute an IPR proceeding of this competitor's patent, requesting a determination that the claims in the patent are unpatentable." Exhibit 30 (Kite Form 10-Q) at 58. As noted above, Kite's IPR was unsuccessful, with the PTAB concluding that Kite failed to meet its burden to prove any claim of the '190 Patent unpatentable.

COUNT 1:

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

55. Plaintiffs re-allege and incorporate by reference the allegations contained in paragraphs 1-54 above.

56. 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 and/or using in the United States without authority, chimeric antigen receptor products that comprise the claimed nucleic acid polymers, including, but not limited to, the KTE-C19 product.

57. On information and belief, Kite has manufactured or caused to be

manufactured KTE-C19 retroviral vector intended for commercial use. On information and belief, Kite has begun to stockpile (for eventual commercial use) vectors containing the nucleic acid polymers falling within the scope of the '190 Patent claims. These retroviral vectors, to be used as part of the KTE-C19 therapy manufacturing process, contain nucleic acid polymers as claimed by at least claims 1-3, 5, 7-9, and 11 of the '190 Patent.

58. Attached as Exhibit 31 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 31 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.

59. Kite's KTE-C19 product meets every limitation of several claims of the '190 Patent, including without limitation claim 1. For example, vectors used with Kite's KTE-C19 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.

60. On information and belief, Kite will infringe 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, and/or offering to sell in the United States without authority, chimeric antigen receptor products that comprise the claimed nucleic acid polymers, including, but not limited to, the KTE-C19 product.

61. On information and belief, Kite does and/or will infringe the '190 Patent in violation of 35 U.S.C. § 271(b) by actively inducing infringement of the '190 Patent, literally and/or under the doctrine of equivalents, with knowledge of the

'190 Patent and knowledge that it will induce 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 or using 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 KTE-C19 product.

62. On information and belief, Kite does and/or will infringe 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 KTE-C19 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.

63. On information and belief, Kite does and/or will infringe 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 will supply or cause to be supplied in or from the United States all or a substantial portion of the components of its KTE-C19 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 KTE-C19 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 KTE-C19 product, including without limitation, Europe.

64. On information and belief, Kite does and/or will infringe 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 will supply or cause to be supplied in or from the United States components of its KTE-C19 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 KTE-C19 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 KTE-C19 product, including without limitation, Europe.

65. 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 and notice of the '190 Patent and its infringement since at least, and through, the filing and service of the Complaint.

66. Kite's infringement of the '190 Patent does and will injure Juno in its business and property rights.

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

68. 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

69. 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 declaration that Kite's activities in connection with its KTE-C19 product do and/or will infringe (whether literally or under the doctrine of equivalents) one or more claims of the '190 Patent under at least 35 U.S.C. §§ 271(a), (b), (c), (f)(1) and (f)(2);

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

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

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

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

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

DATED: September 1, 2017

Respectfully submitted,

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