No. 20-1758

IN THE
United States Court of Appeals for the Federal Circuit

JUNO THERAPEUTICS, INC., SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH,
Plaintiffs-Appellees,
v.
KITE PHARMA, INC.,
Defendant-Appellant.

On Appeal from the United States District Court
for the Central District of California
No. 2:17-cv-07639-PSG-KS
Hon. Philip S. Gutierrez

NONCONFIDENTIAL OPENING BRIEF AND ADDENDUM FOR KITE PHARMA, INC.

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U.S. PATENT NO. 7,446,190: CLAIMS 1-3, 5, 7-9, AND 11 (CLAIMS 3, 5, 9, AND 11 ASSERTED)

1. A nucleic acid polymer encoding a chimeric T cell receptor, said chimeric T cell receptor comprising

(a) a zeta chain portion comprising the intracellular domain of human CD3 ζ chain,

(b) a costimulatory signaling region, and

(c) a binding element that specifically interacts with a selected target, wherein the costimulatory signaling region comprises the amino acid sequence encoded by SEQ ID NO:6.

2. The nucleic acid polymer of claim 1, wherein the binding element is an antibody.

3. The nucleic acid polymer of claim 2, wherein the antibody is a single chain antibody.

5. The nucleic acid polymer of claim 3, wherein the single chain antibody binds to CD19.

7. The nucleic acid polymer of claim 1, wherein the zeta chain portion comprises the sequence obtained by amplification of human zeta chain DNA with the primers of SEQ ID Nos 1 and 2.

8. The nucleic acid polymer of claim 7, wherein the binding element is an antibody.

9. The nucleic acid polymer of claim 8, wherein the antibody is a single chain antibody.

11. The nucleic acid polymer of claim 9, wherein the single chain antibody binds to CD19.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number 20-1758

Short Case Caption Juno Therapeutics, Inc. v. Kite Pharma, Inc.

Filing Party/Entity Kite Pharma, Inc., Appellant

Instructions: Complete each section of the form. In answering items 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance. **Please enter only one item per box; attach additional pages as needed and check the relevant box**. Counsel must immediately file an amended Certificate of Interest if information changes. Fed. Cir. R. 47.4(b).

I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: 08/31/2020

Signature: S/ E. Joshua Rosenkranz

Name: E. Joshua Rosenkranz

1. Represented Entities. Fed. Cir. R. 47.4(a)(1).	**2. Real Party in Interest.** Fed. Cir. R. 47.4(a)(2).	**3. Parent Corporations and Stockholders.** Fed. Cir. R. 47.4(a)(3).
Provide the full names of all entities represented by undersigned counsel in this case.	Provide the full names of all real parties in interest for the entities. Do not list the real parties if they are the same as the entities. ☒ None/Not Applicable	Provide the full names of all parent corporations for the entities and all publicly held companies that own 10% or more stock in the entities. ☐ None/Not Applicable
Kite Pharma, Inc.		Gilead Sciences, Inc.

☐ Additional pages attached

4. Legal Representatives. List all law firms, partners, and associates that (a) appeared for the entities in the originating court or agency or (b) are expected to appear in this court for the entities. Do not include those who have already entered an appearance in this court. Fed. Cir. R. 47.4(a)(4).

☐ None/Not Applicable ☐ Additional pages attached

Munger Tolles and Olson LLP: Blanca Young, Graham Cole, Markus Brazill and Vincent Ling	Fish and Richardson PC: W. Chad Shear, Gregory Booker, John Farrell, Lance Wyatt and Megan Chacon	Gibson Dunn and Crutcher LLP: Omar Amin, Michael Sitzman, Jane Love, Jaysen Chung, Jeffrey Thomas and Timothy Best
Orrick, Herrington & Sutcliffe LLP: Eric Shumsky		

5. Related Cases. Provide the case titles and numbers of any case known to be pending in this court or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal. Do not include the originating case number(s) for this case. Fed. Cir. R. 47.4(a)(5). See also Fed. Cir. R. 47.5(b).

☑ None/Not Applicable ☐ Additional pages attached

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6).

☑ None/Not Applicable ☐ Additional pages attached

TABLE OF CONTENTS

Material has been redacted from page 67 of the Nonconfidential Opening Brief and pages Appx47, Appx48, Appx54, Appx95, Appx98 of the addendum attached to the Nonconfidential Opening Brief. This material has been designated pursuant to the Protective Order entered in *Juno Therapeutics, Inc., et al. v. Kite Pharma, Inc.*, No., 2:17-cv-07639-SJO-KS (C.D. Cal.). The material omitted from page 67 indicates a confidential license valuation. The material omitted from the addendum at Appx47, Appx48, Appx54, Appx95, Appx98 indicates confidential business information containing non-public valuations.

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Regulations

STATEMENT OF RELATED CASES

No appeal in or from the same civil action was previously before this or any other appellate court.

Counsel is not aware of any case pending in this or any other court or agency that will directly affect or be directly affected by this Court's decision in the pending appeal.

INTRODUCTION

Kite Pharma, Inc. co-developed YESCARTA®, a revolutionary immunotherapy that cures many patients afflicted with an especially fatal blood cancer. Kite's work has saved thousands of lives. Equipped with a generic patent, Juno Therapeutics, Inc. attempted to develop a similar treatment, but failed. Juno's "cure" killed so many patients that the FDA shut down clinical testing.

Now Juno's positions threaten to kill innovation. It won a $1.2 billion judgment that, if upheld, would deter wide swaths of lifesaving invention, stifle investment, and reward Juno for Kite's success in solving the very problems Juno could not.

Overclaiming. The patent preempts an entire field of inquiry. Each claim has structural elements that embrace millions of billions of species, constrained only by function. The patent mentions two functioning species (only one for the narrowest claims), providing no chemical structure of either. And the field has all the predictability of a lottery ticket. Fifteen years after the 2002 priority date, Juno tested a billion candidates to identify a tiny subset that might perform the narrowest claims' function, through pure trial and error. In short, the

patent claims a research plan. This Court has repeatedly struck claims like these for lack of written description and enablement.

Expanding the claims. Even the overbroad claims that issued did not cover YESCARTA®. Four-and-a-half years after issuance, the patentee filed a Certificate of Correction that stretched the patent's scope just enough to capture YESCARTA®. By then, Kite's YESCARTA® development was under way and highly public. Such a scope-broadening amendment is forbidden unless it represents a clearly evident correction to a clearly evident error. But if there was an error, it was not evident to the public. As issued, the claim made perfect sense, worked in practice, and was consistent with the specification. So the correction was impermissible, and Kite does not infringe.

Exaggerating the damage. Juno secured an astronomical $1.2 billion judgment and a 27.6% running royalty. The award exceeds YESCARTA®'s revenue through trial, and is multiples of the highest reference license that Juno's expert considered. Juno's expert flouted every basic requirement of damages calculations, including the prohibition against relying on reference licenses that cover more than just the value of a patent and the obligation to apportion.

Affirming this judgment would invite all patentees to follow Juno's example—and stifle innovation.

JURISDICTION

The district court had jurisdiction under 28 U.S.C. §§ 1331 and 1338. The court entered a final judgment on April 8, 2020. Appx30-32. Kite timely appealed on April 23, 2020. Appx32630-32631. This Court has jurisdiction under 28 U.S.C. § 1295(a)(1).

STATEMENT OF THE ISSUES

1. The asserted patent claims genuses defined in functional terms. For the narrowest claims, (1) the structural limitations encompass millions of billions of candidates; (2) only an indeterminate subset of those species function as claimed, with the patent discussing only one such species; and (3) the field is wildly unpredictable. Are the claims invalid for lack of written description?

2. Are those same claims invalid for lack of enablement, where Juno itself—with the benefit of more-developed art 15 years after the priority date—engaged in months of trial-and-error testing and hit nearly a billion dead ends?

3. The patent as issued did not encompass Kite's therapy. The inventors broadened their claims by filing a Certificate of Correction four-and-a-half years after issuance. Such a correction is invalid unless it represents a clearly evident correction to a clearly evident error. But the relevant limitation, as issued, made perfect sense, was consistent with the specification, and functioned. Is the broadening correction invalid?

4. Juno's expert presented a damages opinion that relied on agreements far beyond a patent license and did not apportion. Did the court err in permitting his testimony and finding the award supported by substantial evidence?

5. Must the jury's willfulness finding and the court's enhancement be vacated where Kite had strong defenses to both validity and infringement and abandoning its therapy after clinical success would have cost lives?

STATEMENT OF THE CASE

CAR-T Therapy Is In Its Infancy

Chimeric antigen receptor T-cell ("CAR-T") therapy, long a dream, only recently became reality. The FDA did not approve the first CAR-T

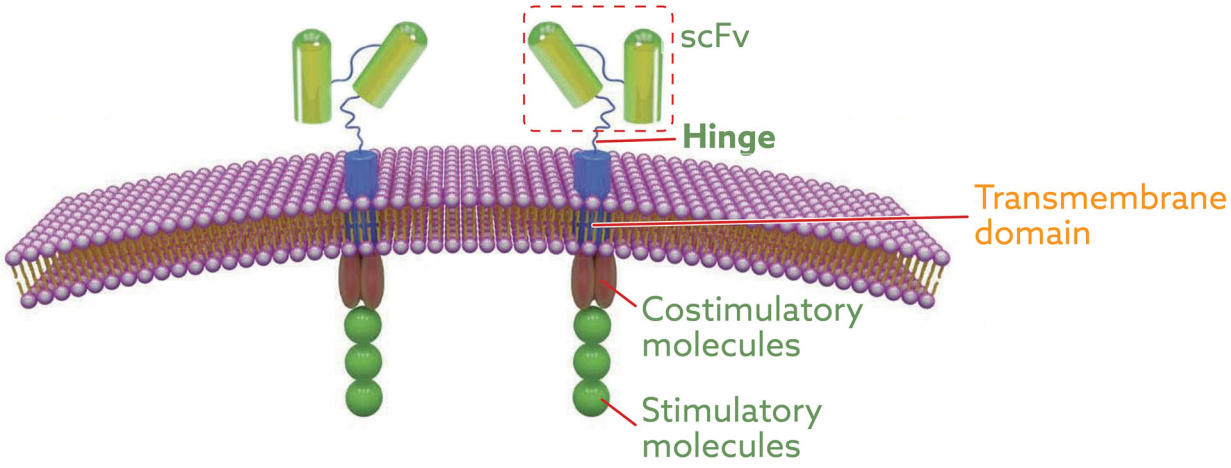
therapy until 2017. Appx33161. By trial, YESCARTA® was one of only two FDA-approved CAR-T therapies. Appx33143; Appx33161. The art was even more immature at the asserted patent's 2002 priority date. The lead inventor described that as the "birth of the CAR-T field," when "most people [were] incredulous about [its] potential." Appx32935; Appx32976.

CAR-T therapy fights diseases by reprogramming our T-cells—a type of white blood cell. A T-cell attacks an enemy cell (such as a cancer cell) by recognizing and binding to an antigen—a distinctive structure on the enemy cell's surface. Appx32907-32908. The reprogramming entails inserting genetic instructions to grow a new receptor that binds to a specific antigen. Appx32913-32914. The new receptor is called a chimeric antigen receptor ("CAR") or chimeric T-cell receptor ("chimeric TCR"). Appx32905; Appx103.

CAR-T technology has developed slowly and unpredictably. The first generation, circa 1993, was a CAR with two parts, both still components of modern CARs. Appx33926-33927; Appx32910. Part one, the "binder," protrudes from the cell's surface. It recognizes and binds to a target antigen. It typically consists of a single-chain variable

fragment (scFv) derived from an antibody. Appx37437; *see* Appx2641-2642. Part two is a "signaling region," inside the T-cell, which sends an "activation signal." The signal directs the T-cell to (1) destroy the enemy cell that the binder has gripped and (2) multiply to attack similar enemy cells. Appx37437. The signaling region consists of a portion of a protein found naturally in a typical human T-cell. Scientists long ago fixed upon a portion of the protein called CD3-zeta (often rendered "CD3 ζ"). Appx35876-35880. Unfortunately, these two-part CARs failed to mount a sustained attack on enemy cells. Appx2640; Appx32909-32912; Appx37400.

Researchers addressed this deficiency in the second generation, circa 1998, by adding a third part. Appx36283-36290; Appx2645-2646.

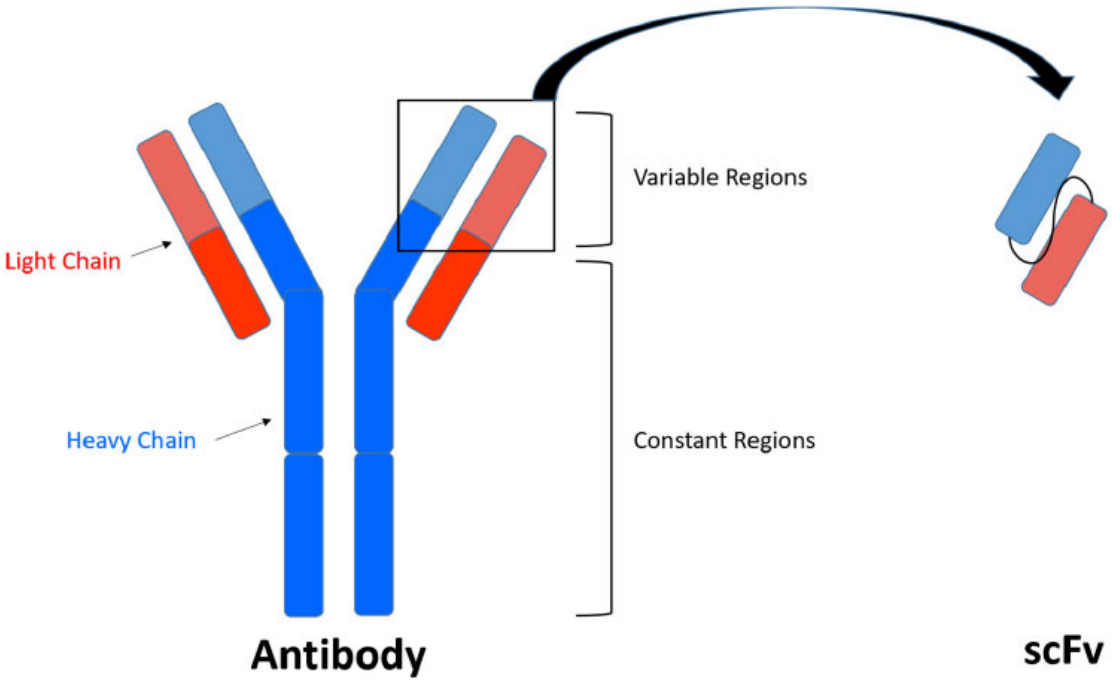


Appx37438 (annotations clarified). Part three—a "costimulatory signaling domain" inside the cell—generates a signal that directs T-cells to multiply. Appx36284; Appx2645-2646; Appx32912. One that worked was "CD28," a naturally occurring T-cell protein. Appx32962-32963; Appx36283-36290; Appx37107; Appx2645-2646. Juno calls these two signaling regions the CAR's "backbone." Appx32906.

Even with this knowledge of three-part CARs, scientists labored for two decades before producing a viable therapy. Appx37443 (citing Appx35881-35884). They had to overcome two challenges relevant here.

First, even where researchers had identified the right target, they still had to design the right scFv binder. Appx37435-37445. A CAR without the right binder is no better than a backbone without a head: The binder alone recognizes and binds to a target (triggering CAR stimulation and T-cell response). scFvs are created by rearranging pieces of antibodies. As illustrated below, antibodies are Y-shaped proteins with "variable regions" at the top, contoured to bind to a specific antigen. Appx2643; Appx33675-33676; Appx33936-33937. Think of the variable regions as three-dimensional puzzle pieces finely crafted to fit to the corresponding contours of a specific antigen.

Appx33675-33676; Appx33936-33937. To make an scFv, researchers take two pieces of an antibody's variable regions—one from the "heavy chain" and one from the "light chain." They select an order for the pieces and link them together with a new "linker sequence":

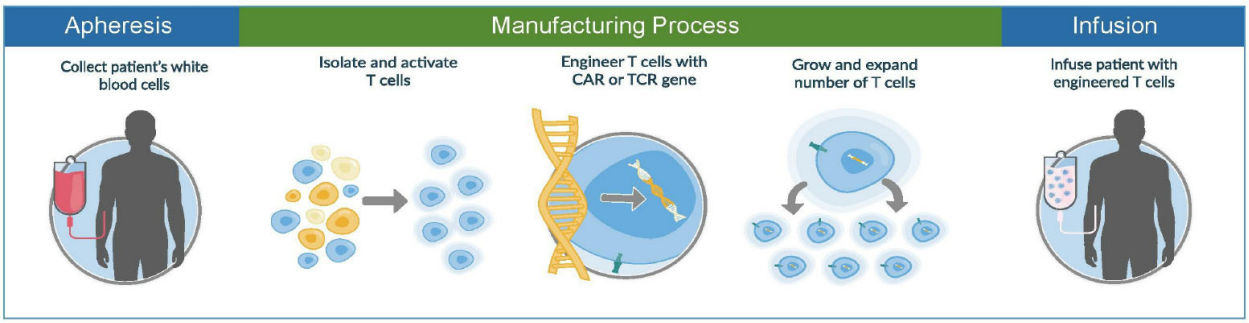


Appx2644; *see* Appx2643-2644.

The specific sequence of amino acids that make up the variable region and linker gives the puzzle pieces their unique three-dimensional shape and binding ability. Appx33675-33676; Appx2643; *see* Appx33937-33938. Even now, there is no known "*a priori* method for determining the ability of a particular antibody to function when" rearranged and "produced as an scFv" with a new linker. Appx35643;

see Appx33687-33688; Appx33701; Appx33955. Consequently, scFv design is rife with uncertainty. *Infra* 27-40, 42-46.

The second high hurdle was the need to solve manufacturing and clinical challenges—which the asserted patent does not address. If you just inject the claimed CAR into a patient's bloodstream, it will not work. Appx32918. Scientists have to design a vector—essentially a virus—that can enter patients' T-cells and deliver the genetic material that encodes the CAR. Appx32918; Appx32995; Appx33160. Then, scientists have to figure out how to make a CAR-T therapy unique to each patient. The patient's T-cells must be harvested, preserved, shipped, re-engineered using the vector, multiplied, and then sent back—alive—for reinfusion, as shown:



Appx36411 (color added); Appx36494. Even now, efforts to do all that for each patient at a commercial scale are rife with failures. *See infra* 12, 69. Compounding the challenge is that time is of the essence. Many

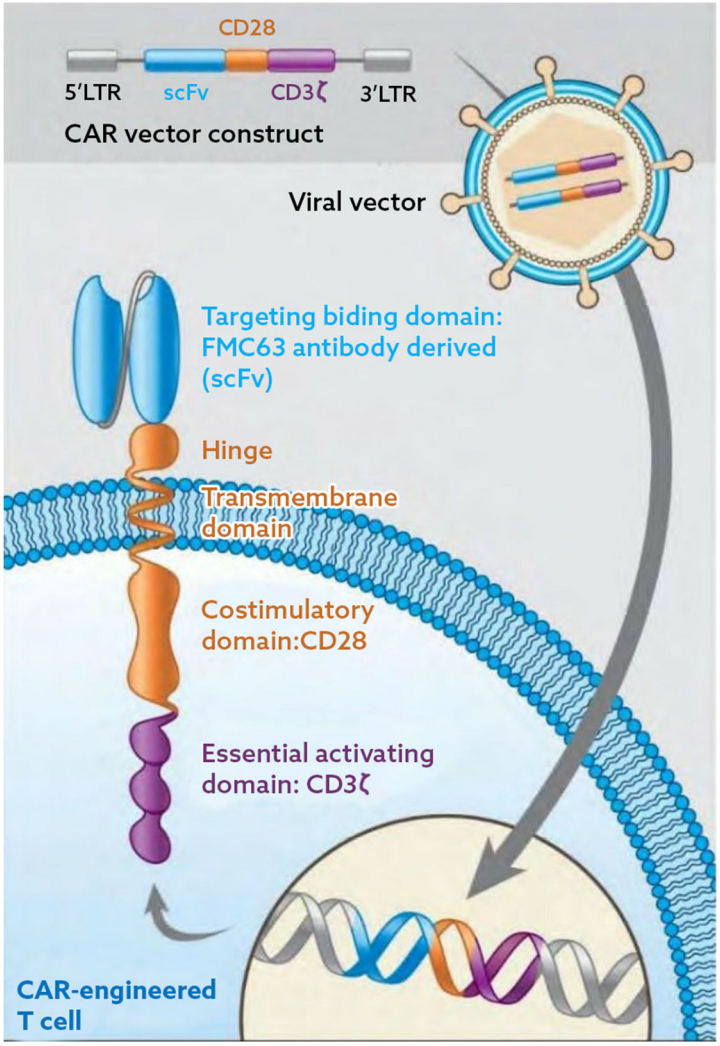
patients will live only weeks without treatment; each additional day in turnaround could spell death. Appx33616-33617; *see* Appx33423-33424.

Kite's YESCARTA® Realizes The Promise Of CAR-T Therapy

Kite, now a Gilead subsidiary, solved these problems to make CAR-T therapy a reality. Kite was founded in 2009 to engineer cancer-fighting therapies. Appx33243-33244; *see* Appx33309-33310. In 2012, it began collaborating with the National Cancer Institute ("NCI") to develop a CAR-T treatment for diffuse large B-Cell lymphoma ("DLBCL"), "one of the most aggressive forms of lymphoma." Appx33592; *see* Appx33314-33325; Appx35820-35871. Before YESCARTA®, DLBCL was often fatal in patients who did not respond to conventional therapies like chemotherapy. Appx33592-33594; *see* Appx33319.

With its FDA approval in 2017, YESCARTA® dramatically changed the odds. Appx33161; Appx33132-33133. It cures over 50% of patients who have unsuccessfully endured at least two lines of treatment, saving thousands of lives. Appx33592-33595; Appx33603-33604; *see* Appx33618.

YESCARTA® uses a three-part CAR illustrated below. Appx36494. The binder (in blue) is an scFv made from a mouse-based ("murine") antibody called FMC63. Appx33700; Appx32974. It targets CD19, an antigen on the surface of DLBCL cells. Appx36494-36495; Appx35936. YESCARTA® also includes portions of the CD3-zeta and CD28 proteins, as primary and costimulatory domains, respectively. Appx36494-36495; Appx35936.



Appx36495 (color added; annotations clarified).

Kite's NCI partners created and disclosed this CAR and its clinical results in seminal papers dating back to 2009. *See, e.g.*, Appx37572-37597; Appx36319-36331; Appx36332-36342; Appx33310-33316. That includes the "first report[]" of an "[e]ffective clinical treatment" of a human patient "with anti-CD19 CAR T cells." Appx37443 (citing Appx36319-36331); *see* Appx32936; Appx33312.

Using that CAR, Kite designed the right vector, addressed clinical challenges, and overcame the logistical challenges in manufacturing numerous individualized treatments. Appx33799. YESCARTA® has the fastest manufacturing of any CAR-T therapy, at 16-17 days' median turnaround. Appx33596-33597; Appx33618; *see* Appx33423; Appx33799. YESCARTA®'s rate of manufacturing success (how often the patient's cells are successfully modified) is also the highest, at 99%. Appx33597; Appx33618. The only other FDA-approved CAR-T therapy for DLBCL (Novartis's KYMRIAH®) has faced "manufacturing and capacity problems" and cannot be made "consistently and timely." Appx11669-11670; *see* Appx33623-33624. The difference can mean life or death. Appx33616-33617.

Juno Licenses The '190 Patent, Which Generically Claims A CAR-T Research Plan

Juno, now a Bristol-Myers Squibb subsidiary, was founded in 2013. Appx33401. Juno is the exclusive licensee of technology, including U.S. Patent No. 7,446,190, owned by Sloan Kettering. Appx260-283 (patent); Appx37509-37553 (license agreement). The patent claims nucleic acid polymers encoding a CAR with at least three parts. Claim 1, the only independent claim, recites:

> 1. A nucleic acid polymer encoding a chimeric T cell receptor, said chimeric T cell receptor comprising
>
> (a) a zeta chain portion comprising the intracellular domain of human CD3 ζ chain,
>
> (b) a costimulatory signaling region, and
>
> (c) a binding element that specifically interacts with a selected target,
>
> wherein the costimulatory signaling region comprises the amino acid sequence encoded by SEQ ID NO:6.

Appx282 (25:30-38).

This three-part structure, with a binder and two signaling domains, mirrors the second-generation approach described above. The claimed binder is nearly limitless. It can have any form, be directed to any target antigen (known or unknown), and be derived from any

source—provided it satisfies the functional condition of "specifically" binding to the selected target (i.e., binding to that target and not others). Thus, the patent claims binding elements for any disease, even though, nearly two decades after the priority date, scientists still have not even identified targets for most cancers, let alone elements that specifically bind to them. Appx32991-32993; Appx26411; Appx37442. The first signaling domain (or "primary" domain) comprises the portion of CD3-zeta commonly used back in first-generation CARs. The second ("costimulatory") signaling domain is made from CD28, the protein used in previous second-generation CARs. The patent distinguishes the invention from prior art by identifying a precise portion of CD28, comprising amino acids encoded by nucleotides listed in SEQ ID NO:6. Appx277; *see* Appx33533-33534; Appx104-105.

At issue are dependent claims 3, 5, 9, and 11. The broadest, claims 3 and 9, add to claim 1 only that the "binding element" must be "a single chain antibody"—i.e., an scFv. Appx282 (25:41-42, 26:35-36). Claims 5 and 11 add a functional requirement that the scFv "bind[] to CD19," a DLBCL antigen. Appx282 (25:45-46, 26:40-41). That means (per claim 1) that the scFv must bind "specifically" to CD19.

The structural limitations of even the CD19-specific claims cover an undisputedly vast range of scFv candidates. Kite's expert, Dr. Christopher Garcia, testified—and Juno did not dispute—that all claims, including the CD19 claims, structurally encompass "millions of billions" of different scFvs. Appx33687-33688. The only way to determine which and how many would bind to CD19 is "to do an experiment where you [made and] tested a very large number of scFvs." Appx33687-33688.

Against the staggering scope of scFvs encompassed by the claimed structure, the patent discloses very little. The specification mentions only two scFvs, from mice, without providing the amino-acid sequence of either. Appx273 (7:43-8:17); Appx275 (11:12-17). Only one, derived from the SJ25C1 antibody, binds to CD19, and YESCARTA® does not use it. *Infra* 29-30, 34-36. The patent says nothing about why or where its CD19 scFv binds or which of its amino acids are key for binding.

By the 2002 priority date, the literature had documented numerous failed attempts to create CD19-specific scFvs. *Infra* 27-28, 30. Even 15 years later, using modern-day technology, Juno itself screened and tested *a billion* scFvs for binding to CD19—identifying

only 60 that did, of which only three were worth further investigation for inclusion in a CAR. Appx33705-33707 (citing Appx37426-37434); *see* Appx37427-37428; Appx37433; Appx26414-26415; Appx37120-37131.

A Belated Certificate Of Correction Extends The '190 Patent Even Further, Capturing YESCARTA®

Broad as it was, the '190 patent as issued did not cover YESCARTA®. SEQ ID NO:6, the nucleotide sequence that encodes the claimed costimulatory region, differed from YESCARTA®'s. That changed in 2013—years after the '190 patent issued and soon after NCI and Kite publicized their collaborative arrangement—when the patentee filed a Certificate of Correction ("CoC"). Appx35269; Appx33245-33247. The "correction" changed SEQ ID NO:6, broadening the claim's scope such that it covered YESCARTA®. *Infra* 27-40, 42-46.

Juno Fails To Bring A Product To Market And Instead Sues Kite, Winning Over $1.2 Billion

Juno has yet to commercialize a CAR-T therapy. Juno tried to develop one, JCAR15, with the benefit of the '190 patent and its lone CD19-specific scFv (different from YESCARTA®'s). Appx33095; Appx36685. It failed catastrophically. The FDA twice halted Juno's clinical trial because multiple patients died. Appx33152-33155. Juno's

failure to adequately solve the manufacturing challenges described above (at 9-10) contributed to those deaths. Appx36765-36766; *see* Appx33150; Appx33157.

Juno ditched JCAR15 in favor of a different CAR-T therapy, JCAR17, that does not practice the '190 patent. Appx33104; Appx33137-33139; Appx33141-33142. For the costimulatory region, JCAR17 does not use CD28. Appx33137; Appx33417-33418.

Juno filed this case on October 18, 2017, the day the FDA approved YESCARTA®. Appx383-396. The district court construed "the amino acid sequence encoded by SEQ ID NO:6" to have different meanings before and after the CoC:

Claim Term	Court's Construction
"the amino acid sequence encoded by SEQ ID NO:6"	**Before the Certificate of Correction:** Amino Acids 113-220 of CD28 (starting with lysine (K)) **After the Certificate of Correction:** Amino Acids 114-220 of CD28 (starting with isoleucine (I))

Appx117. The court held that the patent as issued requires the initial lysine because it "explicitly defined the claim term 'the amino acid encoded by SEQ ID NO:6' by way of the sequence listing and … nothing

in the intrinsic record is sufficient to overcome this express definition." Appx117.

Kite invoked that holding to argue that the CoC must be invalid (and therefore there is no infringement), because it did not satisfy the requirement that a correction be the clearly evident solution to a clearly evident mistake. The court disagreed. Appx8407-8419.

At trial, the court granted Kite less than 12 hours to defend against this billion-dollar case. Kite pressed its CoC defense, along with the defenses that the claims are invalid for lack of written description and enablement. The district court refused to instruct the jury on the governing *Ariad* test for written description, leaving the jury without that critical guidance. And Juno urged the jury to reject Kite's § 112 and CoC defenses with the non sequitur that, in an IPR asserting obviousness, "three trained patent judges look[ed] at issues relative to the validity of the patent." Appx34209-34212.

In the end, the jury rejected Kite's defenses and found Kite's infringement willful. It awarded Juno $778 million in damages: a $585 million upfront payment plus a 27.6% running royalty on net revenues from YESCARTA®. Appx156-160. The court enhanced damages by

50%. Appx56. All told, the final judgment awards Juno over $1.2 billion, plus post-judgment interest and a 27.6% running royalty. Appx30-32.

SUMMARY OF ARGUMENT

I. Juno's patent claims are insufficiently described. The undisputed evidence established all three hallmarks of impermissible functional genus claims. First, structurally, the claims cover a vast and varied set of candidates, numbering in the millions of billions. Second, functionally, only an uncertain fraction of the universe of possible scFv candidates meet the functional limitation of specifically binding to *any* specified target (the requirement of the broadest claims)—or to CD19 in particular (the requirement of the narrowest claims). Fifteen years after the priority date, using modern-day technology, Juno tested a billion scFvs to identify only 60 that bound to CD19. Third, technologically, the claims occupy a highly unpredictable, failure-ridden field that was in its infancy in 2002—and still is. There is no way to predict in advance whether a particular structure will perform the claimed function—making and testing is required.

These claims cannot meet *Ariad*'s requirements for written description, as a matter of undisputed fact. The patent provides no guidance whatsoever as to which sequences will work. Juno's own expert conceded that the patent does not "teach[] any correlation between the amino acid sequence of an scFv and its ability to bind to a target antigen." Appx33955. The patent discusses exactly one scFv that binds to CD19, without disclosing its chemical structure.

At a minimum, the district court's refusal to instruct the jury on *Ariad*'s requirements mandates a new trial.

II. The claims are not enabled. The same undisputed facts—plus two more—show lack of enablement. First, undue time and effort was required at the priority date to make and test structural candidates for functionality. Second, with the benefit of 15 years of knowledge and technology beyond the priority date, Juno investigated nearly a billion dead ends.

III. YESCARTA® does not infringe because the CoC is invalid. The CoC is the only reason the claimed costimulatory region reaches YESCARTA®, as it broadened the claims four-and-half years after the patent issued. That blow to the public-notice function cannot be

sustained because the CoC is not a clearly evident solution to a clearly evident error. No error was evident because the originally claimed sequence was functional and made sense in context. A published CAR using the original sequence worked. And the CoC's sequence was not the only evident solution, because it is in tension with parts of the patent's disclosure. The CoC must be invalidated.

IV. Juno's expert presented a damages opinion so untethered from the '190 patent's value and inconsistent with this Court's precedents that it never should have been admitted and leaves the verdict unsupported by substantial evidence.

First, he included a $150 million equity-based success fee from an agreement establishing a broad collaborative partnership that, all agreed, contained far more value than the bare license to the '190 patent at issue here. But he made no adjustment for that conceded additional value. Second, he ignored the requirement to apportion Kite's contributions to YESCARTA® that Juno itself recognized were valuable and contributed to Kite's success. Worse, he awarded the value of those non-patent-related contributions to Juno by *increasing* nearly threefold the royalty terms from reference licenses in view of the

greater market share Juno expected Kite to garner. Third, he inflated the award even higher by applying multipliers with no factual support.

A verdict based on these flaws must be vacated.

V. Lastly, given the strength of Kite's defenses, Juno presented insufficient evidence of egregious infringement to support a willfulness finding. And the court erred in enhancing damages by failing to independently assess the closeness of the case.

STANDARD OF REVIEW

This Court reviews the district court's legal determinations and jury instructions de novo. *Eko Brands, LLC v. Adrian Rivera Maynez Enters., Inc.*, 946 F.3d 1367, 1372 (Fed. Cir. 2020). The jury's factual findings are reviewed for substantial evidence. *Id.* "Substantial evidence requires more than a mere scintilla," and this Court "must review the record as a whole, taking into consideration evidence that both justifies and detracts from the jury's decision." *Cordis Corp. v. Bos. Sci. Corp.*, 658 F.3d 1347, 1357 (Fed. Cir. 2011).

Written description is "a question of fact." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). "Enablement is a question of law based on underlying factual findings."

Enzo Life Scis., Inc. v. Roche Molecular Sys., Inc., 928 F.3d 1340, 1345 (Fed. Cir. 2019) (quotation marks omitted). Whether the broadening CoC here is valid turns on "a factual question." *Cent. Admixture Pharmacy Servs., Inc. v. Advanced Cardiac Sols., P.C.*, 482 F.3d 1347, 1354 (Fed. Cir. 2007). Willful infringement is also a question of fact. *Polara Eng'g Inc. v. Campbell Co.*, 894 F.3d 1339, 1353 (Fed. Cir. 2018).

Expert testimony's admissibility is reviewed for abuse of discretion, *see Primiano v. Cook*, 598 F.3d 558, 563 (9th Cir. 2010), as are the district court's decisions to enhance damages, *Polara Eng'g*, 894 F.3d at 1353, and deny a new trial on damages due to insufficient evidence, *Experience Hendrix L.L.C. v. Hendrixlicensing.com Ltd*, 762 F.3d 829, 845-46 (9th Cir. 2014).

ARGUMENT

I. The Claims Are Invalid For Insufficient Written Description.

This case starkly illustrates the dangers that arise when an inventor writes a "generic claim" to "a vast genus" that "use[s] functional language to define the [genus's] boundaries." *Ariad*, 598 F.3d at 1349. Here, "the functional [limitations] … simply claim a desired result, … without describing species that achieve that result."

Id. The "overreach" is particularly flagrant for the broadest claims—which purport to cover CAR-Ts for *any* type of disease, even though the inventors had made CAR-Ts targeting only two antigens. Appx271 (4:36-45); Appx32967; *see*; Appx26411; Appx32987-32993; Appx36636; Appx37442. But it is also fatal to the narrowest claims, "limited" to a vast genus of CARs incorporating all scFvs specifically binding to CD19.

For all claims, undisputed facts establish classic features that have led this Court to invalidate patents for insufficient written description: structural claim elements encompassing millions of billions of highly varied candidates, of which only an unknown fraction actually satisfy the recited binding function, with researchers having no way to predict which structures will bind as claimed. § I.A. Given those undisputed facts, the patent's sparse disclosure fails to satisfy either of *Ariad*'s criteria for "sufficient description of a genus": "[1] a representative number of species falling within the scope of the genus or [2] structural features common to the members of the genus." 598 F.3d at 1350-51. This patent impermissibly claims a research plan. § I.B. At a minimum, this Court must order a new trial, because the district court refused to instruct the jury on the governing *Ariad* test. § I.C.

A. The patent functionally claims extremely broad, varied genuses in an unpredictable field.

In evaluating the disclosure of "generic claims" that deploy functional limitations, this Court routinely assesses whether a skilled artisan could have "visualize[d] or recognize[d] the members of the genus," considering (1) the number and variety of candidates described by the structural limitations; (2) the proportion and variety of that universe that satisfies the functional limitations; and (3) the "complexity and predictability of the relevant technology," including "the extent and content of the prior art" and "the maturity of the science or technology." *Ariad*, 598 F.3d at 1349-51 (quotation marks omitted); *see Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1163-65 (Fed. Cir. 2019); *Bos. Sci. Corp. v. Johnson & Johnson*, 647 F.3d 1353, 1364-67 (Fed. Cir. 2011); *Carnegie Mellon Univ. v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1123-26 (Fed. Cir. 2008). The district court ignored the first two factors entirely and misapprehended the third. The undisputed evidence resolved each factor as a matter of law.

Vast structural scope. Because the court did not address the first critical element, Appx63-64, it missed the undisputed fact that the

structural features of the claims encompass a vast and varied universe of scFv candidates. *See supra* 13-16.

The only quantification came from Kite's expert Dr. Garcia. He testified that even the narrowest, CD19-specific claims encompass "millions of billions" of different candidate scFv structures. Appx33687-33688. Juno's expert, Dr. Thomas Brocker, did not counter with his own number. He did not dispute that the candidate population was vast—or even say that Dr. Garcia's "millions of billions" was off-target. He merely pointed to a *different* number in Dr. Garcia's *report* estimating "10 to the 130 [i.e., 10^{130}] different unique sequences" for a generic sequence of 100 amino acids. Appx33939-33940. Dr. Brocker testified that number was high for the claimed invention, because a skilled artisan "would probably not generate … *all those* combinations." Appx33939-33940 (emphasis added). How many fewer that person *would* generate he did not say. A million billion times fewer? That would still be 10^{115}. And Juno's much later work confirms that the candidate pool for a subset of CD19 scFvs is over a billion. Appx33705-33707; Appx32993-32996. It is thus undisputed that the relevant universe includes an enormous number of candidates.

A fraction of candidates are functional. The court also failed to address the second key inquiry. Undisputed testimony established that only a fraction of the universe of scFv candidates would meet the functional limitation of binding to any specified target—or to CD19 in particular. Any one of the following undisputed facts proves the point as a matter of law:

- Again, Juno tested a billion scFvs to identify only 60 that bound to CD19—a proportion of 0.00000006—and that was with the benefit of the patent's teaching and years of accumulated learning. Appx33705-33707.
- A paper Juno's expert cited, predating the priority date, reported that only one of the three scFvs the authors made had any measurable "ability to bind" to CD19. Appx35643; *see* Appx33682; Appx33942.
- Another pre-priority-date paper recounted that "analysis of scFvs … demonstrated that *only one scFv* [of three] … was able to bind [to] the CD19 surface antigen." Appx36182 (emphasis added).
- A named inventor testified that changing a functioning scFv by just three amino acids yielded a CD19 CAR that was "not functional as a receptor." Appx26410; *see infra* 29.

Juno's expert dodged all this evidence: "I can['t] give you a number" of "how many potential CAR constructs fall within the scope of the claims." Appx33957. He admitted it would be "pure speculation" to

estimate what proportion of scFvs bind even just to CD19. Appx33956-33957; *see supra* 15, 26.

Unpredictability. Why did Juno's expert consider it "pure speculation"? Because the pre-2002 literature confirms there was no way to predict ex ante which scFvs would bind to CD19. Even over a decade later, scientists still described "the identification of an optimal scFv [a]s probably the most challenging task in CAR design," Appx37442 (2016 article), so that "design" has "largely been empiric," Appx36636-36638; *see* Appx26415; Appx33682-33683.

Undisputed testimony explained why scFvs were so unpredictable. An scFv's binding ability depends on its "very intricate, complicated spaghetti-like fold." Appx33675; *see* Appx33936-33937 (Dr. Brocker: "three-dimensional orientation" critical "to bind[ing]"). That folding, in turn, is "exquisitely determine[d]" by the scFv's amino-acid sequence. Appx33675. But no one knows how the sequence will affect the shape. Appx33695-33702; Appx35643; *see* Appx33937-33938; Appx26415. Changing a lone amino acid "can result in shape changes to the scFv." Appx33675; *see* Appx26410. And when the shape changes, "it can

prevent the scFv from folding and binding to the target." Appx33676. Again, Dr. Brocker did not disagree.

The inventors understood this. When they filed their patent, only a single publication disclosed an SJ25C1-derived scFv (the type the inventors used for CD19), but it was "not functional as a receptor." Appx26410. The inventors tweaked the variable region by three amino acids and ended up with a functional CD19-specific scFv. The precise sequence was critical, but the inventors did not disclose it in their patent.

Unpredictability is further confirmed by undisputed evidence showing that scFvs that bind to the same target can be "highly diverse." Appx33695-33702; Appx35643. Compare YESCARTA® to the sole CD19-specific scFv discussed in the patent. The two are made from different antibodies that exhibit a "low degree of similarity." Appx33695-33697. The heavy-chain variable sequence of SJ25C1 has only a 39% overlap with FMC63, and the light-chain variable sequences overlap by only 53%. Appx33695-33697. Other CD19-specific scFvs display more structural diversity:

scFv[37]	Yescarta®	HD37	B43	BLY3	HB12A	HB12B	4G7	CAT19
Percent Overlap with SJ25C1 Antibody Variable Heavy Chain Region	39%	83%	87%	85%	70%	82%	68%	79%
Percent Overlap with SJ25C1 Antibody Variable Light Chain Region	53%	52%	57%	56%	54%	52%	46%	55%

Table 2. Percent Overlap of the Variable Regions of the Heavy and Light Chains of the SJ25C1 Antibody and Other CD19-Specific scFvs

Appx38340; *compare* Appx38344; Appx38347.

On the flip side, scFvs with similar sequences may bind to different targets. For example, scFvs more similar to SJ25C1 than FMC63 do not bind to CD19, but instead to antigens on a viral protein that affects shrimp and a bacterial protein that causes Lyme disease. *Compare* Appx38340, *with* Appx38344. And one paper Dr. Brocker cited compared two scFvs "from the same family" and found that only one bound to CD19. Appx35643; Appx35641; *see* Appx33682. In sum, "knowledge of the target tells you nothing about the structure or the sequence of the antibody that will bind to that target." Appx33687 (Dr. Garcia).

Moreover, even with an isolated scFv that binds to CD19, a researcher cannot know if it will still bind when fused to other

sequences to make a CAR. "[W]hen you make an scFv by itself, it folds in a different way than when you make it when it's connected to the CAR." Appx33683-33685 (Dr. Garcia). As a 2016 article confirms, "scFvs behave differently in membrane-bound format, … suggesting that … antigen-binding affinity, and specificity of scFvs should be carefully reassessed and examined in the CAR context." Appx37437. The inventors and a Juno employee confirmed the same. Appx37086 (2013 article by lead inventor and co-inventor: "the structure of the 'spacer region' between an scFv and the transmembrane region … can affect CAR specificity, but no definitive principles have yet emerged"); Appx26415 (Juno employee: "the rules exactly by … which [a] particular CAR is going to work or not have not entirely been worked out"); *see* Appx32987-32988.

The district court ignored all this undisputed evidence of unpredictability in favor of an irrelevancy: general evidence "that scFvs were well-known in the art" and that "CARs used scFvs as binding agents beginning in the early 1990s." Appx63. The court noted that the patent disclosed a "cookbook" method to make "any desired scFv" and one scFv that bound to CD19. Appx63. But knowing how to construct

scFvs does not mean their function is predictable—any more than knowing how to make keys tells you which out of millions of billions of keys will open a bank vault. What matters for the present inquiry is being able to predict which scFvs (in a CAR) will bind to a specified antigen. *See, e.g.*, *Idenix*, 941 F.3d at 1164-65 (knowing how to make nucleosides irrelevant without knowing "what makes them effective"); *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301 (Fed. Cir. 2014) (known modification approach irrelevant where one could not "make predictable changes" to achieve claimed functionality); *Bos. Sci.*, 647 F.3d at 1364 (inadequate written description where "even … minor structural changes to the molecular structure … may have significant and unpredictable effects on functionality," notwithstanding possibility of making and testing).

From *that* perspective, scFv design, both on its own and particularly within the CAR context, was unpredictable in 2002, as the lead inventor confirmed. *See supra* 5.

B. The patent does not disclose representative species or common structural features showing which of the millions of billions of structural candidates would function as claimed.

1. The inventors were required to disclose enough information to distinguish functional from non-functional scFvs. They did not. The patent fails to satisfy *Ariad*'s criteria for written description of a genus: representative species or common structural features. 598 F.3d at 1350.

Taking the latter first, the patent does not disclose common structural features distinguishing which of the millions of billions of possible species will achieve the claimed function from those that will not. It provides no guidance about which sequences will work. Dr. Brocker's concession is dispositive: The patent does not "teach[] any correlation between the amino acid sequence of an scFv and its ability to bind to a target antigen." Appx33955; *see AbbVie*, 759 F.3d at 1300-01. Layer on top the unrebutted testimony that the patent provides no guidance on (1) other design choices that affect binding, such as linkers and the order of heavy and light chains, or (2) the structure of the target antigen, including the specific portion of the antigen the scFv

binds to (the epitope). Appx33679-33680; Appx33691-33693; Appx33698-33701; *see* Appx32968-32969; Appx37086.

The district court ignored all of this in favor of Dr. Brocker's testimony that the patent identified certain "common structural features." Appx63. But Dr. Brocker conceded those structural features are common to "all scFvs," whether or not they bind to CD19 or any other target. Appx33959. That will not do. Written description demands structural features "of species falling within the genus *sufficient to distinguish the genus from other materials*." *Ariad*, 598 F.3d at 1350 (emphasis added); *see Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (inadequate written description where patent "d[id] not define any structural features commonly possessed by members of the genus *that distinguish them from others*" (emphasis added)). Features common to both members *and* non-members do not distinguish one from the other. That disposes of *Ariad*'s structural criterion.

The patent fares no better in providing representative species. It devotes just six lines to exactly one scFv that binds to CD19, without disclosing its (confidential) amino-acid sequence. Appx275 (11:12-17)

(Example 7); *see* Appx32965-32966; Appx33689-33691. Beyond that, the patent references one other scFv that binds to a different antigen, PSMA, on prostate-cancer cells, again not disclosing the sequence. Appx273 (7:43-8:17) (Example 1); *see* Appx33702.

Focusing on the narrowest claims, a lone data point—or even the four or five CD19-specfic scFvs arguably known in the art—cannot be representative of the diverse genus here. "[S]ufficient representative species" must "encompass[] the breadth of the genus." *AbbVie*, 759 F.3d at 1300 (analogizing genus to plot of land, if "the disclosed species only abide in a corner of the genus," written description unsatisfied); *see Carnegie Mellon*, 541 F.3d at 1124. Even when a patent disclosed the amino-acid sequences of 300 claimed antibodies, this Court found written description lacking because the disclosure did not account for the full claim scope's sequence variation—the disclosed antibodies shared 90% or more sequence similarity with each other, but the genus encompassed species, such as the accused product, with 50% or less similarity. *AbbVie*, 759 F.3d at 1291, 1298-1302 (disclosure amounted to "no evidence … [that] any described antibody" was "structurally

similar to," or could be "predictabl[y] change[d]" "to arrive at," "other types of antibodies" claimed); *see Bos. Sci.*, 647 F.3d at 1364.

Written description is all the more lacking here, since (1) the patent provides *no* amino-acid sequence of *any* functioning scFv, or any basic structural information influencing binding specificity and affinity, Appx33693; and (2) the genus includes scFvs, such as YESCARTA®'s, that are very different from, are stronger binders than, and bind to different epitopes than the patent's scFv. *Supra* 15, 33-35; Appx33675; Appx33693; Appx33698. That is not disclosure of representative species. *See In re Alonso,* 545 F.3d 1015, 1021-22 (Fed. Cir. 2008) (genus of antibodies binding to particular target insufficiently described where "[t]he specification [taught] nothing about the structure, epitope characterization, binding affinity, specificity, or pharmacological properties common to the large family of antibodies implicated by the method"); *Idenix*, 941 F.3d at 1164 (written description lacking without "meaningful guidance into what [species] beyond the examples … , if any, would provide the same result").

The sparsity is particularly egregious given that every one of the handful of CD19-specific scFvs arguably known was derived from one

source—mice. Appx35630; Appx35639; Appx35641; Appx35643-35644; Appx35874; Appx36178; *see* Appx32974; Appx33693-33694; Appx36640; Appx37426. Yet the patent seeks to monopolize scFvs from *any* antibody source, including other non-human species, humans, and combinations of the two ("humanized scFvs"). Appx33954-33955. Human and humanized scFvs are particularly valuable because the body is less likely to reject them. Appx33344; Appx36640; Appx37437-37438. But they are notoriously hard to achieve. Lead inventor Dr. Michel Sadelain admitted his lab did not make any such scFvs until at least seven years after the priority date. Appx32974-32976. Even today, making a fully human scFv "is extremely difficult." Appx33955 (Juno's expert); *see* Appx37433.

That, alone, is a fatal mismatch between what the inventors possessed and what they claimed. This Court has found written description inadequate where "nothing in the specification … convey[ed] to one of skill in the art that [the patentee] possessed fully-human antibodies or human variable regions that fall within the boundaries of the asserted claims." *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1350-51 (Fed. Cir. 2011); *see Eli Lilly*, 119 F.3d at 1568

("[D]escription of rat insulin cDNA is not a description of the broad classes of [claimed] vertebrate or mammalian insulin cDNA.").

2. This Court has routinely found more detailed teaching insufficient as a matter of law, even where the universe of candidates was smaller and the art more predictable. The table below captures how this case measures up along the key dimensions.

	Idenix	***Boston Scientific***	***Carnegie Mellon***	**Narrowest claims here**
Structural claim scope	"[A]t least 'many, many thousands.'" (941 F.3d at 1157)	"[T]ens of thousands." (647 F.3d at 1364)	"[T]housands." (541 F.3d at 1125)	"[M]illions of billions." Appx33687-33688.
Functional species arguably disclosed	"[F]our examples on a single sugar." (1161)	39 analogs "known in the art." (1364; *see* 1357-58)	"[T]hree bacterial … genes … had been cloned." (1125)	Five mouse-based scFvs reported in literature. *Supra* 36-37.
Predictable to make functional species?	No. Testing for effectiveness was "routine," but "quantity of experimentation required" was "very high." (1156, 1159-64)	No. Art was "highly unpredictable." (1364-67)	No. "[R]ecombinant plasmids [had to] be carefully constructed" to avoid lethality, but patents gave guidance only for one bacterial species. (1125-26)	No. Highly unpredictable; Juno itself, testing a billion candidates 15 years after the priority date, identifying only 60. *Supra* 15-16.

In short, this patent left a skilled artisan with no way to recognize the claimed species beyond "a trial and error approach to modify" various parameters to "achieve [the] desired result" of binding specifically to CD19, let alone to *any* antigen (per the broader claims). *AbbVie*, 759 F.3d at 1301. That is not written description. It is merely "an indication of a result that one might achieve if one made that invention" and discovered which species "fall within the claim[ed] functional boundaries." *Ariad*, 598 F.3d at 1350, 1353 (quotation marks omitted). The inventors were not entitled to monopolize the entire field based on how little they invented and how much less they disclosed.

C. At a minimum, a new trial is warranted because the court failed to adequately instruct the jury.

At a minimum, a new trial is required because the district court failed to instruct the jury, per *Ariad*, that genus claims "require[]" a representative number of species or common structural elements uniquely identifying the genus. 598 F.3d at 1350-51; *see D Three Enters., LLC v. SunModo Corp.*, 890 F.3d 1042, 1047 (Fed. Cir. 2018); *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1373 (Fed. Cir. 2017); *AbbVie*, 759 F.3d at 1299. The court refused to instruct the jury that written

description depended on those requirements, Appx139; Appx34035-34036, making the instruction fatally "incomplete as given," *Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1307 n.7 (Fed. Cir. 2007) (quotation marks omitted).

The district court was wrong that it was enough merely to "mirror[] the statutory requirements for written description," Appx79, and to follow the Northern District of California's model, Appx79-80. A juror could not have divined *Ariad's* standard based on the statutory language alone. And model patent-law instructions have no "special status" when they "have not been endorsed or approved" by this Court. *Eko Brands*, 946 F.3d at 1378. Nor could the court excuse the legal error by asserting that Kite's proposed "instruction was confusing" because of one word ("genus"). Appx80. It wasn't; this Court uses the same word. Besides, disagreement with one word cannot justify gutting the legal standard.

Given the strength of Kite's evidence on written description, "a correctly instructed jury *could* have concluded" the claims lacked written description. *Wordtech Sys., Inc v. Integrated Networks Sols.,*

Inc., 609 F.3d 1308, 1315 (Fed. Cir. 2010) (emphasis added). The error was therefore not harmless.

II. The Claims Are Invalid For Non-Enablement.

Juno's "[c]laims are not enabled" because "at the effective filing date of the patent, one of ordinary skill in the art could not practice their full scope without undue experimentation." *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380, 1384 (Fed. Cir. 2013). The undisputed facts requiring JMOL of insufficient written description doom enablement too: the vast structural claim scope, only a fraction of structurally sufficient species satisfying the functional requirement of specifically binding to a given target, and rampant unpredictability. *See In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

Particularly relevant to enablement is one set of undisputed facts reflecting the time and effort required to make and determine the functionality of scFvs and CARs encompassed by the full claim scope:

- At the priority date, making one new scFv and testing it for binding would have taken six months to a year. Appx33677-33681.

- At that date, making a CAR incorporating that scFv and testing it for binding would have taken months to well over a year more. Appx33683-33685.

- Even with present-day knowledge, Juno needed months if not years to test a billion CD19-specific scFvs. Appx33705-33707; *supra* 15-16.

That is the very definition of "undue experimentation." Even if it were routine to make and test CARs with each of the millions of billions of possible scFvs, "routine experimentation is not without bounds." *Wyeth*, 720 F.3d at 1386 (quotation marks omitted). The mere invitation here "to engage in an iterative, trial-and-error process to practice the claimed invention" is not enabling as a matter of law, whether or not it is "routine." *Id.* (quotation marks omitted).

Based on these undisputed facts, this patent is invalid as a matter of law, because it provides no guidance on how to make the claimed genus of CARs with scFvs that perform the claimed function beyond synthesizing millions of billions of species and testing each. *See Idenix*, 941 F.3d at 1163 (jury verdict unsustainable where "there were at least many, many thousands of candidate compounds, many of which would require synthesis and each of which would require screening"); *Wyeth*, 720 F.3d at 1384-86 ("synthesiz[ing] and screen[ing] each of at least

tens of thousands of candidate compounds constitutes undue experimentation," even assuming only "routine" processes involved).

The district court's rationale for nevertheless upholding enablement was limited to two related points in a single sentence. The first is the same fallacy the court applied to written description: "[T]he steps to create an scFv were straightforward." Appx65. And it is wrong for the same reason: Knowing how to *make* an scFv is not enough. The inquiry must "focus on the functionality required by the claims," *Enzo*, 928 F.3d at 1346, and "the specification must enable the full scope of the claimed invention," *Trs. of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1364 (Fed. Cir. 2018) (reversing denial of JMOL of non-enablement). That means the narrowest claims cannot be enabled unless the patent teaches how to make the range of scFvs that would, as part of the claimed CAR, specifically bind to CD19 (or any antigen, for the broader claims), without undue experimentation. *See Enzo*, 928 F.3d at 1346. The patent does not.

The district court's second rationale was that the two signaling domains claimed "ha[ve] been successfully used with a number of scFvs [and] Plaintiffs' expert did not know a single scFv that would not work

with the[m]." Appx65. The expert never said, or implied, that a skilled artisan could simply pick any scFv, put it on the claimed signaling regions, and achieve a construct that would bind to a selected target. That would have been absurd given the undisputed evidence of experimentation required to even find a binding scFv in isolation, such as Juno's need to test a billion scFvs to identify only 60 that bound to CD19. *Supra* 15-16.

The testimony the court referenced was about whether an scFv *already known* to bind to an antigen on its own would maintain that function once paired with the claimed signaling regions. Appx33943-33944; Appx33966. All Dr. Brocker said was that he could not name a single functioning scFv that had *lost* that functionality upon pairing. Appx33943-33944; Appx33966. That did not negate the undisputed testimony that scFvs often did lose functionality when incorporated into a CAR. *Supra* 30-31; *see* Appx32987-32988 (lead inventor conceding, if "you wanted to create a fusion protein," "you couldn't predict … with certainty" whether it "would function"). More importantly, it gets Juno nowhere, because it does not diminish the massive experimentation required to identify which of the millions of billions of scFvs in isolation

would specifically bind to CD19 (or any other antigen) in the first place. That alone disposes of enablement.

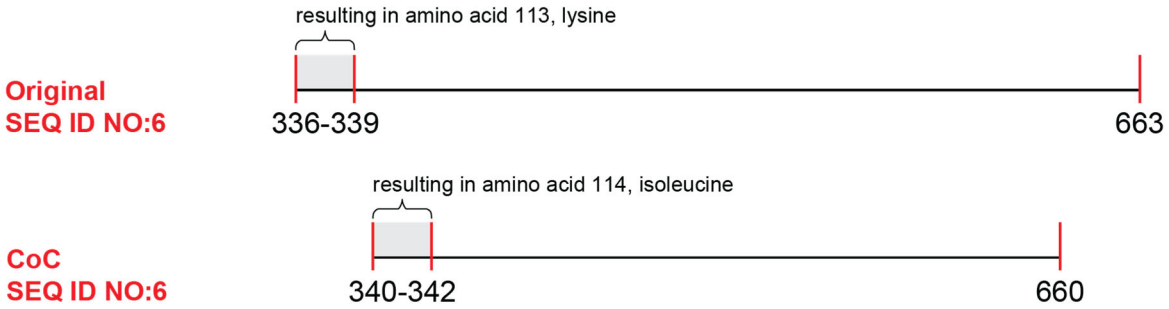
III. Kite Does Not Infringe As A Matter Of Law Because The Certificate Of Correction Is Invalid.

The CoC is invalid as a matter of law. Without it, there can be no infringement, because the claims as issued do not cover YESCARTA®. Appx4881.[1]

The inventors told the public that their invention was limited to CARs with a "costimulatory signaling region compris[ing] the amino acid sequence encoded by SEQ ID NO:6." SEQ ID NO:6 was a specific list of nucleotides (numbered 336-663) that encoded an equally specific amino-acid sequence: amino acids 113-220 of CD28, starting with lysine. Appx282. The reason the claim as issued did not cover YESCARTA® is that YESCARTA®'s costimulatory region consists of amino acids 114-220, omitting 113 and starting with isoleucine. Appx4881.

[1] The district court held on summary judgment that prosecution-history estoppel blocked Juno from asserting the doctrine of equivalents. Appx8407-8419; Appx8414-8415; *see* Appx4874-4880.

The CoC stretched the claim to cover YESCARTA® by removing the first four nucleotides (336-339)—including the trio (or "codon") encoding amino acid 113. Appx33629-33631; *see* Appx2633-2635. Consequently, the "correction" requires nucleotides encoding only amino acids 114-220, starting with isoleucine. Appx283; Appx35265-35273; *see* Appx33629-33631. The difference looks like this:



Juno's attempt to broaden its claims four-and-a-half years after the patent issued strikes at the heart of the public-notice function. To see why, consider this chronology from the perspective of a business deciding where to invest its time and resources:

Pre-Nov. 2008:	NCI creates a CAR with amino acids 114-220. Appx35469-35482.
Nov. 2008:	'190 patent issues claiming a CAR with amino acids 113-220 (not covering NCI's CAR). Appx261.
Sept. 2009:	NCI publishes its CAR with amino acids 114-220. Appx35469-35482.

July 2010:	NCI publishes promising pre-clinical results with its CAR. Appx36278-36282.
Dec. 2011:	NCI publishes promising Phase I clinical results with its CAR. Appx36319-36331.
Aug. 2012:	Kite/NCI initiate and soon publicize collaboration. Appx35820-35871; Appx33246-33248; *see* Appx36386; Appx33316-33325.
June 2013:	Patentee files the CoC covering NCI's CAR. Appx35269.

The public was entitled to take the inventors at their word as to what sequence they were claiming in 2008. Expanding the claims four-and-a-half years down the line (after substantial competitive investment) was neither legal nor fair. A broadening CoC like this "is only valid if it corrects a 'clerical or typographical' error that would have been clearly evident to one of skill in the art reading the intrinsic evidence." *Cent. Admixture*, 482 F.3d at 1353 (quoting *Superior Fireplace Co. v. Majestic Prods. Co.*, 270 F.3d 1358, 1373 (Fed. Cir. 2001)). That means the CoC is invalid unless a skilled artisan reading the original patent and its file history would think that: (A) it was "clearly evident" that the nucleotide sequence in the original SEQ ID NO:6 was a "clerical or typographical error"; and (B) it was "clearly evident" that the way "to correct that error" was to change the

nucleotide sequence to the CoC's sequence. *Id.* No reasonable juror could have reached either conclusion.

A. The intrinsic evidence did not make it "clearly evident" that the original sequence was erroneous.

1. For two independent reasons, the original sequence listing was not a "clearly evident" error.

First, as a matter of law, there is no "clearly evident" error when the claim language the patentee seeks to modify (1) is "'spelled correctly and reads logically in the context of the sentence'"; and (2) results in claims "generally effective for the[ir] stated purpose." *Cent. Admixture*, 482 F.3d at 1354-55 (quoting *Superior Fireplace*, 270 F.3d at 1370). That is the case here. It is undisputed that the original listing yielded a costimulatory signaling region that was part of the known CD28 protein, worked in a CAR, and read logically in view of the claims. A working CAR using the original sequence was published. Appx33646-33648. If the original listing functions, then it is not "clearly evident" to a skilled artisan that it is erroneous.

Second, multiple aspects of the written description support the original version of SEQ ID NO:6:

- The specification explains that one embodiment contains "nucleotides 336-660 of CD28," which encode amino acids 113-220, starting with lysine—exactly what original SEQ ID NO:6 encodes. Appx273 (7:52-53); *see* Appx33640.
- The patent cites multiple articles by lead inventor Dr. Sadelain, spanning five years, describing nucleotide sequences beginning with nucleotide 336, thus encoding amino acids starting with 113. Appx270 (1:66-67) (citing Appx38193); Appx276 (13:13-16) (citing Appx37502); *see* Appx35496 (provisional including 2002 article describing "nucleotides 336-660 of CD28").
- Another sequence in the patent, SEQ ID NO:11, lists amino acids 113-220 of CD28, starting with lysine. Appx278-279.

In contrast, no sequence—anywhere in the patent—lists just amino acids 114-120. Appx33634-33635. That omission is notable given the regulation requiring that "[e]ach sequence disclosed must appear separately in the 'Sequence Listing.'" 37 C.F.R. § 1.821(c).

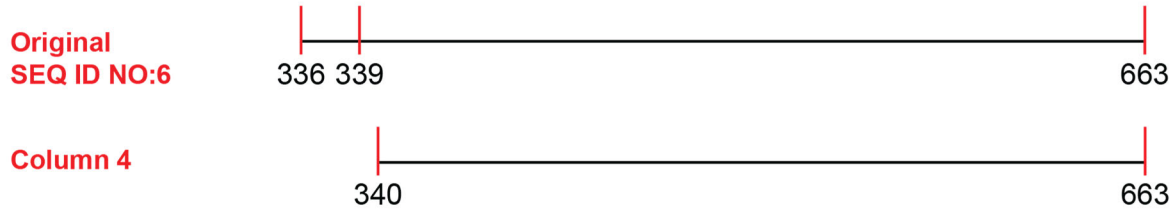
Real-world evidence shows that nothing in patent would have alerted the public of a "clearly evident" error in the claim. In 2013, a Ph.D. venture capitalist, Dr. Thomas Schuetz, was conducting due diligence for a licensing deal with Sloan Kettering. Appx33519-33523. From the specification, he knew that the claimed amino-acid sequence started with lysine and saw nothing askew. Appx33526-33528. His suspicions were aroused only once he secured the "confidential" material Dr. Sadelain used in the lab and noticed a discrepancy

between the patent's claims (including lysine) and Dr. Sadelain's construct (not including lysine). Appx33524; Appx33527-33528; Appx36272-36273; Appx36274-36275; Appx36276-36277; Appx37292-37371. He "[di]dn't understand why" "the two sequences [would be] different." Appx33530. It was not clear to him the patent was wrong. Appx33556. He spoke to the prosecuting attorney and read the prosecution history. Appx33530-33531. None of that helped "clarify things"; he was left "incredibly confused." Appx33530-33531; *see* Appx33556.

2. The district court noted that Juno's expert testified to "inconsistencies" between the original listing and the specification. Appx66. But the court did not conclude that any showed a "clearly evident" error.

Juno invoked column 4, which describes "one embodiment" in which "the CD28 portion suitably *includes* … the portion of CD28 cDNA spanning nucleotides 340 to 663, including the stop codon (amino acids 114-220 …). … *The full sequence* of this region is *set forth in Seq. ID*

No: 6." Appx271 (4:21-28) (emphasis added).[2] There is no inconsistency: The "full sequence" of nucleotides 336 to 663 "includes" the subset of nucleotides 340 to 663. If anything, column 4 disproves Juno's position by confirming that the truncated sequence (340-663) is shorter than "[t]he full sequence … set forth in Seq. ID No: 6":



Even further afield was Juno's citation to certain primers listed in SEQ ID NO:4 and SEQ ID NO:5. Appx277; *see* Appx271 (4:26-28); Appx271 (7:52-56). The asserted claims invoke SEQ ID NO:6, not NO:4 or NO:5. So, as the district court recognized at claim construction, any difference between NO:6 and the other two cannot show that NO:6 was wrong. Appx110. Regardless, there is no inconsistency here either. Primers are sections of DNA that amplify a particular portion of a DNA sequence. Appx115. The patent states that these primers are intended to amplify the "portion of CD28" described in column 4, Appx271

[2] The stop codon "tells the cellular machinery that it has reached the end of the coding region." Appx2635.

(4:26)—not the full NO:6. Amplifying a "portion" of NO:6 does not contradict NO:6.

Even if either of these purported inconsistencies could prove that the original patent contained some mistake, that still would not suffice. A CoC is not validated by "inconsisten[cies]" that "leave unclear which" are "in error." *Superior Fireplace*, 270 F.3d at 1370. Nobody who sees an inconsistency here would know that the *original SEQ ID NO:6* was a "clearly evident" mistake. It is just as likely that any mistake was in column 4 or the primers.

3. Instead of embracing Juno's arguments about inconsistencies, the court sustained the jury's verdict based on a Request for Continued Examination (RCE) seeking—but failing—to amend the original listing to the CoC version. Appx67-68 (referring to Appx35147-35150). This does not show that original SEQ ID NO:6 is a "clearly evident" error either, because, by all outward appearances, the applicants abandoned the RCE amendment.

After some back and forth with the PTO to address deficiencies in the attempted amendment, the applicants ultimately resubmitted the original listing. Appx35208-35232 (final RCE submission); *see*

Appx115. This resubmission asked the PTO to "insert the paper copy in the application [the original NO:6] in place of the previously filed sequence listing [the one consistent with the CoC]." Appx35208. That express instruction is why the original listing, not the CoC version, appears in the issued patent.

Is it possible that a reasonable juror could have thought *both* the original sequence *and* its resubmission were mistakes? Perhaps. But no juror could have thought that conclusion would have been "clearly evident" at the time of issuance. It certainly was not evident to Dr. Schuetz, even with the benefit of additional inside information. Juno had to resort to *extrinsic* testimony blaming a prosecuting attorney who supposedly (1) first listed the wrong nucleotide sequence in original SEQ ID NO:6; (2) caught and planned to correct this initial error; only to (3) reinstate the same error yet *again* by "grabb[ing] the wrong file, the old file, and submitt[ing] it." Appx33831-33832. Juno does not explain how the public would have clearly divined that comedy of errors—which is all that matters.

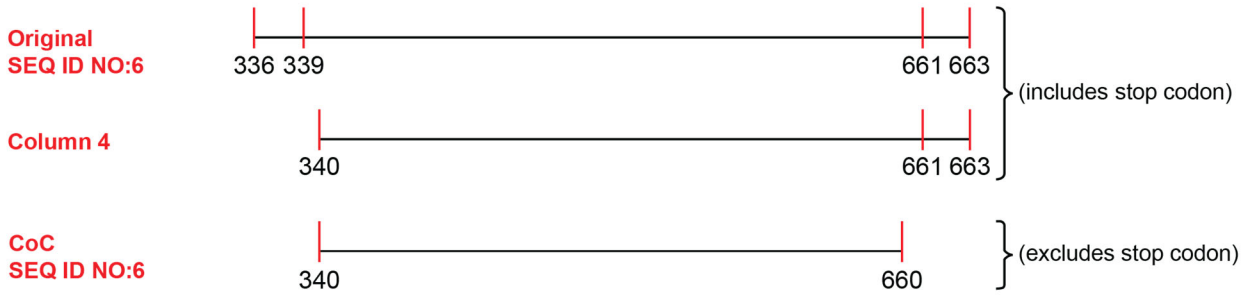
The district court itself made this point at claim construction in rejecting Juno's "conten[tion] that 'any reasonable reader of the

prosecution history would understand that the applicants inadvertently submitted the original, incorrect sequence listing.'" Appx115. It concluded, "[w]hile it is true that this is one possible interpretation of the events, it is also possible for a POSITA to conclude that the applicants intentionally submitted the original sequence listing. Ultimately, the ambiguity of the prosecution history would require a POSITA to guess at the applicants' intent." Appx115 (footnote omitted). Any clue that "require[s] a POSITA to guess" cannot qualify as a "clearly evident" error. As with the purported inconsistencies discussed above, the law "does not allow the mere possibility that one of skill in the art *might* perceive an error to support a broadening correction." *Cent. Admixture*, 482 F.3d at 1355 n.6 (emphasis added); *see Japanese Found. for Cancer Rsch. v. Lee*, 773 F.3d 1300, 1306 (Fed. Cir. 2014) (CoC cannot correct a terminal disclaimer inadvertently "filed due to the mistake of [a] paralegal," where such a filing error is not a "simple mistake[] such as [an] obvious misspelling[] that [is] immediately apparent … on the face of the document" (quotation marks omitted)).

B. The intrinsic evidence did not make it "clearly evident" that the CoC was the solution to any supposed error.

Even assuming a "clearly evident" error, the CoC does not supply the only "clearly evident" solution. As discussed, each purported inconsistency can be solved by "correcting" column 4 or SEQ ID NO:4 and NO:5 to match SEQ ID NO: 6. Worse, there are three additional independent reasons that a skilled artisan would not have necessarily chosen the CoC's "solution."

First, column 4 teaches that the CoC's nucleotide sequence is wrong because it provides a different sequence. It states that its sequence (nucleotides 340-663) "*includ[es]* the stop codon" (the trio of nucleotides marking the sequence's end). Appx271 (4:21-28) (emphasis added). Original SEQ ID NO:6 complies with this direction, but the CoC's sequence *omits* the stop codon:



Thus, even if the CoC sequence—removing the stop codon—could be a conceivable solution to any perceived error, it cannot be the only "clearly evident" solution. *See Cent. Admixture*, 482 F.3d at 1355.

Second, same for the primers Juno relies on. The primers amplify 322 nucleotides. Appx33644; *see* Appx2661-2663. That is one more than the 321 nucleotides listed in the CoC. Appx33857. So, again, the CoC is not *the* "clearly evident" solution.

Third, same, too, for the RCE. The applicants first sought to change the original sequence and then reverted back. That forecloses the CoC sequence as *the* "clearly evident" solution to any error. It is, at best, a muddle of mixed signals. Appx33530-33531; Appx33556.

IV. The Damages Award, Multiples Of Any Reference License, Must Be Vacated.

Rarely has this Court encountered a damages award that so fundamentally flouts the admonition that a "reasonable royalty" must be "carefully tie[d] … to the claimed invention's footprint in the market place." *ResQNet.com, Inc. v. Lansa, Inc.*, 594 F.3d 860, 869 (Fed. Cir. 2010). Juno's expert, Dr. Ryan Sullivan, violated this edict in three ways to yield an award many multiples of all the licenses *he* considered

comparable. First, his royalty rests on agreements that conveyed far more value than the '190 patent. § III.A. Second, he granted Juno the value of Kite's highly valuable noninfringing contributions to YESCARTA®, and, worse, used Kite's contribution, paradoxically, as a reason to inflate the award. § III.B. Third, he applied "multipliers" with no logic or factual support. § III.C.

Dr. Sullivan invoked four real-world agreements:

1. ***Sloan Kettering (MSKCC)-Juno IP License:*** Granted Juno an exclusive license to the '190 patent and other patents and applications and provided Juno "extremely valuable" know-how (discussed below) for commercializing CAR-T therapy. Appx37544; Appx37509-37553 (Agreement); Appx38307-38308 (Amendment); Appx32999.

2. ***MSKCC-Juno Side Letter:*** Established a broad partnership between Juno and MSKCC by giving MSKCC Juno equity and board seats as consideration for clinical trial and research collaboration and IP license. Appx35733-35765 (Agreement).

3. ***St. Jude-Juno:*** Granted Juno an exclusive naked license to an analogous patent, U.S. Patent No. 8,399,645, which covers Juno's JCAR17 construct. Appx35783-35819 (Agreement).

4. ***Juno-Novartis:*** Settlement agreement in which Juno sublicensed that same '645 patent to Novartis for use in KYMRIAH®. Appx36074-36149 (Agreement).

Appx33455-33458. The table below summarizes the terms of these agreements.

	Scope	Rate	Upfront Payment	Contingent Compensation[3]
MSKCC-Juno IP License	Exclusive '190 patent, know-how	7.25%	$6.9M	$3.35M for first FDA approval
MSKCC-Juno Side Letter	License and clinical/research collaboration		$2M in equity	Up to $150M contingent on 30x Juno stock increase
St. Jude-Juno	Exclusive '645 patent, continuations	2.5%	$25M	$17.5M for first FDA approval
Juno-Novartis	Non-exclusive '645 patent, continuations	4.75%	$12.25M	$39.25M for first FDA approval (50% refund if Juno enters market)
Dr. Sullivan's Opinion	Non-exclusive '190 patent	27.6%	$585M	

Dr. Sullivan's proposed royalty dwarfed these real-world valuations: a $585 million upfront payment and a 27.6% running royalty on all YESCARTA® sales. Appx33473; Appx33476. The royalty

[3] The agreements contemplated other contingent payments as well. This table references only those Dr. Sullivan considered applicable. Appx11879.

rate is almost six times the average (4.8%) of the reference licenses. It's also more than five times the only license between two competitors (Juno-Novartis). The upfront payment is more than 11 times the combined upfront and milestone payments contemplated by that license.

Dr. Sullivan got there by cherry-picking the highest component of various agreements, regardless of scope, and inflating them even further through a series of machinations divorced from any semblance of rationality. He began with the MSKCC-Juno Exclusive License Agreement's 7.25% base royalty and $3.35 million milestone payments, which covered far more than just patent rights. Appx33460-33461; Appx33512 (Sullivan). Then, instead of including that agreement's $6.9 million upfront payment, he added the $150 million potential stock-appreciation payment from the separate Side Letter Agreement that launched the broad collaboration between Juno and MSKCC. Appx33462-33463. That $150 million was not an upfront payment, but a highly contingent bonus to reward MSKCC if the prospective collaboration with Juno was so successful that Juno's stock skyrocketed 30-fold, which Juno never expected to happen and which never did.

Appx33796-33797; Appx33484. Illogically, Dr. Sullivan assumed Kite would have granted Juno the massive $150 million payment to reward Juno for the fact that Kite's stock had *already* appreciated 30-fold before the hypothetical negotiation. Appx33462-33463. Thus, he transformed the $6.9 million *actual* upfront fee in the MSKCC-Juno license into a $153.35 million "starting point." Appx33463-33464.

Dr. Sullivan made no downward adjustments to account for the additional value MSKCC conveyed to Juno, the broad research collaboration, the longer license terms, or the fact that those licenses were exclusive. Appx33464-33467; Appx33513-33514. Instead, he applied two adjustments to increase both the royalty and the upfront payment nearly *fourfold*. Appx33464-33467; Appx33473; Appx33475-33476. Essentially, he nearly doubled the already-inflated base amounts because Kite was expected to be a competitor (once Juno entered the market) and then added nearly double the base amount because Kite was expected to be an especially good competitor.

He derived the first near doubling—a 90% increase from his base royalty—by comparing the rate Juno paid St. Jude to license the analogous '645 patent (2.5%) to the rate Juno's competitor Novartis paid

Juno to sublicense the same patent (4.75%). Appx33464-33466. Rather than conclude that a competitor sublicensee would pay 2.25% more in royalty, Dr. Sullivan concluded that competitors pay 90% more, or nearly double, *any* rate paid by a non-competitor. Appx33465-33466; Appx33473. Next, he applied that same 90% rule of thumb to the already-inflated $153.3 million upfront payment, even though the non-sales-based compensation in the two '645 patent agreements was roughly equivalent, regardless of the licensee's competitor status. Thus, Dr. Sullivan transformed the already-high royalty and upfront payment to a 13.78% royalty rate and an upfront payment of $291 million. Appx33465-33466; Appx33473; *see* Appx33476.

Dr. Sullivan did not stop there. He added another 192% increase over the starting license terms—i.e., almost double the base amount. Appx33471-33472. He did so on the theory that Kite was a stronger competitor in 2017 than Novartis had been in 2015, even though Kite's strength resulted in large part from Kite's own innovations. Appx33458; Appx33467-33472; *infra* 68-70. He "quantif[ied]" Kite's competitive strength by comparing Juno's own market-share projections among Novartis and Kite in those two years. Appx33468-33472;

Appx36198. He found that Juno in 2017 would have expected Kite to receive almost three times the revenue Juno projected Novartis to receive in 2015. Appx33469; Appx33471. And Dr. Sullivan concluded that Juno would have demanded a proportional 192% increase to the royalty rate *and* upfront payment rather than being satisfied to collect the vastly higher royalties for those increased sales.

The end result of these gymnastics, a 27.6% royalty and $585 million upfront payment, bears no resemblance to any license in evidence. *Compare Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1329, 1332 (Fed. Cir. 2009) (vacating jury award that was "roughly three to four times the average amount" of any license); *see Wordtech*, 609 F.3d at 1320 ("[A] past royalty range of 3-12% fails to explain a 26.3% hypothetically negotiated rate."). It is also $150 million more than all of YESCARTA®'s *revenue* through trial. Appx33756. Because this Court's cases have analyzed similar defects as both abuses of discretion in admitting evidence and failures of proof, Kite challenges each error under both frameworks. *See Bio-Rad Labs., Inc. v. 10X Genomics Inc.*, 967 F.3d 1353, 1373-74 (Fed. Cir. 2020).

A. The $585 million upfront payment is based on an agreement that vastly overvalues the '190 patent.

The $585 million upfront payment depends almost entirely on Dr. Sullivan's testimony that the reasonable royalty would include the $150 million stock-appreciation payment in the Side Letter. Appx33462-33463. But the Side Letter is not comparable to the hypothetical negotiation and it vastly overstates the value of the '190 patent as a matter of law.

The Side Letter did not license the '190 patent to Juno. The agreement explicitly defined the payment as "consideration" for launching a broad collaborative partnership between Juno and MSKCC that included a "Clinical Studies Agreement" and a "Sponsored Research Agreement" in addition to the MSKCC-Juno "License Agreement." Appx35733; Appx33404-33405 (former Juno CEO); Appx33794-33795. Reflecting that partnership, the Side Letter also granted MSKCC seats on Juno's board and equity in the company. Appx35735-35737. That sort of collaborative agreement bears no resemblance to a hypothetical negotiation to license one patent.

But even if, contrary to the agreement's terms, the Side Letter could be considered consideration for only the IP Licensing Agreement, the $150 million stock-appreciation payment would still necessarily overvalue the patent because the licensing agreement itself granted Juno value far beyond the '190 patent. The agreement included manufacturing and clinical "know how" for creating CAR-T therapies, Appx38309-38311, a benefit to which the agreement assigned significant value, Appx37521, and that Juno's witnesses agreed was "extremely valuable," Appx32999 (Sadelain).

Dr. Sullivan and Juno witnesses conceded that the collaboration and know-how were "valuable." Appx33513; Appx32993-32996; *see* Appx33764 (Kite's expert). So, Dr. Sullivan was required to "account for" and remove that value from the hypothetical negotiation. *Ericsson, Inc. v. D-Link Sys., Inc.*, 773 F.3d 1201, 1227 (Fed. Cir. 2014); *see ResQNet*, 594 F.3d at 872-73. Instead, he admitted he "didn't" "make any adjustment for the licensed technology in the MSKCC Juno agreement compared to the licensed technology at [issue in] the hypothetical negotiation." Appx33513-33514; *see* Appx11722-11723 (Sullivan's Report). That failure "served no purpose other than … 'to

increase the reasonable royalty rate above rates more clearly linked to the economic demand for the claimed technology." *LaserDynamics, Inc. v. Quanta Comput., Inc.*, 694 F.3d 51, 80 (Fed. Cir. 2012).

The district court accordingly abused its discretion in permitting Dr. Sullivan to present an opinion that defied the legal requirements for damages—an error that plainly prejudiced Kite, as the jury adopted Dr. Sullivan's improper opinion wholesale. *Commonwealth Sci. and Indus. Rsch. Organisation v. Cisco Sys., Inc.* ("*CSIRO*"), 809 F.3d 1295, 1303 n.2 (Fed. Cir. 2015) ("[T]his court has often excluded proffered licenses as insufficiently comparable."). And, even if his opinion could clear the admissibility threshold, it cannot constitute substantial evidence to support the damages award because it is not "commensurate with that which the defendant has appropriated." *Bandag, Inc. v. Gerrard Tire Co., Inc.*, 704 F.2d 1578, 1582 (Fed. Cir. 1983); *see Trell v. Marlee Elecs. Corp.*, 912 F.2d 1443, 1447 (Fed. Cir. 1990) (royalty amount from license "involving additional inventions" not substantial evidence); *ResQNet*, 594 F.3d at 873 (same).

The district court was required to act as a gatekeeper precisely because a jury can be easily misled by an expert attesting to a damages

methodology unmoored from reality or economic theory. Here, the mischief is even worse because Juno offered the jury another justification for the upfront payment that was so wrong that even Juno's expert did not embrace it. On summation, it falsely asserted that Celgene, a company that eventually acquired Juno, made "an upfront *royalty* payment" of a "billion dollars" to Juno for CAR-T therapies. Appx34184-34185 (emphasis added); Appx34086. In fact, Celgene paid $850 million to *purchase 9% of Juno* and another $150 million as part of a complex business partnership well beyond the '190 patent. Appx33392; Appx37220-37221; Appx33742-33744. Worse, the court prevented Kite from countering the false assertion with evidence confidential license valuation that [redacted] valued a Kite license to the '190 patent at only [redacted] and a [redacted] Appx97-98; Appx33792-33793; Appx12376-12377. If ever there were real world evidence of what these patent rights were worth, it is that valuation, which the jury never heard.

B. Dr. Sullivan failed to apportion the royalty rate and upfront payment to account for Kite's undisputed contributions to YESCARTA®.

Dr. Sullivan also flouted the rule that a "patentee … must in every case give evidence tending to separate or apportion … between the patented feature and the unpatented features." *CSIRO*, 809 F.3d at 1301 (quoting *Garretson v. Clark*, 111 U.S. 120, 121 (1884)).

1. There is no dispute that Kite made valuable contributions to create the lifesaving therapy, YESCARTA®. If the '190 patent were all that mattered, Juno would long ago have released its own FDA-approved therapy. As Dr. Sullivan acknowledged, "there are other contributors to YESCARTA beyond just the [receptor] construct itself." Appx33447. Specifically, he acknowledged the value of Kite's "manufacturing processes, and administration, and lymphodepletion," catalogued above (at 9-10, 12). Appx33447; *see* Appx33496-33497; *see* Appx32935 (Sadelain). Chief among them is YESCARTA®'s "completely differentiated manufacturing system." Appx33738; Appx36364-36366 (advantages of Kite's process); Appx33341-33342. As discussed (at 9-10), "manufacturing" here is not about how to mass produce an ordinary infusion. It is about the intricate manner in which T-cells are collected,

reprogrammed and multiplied, and then infused back into the patient to deliver a personalized treatment.

Kite's proprietary process is responsible for YESCARTA®'s vastly greater success rate in making functioning CAR-T cells (99% success, compared to Novartis's KYMRIAH®'s 85%), and for Kite's ability to deliver treatment in half the time (an average of 16 days, compared to 30). Appx37184. That means 15% of KYMRIAH® patients will not receive their lifesaving therapy at all; the rest have to wait an average of two additional weeks they may not have left. Appx33616 ("time is of the essence"). It is no understatement to say that the difference is a matter of life and death. Juno's experience proves it: Juno's manufacturing problems led to patient deaths and the FDA shutdown of its JCAR15 trial. *Supra* 16-17.

Unsurprisingly, the market values these features of YESCARTA®. Juno received "consistent customer feedback" about the "importance of manufacturing success rate and turn around time on product preference." Appx37160-37161; *see* Appx33596-33597("[C]ritical factors … are the speed and the success rate of manufacturing … ."); Appx33616-33619; Appx33737-33738. Juno worried that its own

"manufacturing issues may not enable a competitive commercial profile." Appx37159. By Juno's own estimation, Kite's turnaround time would add 7.8% to Kite's market share compared to Juno's 21-day projected turnaround time. Appx37184. While Dr. Sullivan vaguely asserted that manufacturing is not a "demand driver," Appx33497; *see* Appx33447, his more specific testimony conceded the undeniable point that these manufacturing improvements "go towards the sales of the product," Appx33497.

Given this undisputed evidence, Dr. Sullivan was required to "separate the value" of all these noninfringing features. *CSIRO*, 809 F.3d at 1301. Instead, he did the opposite in multiple ways.

First, he afforded Juno the full $150 million stock-appreciation fee based on Kite's stock appreciation from before the hypothetical negotiation without accounting for the appreciation attributable to Kite's unique contributions to YESCARTA®, business decisions, and future outlook. There was no legitimate basis to assume that the '190 patent drove a 30-fold increase in Kite's valuation where Juno attempted to commercialize the same patent and never appreciated 30-fold. Appx33797-33798.

Worse, he then tripled that payment and his base royalty rate to account for how much better YESCARTA® was expected to perform in the market than Novartis—thereby granting Juno the value of Kite's contributions. In this way, Dr. Sullivan not only violated, but downright perverted, the rule that a royalty must be limited to "value attributable to the infringing features of the product." *Finjan, Inc. v. Blue Coat Sys., Inc.*, 879 F.3d 1299, 1309 (Fed. Cir. 2018) (quotation marks omitted); *see Ericsson*, 773 F.3d at 1226 (royalty "must be based on the incremental value that the patented invention adds to the end product"). That made this plainly prejudicial testimony both inadmissible, Appx10823-10825 (Kite's *Daubert* motion); *CSIRO*, 809 F.3d at 1301, and insufficient to support the verdict, *VirnetX, Inc. v. Cisco Sys., Inc.*, 767 F.3d 1308, 1326-28 (Fed. Cir. 2014); *see Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 904 F.3d 965, 978-80 (Fed. Cir. 2018) (vacating unapportioned damages award; ordering new trial).

2. Before trial, the district court did not explain its failure to exercise "its gatekeeping authority to ensure that only theories comporting with settled principles of apportionment were allowed to

reach the jury." *VirnetX*, 767 F.3d at 1328; *see generally* Appx87-100. After trial, the court embraced two invalid reasons.

First, the court credited Dr. Sullivan's "understanding" that apportionment was already "built into" his analysis merely because he relied on "comparable agreements to evaluate reasonable royalties." Appx11711-11712 (Sullivan Report); *see* Appx72 ("apportionment is built into the comparable license framework"). But as the table above shows, Dr. Sullivan identified no reference license that comes within even a third of his 27.6% rate, or a tenth of his $585 million upfront payment.

Where, unlike here, a hypothesized royalty reflects the "market's actual valuation of the patent," this Court has held apportionment may be built in because that valuation excludes any non-patented innovations. *CSIRO*, 809 F.3d at 1303 (expert relied on parties' proposed licensing terms to same patent). But this Court has never held apportionment satisfied where the expert does not even try to establish that the starting license contained the same "proportion of licensed/unlicensed features." *Bio-Rad*, 967 F.3d at 1377; *compare supra* § IV.A. Nor has this Court held apportionment satisfied where,

as here, an expert uses a real-world license as a putative reference point but then multiplies its terms beyond recognition based on factors outside the patent. *See VirnetX*, 767 F.3d at 1326.

Second, the court held that apportionment was not required because Juno presented evidence that the '190 patent was essential and "importan[t]" to YESCARTA®. Appx72. This Court has flatly rejected that reasoning. To avoid apportionment, "[i]t is not enough to merely show that [the invention] … is viewed as valuable, important, or even essential." *LaserDynamics*, 694 F.3d at 68. This is not a case where "the value of the entire [product] can be attributed to the patent[]." *Id.* at 69.

C. The royalty rate and upfront payment are based on grossly excessive and legally impermissible multipliers.

Dr. Sullivan's multipliers were also both inadmissible and insufficient because they were divorced from "sound economic and factual predicates." *Riles v. Shell Expl. & Prod. Co.*, 298 F.3d 1302, 1311 (Fed. Cir. 2002); *see Oiness v. Walgreen Co.*, 88 F.3d 1025, 1032 (Fed. Cir. 1996).

Dr. Sullivan had no factual or economic basis to apply his initial 90% competition adjustment to the upfront payment. As explained, he derived that multiplier from a comparison of *royalty rates* in the St. Jude-Juno and Juno-Novartis agreements. *Supra* 61-62. But unlike the royalty rates, the non-sales-based compensation did not increase by 90% in the Novartis-Juno agreement. Exactly the opposite: Novartis's upfront payment was half of what Juno paid St. Jude, and if Juno enters the market, the milestone payments will be almost exactly the same ($17.5 million versus $19.6 million). *Supra* 59. As applied to the upfront payment, the 90% increase had no factual basis.

Dr. Sullivan's other adjustment is similarly divorced from economic reality because it grants Juno value already accounted for in the $150 million stock-appreciation payment. Again, Dr. Sullivan justified awarding Juno the full $150 million stock-appreciation payment from the Side Letter based on Kite's appreciation from 2015 to 2017. Appx33463-33464; Appx33483-33485; Appx11722. That appreciation necessarily reflected and accounted for Kite's expected success selling CAR-T therapies—the same basis Dr. Sullivan used for his second multiplier to account for Juno's expectation that Kite would

be a formidable competitor. Further tripling (adding 192%) the base royalty and the $150 million stock-appreciation payment based on the same underlying economic factors that purportedly justified the $150 million payment egregiously overcompensates Juno. Juno "can not have it both ways." *Whitserve, LLC v. Comput. Packages, Inc.*, 694 F.3d 10, 30 (Fed. Cir. 2012).

For these additional reasons, the jury's verdict must be vacated.

V. Kite Did Not Willfully Infringe, And The Court Erred In Enhancing Damages.

A. As a matter of law, Kite did not willfully infringe.

To prove willfulness, Juno was required to show that Kite engaged in "egregious, sanctionable behavior"; even "'intentional or knowing' infringement" is not enough. *SRI Int'l, Inc. v. Cisco Sys., Inc.*, 930 F.3d 1295, 1308-09 (Fed. Cir. 2019) (quoting *Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 136 S. Ct. 1923, 1936 (2016) (Breyer, J., concurring)). Juno failed to carry its burden as a matter of law.

Throughout YESCARTA®'s development and through its release, Kite had more than credible defenses to any patent-infringement action. From NCI's development of the CAR through 2013, the patent did not

even purportedly cover YESCARTA®. Only later, after the PTO issued the CoC, did YESCARTA® arguably fall within the patent's scope. *See supra* § III; Appx8413. From 2013 to October 2017, Kite's clinical development of what eventually became YESCARTA® was protected by the Hatch-Waxman Act's safe-harbor provisions. Kite also had concrete backing for its view that the '190 patent was invalid: By February 2016, the PTO had determined there was a "reasonable likelihood" that the asserted claims were obvious when it granted Kite's IPR petition. Appx35280-35281. In 2017, just ten months before YESCARTA® launched, the PTO declined to invalidate the challenged claims, but Kite had an active appeal when Juno sued. *See Kite Pharma, Inc. v. Sloan-Kettering Inst. for Cancer Research*, No. 17-1647 (decided June 6, 2018). Kite also had objectively strong arguments of invalidity under § 112, *supra* §§ I-II, and that the CoC on which infringement depends was invalid, *supra* § III.

There is nothing "egregious" about a pharmaceutical company bringing a lifesaving treatment to market, in reliance on such strong defenses to infringement. To sustain that finding would send a chilling

message to pharmaceutical companies on the verge of releasing lifesaving therapies in contested infringement cases.

The district court concluded a jury could have found Kite willful merely because: (1) there was (disputed) evidence Kite attempted to license the '190 patent; (2) Kite challenged the '190 patent in an IPR; and (3) no witness testified that Kite believed YESCARTA® did not infringe. Appx69-70. None provides substantial evidence of willfulness.

At most, evidence of Kite's purported attempt to license the patent and its IPR showed that Kite knew of the patent and recognized that Juno might assert it against Kite. Because even "intentional or knowing infringement" is insufficient to establish willfulness, *SRI Int'l*, 930 F.3d at 1308, attempting to mitigate a mere potential risk of infringement must be too.

It was also legally impermissible to base willfulness on the absence of trial testimony concerning Kite's subjective belief. Kite produced a witness to testify that Kite did not believe it was infringing. The court excluded that testimony, finding that Kite's subsequent advice of counsel superseded the lay opinion. Appx68-69. The only other evidence Kite could have adduced to prove its subjective belief

would have been informed by a counsel opinion. But Congress in 35 U.S.C. § 298 decreed that an accused infringer's decision not to adduce such evidence "may not be used to prove that the accused infringer willfully infringed." *See SRI Int'l*, 930 F.3d at 1309. The court put Kite in a double bind where the only evidence Kite could have produced was the privileged evidence § 298 expressly says it need not present. And even if Kite somehow could have presented witness testimony uninformed by advice of counsel consistent with the court's order, this Court has held the absence of such testimony "unremarkable" and "insufficient." *Id.*

Following *Halo*, the objective reasonableness of defenses remains a strong indicator of nonwillfulness absent affirmative evidence that the infringer harbored "no doubts about [the patent's] validity or any notion of a defense." *Halo*, 136 S. Ct. at 1932; *WesternGeco L.L.C. v. ION Geophysical Corp.*, 837 F.3d 1358, 1363 (Fed. Cir. 2016), *rev'd on other grounds*, 138 S. Ct. 2129 (2018), *reinstated in relevant part*, 913 F.3d 1067, 1075 (Fed. Cir. 2019). Juno failed to present any such evidence here and failed to carry its burden to prove Kite willful.

B. The Court's enhancement decision rests on legal error.

Kite had compelling defenses that the '190 patent as a whole and the CoC were each invalid. Indeed, earlier in the case, the court itself had expressed "misgivings" about the CoC's validity. Appx8413; *see* Appx116-117. The district court failed to independently assess the strength of those defenses, as required by *Polara Engineering*, 894 F.3d at 1355-56, in wrongly concluding this case was not close.

The district court held the case was not close because the jury awarded Juno all the damages it sought and spent little time deliberating. Appx49. But those litigation facts are no substitute for the requisite judicial assessment. Nor can passing commentary on the credibility of one witness, Appx49, undermine the strength of those defenses, particularly where the testimony bore no relation to the patent's or CoC's validity.

At a minimum, the enhancement award should be vacated and remanded to the district court to consider how the reasonableness of those defenses affects enhancement.

CONCLUSION

This Court should reverse the judgment of invalidity and infringement or at least vacate and remand on written description and damages, including enhancement.

Respectfully submitted,

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August 31, 2020

ADDENDUM*

*Confidential material omitted from the addendum at Appx47, Appx48, Appx54, Appx95, Appx98 indicates confidential business information containing non-public valuations.

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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.,

Case No. 2:17-cv-07639-SJO-KS

~~[PROPOSED]~~ SECOND AMENDED PROTECTIVE ORDER

Judge: Hon. S. James Otero

Defendant.

KITE PHARMA, INC.

Counterclaim Plaintiff,

v.

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

Counterclaim Defendants.

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The Court recognizes that at least some of the documents and information being sought through discovery in the above-captioned action ("Action") are not publicly available and, for competitive reasons, are normally kept confidential by Plaintiffs Juno Therapeutics, Inc., Memorial Sloan Kettering Cancer Center, and Sloan Kettering Institute for Cancer Research (collectively, "Plaintiffs" or "Juno") and Defendant Kite Pharma, Inc. ("Defendant" or "Kite") ("Plaintiffs" and "Defendant" each referred to as "party" and collectively referred to herein as the "parties"). The parties have agreed to be bound by the terms of this Protective Order ("Order") in this Action. The materials to be exchanged throughout the course of the litigation between the parties may contain trade secret or other confidential research, technical, cost, price, marketing or other commercial information, as is contemplated by Federal Rule of Civil Procedure 26(c)(1)(G). The purpose of this Order is to protect the confidentiality of such materials as much as practical during the litigation.

This Order shall apply to all information, documents, and things within the scope of discovery in this Action that are in the possession or custody of, or are owned or controlled by the parties or non-parties, including but not limited to documents and things responsive to requests for production of documents and things under Federal Rule of Civil Procedure 34 (including business records produced pursuant to Federal Rule of Civil Procedure 33(d)); answers to interrogatories under Federal Rule of Civil Procedure 33; responses to requests for admission under Federal Rule of Civil Procedure 36; testimony provided at deposition pursuant to Federal Rule of Civil Procedure 30 or 31; testimony or argument provided at any hearing in this Action; documents and things responsive to, and testimony provided pursuant to any subpoena issued in this Action under Federal Rule of Civil Procedure 45; and documents, things, testimony, or other information obtained through discovery from foreign non-parties, including but

not limited to such discovery taken under the Hague Convention on the Taking of Evidence Abroad in Civil or Commercial Matters. THEREFORE:

DEFINITIONS

1. The term "CONFIDENTIAL INFORMATION" shall mean and include information contained or disclosed in any material that satisfies the requirements of Paragraph 1 of the General Rules below. The term "material" shall mean all documents, communications, depositions, pleadings, exhibits, things and all other material or information subject to discovery in this Action, including responses to requests for production of documents, answers to interrogatories, responses to requests for admissions, deposition testimony, expert testimony and reports and all other discovery taken pursuant to the Federal Rules of Civil Procedure, as well as testimony adduced at trial, trial exhibits, matters in evidence and any other information used or disclosed at trial, hereafter furnished, directly or indirectly, by or on behalf of any party, non-party, or witness in connection with this Action. For the avoidance of doubt, CONFIDENTIAL INFORMATION of a non-party produced in this Action shall be afforded the same degree of protection from disclosure as the CONFIDENTIAL INFORMATION of the parties to this Action. Each party or non party shall act in good faith in designating such information as CONFIDENTIAL INFORMATION.

2. The term "ATTORNEYS' EYES ONLY INFORMATION" shall mean and include CONFIDENTIAL INFORMATION that satisfies the requirements of Paragraph 2 of the General Rules below.

3. The term "BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY" shall mean and include any CONFIDENTIAL INFORMATION disclosed by non-party Bristol-Myers Squibb Company ("BMS") pursuant to the Court's April 29, 2019 Order (Dkt. No. 219) regarding Kite's January 11, 2019 Subpoena to BMS.

4. The term "document(s)" shall have the same meaning as provided in Rule 34 of the Federal Rules of Civil Procedure and applicable local rule, and shall include, without limitation, all original, written, recorded, electronic, or graphic materials, and all copies, duplicates, or abstracts thereof including, but not limited to, notes on documents including information contained therein or derived therefrom.

5. The term "In-House Legal Personnel" shall mean in-house legal personnel in the employ of a party or party's corporate affiliate, whose duties require them to assist Outside Counsel to prepare for trial in this matter, and any administrative staff assisting such personnel.

6. The term "Outside Counsel" shall mean outside counsel of record, and other attorneys, paralegals, secretaries, and other support staff employed by the law firm(s) of the outside counsel of record, or other persons hired or used by these firms for the purpose of preparation and trial of this Action, such as discovery vendors, mock jurors, and trial and jury consultants.

7. The term "Producing Party" shall mean any party or any non-party who produces for inspection, provides access to, provides copies of, or otherwise discloses CONFIDENTIAL INFORMATION in connection with this Action.

8. The term "Receiving Party" shall mean any party who receives the CONFIDENTIAL INFORMATION of a Producing Party.

9. The term "Related Actions" shall mean *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, No. 17-cv-6496 (C.D. Cal.); *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, No. 16-cv-1243 (D. Del.); *Kite Pharma, Inc. v. Juno Therapeutics, Inc.*, No. IPR2015-01719 (P.T.A.B.); and *Kite Pharma, Inc. v. Juno Therapeutics, Inc.*, No. 17-1647 (Fed. Cir.).

GENERAL RULES

1. Material may be designated as CONFIDENTIAL INFORMATION

when the Producing Party believes in good faith that the material qualifies for protection under Federal Rule of Civil Procedure 26(c)(1), contains or pertains to information that is not publicly available, and, for competitive reasons, is normally kept confidential by the Producing Party. This includes but is not limited to confidential research, development, commercial, proprietary, technical, business, financial, sensitive, or private information or material.

2. Material may be designated as ATTORNEYS' EYES ONLY INFORMATION when the Producing Party believes in good faith that the material qualifies for protection as CONFIDENTIAL INFORMATION, is extremely sensitive, and would, if disclosed to the Receiving Party or to a non-party, create a substantial risk of serious harm that could not be avoided by less restrictive means. Any information produced in prior litigations and designated HIGHLY CONFIDENTIAL INFORMATION: ATTORNEYS' EYES ONLY or HIGHLY CONFIDENTIAL INFORMATION: OUTSIDE COUNSEL ONLY shall be treated as ATTORNEYS' EYES ONLY INFORMATION in this Action.

3. Material produced by non-party BMS pursuant to the Court's April 29, 2019 Order (Dkt. No. 219), or any information or testimony derived therefrom, may be designated as BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY. Any use or disclosure of material designated BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY is subject to the restrictions set forth in General Rules Paragraph 12 below.

4. All CONFIDENTIAL INFORMATION shall be used only in connection with the preparation, trial, and appeal of this Action. This limitation shall not apply to the party that created or produced such materials, or otherwise had possession, custody, ownership, or control of the materials prior to the initiation of this lawsuit.

5. The parties may agree to add additional categories of

CONFIDENTIAL INFORMATION from time to time as may be necessary or appropriate. If the parties cannot resolve the issue of whether this Order should be amended to include the proposed new category of CONFIDENTIAL INFORMATION, the dispute may be submitted to the Court via the assigned district judge's procedures for the raising of such matters. Disclosure of material, however, shall still be made, but marked as CONFIDENTIAL INFORMATION, pending resolution of the objection by the parties or the Court, as the case may be.

6. Marking Designated Material as CONFIDENTIAL INFORMATION, ATTORNEYS' EYES ONLY INFORMATION, or BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY shall be made by the Producing Party in the following manner:

a. In the case of documents or any other tangible thing produced, designation shall be made by placing the legend CONFIDENTIAL, ATTORNEYS' EYES ONLY, or BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY, as the case may be, on each page of the document or on the cover or in a prominent place on any other tangible thing prior to production of the document or tangible thing;

b. In the case of electronically stored information ("ESI"), (i) digital image files, such as TIFFs, will be marked by the Producing Party with the appropriate designation on each viewable page or image, and (ii) native documents and databases will be marked by the Producing Party with the appropriate designation using a naming convention that conveys its confidentiality status, or some other appropriate means to communicate the confidential nature of the ESI that is agreed upon by the parties;

c. Any individual response to written interrogatories or requests for admissions or any expert report that contains or constitutes Designated Material shall be labeled or marked by the Producing Party as CONFIDENTIAL,

ATTORNEYS' EYES ONLY, or BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY, as the case may be, at the time it is provided or disclosed to the Receiving Party, by indicating either at the outset of the document embodying the response or in the body of each individual response, the designation applicable to each response. Any document or thing created (e.g., any abstract, summary, memorandum, or exhibit) containing CONFIDENTIAL INFORMATION, ATTORNEYS' EYES ONLY INFORMATION, or BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY subject to this Order, shall likewise be marked or labeled as CONFIDENTIAL, ATTORNEYS' EYES ONLY, or BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY, as the case may be;

d. In the case of deposition testimony, transcripts or portions thereof, designation shall be made by any party either (i) orally on the record during the deposition, in which case the portion of the transcript of the designated testimony shall be bound in a separate volume and marked CONFIDENTIAL INFORMATION, ATTORNEYS' EYES ONLY INFORMATION, or BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY, as the case may be, by the reporter, or (ii) by captioned, written notice to the reporter and all counsel of record, given within thirty days after receipt of the official transcript. All counsel receiving such notice shall be responsible for marking the copies of the designated transcript or portion thereof in their possession or control as directed by the party or deponent. Pending expiration of the thirty days, all parties and, if applicable, any non-party witnesses or attorneys, shall treat the deposition transcript as if it had been designated ATTORNEYS' EYES ONLY INFORMATION; and if any material designated BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY was used or referenced during the deposition, then pending expiration of the thirty days, the deposition

transcript shall be treated as if it had been designated BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY. If the deposition is videotaped, the video technician shall mark the original and all copies of the videotape to indicate that the contents of the videotape are subject to this Order, substantially along the lines of "This videotape contains confidential testimony used in this case. Its contents may not be viewed, displayed, or revealed except by order of the Court or pursuant to written stipulation of the parties." No person shall attend the designated portions of such depositions unless such person is an authorized recipient of CONFIDENTIAL INFORMATION or BMS CONFIDENTIAL INFORMATION under the terms of this Order, as the case may be; and

e. In the event the Producing Party elects to produce materials for inspection, no marking need be made by the Producing Party in advance of the initial inspection. For purposes of the initial inspection, all materials produced shall be considered ATTORNEYS' EYES ONLY INFORMATION, and shall be treated as such pursuant to the terms of this Order. Thereafter, upon selection of specified materials for copying by the inspecting party, the Producing Party shall, within a reasonable time prior to producing those materials to the inspecting party, mark the copies of those materials that contain CONFIDENTIAL INFORMATION with the appropriate confidentiality marking.

7. The Producing Party may redact the following information from documents that it produces:

a. names, addresses, Social Security numbers, tax identification numbers, e-mail addresses, telephone numbers, and any other information that would identify patients;

b. names, addresses, Social Security numbers, tax identification numbers, e-mail addresses, telephone numbers, and any other personal

identifying information of health care providers, including but not limited to individuals, organizations, or facilities that furnish, bill, or are paid for healthcare services or supplies;

c. names, addresses, Social Security numbers, tax identification numbers, e-mail addresses, telephone numbers, and any other personal identifying information (not to include race, age, or gender) of individuals enrolled as subjects in clinical studies or adverse event reports;

d. street addresses, Social Security numbers, tax identification numbers, dates of birth, telephone conference dial-in codes, passwords, home telephone numbers, and cellular telephone numbers of employees;

e. names, addresses, Social Security numbers, tax identification numbers, e-mail addresses, telephone numbers, and other personal identifying information of any clinical investigator submitting an adverse event to the FDA on a MedWatch form;

f. materials that contain information protected from disclosure by the attorney-client privilege, the work product doctrine, or other legal privilege protecting information from discovery in this lawsuit, which shall be identified in a privilege log or otherwise in a manner that complies with Federal Rule of Civil Procedure 26(b)(5).

8. The Producing Party that has redacted information pursuant to Paragraph 6, shall, upon request, identify the nature of the information redacted in a specific document with sufficient detail to allow the Receiving Party to determine whether a challenge to the redacted information may be appropriate. If the Receiving Party has a good-faith basis for challenging the redaction, that party shall inform counsel for the Producing Party in writing of said challenge within fourteen calendar days of receipt of the Producing Party's explanation of the redaction. If, after conferring, the parties cannot resolve the dispute, the Receiving

Party challenging the redaction may move for a ruling on the issue of whether certain information is entitled to redaction. If the Court finds that said information should remain redacted, said information shall remain redacted and may not be used as evidence by either party at trial or at a hearing or be relied upon by either party's experts. If the Court finds that said information should not remain redacted, the Producing Party shall provide or file an unredacted version of the document within fourteen calendar days of the Court's decision or, if the Producing Party challenges such a decision, within fourteen calendar days of the conclusion of any and all proceedings or interlocutory appeals challenging the decision.

9. CONFIDENTIAL INFORMATION shall not be disclosed by the Receiving Party to anyone other than those persons designated herein and shall not be used for any purpose other than this Action as set forth in Paragraph 13, unless and until the parties agree, or the Court orders, that certain specified individuals shall have access to CONFIDENTIAL INFORMATION, or such designation is removed either by agreement of the parties, or by order of the Court.

10. Information designated CONFIDENTIAL INFORMATION shall be viewed only by:

a. Outside Counsel;

b. Officers, directors, and employees (including In-House Legal Personnel) of the Receiving Party or its corporate affiliates;

c. Subject to Paragraph 15 of this Order, outside consultants or experts retained by a Receiving Party in this Action who are not employees or consultants of a Receiving Party or its affiliates;

d. Mock juror or focus group members, provided that, prior to receiving CONFIDENTIAL INFORMATION, such persons execute Exhibit A, agreeing to be bound by the terms of this Order;

e. Any person indicated on the face of the document to be its

originator, author or a recipient of a copy thereof;

f. The Court and its law clerks, staff, and any jury selected to hear this Action;

g. Any mediators engaged by the parties or appointed by the Court;

h. Stenographic reporters, videographers and their respective assistants who are engaged in such proceedings as are necessary for the preparation and trial of this Action;

i. Independent copying services, independent computer consulting and document management services, independent exhibit makers, independent translators, and other support services retained by counsel for purposes of this Action and who are obligated to not disclose CONFIDENTIAL INFORMATION received from counsel;

j. Persons engaged by a party or counsel for a party to prepare graphic or visual aids, or demonstrative exhibits, provided that, prior to receiving CONFIDENTIAL INFORMATION, such persons execute Exhibit A, agreeing to be bound by the terms of this Order; and

k. Others as to whom the Producing Party has given written consent.

11. Information designated ATTORNEYS' EYES ONLY INFORMATION shall be viewed only by (a) those persons described in Paragraph 9(a), 9(c), 9(d), 9(e), 9(f), 9(g), 9(h), 9(i), 9(j), and 9(k), and (b) up to four attorneys who are In-House Legal Personnel (as well as their support staff), who do not have a material role in competitive decision making, as the term is used in *U.S. Steel Corp. v. United States*, 730 F.2d 1465 (Fed. Cir. 1984), in the field of chimeric antigen receptor T cell therapy, and who have signed Exhibit A agreeing to be bound by the terms of this Order ("Designated In-House Counsel"). At least

seven days before any ATTORNEYS' EYES ONLY INFORMATION is disclosed to any attorney who is In-House Legal Personnel, the Receiving Party shall identify the Designated In-House Counsel in writing to the Producing Party.

12. Information designated BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY shall be viewed only by:

a. The outside counsel of record, and other attorneys, paralegals, secretaries, and other support staff employed by the law firm(s) of the outside counsel of record, provided that such personnel shall have no involvement in any matter concerning the merger transaction between BMS and Celgene Corporation ("the BMS-Celgene merger transaction");

b. Subject to Paragraph 15 of this Order, outside consultants or experts retained by a Receiving Party in this Action who are not employees or consultants of a Receiving Party or its affiliates, provided that such persons shall have no involvement in any matter concerning the BMS-Celgene merger transaction;

c. Any person indicated on the face of the document to be its originator, author or a recipient of a copy thereof;

d. Stenographic reporters, videographers and their respective assistants who are engaged in such proceedings as are necessary for the preparation and trial of this Action;

e. The Court and its law clerks, staff, and any jury selected to hear this Action; and

f. Independent computer consulting and document management services retained by counsel for purposes of this Action and who are obligated to not disclose CONFIDENTIAL INFORMATION received from counsel.

13. For the avoidance of doubt, non-party BMS, as a Producing Party of material designated BMS CONFIDENTIAL INFORMATION – OUTSIDE

COUNSEL EYES ONLY, may raise any dispute under this Protective Order with respect to the use or disclosure of material designated BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY before the Court in this Action, subject to the procedures provided for Producing Parties herein.

14. If it becomes necessary for a Receiving Party's outside counsel to seek the assistance of any person, other than those persons referred to in Paragraphs 10, 11, and 12, and to disclose CONFIDENTIAL INFORMATION to such person to properly prepare this Action for trial, the following procedures shall be employed:

a. Outside counsel of the Receiving Party shall notify, in writing, outside counsel for the Producing Party, identifying therein the specific CONFIDENTIAL INFORMATION to be disclosed and the name, address and position (along with a job description) of the person(s) to whom such disclosure is to be made;

b. If no objection to such disclosure is made by outside counsel for the Producing Party within five business days of such notification, outside counsel for the Receiving Party shall be free to make such disclosure to the designated person(s); provided, however, that outside counsel for the Receiving Party shall serve upon outside counsel for the Producing Party, prior to disclosure, an Acknowledgment of Protective Order in the form attached as Exhibit A, whereby such person agrees to comply with and be bound by this Order. The acknowledgment shall be retained by outside counsel for the Receiving Party.

c. If, within five business days, the outside counsel for the Producing Party objects, in writing, to such disclosure, no disclosure shall be made, except by order of the Court upon request by the Receiving Party pursuant the assigned district judge's procedures for the raising of such matters. Before seeking such relief, outside counsel for the Receiving Party shall meet and confer

with outside counsel for the Producing Party in a good faith effort to resolve their differences.

d. Any Party seeking such an order requesting disclosure shall explain why the requested disclosure is appropriate, but the Producing Party shall bear the burden of justifying the confidentiality designation and explaining the harm that would result from the requested disclosure.

15. The following provisions shall control the dissemination of CONFIDENTIAL INFORMATION to consultants and experts:

a. A party proposing to show CONFIDENTIAL INFORMATION to a consultant or expert per Paragraph 10(c) or 11 shall first submit the signed acknowledgment attached hereto as Exhibit A, and a curriculum vitae (a "C.V.") to the other party. The C.V. must include or be accompanied by a document setting forth the consultant's or expert's name, current business affiliation and address, and any known present or former relationships between the consultant or expert and the parties to this Action. The requirements of prior disclosure in this provision will not be a basis for seeking discovery from a non-testifying consultant or expert.

b. A party proposing to show information designated BMS CONFIDENTIAL INFORMATION – OUTSIDE COUNSEL EYES ONLY to a consultant or expert per Paragraph 12(b) shall first submit to BMS the signed acknowledgment attached hereto as Exhibit A; a C.V. meeting the requirements set forth in Paragraph 15(a) above; and any known present or former relationships between the consultant or expert and BMS.

c. Such consultants and experts for the parties shall be entitled to use staff, assistants and clerical workers as they normally do in organizing documents, preparing opinions and doing the other analysis and investigation necessary to assist the experts in completing their assignments.

d. If a party or non-party receiving a notice pursuant to this

Paragraph objects to any CONFIDENTIAL INFORMATION being disclosed to the selected consultant or expert, pursuant to this Order, such party or non-party shall make its objections known in writing to the sender of the notice within seven business days of receipt of the written notification required by this section. Such objection must be for good cause, stating with particularity the reasons for the objection. CONFIDENTIAL INFORMATION may be disclosed to the consultant or expert if the seven business day period has passed and no objection has been made. If an objection is made, then within seven business days of receipt of an objection, the parties shall meet and confer to attempt to resolve their dispute. If the parties or non-parties are unable to resolve their objections, the party or non-party making the objection has seven business days after the meet and confer to deliver the moving party's portion of the Joint Stipulation, pursuant to C.D. Cal. Local Civil Rule 37-2. If the party or non-party making the objection delivers such portion of the Joint Stipulation, the intended disclosure shall not be made unless and until the Court enters an order authorizing such disclosure. If the moving party or non-party does not deliver its portion of the Joint Stipulation within the above seven business days, the objection shall be deemed to have been withdrawn. The party or non-party making the objection shall have the burden of proof that the intended disclosure should not occur. If a timely written notice of objection is provided, no CONFIDENTIAL INFORMATION shall be disclosed to the selected consultant or expert until the objection is resolved by an order of the Court or by an agreement among the parties involved.

e. Each person authorized to receive CONFIDENTIAL INFORMATION under this Order (excluding Outside Counsel, Judges, Magistrate Judges, judicial law clerks, clerical personnel of the Court before which this Action is pending, qualified court reporters, and non-party contractors and their employees involved solely in document management, delivery or copying services for this

Action) to whom CONFIDENTIAL INFORMATION is to be given, shown, disclosed, made available or communicated in any way, shall first execute an Acknowledgment of Protective Order in the form attached as Exhibit A. Outside counsel to whom CONFIDENTIAL INFORMATION is produced shall keep in his or her files an original of each such executed Acknowledgment of Protective Order until sixty calendar days after the final termination of this Action. Upon final termination of this Action and at the written request of the Producing Party, all such executed agreements shall be provided to outside counsel for the Producing Party.

16. All CONFIDENTIAL INFORMATION disclosed by a Producing Party shall be held in confidence by the Receiving Party, and shall be used by the Receiving Party solely for matters related to the prosecution or defense of the claims in this Action, and for no other purpose whatsoever, whether directly or indirectly, unless and until the restrictions herein are removed either by written agreement of counsel for the parties, or by Order of the Court.

17. Each person receiving CONFIDENTIAL INFORMATION shall take reasonable precautions to prevent the unauthorized or inadvertent disclosure of such information. If CONFIDENTIAL INFORMATION is disclosed to any person other than a person authorized by this Order, the party responsible for the unauthorized disclosure must immediately bring all pertinent facts relating to the unauthorized disclosure to the attention of the other parties and, without prejudice to any rights and remedies of the other parties, make every effort to retrieve the improperly disclosed CONFIDENTIAL INFORMATION and prevent further disclosure by the party and by the person(s) receiving the unauthorized disclosure.

18. Absent written consent from the Producing Party, Designated In-House Counsel shall have no involvement in the Prosecution of any patent or patent application relating to chimeric antigen receptor T cell therapy ("Patent

Prosecution Activities") from the time of receipt of any CONFIDENTIAL INFORMATION through and including two years following (a) the entry of a final, non-appealable judgment or order in the liability phase of this Action, or (b) the complete settlement of all claims against all parties in this Action, whichever is later. "Prosecution" as used in this Paragraph means direct participation in drafting, amending, modifying or advising regarding the drafting or amending of patent claims or participation in domestic and/or foreign patent office correspondences in connection with such activities or fee payments related to any such activities. "Prosecution" does not include representing a party in connection with a challenge to or in defense of a patent before a domestic or foreign agency (including, but not limited to, an opposition proceeding, a reissue proceeding, *ex parte* reexamination, *inter partes* reexamination, *inter partes* review, or other post-grant review), provided such representation shall still prohibit a person from participating in the drafting, amendment, modification, or addition of patent claims in the context of an *inter partes* review and/or a challenge to a patent or patent application before a domestic or foreign agency. For the avoidance of doubt, it is agreed and understood that subordinates of individuals who receive access to ATTORNEYS' EYES ONLY INFORMATION may engage in patent prosecution relating to chimeric antigen receptor T cell therapy so long as the individuals who receive access to ATTORNEYS' EYES ONLY INFORMATION do not personally participate in such prosecution and do not communicate any confidential information learned during this Action to such subordinates for any purpose relating to such prosecution.

19. A Producing Party, on its own initiative or at the request of any other party, may remove the designation CONFIDENTIAL INFORMATION.

20. This Protective Order shall be without prejudice to the right of any party to bring before the Court the question of whether any particular item should

no longer be designated as CONFIDENTIAL INFORMATION under the terms of this Order. If counsel for a Receiving Party objects to documents or information designated as such, the following procedure shall apply:

a. Counsel for the Receiving Party shall serve on the Producing Party a written objection to such designation, which shall describe with particularity the documents or information in question and shall state the grounds for objection. Counsel for the Producing Party shall respond in writing to such objection within fourteen calendar days, and shall state with particularity the grounds for asserting that the document or information is CONFIDENTIAL INFORMATION. If no timely written response is made to the objection, the challenged designation will be deemed to be void. If the Producing Party makes a timely response to such objection asserting the propriety of the designation, counsel shall then confer in good faith in an effort to resolve the dispute within five business days.

b. If a dispute as to the designation of a document or item of information as CONFIDENTIAL INFORMATION cannot be resolved by agreement, the proponent of the designation being challenged shall present the dispute in accordance with the Local Rules and the Court's Discovery Order in this Action. The document or information that is the subject of the filing shall be treated as originally designated pending resolution of the dispute.

c. In any motion challenging the classification, the Producing Party shall have the burden of establishing the need for classification as CONFIDENTIAL INFORMATION.

21. Any party may reasonably request, in writing, that a party filing or serving a paper in this Action, such as an expert report or motion, that is marked as CONFIDENTIAL INFORMATION shall produce to the other side a redacted copy of such paper, removing the information that has been designated as

CONFIDENTIAL INFORMATION. Such redacted copy shall be provided within five calendar days of such request or otherwise at a date agreed upon by the parties.

22. This Order shall be effective on the date of its entry by the Court. However, to the extent that any party has produced documents in this Action prior to the entry of this Order that it has indicated contain or pertain to confidential information, those documents will be treated as having been produced marked CONFIDENTIAL INFORMATION pending any re-designation pursuant to this Order.

23. Whenever a deposition taken on behalf of any party involves a disclosure of CONFIDENTIAL INFORMATION of any party:

a. said deposition or portions thereof shall be designated as containing CONFIDENTIAL INFORMATION subject to the provisions of this Order; such designation shall be made on the record whenever possible, but a party may designate portions of depositions as containing CONFIDENTIAL INFORMATION after transcription of the proceedings;

b. the Producing Party shall have the right to exclude from attendance at said deposition, during such time as the CONFIDENTIAL INFORMATION is to be disclosed, any person not authorized to receive such CONFIDENTIAL INFORMATION pursuant to this Order; and

c. the originals of said deposition transcripts and all copies thereof shall bear the legend CONFIDENTIAL INFORMATION.

24. Before any CONFIDENTIAL INFORMATION is filed with the Court for any purpose, the party seeking to file such material shall seek permission of the Court to file said material under seal. The parties will follow and abide by applicable law, including relevant local rules, with respect to filing documents under seal in this Court. The party filing any material pursuant to this paragraph shall also file with the Court and make publicly available at the same time a

redacted version that deletes or obscures any CONFIDENTIAL INFORMATION.

25. This Protective Order is intended to be an Order within the meaning of Federal Rule of Evidence 502(d). The production or disclosure of any information (including documents) in this action that a Producing Party later claims should not have been produced due to a privilege or protection from discovery, including but not limited to any attorney-client privilege, work product privilege, joint defense privilege, or settlement privilege, shall not be deemed to waive any such privilege or protection. A party or non-party may request the return or destruction of such information, which request shall identify the information and the basis for requesting its return. If a receiving party receives information that the receiving party believes may be subject to a claim of privilege or protection from discovery, the receiving party shall promptly identify the information to the Producing Party. When a Producing Party identifies such information as privileged or protected, a receiving party:

a. shall not use, and shall immediately cease any prior use of, such information;

b. shall take reasonable steps to retrieve the information from others to which the receiving party disclosed the information;

c. shall within five (5) business days of the Producing Party's request:

i. return the information and all copies thereof to the Producing Party; or

ii. destroy and confirm to the Producing Party in writing that the information and all copies thereof have been destroyed, except that information existing on disaster recovery backup systems that will be deleted or overwritten in the normal course need not be returned or destroyed.

26. No one shall use the fact or circumstances of production of the

information in this action to argue that any privilege or protection has been waived. After a Producing Party or receiving party identifies the information, the receiving party may file a motion to compel the production of the information on the basis that: (a) the information was never privileged or protected from disclosure; or (b) any applicable privilege or immunity has been waived by some act other than the production of the information in this action. The Producing Party and the receiving party shall meet and confer in accordance with applicable law or Court rules regarding any such motion to compel. Notwithstanding this provision, no party shall be required to return or destroy any information that may exist on any disaster recovery backup system.

27. Nothing in this Order, nor any designation or failure to make any designation of confidentiality hereunder, shall be used or characterized by any party as an admission by a party or a party opponent.

28. The parties agree that a designation of information as CONFIDENTIAL INFORMATION, is not intended to be and shall not be construed as an admission that the CONFIDENTIAL INFORMATION is relevant to any claim or defense or subject to an applicable privilege or protection.

29. Nothing in this Order shall be deemed an admission that any particular CONFIDENTIAL INFORMATION is entitled to protection under this Order, Rule 26(c) of the Federal Rules of Civil Procedure, or any other law.

30. Nothing in this Order shall require disclosure of information, documents or things which a party contends is protected from disclosure by the attorney-client privilege or the work-product doctrine, or any other applicable privilege or immunity. This Order will not preclude any party from moving the Court for an order directing the disclosure of such information, documents or things.

31. Nothing in this Order shall bar counsel from rendering advice to

their clients with respect to this Action and, in the course thereof, relying upon any information designated as CONFIDENTIAL INFORMATION, provided that the contents of the information shall not be disclosed.

32. This Order shall be without prejudice to the right of any party to oppose production of any information for lack of relevance or any other ground other than the mere presence of CONFIDENTIAL INFORMATION. The existence of this Order shall not be used by either party as a basis for discovery that is otherwise not proper under the Federal Rules of Civil Procedure.

33. Drafts of expert reports and notes or outlines for draft reports shall not be discoverable by any party and do not need to be identified on a privilege log. Communications between experts and counsel relating to the preparation of expert reports shall not be discoverable and do not need to be identified on a privilege log, except that any facts and/or documents provided to an expert, on which the expert relies, whether from counsel or any other source, and the source of those documents and/or information are discoverable. Similarly, privileged communications (including any notes and memoranda) do not need to be identified on a privilege log if they (a) involve a Party's outside counsel in this Action or a Related Action and (b) occurred during the pendency of or in reasonable anticipation of this Action or a Related Action. The materials, communications and other information exempt from discovery under the foregoing sentences shall be treated as protected by the attorney-client privilege and/or attorney work product doctrine.

34. Nothing herein shall be construed to affect in any way the evidentiary admissibility of any document, testimony, or other matter at any court proceeding related to this Action. The marking of CONFIDENTIAL INFORMATION pursuant to this Order shall not, for that reason alone, bar its introduction or use at any court proceeding related to this Action pursuant to such

terms and conditions as the Court may deem appropriate, consistent with the need for a complete and accurate record of the proceedings; provided, however, that every effort shall be made, through the use of procedures agreed upon by the Parties or otherwise, to preserve the confidentiality of CONFIDENTIAL INFORMATION.

35. No reference may be made at the trial in this Action, in the presence of a jury, to the existence of this Order or to the effect that certain material is subject to this Order.

36. Upon final termination of this Action, all persons subject to the terms hereof shall use commercially reasonable efforts to collect and return to the respective parties all CONFIDENTIAL INFORMATION and all copies, excerpts, and summaries thereof within 60 calendar days of final termination of this Action (including any appeals), including all copies of such designated materials which may have been made. Alternatively, all persons subject to the terms of this Order may elect to destroy such materials and documents. Notwithstanding the foregoing, Outside Counsel for deponents or each party may retain: one paper copy of all court pleadings and briefs containing such designated materials; one paper copy of all deposition transcripts and deposition exhibits containing such designated materials; paper copies of attorney work product or other documents incorporating or referring to such designated materials; and Outside Counsel's electronic files other than the production sets of documents and things. All such documents retained by Outside Counsel shall remain subject to the terms of this Protective Order. The commercially reasonable efforts contemplated by this paragraph do not require the return or destruction of materials that (a) are stored on backup storage media made in accordance with regular data backup procedures for disaster recovery purposes, (b) are located in the email archive system or archived electronic files of departed employees, (c) are subject to litigation hold obligations,

or (d) are otherwise required by law to be retained. The fulfillment of the obligations imposed by this paragraph, whether by return, destruction, or both, shall be certified in writing by the Receiving Party within sixty calendar days.

37. All obligations and duties arising under this Order shall survive the termination of this Action. The Court retains jurisdiction indefinitely over the parties, and any persons provided access to CONFIDENTIAL INFORMATION under the terms of this Order, with respect to any dispute over the improper use of such designated materials.

38. The restrictions and obligations set forth herein shall not apply to any information that: (a) the parties agree should not be designated CONFIDENTIAL INFORMATION; (b) is already public knowledge; (c) has become public knowledge other than as a result of disclosure by the Receiving Party, its employees, or its agents in violation of this Order; or (d) has come or shall come into the Receiving Party's legitimate knowledge independently of the production by the designating party. Prior knowledge must be established by pre-production documentation.

39. The restrictions and obligations herein shall not be deemed to prohibit discussions of any CONFIDENTIAL INFORMATION with anyone if that person already has or obtains legitimate possession thereof.

40. Nothing herein shall be construed to limit in any way a party's use of its own CONFIDENTIAL INFORMATION.

41. In the event that a new party is added, substituted or brought in, this Order will be binding on and inure to the benefit of the new party, subject to the right of the new party to seek relief from or modification of this Order.

42. If discovery is sought of a person not a party to this Action requiring disclosure of such non-party's CONFIDENTIAL INFORMATION, the CONFIDENTIAL INFORMATION disclosed by any such non-party will be

accorded the same protection as the parties' respective CONFIDENTIAL INFORMATION, and will be subject to the same procedures as those governing disclosure of the Parties' respective CONFIDENTIAL INFORMATION pursuant to this Order.

43. During the course of this Action, a party may be requested to produce to another party information subject to contractual or other obligations of confidentiality owed to a non-party by the party receiving the request. The party subject to such contractual or other obligation of confidentiality shall timely contact the non-party to determine whether such non-party is willing to permit disclosure of the information under the terms of this Order. If the non-party is willing to permit such disclosure, the information shall be produced in accordance with this Order. If the non-party is not willing to permit disclosure of the information under the terms of this Order, the Requesting Party in the Action shall be notified and any information withheld on the basis of such contractual or other confidentiality obligation shall be identified on a separate index stating the reason for withholding the document and the non-party to whom the obligation of confidentiality is owed. This Order shall not preclude any party from seeking an order compelling production of such information.

44. Nothing herein shall be construed to prevent disclosure of CONFIDENTIAL INFORMATION if such disclosure is required by law or by order of the Court. In the event that a Producing Party's CONFIDENTIAL INFORMATION is sought from a Receiving Party by any person not a party to this Action, by subpoena, by service with any legal process, by order or otherwise, prompt written notice shall be given to the Producing Party. Such notice shall include a copy of such subpoena, legal process or order. If the Producing Party does not move to quash and/or for a protective order within the time allowed for production by the subpoena or other request (or within such times as a court may

direct or as may be agreed upon by the parties) or notifies the Receiving Party in writing that it will not file a motion, the Receiving Party may disclose information in response to the subpoena or other request. The Receiving Party will not produce any of the CONFIDENTIAL INFORMATION while a Producing Party's motion to quash or for a protective order is pending, or while an appeal from or request for appellate review of such motion is pending, unless a court orders production of the CONFIDENTIAL INFORMATION that is subject to this Order. Nothing in this Order shall be construed as authorizing a party to disobey a lawful subpoena issued in another action. Nothing in this Order shall be construed as requiring anyone covered by this Order to contest a subpoena or other process, to appeal any order requiring production of CONFIDENTIAL INFORMATION covered by this Order or to subject itself to penalties for non-compliance with any subpoena, legal process or order. Any persons seeking such CONFIDENTIAL INFORMATION who take action to enforce such subpoena or other legal process shall be apprised of this Order.

45. Transmission by facsimile and/or e-mail is acceptable for all notification purposes herein.

46. To the extent that the parties have agreed on the terms of this Order, such stipulation is for the Court's consideration and approval as an Order. The parties' stipulation shall not be construed to create a contract between the parties or between the parties and their respective counsel.

47. This Order is entered without prejudice to the right of any Party to apply to the Court at any time for additional protection, to release, rescind, or modify the restrictions of this Order, to determine whether a particular person shall be entitled to receive any particular information, or to seek relief from the production or disclosure of any information in this action that a Producing Party later claims should not have been produced. On any request seeking

disclosures beyond those authorized by this Order, the burden will be on the Receiving Party to justify the disclosure.

48. By entering this Order and limiting the disclosure of information in this case, the Court does not intend to preclude another court from finding that information may be relevant and subject to disclosure in another case. Any person or party subject to this Order who becomes subject to a motion to disclose another party's CONFIDENTIAL INFORMATION pursuant to this Order shall promptly notify that party of the motion so that the party may have an opportunity to appear and be heard on whether that information should be disclosed.

IT IS SO ORDERED.

DATED: May 7, 2019

Hon. Karen L. Stevenson
United States Magistrate Judge

EXHIBIT A

IN THE UNITED STATES DISTRICT COURT FOR THE CENTRAL DISTRICT OF CALIFORNIA

WESTERN DIVISION

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

Plaintiffs/
Counterclaim Defendants,

vs.

KITE PHARMA, INC.,

Defendant/
Counterclaim Plaintiff.

CASE NO.: 17-cv-07639-SJO-KS

EXHIBIT A TO PROPOSED AMENDED PROTECTIVE ORDER

AGREEMENT TO BE BOUND BY PROTECTIVE ORDER

Judge: Hon. S. James Otero

I, _____, hereby acknowledge and agree that:

1. My address is _____.
2. My present employer(s) is/are _____.
3. My present occupation(s) or job description(s) is/are _____ _____.
4. I have read and understood the provisions of the Amended Protective Order in this case signed by the Court in the above-captioned matter, and I will comply with all provisions of the Amended Protective Order.
5. I will hold in confidence and not disclose to anyone not qualified under the Amended Protective Order any CONFIDENTIAL INFORMATION or any words, summaries, abstracts, or indices of such information disclosed to me.
6. I will limit use of designated information disclosed to me solely for purpose of this action pursuant to the provisions of the Amended Protective Order.
7. No later than the final conclusion of the case, I will destroy or return all designated materials and information, as well as all summaries, excerpts, abstracts, and indices thereof which come into my possession, and documents or things which I have prepared relating thereto, to counsel for the party for whom I was employed or retained.

I declare under penalty of perjury that the foregoing is true and correct.

_____ _____
Dated Signature

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA
WESTERN DIVISION

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

Plaintiffs,

v.

KITE PHARMA, INC.,

Defendant.

AND RELATED COUNTERCLAIMS

Case No. 2:17-cv-07639-PSG-KSx

~~[PROPOSED]~~ FINAL JUDGMENT

Hon. Philip S. Gutierrez

Courtroom 6A

This action came on for jury trial on December 3, 2019, in Courtroom 10C of the above-entitled Court, the Honorable District Court Judge S. James Otero presiding. On December 13, 2019, the jury returned a unanimous verdict in favor of Plaintiffs Juno Therapeutics, Inc., and Sloan Kettering Institute for Cancer Research ("Plaintiffs"), and against Defendant Kite Pharma, Inc. ("Kite"). Dkt. No. 593 (redacted version); Dkt. No. 594 (sealed version). The Court has now considered and resolved each side's consolidated post-trial motions.

NOW THEREFORE, IT IS ORDERED, ADJUDGED, AND DECREED THAT JUDGMENT IS HEREBY ENTERED IN THIS MATTER AS FOLLOWS:

1. Kite has infringed claims 3, 5, 9, and 11 of United States Patent No. 7,446,190 ("the '190 Patent") since October 18, 2017, by making, selling, and/or offering to sell Yescarta® in the United States.

2. Kite's infringement of claims 3, 5, 9, and 11 of the '190 Patent has been willful.

3. Claims 3, 5, 9, and 11 of the '190 Patent are not invalid for lack of enablement or written description.

4. The '190 Patent's Certificate of Correction is not invalid.

5. Judgment is entered against Kite on its counterclaims of non-infringement and invalidity.

6. Plaintiffs shall recover: (1) $778,343,501 on the jury verdict, comprising (a) a $585,000,000 upfront payment; and (b) $193,343,501, calculated as a 27.6% running royalty on each of (i) Kite's net revenues from sales of Yescarta® from October 18, 2017 through September 30, 2019, which were $603,650,765; and (ii) Kite's net revenues from sales of Yescarta® from October 1, 2019 to December 12, 2019, which were $96,869,167; (2) pre-judgment interest on the jury's verdict in the amount of $32,807,300, and (3) enhanced damages of $389,171,750.50.

7. As provided in 28 U.S.C. § 1961, Plaintiffs shall also recover post-judgment interest on all amounts listed in paragraph 6 above, at a rate of 0.15%, compounded annually, from the date of this Judgment until the Judgment is paid.

8. Kite shall pay Plaintiffs a running royalty of 27.6% of its net revenues for Yescarta® and any other therapy using the same infringing CAR from December 13, 2019 to the expiration date of the '190 Patent, August 28, 2024. Kite shall disclose its net revenues for Yescarta® and any other therapy using the same infringing CAR to Plaintiffs by the second Monday following the end of each quarter and wire Plaintiffs a corresponding royalty payment by that same date. Further, within ten (10) days of entry of this Judgment, the parties shall submit to the Court proposed terms for inspection and reporting procedures regarding the therapies and revenues subject to the ongoing royalties awarded in this paragraph.

Dated: April 8, 2020

HONORABLE PHILIP S. GUTIERREZ
UNITED STATES DISTRICT JUDGE

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

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CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

TITLE: Juno Therapeutics, Inc., et al. v. Kite Pharma, Inc.

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PRESENT: THE HONORABLE S. JAMES OTERO, UNITED STATES DISTRICT JUDGE

Victor Paul Cruz	Not Present
Courtroom Clerk	Court Reporter
COUNSEL PRESENT FOR PLAINTIFFS:	**COUNSEL PRESENT FOR DEFENDANTS:**
Not Present	Not Present

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PROCEEDINGS (in chambers): ORDER RE: PLAINTIFFS' CONSOLIDATED POST-TRIAL MOTION [ECF No. 655]

This matter comes before the Court on Plaintiffs' Juno Therapeutics, Inc. ("Juno") and Sloan Kettering Institute for Cancer Research ("SKI") (collectively, "Plaintiffs") Consolidated Post-Trial Motion ("Motion") filed on January 21, 2020. (Motion, ECF No. 655.[1]) Defendant Kite Pharma, Inc. ("Defendant" or "Kite") filed its Opposition to Plaintiffs' Post-Trial Motion ("Opposition" or "Opp.") on February 10, 2020. (Opp., ECF No. 672-2.[2]) Plaintiffs filed their Reply in Support of Plaintiffs' Consolidated Post-Trial Motion ("Reply") on February 24, 2020. (Reply, ECF Nos. 694, 696-2.[3]) Plaintiffs subsequently filed a Notice of Supplemental Authority ("Notice") on March 10, 2020. (Notice, ECF No. 713.) Defendant filed a Response ("Response") on March 12, 2020. (Response, ECF No. 715.)

Plaintiffs also filed a [Proposed] Final Judgment ("Proposed Final Judgment," ECF No. 658[4]) and Local Rule 58-7 Memorandum Regarding Pre- and Post-Judgment Interest ("L.R. 58-7 Memorandum," ECF No. 658-1[5]) on January 21, 2020. Defendant filed Objections to Plaintiffs' Proposed Final Judgment ("Objections") on February 10, 2020. (Objections, ECF No. 671.) Plaintiffs filed their Reply in Support of Proposed Final Judgment ("Final Judgment Reply") on February 24, 2020. (Final Judgment Reply, ECF No. 695.)

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[1] Plaintiffs' Memorandum in Support of Plaintiffs' Motion is located at ECF No. 656, and the sealed version is located at ECF No. 685. Unless otherwise noted, all citations to Plaintiffs' Motion refer to the sealed memorandum, ECF No. 685.

[2] Unless otherwise noted, all citations to Defendant's Opposition refer to the sealed Opposition, at ECF No. 693.

[3] Unless otherwise noted, all citations to Plaintiffs' Reply refer to the sealed Reply, at ECF No. 712.

[4] Unless otherwise noted, all citations to Plaintiffs' Proposed Final Judgment refer to the sealed Proposed Final Judgment, at ECF No. 686.

[5] Unless otherwise noted, all citations to Plaintiffs' L.R. 58-7 Memorandum refer to the sealed L.R. 58-7 Memorandum, at ECF No. 686-1.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

In setting the post-trial briefing schedule, the Court indicated that it would take the matters under submission following the filing of reply motions. (Order, ECF No. 639 at 5; *see also* Fed. R. Civ. P. 78(b).)

For the following reasons, the Court **GRANTS-IN-PART** Plaintiffs' Consolidated Post-Trial Motion [ECF No. 655]. Final Judgment to follow.

I. BACKGROUND

This is a patent infringement action involving U.S. Patent No. 7,446,190 ("the '190 Patent"), titled "Nucleic Acids Encoding Chimeric T Cell Receptors." The '190 Patent issued on November 4, 2008 and incorporates a provisional application filed on May 28, 2002. ('190 Patent Caption.) The claimed invention provides "nucleic acid polymer encoding [] chimeric TCR's [T Cell Receptors] . . . ." ('190 Patent, col. 2:11-14.) The chimeric TCRs encoded by the claimed invention "combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain ("zeta chain portion"), a signaling region from a costimulatory protein such as CD28 with a binding element that specifically interacts with a selected target." ('190 Patent, col. 2:14-18.) These TCRs are designed to "specifically interact[] with a cellular marker associated with target cells," resulting in the stimulation of a T cell immune response to the target cells. ('190 Patent, col. 2:30-36.)

Plaintiffs initiated this action on October 18, 2017, alleging that Defendant infringes the '190 Patent through the use, sale, offer for sale, or importation of one of Defendant's immunotherapy treatments, YESCARTA®. YESCARTA® is described as 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." (Second Amended Complaint ("SAC") ¶ 18, ECF No. 484.) Plaintiffs assert that YESCARTA® infringes the '190 Patent by utilizing nucleic acid polymers encoding chimeric TCRs within the scope of the '190 Patent claims. (SAC ¶ 26.) Defendant, in turn, filed counterclaims seeking declaratory judgments of non-infringement and invalidity of the '190 Patent. (*See generally*, Answer to SAC and Counterclaims, ECF No. 617.)

On December 13, 2019, the jury entered a unanimous verdict in favor of Plaintiffs, finding: (1) Defendant had not proven by clear and convincing evidence that the Certificate of Correction was invalid, (2) Defendant had not proven by clear and convincing evidence that any of claims 3, 5, 9, and 11 of the '190 Patent were invalid for lack of enablement or written description, (3) Plaintiffs proved by a preponderance of the evidence that Defendant's infringement of the corrected claims of the '190 Patent was willful, and (4) Plaintiffs proved by a preponderance of the evidence the damages owed were a $585,000,000 upfront payment, and 27.6% running royalty. (Redacted Jury Verdict, ECF No. 593.)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

Following the jury's return of the verdict, the Court set a post-trial briefing schedule for both parties and deferred entry of judgment. (Order, ECF No. 639.)

II. LEGAL STANDARDS

A. Prejudgment Interest

In patent cases, "[p]rejudgment interest should ordinarily be awarded absent some justification for withholding such an award." *DDR Holdings, LLC v. Hotels.com, L.P.*, 773 F.3d 1245, 1262 (Fed. Cir. 2014) (citing *Gen. Motors Corp. v. Devex Corp.*, 461 U.S. 648 (1983)). Prejudgment interest generally runs from the earliest date of infringement of any patent. *Comcast IP Holdings I LLC v. Sprint Commc'ns Co., L.P.*, 850 F.3d 1302, 1315 (Fed. Cir. 2017). "Courts have discretion to determine the appropriate rate of prejudgment interest to be awarded." *Deckers Outdoor Corp. v. Superstar Int'l, Inc.*, No. CV 13-0566 AG (PJWx), 2014 WL 12588480, at *2 (C.D. Cal. Aug. 18, 2014) (citations omitted). Ultimately, prejudgment interest seeks to provide full compensation to the patent owner for "the forgone use of the [royalties] between the time of infringement and the date of judgment." *Gen. Motors*, 461 U.S. at 656.

B. Enhancement

Section 284 of the Patent Act states that "the court may increase . . . damages up to three times the amount found or assessed." 35 U.S.C. § 284. "Awards of enhanced damages under the Patent Act over the past 180 years establish that they are not to be meted out in a typical infringement case, but are instead designed as a 'punitive' or 'vindictive' sanction for egregious infringement behavior." *Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 136 S. Ct. 1923, 1932 (2016). Entitlement to enhanced damages must be proven by a preponderance of the evidence. *Id.* at 1934.

In *Halo*, the Supreme Court rejected the Federal Circuit's test from *In re Seagate Technology, LLC*, 497 F.3d 1360, 1371 (Fed. Cir. 2007), for enhanced damages. *Seagate* had required a determination of willful infringement to award enhanced damages, where willfulness was measured through a two-part test that included an "objective recklessness prong" and a subjective prong. The Supreme Court found "[t]he subjective willfulness of a patent infringer, intentional or knowing, may warrant enhanced damages, without regard to whether his infringement was objectively reckless." *Id.* at 1933. *Halo* concluded:

> Section 284 allows district courts to punish the full range of culpable behavior. Yet none of this is to say that enhanced damages ***must*** follow a finding of egregious misconduct. As with any exercise of discretion, courts should continue to take into account the particular circumstances of each case in deciding whether to award

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

> damages, and in what amount. Section 284 permits district courts to exercise their discretion in a manner free from the inelastic constraints of the *Seagate* test. Consistent with nearly two centuries of enhanced damages under patent law, however, such punishment should generally be reserved for egregious cases typified by willful misconduct.

Id. at 1933-34. Since then, the Federal Circuit has further clarified that "conduct r[ising] to the level of wanton, malicious, and bad-faith behavior [is] ***required*** for willful infringement." *SRI Int'l, Inc. v. Cisco Sys., Inc.*, 930 F.3d 1295, 1309 (Fed. Cir. 2019) (emphasis added).

Regarding the analysis for willful infringement, although the Federal Circuit's "decision in *Read* [is] relevant to an award of enhanced damages, a "district court is not required to discuss the *Read* factors." *Presidio Components, Inc. v. Am. Tech. Ceramics Corp.*, 875 F.3d 1369, 1382-83 (Fed. Cir. 2017); *see also Read Corp. v. Portec, Inc.*, 970 F.2d 816 (Fed. Cir. 1992). The *Read* factors are:

> (1) whether the infringer deliberately copied the ideas or design of another;
> (2) whether the infringer, when he knew of the other's patent protection, investigated the scope of the patent and formed a good-faith belief that it was invalid or that it was not infringed;
> (3) the infringer's behavior as a party to the litigation;
> (4) defendant's size and financial condition;
> (5) closeness of the case;
> (6) duration of defendant's misconduct;
> (7) remedial action by the defendant;
> (8) defendant's motivation for harm; and
> (9) whether defendant attempted to conceal its misconduct.

See Read Corp., 970 F.2d at 826-27.

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

C. Ongoing Royalty Rate

An ongoing royalty permits an adjudged infringer to continue using a patented invention for a price. *See Paice LLC v. Toyota Motor Corp.*, 504 F.3d 1293, 1313 n.13 (Fed. Cir. 2007) (defining an ongoing royalty and distinguishing a compulsory license). The Federal Circuit has identified 35 U.S.C. § 283, which authorizes "injunctions in accordance with the principles of equity," as statutory authority for awarding ongoing royalties. *See id.* at 1314 (citing § 283); *see also* Mark A. Lemley, The Ongoing Confusion over Ongoing Royalties, 76 Mo. L. Rev. 695, 695-99 (2001) (analyzing authority for ongoing royalties under §§ 283 and 284). Accordingly, while this remedy involves monetary relief, there is no Seventh Amendment right to a jury trial for ongoing royalties. *See Paice*, 504 F.3d at 1315-16 ("[T]he fact that monetary relief is at issue in this case does not, standing alone, warrant a jury trial.").

The Federal Circuit has held that ongoing royalties are a discretionary remedy. "There are several types of relief for ongoing infringement that a court can consider: (1) it can grant an injunction; (2) it can order the parties to attempt to negotiate terms for future use of the invention; (3) it can grant an ongoing royalty; or (4) it can exercise its discretion to conclude that no forward-looking relief is appropriate in the circumstances." *Whitserve, LLC v. Computer Packages, Inc.*, 694 F.3d 10, 35 (Fed. Cir. 2012). "Under some circumstances, awarding an ongoing royalty for patent infringement in lieu of an injunction may be appropriate." *Paice*, 504 F.3d at 1314. However, the remedy is not automatic: "awarding an ongoing royalty where 'necessary' to effectuate a remedy, be it for antitrust violations or patent infringement, does not justify the provision of such relief as a matter of course whenever a permanent injunction is not imposed." *Id.* at 1314-15.

Determination of ongoing royalties differs from evaluation of a reasonable royalty during trial because the jury has reached a liability verdict and other economic factors may have changed. "Prior to judgment, liability for infringement, as well as the validity of the patent, is uncertain, and damages are determined in the context of that uncertainty. Once a judgment of validity and infringement has been entered, however, the calculus is markedly different because different economic factors are involved." *Amado v. Microsoft Corp.*, 517 F.3d 1353, 1362 (Fed. Cir. 2008). A district court may also consider "additional evidence of changes in the parties' bargaining positions and other economic circumstances that may be of value in determining an appropriate ongoing royalty." *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1343 (Fed. Cir. 2012). *But see Lemley*, *supra*, at 704-05 ("Juries are already required to assume that the patent is valid and infringed when setting past damages. There is no reason to think that asking the same question twice should produce different answers in most cases.") (footnotes omitted).

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

III. DISCUSSION

In their Motion, Plaintiffs argue for: (A) jury verdict damages through December 12, 2019 (*i.e.*, through trial); (B) prejudgment interest at the prime rate; (C) enhanced damages; and (D) an award of going royalties. Each argument is addressed in turn.

A. Damages through December 12, 2019

Plaintiffs request damages on the jury verdict to be updated, based on Defendant's subsequently-disclosed revenues from YESCARTA® through the end of trial. The jury determined Defendant owed Plaintiffs a $585 million upfront payment, with a running royalty rate of 27.6% on YESCARTA® revenues through trial. (Motion 4.) Defendant previously disclosed total revenues of $603,650,765 through September 30, 2019. (*Id.*) Defendant has since disclosed total revenues of $700,519,932 through December 12, 2019. (Motion 4-5.) Based on Defendant's updated revenue information and the jury's upfront payment and running royalty, the updated damage award totals $778,343,501. (Motion 5.)

Defendant did not respond to Plaintiffs' request directly. (*See generally* Opp.)

The Court, having received no opposition, updates the jury award to $778,343,501.

B. Prejudgment interest at prime rate

Plaintiffs argue the Court should order Defendant to pay pre-judgment interest on the jury's award at the prime rate, compounded quarterly. (Motion 5.) First, Plaintiffs argue that courts recognize the prime rate as the most accurate estimate in patent cases, because it represents the rate charged by banks to its most credit-worthy customers. (*Id.* (citing *Opticurrent, LLC v. Power Integrations, Inc.*, No. 17-cv-3597, 2019 WL 2389150, at *19 (N.D. Cal. June 5, 2019)).) Plaintiffs argue that district courts both inside and outside of California have awarded the prime rate (Motion 5-6 (citing cases)), as well as the Federal Circuit, even where the patent owner has not shown that it borrowed at that rate or a higher rate. (Motion 6 (citing *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 939 F.2d 1540, 1545 (Fed. Cir. 1991)).) Second, Plaintiffs argue quarterly compounding is common (*id.* (citing cases)), and aligns well with the quarterly sales data Defendant provides in this case (*id.*).

Defendant responds that the Treasury bill rate is appropriate for fixing the rate of pre-judgment interest for federal claims, unless the trial judge finds, on substantial evidence, that the equities of a particular case require a different rate. (Opp. 29.) The Treasury bill rate accords with sound economics by compensating Plaintiffs for the time value of money, but not investment risk that Plaintiffs did not bear. (Opp. 29-30 (citing cases).) Prejudgment interest need not be

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

compounded at all. (Opp. 30.) If compounding is ordered, although some courts have ordered annual compounding, Defendant accepts quarterly compounding of prejudgment interest. (*Id.*)

Plaintiffs reply pre-judgment interest, arising under § 284, is routinely treated as governed by Federal Circuit law. (Reply 14-15.) The prime rate is the most accurate estimate of the likely rate a large corporation would be charged by a bank, and the license previously entered into by Juno and Memorial Sloan Kettering ("MSK License") calls for an even higher rate for late royalty payments. (Reply 15.) The prime rate reflects the cost of borrowing money the patentee should have had, even without any showing that the patent owner actually borrowed at that rate or higher. (*Id.*)

As a preliminary matter, the Court determines prejudgment interest is warranted. The Court has not been presented with any justification for withholding prejudgment interest. Thus, the Court follows the ordinary course and finds prejudgment interest will place Plaintiffs in as good a position as if Defendant had entered into a reasonable royalty agreement in the first place. *See Gen. Motors Corp.*, 461 U.S. at 655; *see also DDR Holdings, LLC*, 773 F.3d at 1262.

Turning next to the amount of prejudgment interest, the Federal Circuit "has recognized that the district court has substantial discretion . . . ." *Gyromat Corp. v. Champion Spark Plug Co.*, 735 F.2d 549, 556 (Fed. Cir. 1984). "A court may use the prime rate, the prime rate plus a percentage, the United States Treasury Bill ('T-Bill') rate, a state statutory rate, the corporate rate, or whatever rate the court deems appropriate under the circumstances." *Fujifilm Corp. v. Motorola Mobility LLC*, 182 F. Supp. 3d 1014, 1042-43 (N.D. Cal. 2016) (citations omitted).

Here, Plaintiffs have not argued that they actually borrowed money at a rate higher than the T-bill rate, or that they did so ***because*** they did not possess the money from a reasonable royalty agreement. *Laitram Corp. v. NEC Corp.*, 115 F.3d 947, 955 (Fed. Cir. 1997) (awarding T-bill rate, where the district court determined there was no evidence that plaintiff borrowed money at a higher rate, or that there was a causal connection between the loss of use of money as a result of defendant's infringement and a need to borrow money). Nor have Plaintiffs argued that the litigation was protracted, or that their poor financial condition required borrowing above the prime rate. *Uniroyal*, 939 F.2d at 1545 (awarding prime rate where protracted nature of litigation and party's poor financial condition required borrowing above a prime rate). Although *Uniroyal* holds that evidence that a patentee borrowed money at a higher rate is not necessary to support a prime rate award, *Uniroyal* does not hold that the absence of such evidence still mandates an award at a prime rate. 939 F.2d at 1545. And although the MSK License lists a higher interest rate for late payments as a penalty, the Court does not find this probative of an interest rate Plaintiffs would have received if affirmatively seeking a loan. The Court also notes that *Hockerson-Halberstadt, Inc. v. Propet USA, Inc.* is inapposite because the salient issue in that case was the proper date from which to calculate prime interest. 62 Fed. Appx. 322, 334 (Fed.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

Cir. 2003) (remanding to determine prejudgment interest where district court awarded the prime rate in effect when the order issued in 2002, rather than the interest rate in effect in 1995 when infringement began, which was over double the awarded rate).

In light of the above, the Court awards the Treasury bill rate.[6] The Court finds this rate most consistent with the evidence and arguments presented in this case. *See Apple Inc. v. Samsung Elecs. Co.*, 67 F. Supp. 3d 1100, 1122 (N.D. Cal. 2014) (awarding Treasury bill rate, where although plaintiff submitted a declaration stating it borrowed at rates higher than the Treasury bill rate, plaintiff maintained substantial cash reserves and did not present any evidence it needed to borrow money ***because*** it was deprived of the damages award).

Thus, the Treasury bill rate, compounded quarterly, is awarded for prejudgment interest, which shall not apply to the enhancement award.

C. Enhanced damages

Plaintiffs argue that the Court should award enhanced damages in the same amount as the jury's damages award. (Motion 7.) Plaintiffs argue enhancement is a vindictive or punitive sanction designed to prevent a caught infringer from being punished by paying no more than the reasonable royalty it would have paid in the first place. (*Id.*) Here, the jury determined that Defendant knew of Plaintiffs' patent and intentionally infringed at least one asserted claim. (*Id.*) The supporting evidence demands a meaningful enhancement, as analyzed under the *Read* factors. (Motion 8.) Courts have awarded enhancements in the amount of the jury's award for less egregious conduct. (Motion 25 (citing *Arctic Cat v. Bombardier Recreational Prods., Inc.*, 198 F. Supp. 3d 1343 (S.D. Fla. 2016); *Saint-Gobain Autover USA, Inc. v. Xinyi Glass N. Am., Inc.*, 707 F. Supp. 2d 737 (N.D. Ohio 2010)).)

Defendant responds that Gilead, Defendant's parent company, launched YESCARTA® with knowledge of the '190 Patent and the inevitability that Plaintiffs would sue Defendant for infringement. (Opp. 1.) The *Read* factors may be convenient guidelines, but they are not the only factors that may be relevant, and this Court is not bound to apply them. (Opp. 1-2.) Defendant further responds that when the alleged misconduct is a cure for a potentially fatal disease, and the damages award is one of the largest ever returned, the additional sanction of enhancement is just not warranted. (Opp. 2 (citing *Idenix Pharms. LLC v. Gilead Scis., Inc.*, 271 F. Supp. 3d 694, 703 (D. Del. 2017)).) Defendant has administered YESCARTA® to over 2,250 terminal cancer patients, and Plaintiffs have not had, and still do not have, an FDA-approved

[6] *Opticurrent* awarded the prime rate "as that would likely be the loan rate that [plaintiff,] as a large corporation, would be charged by a bank." 2019 WL 2389150, at *19. While *Opticurrent* presents a relevant consideration, the Court finds the T-bill rate more appropriate, for the reasons listed.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

CAR-T therapy. (Opp. 2.) Although Novartis has its KYMRIAH® product, it has experienced significant manufacturing problems, and Defendant's and Novartis's combined capacity does not meet the need of eligible patients. (Opp. 2-3.)

Plaintiffs reply enhancement is justified and necessary to punish and deter Defendant's unscrupulous conduct. (Reply 1.) That Defendant's therapy is life-saving does not provide Defendant a pass. (*Id.*) Enhanced damages are appropriate, even in cases involving lifesaving goods. (Reply 1-2 (citing cases).) Defendant had the option of taking a license or designing around the '190 Patent, but chose not to take either option. (Reply 2.)

The Court provides initial analysis pursuant to *Halo*, as clarified by the Federal Circuit in *SRI International*. *See Halo*, 497 F.3d at 1371 (permitting courts to exercise discretion and stating "punishment should generally be reserved for egregious cases typified by willful misconduct"); *see also SRI Int'l*, 930 F.3d at 1309 ("[C]onduct r[ising] to the level of wanton, malicious, and bad-faith behavior [is] ***required*** for willful infringement." (emphasis added)). In doing so, the Court may consider evidence that was not available to the jury. The Court notes it benefits from its experience presiding over this case since its inception in October 2017[7] (including reviewing all filings of the parties throughout the course of the case), and having presided over trial (including personally observing the live testimony of 18 witnesses, and designated testimony of 5 witnesses, in the case).

Based on the benefit of the Court's extensive history and familiarity with the case, the Court notes that in its view, the testimony of Dr. Arie Belldegrun, former CEO of Defendant, was not credible. He testified repeatedly that in 2013, he did ***not*** attempt to license the '190 Patent from SKI. Instead, he insisted that he only sought opportunities for clinical trial testing sites. His testimony was contradicted by Dr. Yashodhara Dash of MSK (the other participant in the meetings, who the Court views as having testified credibly), Dr. Aya Jakobovits, former President of Defendant, and other evidence introduced during trial. The jury's verdict likewise demonstrates that it, as the finder of fact, did not believe Dr. Belldegrun's testimony.

Having discredited Dr. Belldegrun's testimony, the record clearly demonstrates that Defendant, despite believing the '190 Patent to be important in 2013 to the product later released as YESCARTA®, did not obtain a license. Defendant's filing of an IPR against the '190 Patent (and its subsequent labeling of IPR institution as one of the three top highlights for Defendant in 2016), likewise demonstrates the importance of the '190 Patent to Defendant. And yet, following these actions, Defendant admits in its Opposition that it ***sped up*** release of its YESCARTA® therapy to market, despite being fully aware of the '190 Patent and "inevitable" litigation. Now, Defendant points to its defenses asserted ***during*** litigation as justification for its actions ***preceding*** litigation.

[7] Order, ECF No. 11.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

Thus, the Court considers the totality of Defendant's actions, where the Court views the following as undisputed: Defendant knew of the Sadelain backbone claimed in the '190 Patent at least as of 2013, attempted aggressively to license the '190 Patent, affirmatively attempted to invalidate the '190 Patent by filing an IPR, then when neither of those steps was successful, chose to accelerate YESCARTA® to market to its own advantage and to Plaintiffs' corresponding detriment, all while knowing that Plaintiffs' assertion of the '190 Patent in this litigation was, by Defendant's own admission, "inevitable." (Opp. 1:7.) The Court finds this behavior rises to the level of wanton, malicious and bad-faith behavior required for willful infringement. *SRI Int'l*, 930 F.3d at 1309.

The Court next addresses Defendant's argument that an enhancement is not warranted because the misconduct resulted in a life-saving therapy. Defendant relies on *Idenix* for the proposition that an additional sanction is not warranted, where the misconduct bears on a life-saving treatment, and the jury's damages award was the largest ever returned in a patent trial. *Idenix*, 271 F. Supp. 3d at 703. While the Court agrees that the misconduct did result in a life-saving treatment that saved lives, and that the jury's damages award is substantial, the *Idenix* court carefully voiced its view that based on its extensive familiarity with the entire course of the case, substantial contrary evidence was presented by defendant. The Court does not observe the same circumstances here, particularly due in large part to Dr. Belldegrun's testimony. Moreover, that a treatment is life-saving does not automatically preclude an award of enhanced damages. *See, e.g.*, *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317 (Fed. Cir. 2016) (upholding 50% enhancement for potentially life-saving products).

Thus, the Court weighs the wanton and bad-faith behavior of Defendant in rushing a product to market despite having failed in its licensing and invalidating attempts, against the fact that Defendant's actions have resulted in a life-saving treatment for thousands of terminal cancer patients. The Court in its discretion determines that after weighing the relevant facts, a 50% enhancement is appropriate. While Defendant's flagrant actions cannot be completely pardoned, Defendant's therapy singlehandedly saved the lives of thousands of terminal cancer patients, many of whom otherwise faced a certain death sentence. The immeasurable benefit to the public interest thus warrants mitigation. While the Court's enhancement determination here is dispositive, the Court provides additional analysis of the *Read* factors, which further supports the Court's determination.

1. *Read* Factor 1 – deliberately copied

Plaintiffs argue *Read* Factors 1 and 6 support enhancement. Defendant has long been aware that its collaborators copied Dr. Sadelain's two-part backbone, which forms the essence of Dr. Sadelain's invention in the '190 Patent. (Motion 9.) Dr. Rosenberg, a scientist at the National Cancer Institute ("NCI"), demanded information from Dr. Sadelain, who then directed Dr.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

Rosenberg to a paper disclosing his backbone. (Motion 9-10.) Dr. Rosenberg later published a case report describing a sequence corresponding to the portion Dr. Sadelain shared in 2007. (Motion 10.) Evidence demonstrated Defendant understood the link between Dr. Rosenberg and Dr. Sadelain, including internal emails. (Motion 10-11.) Defendant repeatedly attempted to license the '190 Patent from Plaintiffs, and although unsuccessful, proceed to commercialize YESCARTA® anyway. (Motion 11-12.) Defendant subsequently filed an unprovoked IPR challenging the '190 Patent, and as part of the IPR learned that Plaintiffs believed Dr. Rosenberg had copied Dr. Sadelain's CAR. (Motion 12-13.) Despite the PTO denying invalidation of the '190 Patent, Defendant proceeded to commercialize YESCARTA®. (Motion 13.)

Defendant responds that Dr. Rosenberg is a towering figure in the field of immunotherapy, the '190 Patent had not yet issued when he spoke with Dr. Sadelain, and Dr. Sadelain never told Dr. Rosenberg he was seeking patent protection. (Opp. 3-4.) Moreover, Dr. Rosenberg (and eventually Defendant) developed a CAR using a different scFv. (Opp. 4.) Dr. Rosenberg openly cited Dr. Sadelain's work in two publications, and Defendant understood that the costimulatory regions referenced in the '190 Patent (amino acids 113-220) and NCI (amino acids 114-220) CAR's were different. (Opp. 4-5.) The internal emails do not constitute evidence of copying because they discussed what the difference was between Dr. Rosenberg's and MSK's constructs. (Opp. 5-6.) Plaintiffs' evidence of Defendant's alleged attempts to license the '190 Patent and the IPR reflect at most Defendant's recognition that Plaintiffs might assert the '190 Patent against it. (Opp. 6.)

Plaintiffs reply Defendant copied Dr. Sadelain's CAR backbone and continues to perpetuate misconduct to this day. (Reply 2.) Factor 1 focuses on whether a defendant copied the ideas of another, regardless of when the patent issued. (*Id.*) Defendant does not suggest it or Dr. Rosenberg developed YESCARTA® independently, or that Defendant failed to ask Dr. Rosenberg about the source of his CAR construct. (Reply 2-3.) Although Defendant relies on Dr. Bot's 2012 homology analysis, Defendant admitted before trial it did not rely on Dr. Bot's homology analysis after 2012. (Reply 3.)

The proper inquiry under Factor 1 is not limited to a patent itself, but rather the "ideas or design of another," including the "commercial embodiment, not merely the elements of a patent claim." *Read*, 970 F.2d at 827. Defendant does not deny that it deliberately copied the work of Drs. Rosenberg and Sadelain, and instead tries to: distinguish the constructs, and claim that the '190 Patent had not issued when Defendant communicated with Drs. Rosenberg and Sadelain. Under the proper inquiry, the Court determines that Defendant deliberately copied the ideas later contained in the '190 Patent (*i.e.*, the Sadelain backbone), and that this factor thus weighs in favor of enhancement.

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

2. *Read* Factor 2 – good-faith belief

Plaintiffs argue Defendant presented no evidence of good-faith belief of non-infringement or invalidity to the jury. (Motion 14.) To the contrary, despite repeated indications Dr. Rosenberg copied Dr. Sadelain's backbone, Defendant refrained from inquiring, despite having close working relationships with Dr. Rosenberg. (*Id.*) By 2017, the PTO issued the Final Written Decision ("FWD"), and Defendant conceded that it literally infringes the '190 Patent, subject to its CoC defense. (Motion 14-15.) Defendant admitted no testimony or documentary evidence suggesting Defendant had a good-faith belief of its defenses, or that anyone relied on such a belief when YESCARTA® launched. (Motion 15.) Plaintiffs argue defenses contrived after the fact for litigation purposes are irrelevant to enhancement because culpability is measured at the time of the challenged conduct. (*Id.*)

Defendant responds that Plaintiffs ignore Defendant's CoC, written description, and enablement defenses presented at trial. (Opp. 18.) During its opening statement, Defendant's counsel stated Defendant had very, very good reasons for believing it does not infringe, based on these three defenses. (Opp. 18-19.) Defendant attempted to introduce evidence from Dr. Bot that prior to the CoC, the '190 Patent did not cover Dr. Rosenberg's construct. (Opp. 19.) By the time the CoC issued, Defendant had consulted with attorneys, and Defendant exercised its right to maintain privilege over those communications. (*Id.*) Defendant then could not present further evidence from fact witnesses as to their subjective beliefs, for fear of waiving that privilege. (Opp. 19-20). The proper legal inquiry is Defendant's good-faith belief at the time of first infringement. (Opp. 20.) Here, at that time, Defendant had pursued appeal of the adverse IPR decision, and asserted the defenses that it tried to the jury. (*Id.*) Because Defendant maintained privilege that prevented it from introducing further evidence of its subjective good faith, § 298 prohibits any negative inference being drawn from assertion of privilege, thus this factor should either weigh against enhancement, or at most, be deemed neutral. (*Id.*)

Plaintiffs reply that Defendant cannot rely on its litigation defenses where it never offered any evidence that anyone relied on its litigation defenses when it made its decision to knowingly infringe. (Reply 8.) Plaintiffs further reply that Defendant cannot rely on its assertion of privilege, where § 298 says failure to obtain or present advice of counsel may not be used to prove willfulness. Defendant submitted no evidence of any type to establish its good-faith belief. (*Id.*)

The proper inquiry under *Read* is "whether the infringer, ***when he knew of the other's patent protection***, investigated the scope of the patent and formed a good-faith belief that it was invalid or that it was not infringed." *Read*, 970 F.2d at 827 (emphasis added). The parties instead focus on Defendant's good-faith belief at the time of first infringement, which is the relevant inquiry for determining whether infringement was willful. But that issue has already been decided, as the jury entered a verdict of willful infringement. Instead, the Court notes that Defendant has not

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

presented evidence of any investigation and good-faith belief of noninfringement or invalidity when Defendant knew of the '190 Patent. To the extent Defendant attempts to point to Dr. Bot's 2012 homology analysis as evidence of its good-faith defense, the Court freely considers it and finds it does not tip the scale. During the enhancement phase, the Court may consider evidence and information the jury did not have. The Court finds that Dr. Bot's homology analysis in 2012 bears little relevance to Defendant's good-faith defense, where it was superseded by Defendant seeking and receiving advice of counsel.

Even evaluating Defendant's good-faith belief at the time of first infringement, Defendant relies on its litigation defenses presented at trial. But the first evidence of Defendant's litigation defenses appears in its Answer, filed on November 27, 2017. (Answer, ECF No. 22.) The parties agree the date of first infringement is October 2017. Thus, Defendant still does not present evidence to show it held those views at the time infringement began, much less that it relied on its views when it chose to infringe.

Nor does 35 U.S.C. § 298 weigh in Defendant's favor. Section 298 says that failure of an infringer to present advice of counsel "may not be used to prove that the accused infringer willfully infringed the patent . . . ." As discussed above, the determination that the accused infringer willfully infringed the patent has already been made. Now, the proper inquiry under *Read* is whether Defendant investigated the patent and formed a good-faith belief when it learned of the '190 Patent. Even omitting any negative inference (as precluded by § 298 for a finding of willful infringement), the Court determines that no fact testimony was presented regarding a good-faith defense. That Defendant strategically chose to exercise privilege and not present an advice of counsel opinion did not preclude it from presenting fact testimony. Thus, the second factor weighs in favor of enhancement.

3. *Read* Factor 3 – behavior as a party

Plaintiffs argue that Defendant's litigation misconduct was exceptional and egregious. (Motion 17.) Defendant elicited false, misleading, and incredible testimony. (Motion 17.) Dr. Belldegrun testified he contacted Plaintiffs simply to seek clinical trial sites, where evidence demonstrated his interest in licensing the '190 Patent. (Motion 17-18.) Dr. Belldegrun further denied any pre-suit concern of the '190 Patent, where Defendant had attempted to license the patent and invalidate the patent. (Motion 18.) Dr. Belldegrun further denied Defendant was motivated by a first-mover advantage. (*Id.*) Defendant's intent to call Dr. Schuetz to testify was obscured, leading to his deposition on the Sunday morning before trial. (*Id.*) Dr. Schuetz was further presented as an independent third-party witness, where he had substantial ties to Defendant and Gilead, including being represented by Defendant's counsel. (Motion 19.) Furthermore, Defendant filed repetitive motions that forced Plaintiffs and the Court to expend time and resources addressing repetitive and unjustified requests, including Dr. Bot's homology analysis

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

and Plaintiffs' damages case. (Motion 20.) Defendant affirmatively misrepresented its good-faith defense all while knowing it had no non-attorney evidence to offer at trial, then later claimed prejudice by mischaracterizing its privilege assertion. (Motion 21.) Defendant further attempted to take advantage of its own use of an erroneous jury verdict form resulting from its own duplicitous conduct. (*Id.*) Defendant's unreasonable handling of witnesses warrants enhancement. (Motion 22 (citing *Fractus, S.A. v. Samsung Elecs. Co.*, 876 F. Supp. 2d 802 (N.D. Tex. 2012)).) Defendant's unreasonable and vexatious litigation tactics further warrant enhancement. (Motion 22-23 (citing *Liqwd, Inc. v. L'Oréal USA, Inc.*, No. 17-cv-14, 2019 WL 6840353 (D. Del. Dec. 16, 2019)).)

Defendant responds that its introduction of Dr. Belldegrun's testimony (which conflicted with Dr. Dash's testimony) is not misconduct. (Opp. 7.) Dr. Belldegrun's trial testimony tracked his deposition testimony, and Plaintiffs do not cite facts suggesting Dr. Belldegrun's trial testimony was false. That Dr. Dash's testimony contradicted Dr. Belldegrun's testimony does not show it was false (Dr. Dash likewise was biased, contradictory of her deposition at times, and exaggerated). (Opp. 8.) Ms. Champski's third-party hearsay statement that Defendant was interested in licensing from MSK should be afforded less trustworthiness, as she never testified, nor was she deposed. (Opp. 8-9.) Dr. Jakobovits did not contradict Dr. Belldegrun, where her recollection was refreshed by a vague email referring to a collaboration/license. (Opp. 9.) Defendant's responses to Plaintiffs' damages contentions (which represented the parties had licensing discussions in 2013 and 2014) were preliminary in nature and unverified. (*Id.*) And Defendant did in fact pursue other sites for clinical trials over a year before Defendant began its trials. (Opp. 9-10.) Dr. Belldegrun only contacted the Office of Technology Development ("OTD") after being referred by Dr. Sadelain. (Opp. 10.) Dr. Belldegrun's testimony was corroborated by evidence, and no other documents or witnesses besides Dr. Dash gave a conflicting account. (Opp. 11.) And Plaintiffs—not Defendant—elicited allegedly implausible testimony from Dr. Belldegrun. (*Id.*) Regarding Dr. Schuetz, the Court already addressed Plaintiffs' arguments regarding his appearance at trial, his communications with Gilead ended months before trial, Dr. Schuetz was reimbursed for his expenses and time away from work, Dr. Schuetz wanted to be represented by Defendant's counsel based on Plaintiffs' counsel's behavior, and Plaintiffs mischaracterize their request for Dr. Schuetz to sign an affidavit stating he had not reviewed the prosecution history for the '190 Patent. (Opp. 12-14.) Finally, Defendant's advocacy was reasonable, where zealous advocacy is an ethical responsibility. (Opp. 14.) Defendant's requests regarding use of the claim construction order as impeachment, Dr. Bot's homology analysis, Plaintiffs' damages, Dr. Sullivan's demonstratives, its good-faith basis for noninfringement, and verdict form were reasonable and within its rights. (Opp. 14-17.)

Plaintiffs reply Dr. Belldegrun lied under oath at trial, as demonstrated by Defendant's failure to assert the testimony it elicited was truthful. (Reply 4.) Plaintiffs clarify the facts Defendant claims were undisputed from Dr. Belldegrun's testimony. (*Id.*) Similarly, internal emails demonstrate

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CONFIDENTIAL MATERIAL OMITTED

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

Dr. Belldegrun sought a license. (Reply 5.) Any writing could have been used to refresh the recollection of Dr. Jakobovits. (*Id.*) Defendant's damages contentions are now claimed to be false, and Defendant blames Plaintiffs for Defendant's own failure to investigate, or later supplement, amend, or modify. (*Id.*) Although Dr. Dash testified that she was aware of documents referencing clinical trials with licensing for a collaboration with a different entity, those documents having nothing to do with Defendant or Dr. Belldegrun. (Reply 6.) Regarding Dr. Schuetz, Defendant mischaracterizes Plaintiffs' counsel's interactions, including Plaintiffs seeking an affidavit, and Dr. Schuetz not being an independent witness where he admitted having consulting and legal services agreements with Defendant's counsel and being paid for by Defendant (and Gilead). (Reply 6-7.) Plaintiffs further reply that Defendant kept relitigating issues, even where (contrary to what Defendant claims), the Court provided explanations when it denied Defendant's requests on the record. (Reply 7.)

The Court does not find that the actions of Defendant or its counsel amount to litigation misconduct. The Court has already stated its view of Dr. Belldegrun's testimony. But the Court is not of the view that Defendant's counsel's eliciting testimony from Dr. Belldegrun constituted litigation misconduct, where Defendant was entitled to present its own story and its own version of events. Likewise for Dr. Schuetz, Defendant was entitled to argue Dr. Schuetz was an independent witness, and Plaintiffs were entitled to elicit biases on cross-examination (as they did). The Court views Defendant's counsel's conduct as zealous representation of its client. Finally, the Court also finds that Defendant's re-raising of certain issues in different contexts also did not constitute litigation misconduct. A party may waive certain rights on appeal by not preserving its objections for the record, and the Court does not find that Defendant's behavior was excessive or unwarranted. The third factor thus weighs in Defendant's favor.

4. *Read* Factor 4 – size and financial condition

Plaintiffs argue Defendant's large size and financial standing support enhancement, where Gilead purchased Defendant for $12 billion shortly before YESCARTA® went on the market, which warrants a review of Gilead's (not Defendant's) financial condition. (Motion 23.) Gilead's total assets are nearly $60 billion, including $9 billion in cash and cash equivalents, its market capitalization is over $79 billion, and its total revenues in the third quarter of 2019 were over $5.6 billion. (Motion 23-24.) In light of Gilead's financial condition, the amount of enhancement should be sufficiently meaningful to send a message that such practices will not be countenanced. (Motion 24.)

Defendant responds Plaintiffs sued Defendant, not Gilead, and Defendant is a comparatively small corporation. (Opp. 23.) Defendant's actual revenues through 2019 were $724 million, and [redacted] (*Id.*) Enhancement would

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CONFIDENTIAL MATERIAL OMITTED

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

therefore be unduly punitive. (*Id.*) Plaintiffs' cited authority is distinguishable because it enhanced considerably more modest awards, ranging from $700,000 to $15.5 million. (Opp. 24.)

Plaintiffs reply Defendant and Gilead function as a single company, and Gilead is responsible for the actions at issue. (Reply 11.) Even if the focus were on Defendant, Defendant can sustain the penalty, [redacted] where Dr. Rao's analysis runs only through 2022, and where Dr. Rao does not provide additional information about cost categories. (Reply 11-12.) Moreover, the law disregards whether an infringer would be profitable after a reasonable royalty. (Reply 12.)

The Court finds that consideration of Gilead's size and financial status, as it acquired Defendant before YESCARTA® went on the market, is appropriate. This is especially so where although Gilead did not become a party to this litigation, Gilead paid for Dr. Schuetz to testify on Defendant's behalf in this litigation, demonstrating its ties to this litigation and to Defendant. Gilead's total assets of nearly $60 billion, and $9 billion in cash and cash equivalents, are substantial and merit an enhancement to send a strong message. *See, e.g.*, *Johns Hopkins Univ. v. Cellpro*, 978 F. Supp. 184, 195 (D. Del. 1997) ("Punishing a larger company in a stronger financial condition may call for higher damages, where a lower number may be equally effective in punishing a smaller company."). In fact, within the last few years, a different court similarly determined that Gilead's size and financial condition were large and healthy. *Idenix*, 271 F. Supp. 3d at 701 (concluding that although Gilead's size and financial condition "as a general matter could support enhancement," they did not in that particular case).

Even considering only the size and financial condition of Defendant, although Defendant is comparatively small when compared to Gilead, the Court finds that revenues of $724 million, and nearly $100 million in revenues from October to December 2019 are significant.

Thus, the Court finds this factor weighs in favor of enhancement.

5. *Read* Factor 5 – closeness of case

Plaintiffs argue the case was not close, where the nine-member jury returned a unanimous verdict accepting all of Plaintiffs' arguments, and rejecting all of Defendant's arguments. (Motion 16.) Specifically, the jury rejected Defendant's CoC and invalidity defenses, Defendant stipulated to literal infringement of claims as corrected by the presumptively-valid CoC, the jury determined Defendant's infringement was willful, and it found Plaintiffs' damages expert credible. (Motion 16-17.)

Defendant responds that the mere fact that Defendant did not prevail does not suggest the case

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

was not close. (Opp. 22.) Defendant asserted a substantial challenge to the CoC. (Opp. 23.) When Defendant moved for summary judgment on this issue, the Court acknowledged doubts about Plaintiffs' position. (*Id.*) Plaintiffs offered no new evidence on this point, and Defendant introduced Dr. Schuetz's testimony, rendering this defense a hotly-contested issue. (*Id.*) Defendant also presented substantial written description and enablement defenses, and Plaintiffs did not even attempt to move for summary judgment on these issues. (*Id.*)

Plaintiffs reply the jury returned a sweeping, across-the-board verdict, including Plaintiffs' requested damages in full. (Reply 10.) That a case proceeds to trial does not mean the jury's call was close. (*Id.* (citing cases).)

The Court finds that although Defendant's failure to prevail on a single issue does not automatically render a case close, the Court's view of the live testimony, including the incredibility of Dr. Belldegrun's testimony as noted above, merits a finding that this factor weighs in Plaintiffs' favor. Plaintiffs prevailed on every single issue presented to the jury, including a damages award that, as Defendant noted in its briefing on January 21, 2020, "is listed as the seventh-largest patent jury award ever, according to Docket Navigator." (Defendant's Motion for Judgment as a Matter of Law, ECF No. 659, at 35 n.6.) Also weighing in Plaintiffs' favor is the speed with which the jury returned the verdict, where it returned a verdict the morning after beginning deliberation. Defendant does not provide any authority concluding that a party's failure to move for summary judgment on an issue suggests the case was close. The Court is unpersuaded by this argument, given the different standards that apply. Thus, the Court finds this factor weighs in Plaintiffs' favor.

6. *Read* Factor 6 – duration of misconduct

As set forth above in Read Factor 1 (*see supra*, Section III.C.1), Plaintiffs argue Defendant's longstanding (since at least 2012) knowing copying of Plaintiffs' technology supports enhancement. (Motion 7-13.)

Defendant responds that its alleged misconduct has been of short duration, where it did not begin until October 2017, when Defendant launched YESCARTA®. (Opp. 17-18.) Defendant cannot be charged with any misconduct prior to that date, because Kite did not even exist (2007-2008), the pre-CoC '190 Patent did not cover the CAR Defendant developed (2008-2013), and Defendant's further development work was exempt from any claim of infringement under the safe harbor provisions of the Hatch-Waxman Act, 35 U.S.C. § 271(e). (Opp. 18.)

Plaintiffs reply that the history leading up to infringement is relevant and significant, especially because Defendant had so many years to change course. (Reply 3.) Even if not, Defendant's 2017-to-date actions would suffice, where over the last two years it has shown no signs of

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

ceasing or implementing remedial measures. (Reply 3-4.)

The jury already determined the CoC is valid, which means the '190 Patent, as originally issued, contained a clearly evident error and solution from the perspective of a POSITA. Thus, even before issuance of the CoC, Defendant should have been on notice of its misconduct. However, even evaluating Defendant's actions from 2013 onward, ***after*** the CoC issued, the Court finds Defendant's misconduct was of a lasting duration, as it had many years to develop, test, apply for approval for, and obtain a license to the '190 Patent for, YESCARTA® before its release in 2017. Even if the safe harbor provision of the Hatch-Waxman Act applied to Defendant's actions before 2017, Defendant's continuing actions post-2017 would weigh in favor of enhancement.

7. *Read* Factor 7 – remedial action

As set forth above in *Read* Factor 2 (*see supra*, Section III.C.2), Plaintiffs argue Defendant's failure to take any remedial steps, despite its lack of good-faith belief of non-infringement or invalidity, supports enhancement. (Motion 14-15.)

Defendant responds that by June 2013 (when the CoC issued), Dr. Rosenberg had already conducted Phase I clinical trials, and Defendant was in preparation to conduct Phase I/II trials that led to FDA approval for YESCARTA®. (Opp. 20-21.) Remedial efforts are not simple and would have required many years of research and development. (Opp. 21.) Defendant had to decide whether to: (1) continue developing YESCARTA® and rely on its defenses to an infringement claim, or (2) pull the plug on YESCARTA® and switch to a different construct. (Opp. 21.) Defendant in 2014 or 2015 decided to accelerate development of YESCARTA®. (*Id.*) Defendant also decided to develop a different CAR construct for its next-generation therapy. (*Id.*) Defendant has continued developing its non-infringing construct as part of its next-generation dual-targeting CAR-T therapy. (*Id.*)

Plaintiffs reply Defendant willfully barreled ahead and infringed, having failed to license or invalidate the '190 Patent. (Reply 9.) Defendant's bizarre response showing it took remedial steps is to state that it rushed an infringing product to market, without a license. (*Id.*) Plaintiffs argue they have always been open to a reasonable sublicense. (*Id.*)

The Court understands Defendant's argument to be that remedial steps would simply have been too difficult to take, and Defendant's response was thus to ***speed up*** the date on which it began its infringing behavior. Such an argument certainly cannot sway this factor in Defendant's favor. Defendant has not argued that it even attempted to change its product or re-approach Plaintiffs regarding licensing, even where Plaintiffs state they have always been open to a reasonable sublicense. The Court recognizes that "reasonable" is in the eye of the beholder, but Defendant's failure to put forth any evidence or argument that it even attempted to sublicense

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

the '190 Patent merits a finding that this factor weighs in Plaintiffs' favor.

8. *Read* Factor 8 – motivation for harm

Plaintiffs argue Defendant's goal of obtaining a competitive advantage at Plaintiffs' expense supports enhancement. (Motion 15.) Plaintiffs and Defendant are longstanding competitors and each attempted to beat the other to market, as demonstrated by Defendant's internal documents. (Motion 16.) Any first-mover advantage to Defendant would create reciprocal harm to Plaintiffs, as they were direct competitors in a relatively small market. (*Id.*)

Defendant responds that mere motivation to make a profit does not distinguish this case from the garden-variety infringement case. (Opp. 21.) Defendant's sales have not come at Juno's expense, as Juno is not on the market. (Opp. 22.) Moreover, even Defendant and Novartis combined cannot treat all eligible patients. (*Id.*)

Plaintiffs reply Defendant's goal was to get to market first because it believed doing so would allow it to dominate the market. (Reply 10.) Although Defendant argues it and Novartis cannot serve the entire market, it does not argue that Defendant, Novartis, and Juno combined could not serve the entire market. (*Id.*)

The Court finds that Defendant's goal was more than just simply to make a financial profit. As the evidence overwhelmingly shows, Defendant raced to get its product to market to benefit from the "first mover advantage," where it would enter the market early and grab market share, in order to preclude Plaintiffs from later obtaining that same market share. And it did so by improperly using Plaintiffs' patented CAR. Thus, the benefit conferred to Defendant by its improper head start was to direct detriment of Plaintiffs. This is also confirmed by internal documents, such as a Gilead internal document asking "Why Kite instead of Juno? . . . **First mover** advantage." Ex. 21 (PX78 at 5 (emphasis in original)). Thus, even though Plaintiffs have not yet jointed the market, Defendant's unfair head start was designed to impede Plaintiffs' progress when they do so. This factor weighs in Plaintiffs' favor.

9. *Read* Factor 9 – attempt to conceal

Plaintiffs argue evidence shows Defendant attempted to conceal its wrongful conduct, such as Dr. Belldegrun's licensing testimony, and Defendant's internal emails regarding Dr. Rosenberg's public statements acknowledging Dr. Sadelain. (Motion 24.) Defendant's attempts continue, where it continued to assert (after the verdict) to press outlets that Defendant independently developed YESCARTA®. (Motion 24.)

Defendant responds that there is no evidence that Defendant tried to conceal its infringing

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

conduct. (Opp. 24.) Dr. Rosenberg published articles disclosing the YESCARTA® construct, gave Dr. Sadelain credit for contributing, and deposited the sequence in Genbank. (*Id.*) For the reasons set forth for *Read* Factor 1, Plaintiffs did not identify any false and misleading testimony from Dr. Belldegrun. (*Id.*; *see supra*, Section III.C.1.) Defendant's internal reaction to Dr. Rosenberg's statement in a New York Times article crediting Dr. Sadelain did not conceal anything. (Opp. 24.) Defendant's post-trial statement of opinion is one Defendant may express. (*Id.*)

Plaintiffs reply improper concealment reaches concealment of misconduct, not just concealment of sales. (Reply 12.) Defendant's discussion of Dr. Rosenberg crediting Dr. Sadelain shows Defendant sought to conceal Dr. Sadelain's inventive role, and the law considers unsuccessful concealment still to be concealment. (*Id.*)

The Court finds that Defendant's internal emails lamenting Dr. Rosenberg's public statements that NCI's research "owe[d] a lot" to Dr. Sadelain do not necessarily constitute an attempt by Defendant to conceal its infringing conduct. The correspondence certainly demonstrates an attitude consistent with a desire to conceal, but falls short of recognizing any attempt to conceal. While the Court finds that Dr. Belldegrun's testimony, which has been discredited, demonstrates an attempt to conceal the fact that Defendant sought a license to the '190 Patent, ultimately the Court is not persuaded that that testimony falls squarely within *Read* factor 9 (for which *Read* cites authority where a party failed to preserve its record and cooperate at trial). The Court finds this factor neutral.

Taking all the *Read* factors together, the Court's previous determination is supported by the analysis. *Read* factors 1, 2, 4, 5, 6, 7, and 8 weigh in favor of enhancement, whereas factor 3 weighs against enhancement, and factor 9 is neutral. The Court maintains its position that enhancement is proper, and taking into account all of the circumstances regarding enhancement, determines a 50% enhancement proper.

D. Ongoing royalties

Plaintiffs argue Defendant's continued infringement warrants an ongoing royalty rate of at least 33.1% (20% more than the jury's rate) for ongoing sales of infringing therapies. (Motion 26-27.) The increase accounts for the parties' changed circumstances, including that a verdict of no invalidity and infringement amounts to a substantial shift in bargaining position, post-verdict infringement is necessarily willful, and courts frequently impose a post-verdict ongoing royalty rate higher than a reasonable royalty found at trial. (Motion 27-28.) One study demonstrated that between 2007 and 2015, the ongoing rate was higher than the jury's in two thirds of the cases studied. (Motion 28.) Here, the parties' economic circumstances have changed since October 2017, the date of the hypothetical negotiation. (Motion 29.) Specifically, Bristol-Myers

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

Squibb ("BMS"), Juno's ultimate corporate parent, has announced a biologics license application ("BLA") for JCAR017, including to treat relapsed/refractory mantel cell lymphoma ("MCL"). (*Id.*) Gilead has also announced Defendant submitted a BLA for CAR-T therapy to treat MCL. (*Id.*) Plaintiffs' further progress for JCAR017, as well as Defendant's new BLA, was not previously accounted for in Dr. Sullivan's competition adjustment. (*Id.*) At a minimum, the 27.6% rate found by the jury is necessary. (Motion 30.)

Defendant responds that the 27.6%[8] royalty award is punitive, not apportioned, and unsupported by comparable licenses or other substantial evidence. (Opp. 25.) There is no basis for further increase, where Dr. Sullivan opined the royalty rate applies throughout the patent term, and Plaintiffs' Motion contradicts Dr. Sullivan's testimony. (*Id.*; *see also id.* (citing *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1380 (Fed. Cir. 2008)).) Moreover, the upfront payment precludes injunctive relief, which weighs against an increased royalty. (Opp. 26.) Without the threat of an injunction, the parties' negotiating positions would remain the same—the initial hypothetical negotiation assumes validity and infringement. (Opp. 26.) Courts frequently decline to increase the forward royalty rate found by the jury. (Opp. 26-27 (citing cases).) The Federal Circuit has rejected enhancing ongoing royalties based on willfulness, where an injunction is unavailable. (Opp. 27.) Here, the upfront payment precludes an injunction, and the equities highly disfavor an injunction for a product that fills an unmet need in terminal cancer patients. (Opp. 27-28.) Defendant further responds that a hypothetical negotiation today would lead to a lower royalty: (1) Defendant's actual revenues have been dramatically lower than projections at the hypothetical negotiation, and (2) the hypothetical negotiation assumed Plaintiff would already have launched an approved product by mid-2019, where in fact JCAR017 may now be available in late 2020 at the earliest, translating into a shorter period of competition than originally anticipated. (Opp. 28-29.)

Plaintiffs reply that *Innogenetics* holds an upfront payment compensating through the full term of the patent is inconsistent with an injunction against practicing the patent, but says nothing about the rate of the future royalty. (Reply 13.) Moreover, there is a fundamental difference between a reasonable royalty for pre-verdict infringement and damages for post-verdict infringement. Here, a running royalty rate adjusts for revenues lower than projected, because the running royalty takes a percentage of the lower amount. (Reply 14.) Plaintiffs further reply that the imminent entry of JCAR017 requires a higher royalty rate. (*Id.*) Plaintiffs further reply Defendant would agree to a higher royalty rate in 2019, because it now has a greater market share than anticipated in 2017. (*Id.*) Plaintiffs further argue Dr. Sullivan's trial analysis did not account for the mantle cell lymphoma indication, and accounting for it now increases the degree

[8] Defendant referred to the "26.7% royalty award," Opp. at 25:4, but the Court assumes this to be a typographical error, as Defendant referred elsewhere in its Opposition to the correct 27.6% royalty, and has not otherwise disputed what the jury awarded.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CONFIDENTIAL MATERIAL OMITTED

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

of competition. (*Id.*)

The Court finds that in a post-trial hypothetical negotiation, some factors weigh in favor of a higher royalty rate. The jury found the '190 Patent valid and infringed, which strengthens Plaintiffs' position. Although a hypothetical negotiation assumes a patent is valid and infringed, a determination on the merits can strengthen a party's position. *See ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*, 694 F.3d 1312, 1342 (Fed. Cir. 2012) ("When patent claims are held to be not invalid and infringed, this amounts to a substantial shift in the bargaining position of the parties." (citations omitted)). Additionally, Plaintiffs presented evidence that both Plaintiffs and Defendant have submitted BLAs to treat MCL. Dr. Sullivan did not account for this fact in his previous competition adjustment, and if considered, would increase the adjustment as the parties would be in direct competition to treat MCL. Finally, *Innogenetics* does not preclude an increase in royalty rate. Unlike in *Innogenetics*, Dr. Sullivan did not opine that the market entry fee was "paid in anticipation of [defendant's] long-term license to sell its products," or that "his proposed amount of damages was not capped by the date of the jury award." *Innogenetics*, 512 F.3d at 1380.

However, other factors weigh in favor of a lower royalty rate. Neither party disputes that revenues for YESCARTA® have been lower than originally estimated at the time of the hypothetical negotiation in 2017. Specifically, while in 2017, Defendant estimated [redacted] While Plaintiffs argue this is taken into account because the royalty is a percentage, a smaller revenue can still weigh in favor of a lower royalty rate, because the resulting margin is smaller. Additionally, although at the original hypothetical negotiation, the parties expected Plaintiffs to have already entered the market, Plaintiffs have yet to do so. Given the limited term of the patent, Plaintiffs will face competition for a comparatively shorter time than anticipated in 2017.

After careful consideration of all of the factors, the Court declines to change the royalty rate awarded by the jury. The Court emphasizes that in deciding not to change the royalty rate, it has performed a careful analysis of the parties' changed circumstances, as noted above. *EcoServices, LLC v. Certified Aviation Servs., LLC*, 340 F. Supp. 3d 1004, 1028 (C.D. Cal. 2018) ("For determining an ongoing post-judgment royalty rate, the rate the jury adopted is significant as a starting point, but the court cannot simply apply the jury's pre-verdict royalty award to the post-verdict infringement, without considering the impact of changed circumstances." (citations omitted)).

Thus, the Court imposes a 27.6% running royalty. Infringing sales occurring between entry of the verdict and entry of judgment shall be subject to the running royalty rate, and shall not be subject to enhancement.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

E. Entry of final judgment

Plaintiffs' L.R. 58-7 Memorandum requests pre-judgment interest (*see supra*, Section III.B) and post-judgment interest at a rate equal to the weekly average 1-year constant maturity Treasury yield, as published by the Board of Governors of the Federal Reserve System, for the calendar week preceding the date of the judgment, computed daily to the date of payment, compounded annually. (L.R. 58-7 Memorandum 1-2.)

Defendant maintains its objections presented in its Motion for Judgement as a Matter of Law (JMOL, ECF No. 659), reserves its rights to submit additional objections and motions after final judgment, and notes it objected to Plaintiffs' calculation of prejudgment interest (*see supra*, Section III.B). Defendant further objects to Plaintiffs' proposed accounting and payment procedures as premature, stating if the Court denies Defendant's JMOL, Defendant "will post a supersedeas bond to stay enforcement of the judgment . . . ." (Objections 1.)

Plaintiffs reply that: (1) prejudgment interest should be calculated using the prime rate (*see supra*, Section III.B); (2) the judgment should include procedures for computing and paying ongoing royalties, as a supersedeas bond does not stay execution until a court approves it; and (3) any subsequent JMOL or new trial motions would be untimely and improper. (Final Judgment Reply 1.)

The Court finds that the Treasury bill rate is appropriate for pre-judgment interest. (*See supra*, Section III.B.) The Court further finds that Defendant not having presented any opposition, post-judgment interest shall be calculated according to Plaintiffs' proposal.

Regarding entry of final judgment, the Court finds it efficient to enter judgment with accounting and payment procedures in place. Defendant not having presented any opposition, the Court will enter the procedures proposed by Plaintiffs. The Court will consider any supersedeas bond and corresponding request to stay if and when one is filed.

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: April 2, 2020**

IV. RULING

For the foregoing reasons, the Court **GRANTS-IN-PART** Plaintiffs' Consolidated Post-Trial Motion [ECF No. 655]. Specifically, the following is held:

(1) Plaintiffs are awarded $778,343,501 on the jury verdict for Defendant's infringement from October 18, 2017 through December 12, 2019;
(2) The Treasury bill rate, compounded quarterly, is awarded for prejudgment interest, which shall not apply to the enhancement award;
(3) The damages award is enhanced by 50%; and
(4) A 27.6% running royalty is awarded.

Final Judgment to follow.

IT IS SO ORDERED.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

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CASE NO.: 2:17-cv-07639 SJO-KS **DATE: March 24, 2020**

TITLE: Juno Therapeutics, Inc., et al. v. Kite Pharma, Inc.

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PRESENT: THE HONORABLE S. JAMES OTERO, UNITED STATES DISTRICT JUDGE

Victor Paul Cruz	Not Present
Courtroom Clerk	Court Reporter

COUNSEL PRESENT FOR PLAINTIFFS:	**COUNSEL PRESENT FOR DEFENDANTS:**
Not Present	Not Present

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PROCEEDINGS (in chambers): ORDER RE: DEFENDANT'S MOTION FOR JUDGMENT AS A MATTER OF LAW PURSUANT TO FED. R. CIV. P. 50(B) AND/OR A NEW TRIAL PURSUANT TO FED. R. CIV. P. 59 [ECF No. 659]

[Portions of the parties' briefing filed in support of and in opposition to the motion ruled upon in this Order were filed under seal. The parties are expected to file a joint report within five days of this ruling proposing redactions of any confidential material. If the parties fail to file a joint report, this Order will be publicly issued as-is.]

This matter comes before the Court on Defendant Kite Pharma, Inc.'s ("Defendant" or "Kite") Motion for Judgment as a Matter of Law Pursuant to Fed. R. Civ. P. 50(b) and/or a New Trial Pursuant to Fed. R. Civ. P. 59 ("JMOL") filed on January 21, 2020. (JMOL, ECF No. 659.[1]) Plaintiffs Juno Therapeutics, Inc. ("Juno") and Sloan Kettering Institute for Cancer Research ("SKI") (collectively, "Plaintiffs") filed their Opposition to Defendant's Motion for Judgment as a Matter of Law and/or a New Trial ("Opposition" or "Opp.") on February 10, 2020. (Opp., ECF Nos. 673.[2]) Defendant filed its Reply in Support of a Motion for Judgment as a Matter of Law Pursuant to Fed. R. Civ. P. 50(b) and/or a New Trial Pursuant to Fed. R. Civ. P. 59 ("Reply") on February 24, 2020. (Reply, ECF No. 699.[3]) In setting the post-trial briefing schedule, the Court indicated that it would take the matter under submission following the filing of reply motions. (Order, ECF No. 639 at 5; *see also* Fed. R. Civ. P. 78(b).) For the following reasons, the Court **DENIES** Defendant's Motion for Judgment as a Matter of Law Pursuant to Fed. R. Civ. P. 50(b) and/or a New Trial Pursuant to Fed. R. Civ. P. 59 [ECF No. 659].

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[1] Defendant subsequently filed a Corrected Memorandum in support of its JMOL on February 20, 2020, which the Court has considered in this Order. (ECF No. 692.) Unless otherwise noted, all citations to Defendant's JMOL refer to the Corrected Memorandum, ECF No. 692.

[2] Plaintiffs subsequently filed a Corrected Opposition to Defendant's JMOL on February 10, 2020, which the Court has considered in this Order. (ECF No. 683.) Unless otherwise noted, all citations to Plaintiffs' Opposition refer to the Corrected Opposition, ECF No. 683.

[3] Unless otherwise noted, all citations to Defendant's Reply refer to the sealed Reply, at ECF No. 709.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: March 24, 2020**

I. BACKGROUND

This is a patent infringement action involving U.S. Patent No. 7,446,190 ("the '190 Patent"), titled "Nucleic Acids Encoding Chimeric T Cell Receptors." The '190 Patent issued on November 4, 2008 and incorporates a provisional application filed on May 28, 2002. ('190 Patent Caption.) The claimed invention provides "nucleic acid polymer encoding [] chimeric TCR's [T Cell Receptors] . . . ." ('190 Patent, col. 2:11-14.) The chimeric TCRs encoded by the claimed invention "combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain ("zeta chain portion"), a signaling region from a costimulatory protein such as CD28 with a binding element that specifically interacts with a selected target." ('190 Patent, col. 2:14-18.) These TCRs are designed to "specifically interact[] with a cellular marker associated with target cells," resulting in the stimulation of a T cell immune response to the target cells. ('190 Patent, col. 2:30-36.)

Plaintiffs initiated this action on October 18, 2017, alleging that Defendant infringes the '190 Patent through the use, sale, offer for sale, or importation of one of Defendant's immunotherapy treatments, YESCARTA®. YESCARTA® is described as 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." (Second Amended Complaint ("SAC") ¶ 18, ECF No. 484.) Plaintiffs assert that YESCARTA® infringes the '190 Patent by utilizing nucleic acid polymers encoding chimeric TCRs within the scope of the '190 Patent claims. (SAC ¶ 26.) Defendant, in turn, filed counterclaims seeking declaratory judgments of non-infringement and invalidity of the '190 Patent. (*See generally*, Answer to SAC and Counterclaims, ECF No. 617.)

On October 9, 2018, the Court issued the Claim Construction Order construing, *inter alia*, the following claim term:

Claim Term	Court's Construction
"the amino acid sequence encoded by SEQ ID NO:6"	**Before the Certificate of Correction:** Amino Acids 113-220 of CD28 (starting with lysine (K)) **After the Certificate of Correction:** Amino Acids 114-220 of CD28 (starting with isoleucine (I))

(Claim Construction Order, ECF No. 100.) In relevant part, the Court's Claim Construction Order was based upon the following: (1) Applicants filed Provisional Application No. 60/383,872 and incorporated a journal article identifying "nucleotides 336-660 of CD28"; (2) Applicants subsequently filed a non-provisional patent application incorporating the same language and defining SEQ ID NO:6 in accordance with this description; (3) following approval by the patent

examiner, applicants filed a Request for Continuing Examination ("RCE") noting an error in the presentation of SEQ ID NO:6 and requesting removal of the first four nucleotides, such that the first codon corresponds to isoleucine, amino acid 114 of CD28, rather than lysine, amino acid 113; (4) the Patent and Trademark Office ("PTO") rejected the amended listing as damaged or unreadable; (5) the applicants provided a new copy again reflecting the changes to the presentation of SEQ ID NO:6; (6) the PTO again rejected the filing, for failure to comply with PTO formatting requirements; (7) the applicants for the third time filed an amended sequence listing, however the listing did not reflect the changes to SEQ ID NO:6; (8) the '190 Patent initially issued without the amendments contained in the RCE; (9) in mid-2013, the patentees requested, and the PTO granted, a CoC that altered the definition of SEQ ID NO:6 from the sequence beginning with nucleotide 336 (encoding amino acid 113) of the CD28 protein to the sequence beginning with nucleotide 340 (encoding amino acid 114) of the CD28 protein. (*Id.*)

On December 13, 2019, the jury entered a unanimous verdict in favor of Plaintiffs, finding: (1) Defendant had not proven by clear and convincing evidence that the Certificate of Correction was invalid, (2) Defendant had not proven by clear and convincing evidence that any of claims 3, 5, 9, and 11 of the '190 Patent was invalid for lack of enablement or written description, (3) Plaintiffs proved by a preponderance of the evidence that Defendant's infringement of the corrected claims of the '190 Patent was willful, and (4) Plaintiffs proved by a preponderance of the evidence the damages owed were a $585,000,000 upfront payment, and 27.6% running royalty. (Jury Verdict, ECF No. 594.)

Following the jury's return of the verdict, the Court set a post-trial briefing schedule for both parties and deferred entry of judgment. (Order, ECF No. 639.)

II. LEGAL STANDARDS

A. Judgment as a Matter of Law

The Federal Rules of Civil Procedure provide for the issuance of judgment as a matter of law upon a motion "made at any time before the case is submitted to the jury." Fed. R. Civ. P. 50(a)(2). The Rules further provide that "[i]f the court does not grant a motion for judgment as a matter of law under Rule 50(a), the court is considered to have submitted the action to the jury subject to the court's later deciding the legal questions raised by the motion." Fed. R. Civ. P. 50(b). Moreover, "[n]o later than 28 days after the entry of judgment—or if the motion addresses a jury issue not decided by a verdict, no later than 28 days after the jury was discharged—the movant may file a **renewed** motion for judgment as a matter of law and may include an alternative or joint request for a new trial under Rule 59." Fed. R. Civ. P. 50(b) (emphasis added).

"A Rule 50(b) motion for judgment as a matter of law is not a freestanding motion. Rather, it is a renewed Rule 50(a) motion." *E.E.O.C. v. Go Daddy Software, Inc.*, 581 F.3d 951, 961 (9th Cir. 2009). Thus, "[u]nder Rule 50, a party must make a Rule 50(a) motion for judgment as a matter of law before a case is submitted to the jury," and "[i]f the judge denies or defers ruling

on the motion, and if the jury then returns a verdict against the moving party, the party may renew its motion under Rule 50(b)." *Id.* "Because it is a renewed motion, a proper post-verdict Rule 50(b) motion is limited to the grounds asserted in the pre-deliberation Rule 50(a) motion." *Id.* "Thus, a party cannot properly 'raise arguments in its post-trial motion for judgment as a matter of law under Rule 50(b) that it did not raise in its preverdict Rule 50(a) motion.'" *Id.* (citing *Freund v. Nycomed Amersham*, 347 F.3d 752, 761 (9th Cir. 2003)). Notwithstanding this requirement, "Rule 50(b) 'may be satisfied by an ambiguous or inartfully made motion' under Rule 50(a)." *Id.* (citing *Reeves v. Teuscher*, 881 F.2d 1495, 1498 (9th Cir. 1989)).

A district court can grant a Rule 50 motion for judgment as a matter of law only if "there is no legally sufficient basis for a reasonable jury to find for that party on that issue." *Jorgensen v. Cassiday*, 320 F.3d 906, 917 (9th Cir.2003) (quoting *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 149 (2000)). "In entertaining a motion for judgment as a matter of law, the court may not make credibility determinations or weigh the evidence." *Krechman v. Cty. of Riverside*, 723 F.3d 1104, 1110 (9th Cir. 2013) (citations omitted). The evidence must be viewed "in the light most favorable to the non-moving party, and all reasonable inferences are drawn in that party's favor." *El-Hakem v. BJY Inc.*, 415 F.3d 1068, 1072 (9th Cir. 2005).

B. New Trial

Rule 59(a) provides that "[t]he court may, on motion, grant a new trial on all or some of the issues . . . after a jury trial, for any reason for which a new trial has heretofore been granted in an action at law in federal court." Fed. R. Civ. P. 59(a)(1)(A). "Unlike with a Rule 50 determination, the district court, in considering a Rule 59 motion for new trial, is not required to view the trial evidence in the light most favorable to the verdict. Instead, the district court can weigh the evidence and assess the credibility of the witnesses." *Experience Hendrix L.L.C. v. Hendrixlicensing.com Ltd.*, 762 F.3d 829, 842 (9th Cir. 2014) (citing *Kode v. Carlson*, 596 F.3d 608, 612 (9th Cir. 2010) (per curiam)). "However, a district court may not grant a new trial simply because it would have arrived at a different verdict." *Silver Sage Partners, Ltd. v. City of Desert Hot Springs*, 251 F.3d 814, 819 (9th Cir. 2001) (citing *United States v. 4.0 Acres of Land*, 175 F.3d 1133, 1139 (9th Cir. 1999)). A new trial is appropriate under Fed. R. Civ. P. 59 "only if the jury verdict is contrary to the clear weight of the evidence." *DSPT Int'l, Inc. v. Nahum*, 624 F.3d 1213, 1218 (9th Cir. 2010).

III. DISCUSSION

Defendant moves for judgment as a matter of law on: (A) its written description defense; (B) its enablement defense; (C) its defense that the CoC is invalid; (D) its good-faith defense to willfulness; and (E) the opinion of Plaintiffs' damages expert, Dr. Ryan Sullivan. Defendant also: (F) moves for a new trial based on: (1) the verdict form; (2) Dr. Sullivan's testimony; (3) large figures; (4) the written description instruction; (5) Plaintiffs' IPR statements; (6) Plaintiffs'

introduction of certain evidence; (7) the time limit; and (8) cumulative prejudice. Each ground is addressed below.

A. Written Description

Defendant argues that the '190 Patent claims are invalid for lack of written description as a matter of law. (JMOL 2 (citing *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1350-51 (Fed. Cir. 2010) (*en banc*) (holding adequate description of a genus requires disclosure of either: (1) a representative number of species falling within the genus, or (2) structural features common to the members of the genus so that one of skill in the art can visualize or recognize the members of the genus)).) Defendant further argues that the '190 Patent claims a broad genus that covers an enormous number of functionally-identified CAR constructs. (JMOL 3.) Defendant further argues that the CAR-T field was new and unpredictable when the '190 Patent was filed, and remains unpredictable even today. (JMOL 4.) Similarly, the use of single chain variable fragments ("scFvs") in CARs was also unpredictable. (*Id.*) Because the '190 Patent claims a broad genus, and because the CAR-T field was new and unpredictable, the written description does not satisfy the two-part test presented in *Ariad*. (*Id.*) Specifically, the specification does not adequately describe the two CARs disclosed as examples because it does not disclose a DNA or amino acid sequence, and for one example, does not disclose the amino acid sequence of the scFv. (JMOL 5.) Moreover, even looking outside the specification (which would be improper), no published materials would permit a person of ordinary skill in the art ("POSITA") to identify the scFvs. (*Id.*) Additionally, the two CARs disclosed as examples, even if they were adequately disclosed, would not be representative of the billions of CAR constructs claimed in the '190 Patent. (JMOL 6.) For example, in *AbbVie*, the Federal Circuit determined that there was no evidence demonstrating any antibody described in the patent was structurally similar to the accused product (which was a member of the claimed genus). (JMOL 7 (citing *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285 (Fed. Cir. 2014)).) Similar to *AbbVie*, the scFvs disclosed in the '190 Patent are not representative of the claimed genus, because YESCARTA® and other species encompassed within the genus are structurally and functionally different. (JMOL 8.) Nor does the specification disclose common structural features sufficient to allow a POSITA to visualize or recognize members of the genus. (JMOL 8-9.) Plaintiffs' expert Dr. Brocker's testimony to the contrary was insufficient. He testified only to common structural features (such testimony is insufficient under the law), and he applied the wrong legal standard (first by assuming the scFv portion was not part of the claimed invention, and by conflating the written description and enablement requirements). (JMOL 9-10.)

Plaintiffs respond that Defendant cannot meet its burden of demonstrating the evidence overcoming the presumption of validity is clear and convincing, and undisputed. (Opp. 2.) The record demonstrates scFvs were an old and well-known component of CARs, and the Federal Circuit has already determined scFvs (as a CAR component) were known as early as 1995. (*Id.*

(citing *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005)).) The '190 Patent discloses a novel combination of known elements—a binding element (*i.e.*, scFv), and signaling element (CD28 and zeta chain). (Opp. 3.) At the time the '190 Patent was filed, scFvs were routine and well-known in the CAR field (as demonstrated by papers, witness testimony, and expert witness testimony), thus the law states that the specification should preferably omit routine technology that is well known. (Opp. 4-6.) Specifically, CD19-specific scFvs were shown to be well known in the art, even by Defendant's own witnesses. (Opp. 6.) The '190 Patent additionally provides examples of scFvs that can be used with the invention, and real-world evidence shows that POSITAs did make the three-part CAR claimed in the '190 Patent. (Opp. 7.) Plaintiffs further respond that the Federal Circuit recognized in 1995 that scFvs were a well-known component of CARs, which Defendant itself relied upon to overcome a written description objection during prosecution. (Opp. 8-9 (citing *Capon*, 418 F.3d at 1439 and other authority).) Plaintiffs further respond that Defendant baldly mischaracterizes the '190 Patent's claims as functional genus claims by virtue of their scFv element, but the claims are composition claims reciting a three-part structure. (Opp. 9-10.) Plaintiffs further argue the *Ariad* test is inapplicable here because the test is relevant to novel compounds, not those known in the art. (Opp. 11-12.) Even if relevant, *Ariad* is satisfied because the patent discloses the CAR backbone, two scFvs successfully used with the backbone, additional scFvs, and the CD19 scFv is representative of scFvs in the context of CARs. (Opp. 12.) Defendant's contention that the two examples are not representative is unpersuasive because the claims recite scFvs as part of a CAR, not any possible scFv chain. (Opp. 13.) Plaintiffs further argue that Defendant's argument that Dr. Brocker used the wrong test is forfeited, because it was not raised in Defendant's Rule 50(a) motion. (Opp. 14.) Even if procedurally proper, Defendant misrepresents Dr. Brocker's testimony—he actually testified that single-chain scFvs had been known and were separate from the Sadelain two-part backbone invention. (Opp. 14-15.)

Defendant replies that Dr. Sadelain only made and disclosed two CARs in the '190 Patent, and for those two CARs, the patent does not disclose the structure of the scFv portion. (Reply 1.) Plaintiffs suggest the scFv portion is not the crux of the invention, where the law states that written description is the same whether the claim is to a novel compound or a novel combination of known elements. (*Id.*) Plaintiffs cannot satisfy *Ariad* where the specification discloses only two incomplete examples, each claim covers an enormous number of CARs, the CARs are diverse, the field was new and unpredictable, the two disclosed examples are not representative, and the patent does not describe structural features common to scFvs targeting CD19. (Reply 2-6.) Defendant further replies that knowledge outside the patent cannot substitute for an adequate description of the claims, and *Capon* did not hold there was sufficient written description for the claimed CARs. (Reply 6-7.)

In order for Defendant to succeed on its JMOL, it must show that the *Ariad* test was satisfied by clear and convincing, undisputed evidence. *Ariad* holds that "a sufficient description of a genus

. . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can visualize or recognize the members of the genus. 598 F.3d at 1350 (citations omitted). *Ariad* further recognizes that the inquiry is a highly factual one that "will necessarily vary depending on the context," and that "the level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." *Id.* at 1351. The '190 Patent claims a three-part CAR, where the two-part Sadelain backbone permitted T-cells to proliferate, permitting patients' immune systems to continue targeting tumor cells following a single treatment. The parties' written description dispute centers around the sufficiency of the written disclosure for the third piece of the CAR—a binding element, which is limited to scFvs in the asserted claims.

During trial, both parties presented conflicting evidence for scFvs for both *Ariad* factors. ***First***, Plaintiffs presented evidence and testimony that a representative number of species was disclosed. Plaintiffs highlighted the '190 Patent's disclosure of several scFvs (two directed to PSMA and CD19). Plaintiffs also presented testimony that scFvs were well-known in the art. *See UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629, 648 (E.D. Tex. 2017) ("[W]hen a genus is well understood in the art and not itself the invention but is instead a component of the claim, background knowledge may provide the necessary support for the claim."). Plaintiffs presented testimony and argument that scFvs had been made since at least 1988, and CARs utilized scFvs as binding elements beginning in the early 1990s. Plaintiffs' expert Dr. Brocker testified that a paper he authored in 1993 noted the interchangeability of scFvs in CAR design. A separate paper authored by Krause and Finney stated scFvs had been successfully used as the binding element in CARs in 1998. Plaintiffs further presented testimony that the '190 Patent disclosed the Orlandi method, which could be used as a "cookbook" to make any desired scFv. Plaintiffs further presented testimony that a dishwasher from Dr. Brocker's lab in fact used Orlandi's method to make an scFv that Dr. Brocker used in his research.

Second, Plaintiffs presented evidence and testimony that a POSITA would be able to recognize the members of the genus, based on the disclosure of structural features of scFvs. Plaintiffs presented evidence that the '190 Patent describes two specific scFvs that share common structural features. As discussed in the preceding paragraph, Plaintiffs also presented evidence that scFvs were well known in the art, including the common structural features they share. In light of the testimony presented, including the disclosures within the four corners of the patent, Defendant cannot satisfy its burden of showing the *Ariad* test elements were undisputed.

That Defendant disputes Plaintiffs' testimony and evidence, or presented its own conflicting evidence, is not grounds for JMOL. *See Krechman*, 723 F.3d at 1110 (court may not make credibility determinations or weigh the evidence during JMOL).

Thus, the Court denies Defendant's JMOL on written description.

B. Enablement

Defendant argues the '190 Patent does not enable the full scope of the claims as a matter of law because the art was nascent and unpredictable, the claims' structural limitations cover an untold number (millions of billions) of constructs, only a subset of those constructs bind to a particular target (but the '190 Patent does not disclose which), and the effective constructs must be discovered via screening. (JMOL 11-13 (citing *Wyeth & Cordis Corp. v. Abbott Labs.*, 720 F.3d 1380 (Fed. Cir. 2013); *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149 (Fed. Cir. 2019)).) Regarding screening, Plaintiffs presented no testimony regarding the effort this would take in the 2002 timeframe. (JMOL 13.) Defendant's expert, Dr. Garcia testified that making and testing a single scFv could take months to more than a year. (*Id.*) Juno's efforts to create a human scFv for CD19 demonstrate the time and effort required, where Juno screened one billion scFvs to identify three candidates for use in a CAR. (*Id.*) Although Plaintiffs' expert Dr. Brocker testified that the synthesis and testing were so easy that a dishwasher could perform them, the mere fact that those steps were required for claims covering a large number of compounds in an unpredictable field demonstrates that the claims were not enabled. (JMOL 14.)

Plaintiffs respond that Defendant cannot demonstrate that it proved enablement by clear and convincing, undisputed evidence. (Opp. 15.) Specifically, Defendant did not dispute the '190 Patent explains how to make and test the two-part Sadelain backbone, it challenges the third element of scFvs, which were not a new and unpredictable field. (Opp. 15-16.) Dr. Brocker testified that making and testing scFvs was not more than standard laboratory procedure, and the Sadelain backbone has worked with every scFv with which it was tested. (Opp. 16.) Dr. Garcia's testimony to the contrary was generalized and rebutted by Dr. Brocker's testimony and other evidence. (Opp. 17.)

Defendant replies that Plaintiffs' argument addresses only whether a POSITA could make a single embodiment, but the correct legal inquiry is the level of experimentation required to practice the full claim scope. (Reply 8.) Defendant argues that Plaintiffs started with a pool of a billion scFvs to identify only 60 that bound to CD19, Plaintiffs have no evidence that functioning of scFvs in the CAR field was predictable in 2002, Plaintiffs point only to generic techniques to produce an scFv, Plaintiffs do not rebut Dr. Garcia's testimony that making and testing a single functional scFv for a CAR could make months, if not years, with a success rate of 25%, and Dr. Sadelain's testimony that he made up to 30 functional CARs with different scFvs after filing his patent did not disclose the time and effort (or failures) relating to those CARs. (Reply 8-9.)

The enablement inquiry turns on whether a POSITA would have to engage in undue

experimentation to make and use the claimed invention. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). At trial, Plaintiffs presented evidence and testimony that a POSITA would not. Specifically, Plaintiffs presented testimony including that in 2002, scFvs were not a new and predictable field, that the steps to create an scFv were straightforward, that the Sadelain backbone has been successfully used with a number of scFvs, that Plaintiffs' expert did not know a single scFv that would not work with the Sadelain backbone. Defendant's arguments to the contrary were appropriate for cross-examination, not for JMOL. Drawing all inferences in Plaintiffs' favor, there was a legally sufficient basis for the jury's verdict.

Thus, the Court denies Defendant's JMOL for enablement.

C. CoC

Defendant argues that the CoC is invalid as a matter of law. Although the question of whether a clerical or typographical error (or how to correct the error) was clearly evident is a question of fact, judgment as a matter of law is warranted when the material facts are undisputed. (JMOL 14-15 (citing *Cent. Admixture Pharm. Servs., Inc. v. Advanced Cardiac Sols. P.C.*, 482 F.3d 1347 (Fed. Cir. 2007)).) Here, no reasonable juror could have found the CoC valid because a POSITA would not know which of two possible costimulatory sequences was claimed—amino acids 113-220 (originally-issued patent), or amino acids 114-220 (as amended by CoC). (JMOL 15.) Defendant argues none of the original claims, specification, or cited publications unambiguously point to disclosure of amino acids 114-220. (JMOL 15-16.) The specification lists both sequences and does not disclose a clearly evident correction and clearly evident error. (JMOL 16-17.) The prosecution history is also ambiguous, because although the patentee submitted an updated sequence listing with the RCE, the scientific explanation provided by patentee for correcting the error did not indicate a clear error as to SEQ ID NO:6. (JMOL 17.) Specifically, there was no clear error because the sequence in SEQ ID NO:6 need not be divisible by three, the stop codon at the end of the sequence is irrelevant to whether the first encoded amino acid is correct, the RCE's sequence merely identified an inconsistency from original SEQ ID NO:6, the RCE's statement that the correction conformed to the construct used in the examples is incorrect because the specification still described one example as beginning with nucleotide 336 (corresponding to amino acid 113), not nucleotide 340 (corresponding to amino acid 114). (JMOL 17-19.) Patentee's submissions containing the disclosure of amino acids 114-220 were rejected for formal defects, until ultimately the 336-663 nucleotide listing was reintroduced. (JMOL 19-20.) Plaintiffs did not introduce evidence creating a genuine dispute of material fact, based on the foregoing. (JMOL 20.) Instead, Plaintiffs' evidence impermissibly relied on material outside the intrinsic record, such as Dr. Schuetz, a third party, who requested Dr. Sadelain's complete sequence (not disclosed in the patent) before determining the error, Plaintiffs' expert Dr. Quackenbush did not give import to disclosures unfavorable to his opinion that amino acids 114-220 were intended, Dr. Quackenbush's opinions

contradicted the prosecution history, although Plaintiffs argued Dr. Sadelain only worked on CARs beginning with amino acid 114 (not disclosed in the intrinsic record), an article that formed the basis for the patent filing contained inconsistencies (including disclosure of sequences starting with both 113 and 114). (JMOL 20-23.) The Court already rejected Plaintiffs' arguments during claim construction, and the relevant evidence at trial confirmed the Court's findings, thus the Court should enter JMOL that the CoC is invalid. (JMOL 23.)

Plaintiffs respond that there were material factual disputes for the jury to decide, and Plaintiffs presented the testimony of Dr. Quackenbush that a POSITA would have understood SEQ ID NO:6 to begin at amino acid 114 (based on the prosecution history, including the RCE). (Opp. 18.) Defendant cites no cases finding a CoC invalid where the prosecution history contains a request for the correction in the CoC. (Opp. 19.) Defendant likewise points to scattered references to nucleotides encoding amino acid 113 and an extraneous sequence beginning with lysine, but these references do not serve as clear and convincing evidence (nor is it undisputed) of the invalidity of the CoC, where Plaintiffs presented evidence and testimony to the contrary. (Opp. 20.) Specifically, Dr. Quackenbush explained that the RCE showed four extraneous nucleotides crossed out at the beginning of corrected SEQ ID NO:6, and further explained why the correction was necessary. (Opp. 20-21, 22-23.) Dr. Quackenbush further testified that the '190 Patent itself would have indicated to a POSITA the four initial nucleotides should be removed. (Opp. 21-22.) Moreover, Defendant's argument is forfeited, because it was not raised in its Rule 50(a) motion, and its arguments regarding the correctness of the RCE are irrelevant to the CoC inquiry. (Opp. 23.) Plaintiffs further respond that Defendant's criticisms of Dr. Quackenbush (besides being improper because they were also not raised in their Rule 50(a) motion), were proper considerations for cross-examination, not JMOL. (Opp. 24-25.) Plaintiffs further respond to the criticisms by responding that Dr. Quackenbush did not ignore certain evidence, nor did he rely on extrinsic evidence. (Opp. 27.) Plaintiffs further respond that Dr. Schuetz's testimony that he discovered a mistake based on information outside the intrinsic record does not mean that Dr. Schuetz would not have identified an error based on the intrinsic record, Dr. Bot admitted he did not review the RCE or prosecution history in determining SEQ ID NO:6 began with amino acid 113, and Dr. Junghans' testimony that he made a CAR using amino acids 113-220 is irrelevant because he testified he had not read the '190 Patent, let alone the full intrinsic record at that point. (Opp. 27.)

Defendant replies that a CoC is improper for broadening the scope of a claim, where SEQ ID NO:6 did not contain a correctable error. (Reply 9-10.) Defendant further replies that the claims specified that SEQ ID NO:6 began with amino acid 113. (Reply 10.) The RCE does not resolve any purported ambiguity because the RCE was superseded by the patent prosecutor filing substitute sequence listings showing SEQ ID NO:6 to begin with amino acid 113, a POSITA would not uncritically accept the statements in the RCE, and the RCE does not show the original sequence had a clearly evident error. (Reply 11-12.) Dr. Quackenbush's testimony contradicts

the intrinsic record and the Court's claim construction ruling. (Reply 12.) Defendant further replies that real-world evidence, such as MSK's failure to notice the error for four and a half years, Dr. Bot's and Dr. Junghan's interpretations as beginning with amino acid 113, and Dr. Schuetz's tainted testimony as a result of meeting with counsel, weighs against such a finding. (Reply 13.)

For Defendant to prevail on its JMOL finding the CoC invalid, Defendant must show there was no legally sufficient basis for a reasonable jury to find in its favor. *Jorgensen*, 320 F.3d at 917. "Invalidating a certificate of correction for impermissible broadening therefore requires proof of two elements: (1) the corrected claims are broader than the original claims; and (2) the presence of the clerical or typographical error, or how to correct that error, is not clearly evident to one of skill in the art." *Central Admixture Pharm. Servs., Inc. v. Adv. Cardiac Sols., P.C.*, 483 F.3d 1347, 1353 (Fed. Cir. 2007). The Court previously ruled on the first element when it determined that the CoC altered the starting amino acid encoded by SEQ ID NO:6. (*See* Markman Order, ECF No. 100, at 17 (starting at amino acid 113 before the CoC, amino acid 114 after the CoC).) The Court previously declined to rule on the second element when it denied Defendant's motion for summary judgment of noninfringement, finding that "a clear and genuine dispute of fact" existed regarding whether "the error and correction would have been clearly evident to a POSITA examining the record." (Summary Judgment Order, ECF No. 246, at 7.) At trial, both parties presented extensive testimony and evidence regarding the validity of the CoC. Now, in order for Defendant to prevail on its JMOL, it must show that despite Plaintiffs' extensive testimony and evidence, there was no sufficient basis for the jury's finding.

The Court finds that Plaintiffs presented sufficient testimony on which a jury could base its determination. It is undisputed that during patent prosecution, Plaintiffs sought an RCE in which it stated that "an error occurred in the presentation of Seq. ID No. 6," and that "the amino acids of the CD28 Sequence (144-220 contained a typographical error and should have been 114-220)." (RCE, Sept. 4, 2007.) Plaintiffs also submitted an amended SEQ ID NO:6 crossing out the first four nucleotides.

caaaattgaa

(RCE, Sept. 4, 2007.) The amended listing, and subsequent attempted amendment were both rejected for improper formatting. The third attempt reverted back to the original SEQ ID NO:6. Plaintiffs' expert Dr. Quackenbush then testified that as a POSITA, he understood the intrinsic record (including the '190 Patent claims, specification, and prosecution history) to show the uncorrected SEQ ID NO:6 solely as a result of a mistaken file submission, and that the RCE's unambiguous correction clearly showed the amino acid sequence beginning at 114. (Tr. 1149:7-1152:10.) Dr. Quackenbush further testified that the RCE stated that the first codon is "att,"

which corresponds to a sequence starting at position 114. (Tr. 1151:8-18.) Although there was additional testimony and evidence supporting Plaintiffs' position, the Court finds that at least these specific examples provide a basis for the jury to have concluded the CoC was valid.

Defendant raises a number of points as to the merits of Plaintiffs' arguments, such as various citations in the specification to a sequence beginning at the equivalent of amino acid 113, the ambiguity of the RCE and subsequent amended submissions, the inadequacy of testimony by Dr. Schuetz, the bias of Dr. Schuetz, Dr. Quackenbush's failure to properly consider certain aspects of the patent and the prosecution history, an article by Dr. Sadelain, Plaintiffs' failure to notice the error for four and a half years, and the conflicting testimony of Dr. Bot and Dr. Junghans. But in light of the totality of the testimony presented, the Court cannot determine that there did not exist a genuine issue of fact whether a POSITA would have recognized a clearly evident error and solution, based on the intrinsic record of the '190 Patent. *See Krechman*, 723 F.3d at 1110 ("In entertaining a motion for judgment as a matter of law, the court may not make credibility determinations or weigh the evidence."); *see also El-Hakem*, 415 F.3d at 1072 (holding the evidence must be viewed "in the light most favorable to the non-moving party, and all reasonable inferences are drawn in that party's favor.").

Thus, the Court denies Defendant's JMOL for a finding that the CoC is invalid.

D. Willfulness

Defendant argues Plaintiffs failed to show Defendant launched YESCARTA® without doubts about its validity or any notion of a defense. (JMOL 24.) Plaintiffs argued Defendant failed to present witnesses stating they did not believe Defendant infringed, but Defendant was not permitted to present such witnesses because it asserted privilege. (*Id.*) Plaintiffs also focused on communications between Dr. Sadelain with Dr. Rosenberg (a physician at the National Cancer Institute), Dr. Belldegrun's communications with Dr. Dash, and Defendant's filing of an IPR in 2015. (*Id.*) However, these events took place years before Gilead acquired Defendant and decided to launch YESCARTA®. (*Id.*) When sued, Defendant promptly raised the defenses it raised at trial, and no evidence at trial suggested Defendant lacked a good-faith belief in its defenses. (*Id.*)

Plaintiffs respond that Defendant cannot show no reasonable jury could have concluded Defendant's infringement was willful. (Opp. 28.) Defendant cannot do this where Plaintiffs introduced evidence that Defendant knew its collaborators copied the Sadelein backbone, tried to license the '190 Patent unsuccessfully, tried to invalidate the '190 Patent unsuccessfully, and then to commercialize YESCARTA® anyway. (*Id.*) The law considers conduct pre-dating infringement as a factor. (Opp. 28-29.) Dr. Bot's excluded homology analysis was excluded because it was superseded by other events, including advice of counsel and Defendant's

licensing and IPR attempts, which rendered the evidence irrelevant, or at the very least, prejudicial. (Opp. 29.) The Court precluded no other percipient witness testimony. (*Id.*) On Defendant's litigation defenses, Defendant forfeited this argument by not raising it in its Rule 50(a) motion, but even if not, proof of an objectively reasonable litigation defense is no longer a defense to willful infringement. (Opp. 29-30.) Even if it was, Defendant did not offer any evidence of actual reliance. (*Id.*)

Defendant replies that the following undisputed facts foreclose a finding of willful infringement: no infringing conduct before the launch, Gilead (not Drs. Belldegrun or Jakobovitz) decided to launch YESCARTA®, and Plaintiffs offered no evidence regarding Gilead's willful infringement. (Reply 13-14.) These facts do not support a finding of willful infringement because the inquiry focuses on the mind of the infringer at the time of infringement. (Reply 14.)

For Defendant to prevail of its JMOL finding no willful infringement, it must show that no reasonable jury could have concluded that Defendant acted despite a risk of infringement known or so obvious that it should have been known to the accused infringer. The conduct is required to be wanton, malicious, or in bad faith. *See SRI Int'l, Inc. v. Cisco Sys., Inc.*, 930 F.3d 1295 (Fed. Cir. 2019) (clarifying the standard for willful infringement set forth in *Halo Elecs., Inc. v. Pulse Elecs., Inc.,* 136 S. Ct. 1923, 1932 (2016)). The infringer's state of mind is determined at the time of infringement, but conduct predating infringement may be relevant to determine the infringer's state of mind at the time of infringement. *Polara Eng'g Inc. v. Campbell Co.*, 894 F.3d 1339, 1353-54 (Fed. Cir. 2018).

The Court finds that Plaintiffs presented sufficient evidence of willfulness that a reasonable jury could find in its favor. Plaintiffs presented evidence and testimony that Defendant knew that Dr. Rosenberg from National Cancer Institute ("NCI") copied Dr. Sadelain's backbone, as demonstrated by Defendant's attempting to be the first to license and to invalidate the '190 Patent. Plaintiff's fact witness Dr. Dash testified that Dr. Belldegrun was so desperate to pursue a license to the '190 Patent that he appeared at her office, despite not having a meeting. Dr. Jakobovitz similarly testified that Dr. Belldegrun met with Plaintiffs in an attempt to license the '190 Patent. Plaintiffs further argued that Defendant's filing of the IPR against the '190 Patent demonstrated the importance of the '190 Patent to Defendant. In light of at least these examples of testimony and evidence, a reasonable jury could have entered a finding of willfulness.

Defendant's argument that it was precluded from introducing fact witness testimony relating to its belief of non-infringement does not change this outcome. Dr. Bot's homology analysis, performed in 2012, was excluded as having little relevance to the determination of willfulness in 2017, where Defendant subsequently obtained advice of counsel, attempted to license the '190 Patent, and filed an IPR against the '190 Patent. Thus, exclusion of Dr. Bot's testimony was not because Defendant claimed privilege over its advice of counsel. It was because Dr. Bot's

analysis bore little relevance to the willfulness determination where it was superseded by other events, and what little relevance it did bear was outweighed by prejudice.

Finally, Defendant's argument that Gilead, not Defendant, was the one who decided to launch YESCARTA® does not provide a sufficient basis for finding that no reasonable jury could have determined Defendant willfully infringed YESCARTA®. The testimony regarding Dr. Rosenberg, in addition to the testimony of Dr. Dash, Dr. Sadelain, Dr. Belldegrun, and Dr. Jakobovitz weighs in favor otherwise.

Thus, the Court denies Defendant's JMOL for a finding of no willful infringement.

E. Sullivan

Defendant argues Plaintiffs presented no legally or factually sufficient basis for damages, and the proper award is the opinion Defendant's damages expert, Dr. Mohan Rao, would have presented at trial but was precluded from doing so by the Court's *Daubert* Order. (JMOL 25.) Dr. Sullivan testified his opinion was based upon a license agreement ("MSK License") between Juno and Memorial Sloan Kettering[4] ("MSK"), which contained a royalty rate up to 7.25%, $6.9 million upfront payment, and potential milestone payments of $3.35 million through first approval. (JMOL 26.) Juno and MSK also entered into a Side Letter Agreement, which set a maximum stock appreciation success fee of $150 million. (*Id.*) Defendant argues Dr. Sullivan's use of the success fee was not tied to use of the '190 Patent, where the Side Letter Agreement reflected a broad collaboration between an academic institution and a startup. (JMOL 27.) Dr. Rao testified that success fees are based on a relationship with an extensive collaboration, not between two mature pharmaceutical companies. (*Id.*) Even if the success payment was proper, Dr. Sullivan did not explain what portion should be allocated to the '190 Patent. (JMOL 27-28.) Moreover, the expected value of the success fee depended on the parties' expectations about Juno's future appreciation, and Juno's auditors assigned the success fee a de minimis value. (JMOL 28.) Dr. Sullivan improperly substituted the appreciation of Defendant's stock for Juno's stock, and improperly opined Defendant would have agreed to pay the stock success fee. (JMOL 29.) The evidence showed that Defendant's and YECARTA®'s value was driven by factors other than the patented construct, including clinical trials, manufacturing, lymphodepletion, physician outreach, and future therapies. (JMOL 29-30.) Defendant further argues the 27.6% running royalty does not apportion, where Dr. Sullivan did not value other essential inputs, such as manufacturing, business risks, or significant features. (JMOL 31.) Defendant further argues Dr. Sullivan's upward adjustments (markup from previous Novartis license, competitor adjustment) were illogical and unsupported, including for his adjustment to the success fee. (JMOL 31-33.) Dr.

[4] MSK was dismissed as a party, but the Court did not preclude Plaintiffs from arguing that MSK would have been present at a hypothetical negotiation.

Sullivan's opinion departed from comparable licenses and rendered his opinion out of line with economic reality. (JMOL 33-34.)

Plaintiffs respond that Dr. Sullivan's analysis was proper, and Defendant continues to rely on its own interpretation of the MSK License to argue no reasonable jury could have found in Plaintiffs' favor. (Opp. 31-32.) The MSK License (via Side Letter) provided a $150 million payment based upon a multiple of initial equity value, and witnesses testified the success payment was important, intended to provide upside without increasing equity burden, and has actually been paid. (Opp. 31-32.) Unlike the stock swap which was excluded by the Court, the success payment does not exchange Juno's shares for Kite's shares. (Opp. 33.) Apportionment was built into the comparable license framework, and even if not, Dr. Sullivan testified that the success payments would have been triggered solely off the $6.2 billion valuation for YESCARTA® at the time of the hypothetical negotiation. (*Id.*) Plaintiffs further respond that the Court already rejected Defendant's challenges to Dr. Sullivan's adjustments, and even if not, these challenges are inappropriate for a JMOL, which does not permit a challenge to the sufficiency of the evidence. (Opp. 34.) Moreover, the evidence at trial supported Dr. Sullivan's adjustments: (1) the first adjustment (hypothetical negotiation between competitors, not collaborators) uses a ratio, which was supported by the testimony of Dr. Dash and Dr. Belldegrun (Opp. 35); (2) the second adjustment (hypothetical negotiation on the eve of launch) accounted for the greater anticipated economic harm Juno expected due to Defendant being on the eve of launch, which was supported by the testimony of Dr. Dash, Dr. Dulac, Dr. Gilbert, Dr. Belldegrun, and Mr. Bishop (Opp. 35-36.) Plaintiffs further respond that the jury's damages award did not violate apportionment requirements, because apportionment is built into the comparable-license approach, and Defendant's authority addresses multi-component electronic devices or software programs, not biotechnology. (Opp. 36-37.) Although Defendant touted other components as drivers of value (lymphodepletion, manufacturing), Plaintiffs introduced contradicting evidence (lymphodepletion leading to higher toxicities, first-generation manufacturing process), based on which the jury could have concluded these other components added little overall value to YESCARTA®. (Opp. 37-38.)

Defendant replies that the damages award is not apportioned because the '190 Patent is only one component of YESCARTA® therapy and does not account for a complex manufacturing process. (Reply 15.) The superiority of Juno's manufacturing and lymphodepletion regimen for JCAR017 is not relevant to whether Defendant's processes have contributed to demand. (*Id.*) Apportionment was not built into Dr. Sullivan's analysis, where he did not use the same license rate as comparable license agreements, and Plaintiffs presented no evidence that Defendant would have been willing to pay the success fee for a naked license to the '190 Patent. (Reply 16-17.) Moreover, there was no evidence tying the success fee to the '190 Patent, as the payments consistent of various other components. (Reply 17.) Defendant further replies that the success fee was improper because Dr. Rao's testimony that a success fee would not be part

of a negotiation between two companies was unrebutted, the success fee was not apportioned to the '190 Patent, there was no evidence to support the appropriateness of transfer of the equity-based fee to a different company at a different time, and the 30-fold increase in Defendant's stock resulted from factors other than the '190 Patent. (Reply 18.) Defendant further replies that Dr. Sullivan's adjustments were unreliable because they resulted in Defendant paying five times as much as Novartis, Juno did not expect competing for a significant part of the patent term, and the adjustment to the success fee was unjustified. (Reply 18-19.)

Regarding the success payment, the Court already ruled that Dr. Sullivan's testimony regarding the $150 million success payment was permissible. Unlike the stock swap that the Court excluded, the success payment did not substitute the shares of one company for another. Instead, the success payment was based on Dr. Sullivan's opinion that the parties at the hypothetical negotiation would have agreed to the term based on the inclusion of the term to the MSK License (via the Side Letter), and based on the parties' consideration of the $6.2 billion valuation of YESCARTA®. That Defendant disagreed with the inclusion of the success payment was a theory presented to and, based on the verdict, rejected by the jury.

Regarding apportionment (of both the licensing rate and success payment), the Federal Circuit has held that apportionment is built into the comparable license framework. *Commonwealth Sci. & Indus. Research Org. v. Cisco Sys.*, 809 F.3d 1295, 1303 (Fed. Cir. 2015). However, even assuming not, Plaintiffs presented testimony and evidence regarding the importance of the '190 Patent to YESCARTA®, and to Defendant's overall business. Specifically, Defendant tried unsuccessfully, multiple times, to develop non-infringing alternatives. Defendant's own witnesses (for example, Dr. Komanduri) likewise testified to the importance of the '190 Patent's CAR construct to CAR-T therapy. That Defendant argued other factors contributed to the success of YESCARTA® does not as a matter of law render the conclusion that apportionment is required, especially where Plaintiffs introduced conflicting testimony regarding the importance of the '190 Patent to YESCARTA®. Plaintiffs' damages testimony properly considered apportionment, and there was thus a legally sufficient basis for the damages award by the jury.

Regarding Dr. Sullivan's adjustments, the Court already previously rejected Defendant's argument that they were improper. Dr. Sullivan testified that he performed two adjustments, one to account for the fact that the MSK License involved parties who would want to collaborate, whereas the hypothetical negotiation involved two commercial competitors less likely to be agreeable. The second adjustment accounted for Plaintiffs allowing a commercial competitor to enter the marketplace with a competing product before them. The Court finds that the testimony at trial provided a legally sufficient basis for the jury to enter Plaintiffs' damages award, including enhancements.

Thus, the Court denies Defendant's JMOL regarding Dr. Sullivan.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: March 24, 2020**

F. New Trial

1. Verdict Form

Defendant argues that in closing argument, it used a version of the verdict form that specified the period for the upfront payment should extend through trial. (JMOL 36.) Defendant asked the jury to disregard Plaintiffs' damages requests, as Plaintiffs requested damages extending beyond trial. (JMOL 36-37.) When Plaintiffs pointed to the term of upfront payment reflected in the form, the Court stated Defendant's verdict form was different from the one the Court would provide to the jury, and the Court-provided verdict form did not include the limitation for the upfront payment through trial. (JMOL 37.) Defendant argues it was prejudiced because it could not present a payment number for damages past trial, and its credibility was tarnished. (JMOL 37-38.)

Plaintiffs respond that Defendant knew or should have known that it was using an incorrect version of the verdict form. (Opp. 38.) The Court repeatedly denied Defendant's requests to: (1) limit Plaintiffs' evidence and testimony during trial regarding the upfront payment to the time period through trial, and (2) revise the verdict form to include language limiting the upfront payment through trial. (Opp. 38-39.) The Court at every turn denied Defendant's requests, and Defendant itself had received at least five versions of the verdict form omitting the language. (Opp. 39.) It was thus unreasonable for Defendant to believe that the Court, after consistently rejecting Defendant's request throughout trial and earlier versions of the verdict form, would have accepted Defendant's request in a later verdict form without any comment or explanation on the record. (*Id.*) As the Court stated on the record, Defendant used the verdict form without first clearing it with the Court, and the jury was provided with the verdict form that was approved by the Court on the record with both parties. (*Id.*) Moreover, Defendant witnessed Plaintiffs arguing from the correct verdict form (that was displayed on multiple monitors at Defendant's counsel's table), yet Defendant remained silent regarding the verdict form (it was Plaintiffs who pointed out Defendant's use of the wrong form). (Opp. 39-40.) Plaintiffs further respond that there was no prejudice, where the Court had consistently denied Defendant's requests to limit damages through trial, and Defendant's trial presentation never deviated from its view that the upfront payment should be prorated. (Opp. 40.) Moreover, Defendant did present Dr. Rao's upfront payment that was not prorated—$88 million. (*Id.*)

Defendant replies that it used the form it received, which included language it had previously requested. (Reply 19.) The Court's rulings throughout trial did not reject Defendant's request to limit damages through trial. (*Id.*) The parties discussed changes with the Court on the morning of December 11, and the form distributed included the changes discussed that morning, as well as a change to the term of upfront payment. (Reply 20.) The Court also incorporated other

changes without comment on the record, including two agreed-upon changes and the order of questions presented. (Reply 20.) Defendant was prejudiced because it did not suggest to the jury to use the $88 million upfront payment, although the figure was noted. (Reply 20-21.) Defendant also notes its credibility was harmed by criticizing Dr. Sullivan's upfront payment. (Reply 21.)

As a preliminary matter, the Court notes that it has already ruled upon Defendant's motion for a new trial based on the verdict form. First, the Court ruled on Defendant's oral motion for a mistrial on the record:

> Mr. Dane, you used the verdict form without clearing it first with the Court. So I just want to make sure that is clear. And this – the verdict form that is being given to the jury today is the verdict form that was initially approved . . . by the Court on the record.

(Tr. 1543:18-24.) Second, the Court provided further explanation in a written order following trial. (Order, ECF No. 584.) Specifically, the Court found the motion for mistrial did not bear merit because: (1) the Court's ruling on the record was clear, (2) the verdict form provided to the jury was consistent with the Court's ruling, and (3) any error was not prejudicial to Defendant where its damages expert consistently argued damages should be limited through trial, and (4) removal of the express limitation of damages through trial did not preclude the jury from entering the award argued by Defendant's counsel. (Order, ECF No. 584, at 2-3.)

Nevertheless, the Court once again addresses Defendant's request. On December 10, 2019, the Court heard arguments from both parties regarding the proposed verdict form. One issue was whether Question 5a (regarding the upfront payment for damages) should include a note expressly limiting damages through the end of trial. Defendant, who argued throughout trial the upfront payment should be prorated through the end of trial, requested inclusion of the language. Plaintiffs, who argued throughout trial the upfront payment should not be pro-rated, opposed Defendant's request. The Court distributed an updated verdict form at the end of December 10, 2019, which did not include the limitation. On December 11, 2019, the Court noted Plaintiffs had submitted an updated jury verdict form. (Tr. 1321:13-14; *see also* ECF No. 554.) The form did not include the limitation. Each party made an unopposed request to the verdict form unrelated to the limitation. (Tr. 1321:14-1322:8 (requesting changes re party names and willful infringement).) The Court granted both modifications to Plaintiffs' updated jury verdict form. (Tr. 1322:9-12.) Plaintiffs' updated jury verdict form, including the two unopposed modifications, was the form provided to the jury for deliberation.

In light of these facts, the Court finds that its ruling on the record was clear and unambiguous. Plaintiffs' updated jury verdict form, with the two unopposed modifications, was the final verdict

form. Although there appears to be some confusion as to the potential distribution of a different version,[5] Defendant was at least on inquiry notice that what it believed to be the final verdict form was incorrect, because: (1) the Court permitted Dr. Sullivan to testify to an un-prorated upfront payment during trial, (2) the Court never granted Defendant's request to include the limitation on the record, (3) the Court's previous revisions to the verdict form without comment in the record were for non-substantive, unopposed, changes, (4) in addition to the two proposed forms provided by the Court on December 10, Plaintiffs sent an additional two proposed forms to Defendant, none of which included the limitation, (5) Defendant received Plaintiffs' updated jury verdict form (omitting the language) the morning of December 11, (6) Plaintiffs' updated verdict form had only two unopposed modifications incorporated on the record, (7) Defendant had the opportunity to see Plaintiffs utilize a different verdict form, (8) Defendant had a full day to verify the correct form because it received the form on December 11, but did not use it during its closing argument until December 12, and yet (9) as noted on the record, Defendant did not confirm the final verdict form with the Court before using it.

Moreover, Defendant was not prejudiced, where it presented the same damages theory throughout trial. Removal of the limitation did not preclude the jury from awarding Defendant a pro-rated upfront payment. Defendant referenced what its expert used as the full upfront payment ($88 million), so the jury was aware what amount they could award, if they agreed with Defendant. (Tr. 1502:17-23 ("For the upfront payment, he used the $88 million that potentially could have been paid over the whole term of the Novartis license . . . , and then he prorated it . . . . And that's proper to prorate it because of the limited period of damages.").); *see also Ruvalcaba v. City of Los Angeles*, 167 F.3d 514 (9th Cir. 1999) (relief warranted only where prejudice results). As to Defendant's argument that its credibility was tarnished, the Court notes that Defendant's counsel's arguments regarding the entirety of its damages case (including comparable license analysis, upfront payment, reasonable royalty, revisiting testimony of Dr. Sullivan and Dr. Rao) totaled 11 minutes, out of the 142 minutes Defendant argued.[6] Thus, Defendant's showing of the verdict form during a portion of the 11 minutes, out of 142 minutes of closing argument, was minimal. While the Court does not believe Defendant's use of the verdict form caused any prejudice, any prejudice was minimal considering the minimal use of the form, when compared to the entirety of Defendant's closing argument.[7,8]

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[5] Plaintiffs state that contrary to Defendant's assertion, they never received an incorrect version of the verdict form prior to closing arguments. However, given Defendant's counsel's declarations, the Court assumes for purposes of this Order that Defendant received an incorrect version of the verdict form.

[6] The Court's records indicate Defendant's counsel's closing argument on December 11 spanned 1:59pm (Tr. 1417:15) – 3:29pm (Tr. 1465:7), and on December 12 spanned 8:45am (Tr. 1475:5) – 9:37am (Tr. 1506:1). Counsel's damages argument on December 12 spanned 9:26am (Tr. 1498:24) – 9:37am (Tr. 1506:1).

[7] The Court notes the jury, while sending notes on other issues, did not send a note requesting clarification regarding the jury verdict form.

[8] The Court notes its view that Defendant's use of the incorrect verdict form was minimal and no more prejudicial than other events during Defendant's closing, such as Defendant presenting a slide listing its own witness as a

Thus, the Court again denies Defendant's motion for a new trial based on the verdict form.

2. Sullivan's Testimony

Defendant argues Plaintiffs introduced testimony about future harms not disclosed in Dr. Sullivan's report. (JMOL 38.) Dr. Sullivan was limited to past damages (not future anticipated harm), as the Court had limited Dr. Sullivan to testifying that his upfront payment was for harms realized at the hypothetical negotiation, not any future anticipated harm. (JMOL 38-39.) Dr. Sullivan then testified the $585 million upfront payment necessarily applied through the term of the '190 Patent, thus his conflicting opinions about whether his proposed royalty fully compensates for future harms are irreconcilable and provide an improper basis for the jury's award. (JMOL 39-40.) Dr. Sullivan's testimony regarding his royalty compensating for future harms prejudiced Defendant, who would otherwise have presented testimony regarding anticipated non-infringing constructs. (JMOL 40.)

Plaintiffs respond that the Court already rejected Defendant's argument that Dr. Sullivan's testimony exceeded the scope of his expert report. (Opp. 41.) Plaintiffs further respond that Dr. Sullivan testified consistent with his opinion that the upfront payment is for harms realized at the hypothetical negotiation, not compensation for future harm. (*Id.*) Plaintiffs further respond that Dr. Sullivan did not give conflicting opinions on lost profits—Defendant conflated the hypothetical negotiation with post-trial relief. (*Id.*) Plaintiffs further respond that Defendant was not prejudiced by not presenting anticipated non-infringing constructs, because Defendant's non-infringing alternatives theory was so weak and speculative that Defendant withdrew its theory before trial. (Opp. 41-42.)

Defendant replies that Plaintiffs did not identify other opinions of Dr. Sullivan where he contradicted himself so as not to give confusing and self-contradictory testimony. (Reply 21.) Defendant further replies that it was prejudiced by not pursuing a theory regarding non-infringing alternatives which the parties would have expected to be available after the time of trial. (*Id.*)

The Court holds that for the reasons noted above (*see supra*, Section III.E), even under the standard for a motion for a new trial where the Court may "weigh the evidence and assess the credibility of the witnesses," the Court cannot conclude that the jury verdict is contrary to the clear weight of the evidence. The Court already ruled on Defendant's *Daubert* motion to exclude certain testimony by Dr. Sullivan and found that his testimony was not inconsistent with his

witness for Plaintiffs. (Tr. 1459:10-14 ("Oh, and I apologize, . . . there is an error on the slide. Dr. Schuetz was, of course, not a Juno witness, so I apologize for that. He was one of our witnesses, and that should not indicate that he was a Juno witness.").)

disclosed opinion that the upfront payment is for "harms realized at the hypothetical negotiation." (ECF No. 659 at 39.) To the extent Defendant argues it was prejudiced by its inability to develop and present non-infringing alternatives that would exist post-trial, Defendant: (1) was in possession of evidence of non-infringing alternatives post-trial (*see* DX2011c.8 (multi-generation forecast for 2020); *see also* DX0125c (clinical trials)), (2) to the extent Dr. Sullivan's testimony was inconsistent, Defendant never requested reopening discovery to develop its purported non-infringing alternatives theory, (3) it remains unclear to this Court why Defendant would require discovery of its ***own*** non-infringing alternatives, and (4) Defendant had the opportunity to address any inconsistency in Dr. Sullivan's damages theory in its opposition to Plaintiffs' post-trial briefing re damages. (*See* ECF Nos. 672-2, 693.)

For these reasons, the Court denies Defendant's motion for a new trial based on Dr. Sullivan's testimony.

3. Large Figures

Defendant argues Dr. Sullivan's testimony was tied to large figures (projected profits, YESCARTA® valuation, negative impact to Juno, upfront payment from separate agreement, and royalty rates for late-stage technologies). (JMOL 41.) Defendant argues these figures were not apportioned, highly speculative, not sufficiently similar, and should not have been permitted, even as a check on the reasonableness of a damages award. (JMOL 42.)

Plaintiffs respond that the data points were highly relevant. As an initial matter, Defendant's failure to object to the admissibility of multiple data points to which it now objects, means it has waived its right to seek a new trial. (Opp. 42.) However, even if Defendant had not waived its right, each of the data points is relevant to the damages analysis. (Opp. 43.)

Defendant replies that it preserved its objections by moving *in limine* to preclude Plaintiffs from referring to high dollar figures Dr. Sullivan did not rely upon in his calculations. (Reply 21.) Plaintiffs then misrepresented to the jury large numbers as real anchors in the real world, skewing the jury's damages horizon. (Reply 22.) Defendant was also not permitted to introduce an estimated upfront payment between Juno and Celgene. (*Id.*)

As a threshold matter, Defendant failed to object to and receive a ruling on multiple figures it now disputes. *See* 11 Wright & Miller, Fed. Practice and Procedure § 2805 (3d ed. 2002) (stating a new trial will not be granted on issues not called to the court's attention, "unless the error was so fundamental that gross injustice would result"). True, Defendant filed a motion *in limine* to preclude generally testimony of "high dollar figures that Sullivan does not use in his calculations" (ECF No. 309 at 1, 12) (and the Court did in fact exclude all but one of the figures contained in the motion *in limine*) and filed objections "regarding projected or actual licensing figures that

neither expert has relied upon," however these broad objections cannot satisfy the requirement for calling a court's attention to an inadmissible figure during live testimony.

Nevertheless, the Court determines on the merits that the figures presented by Plaintiffs do not warrant a new trial.

$7.1 billion projected profits through patent term. Although Defendant did not object to this figure during testimony, the Court determines that Gilead's projected profits for YESCARTA® through the term of the '190 Patent are a relevant consideration to the hypothetical negotiation, and specifically to what Plaintiffs would have considered paying. Defendant's argument that the figure should have been apportioned is an issue of fact appropriate for cross-examination, where Plaintiffs argued the '190 Patent was critical to YESCARTA®, and Defendant argued factors other than the '190 Patent contributed to the success of YESCARTA®.

$6.2 billion alleged value of YESCARTA®. The Court already rejected Defendant's motion *in limine* to exclude this figure, as it determined that Gilead's value assigned to YESCARTA® had a nexus to the accused product. (Order, ECF No. 473, at 9.) Furthermore, this figure is relevant as the value that Gilead attributed to YESCARTA®. Defendant's argument that the figure should have been apportioned is an issue of fact appropriate for cross-examination, where Plaintiffs argued the '190 Patent was critical to YESCARTA®, and Defendant argued factors other than the '190 Patent contributed to the success of YESCARTA®.

$1.3 billion projected annual negative impact to Juno. Although Defendant did not object to this figure during testimony, the Court determines that the negative annual revenue Juno anticipated from Defendant's market entry as a result of its license to the '190 Patent is relevant to Dr. Sullivan's damages calculation and appropriate to consider under the law. *See Georgia-Pacific Corp. v. U.S. Plywood Corp.*, 318 F. Supp. 1116, 1121 (S.D.N.Y. 1970) (considering "the anticipated amount of profits that the prospective licensor reasonably thinks he would lose as a result of licensing the patent").

$1 billion upfront payment from Celgene-Juno Agreement, 20-30% royalty rates for late-stage technologies. Defendant did not object to these figures during testimony, but the Court notes that even if Defendant had objected to and excluded these figures at trial, the jury verdict would not be rendered contrary to the clear weight of the remaining evidence.

Thus, the Court denies Defendant's motion for a new trial based on large figures.

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4. Written Description Instruction

Defendant argues the written description jury instruction provided to the jury was flawed because it did not correctly cover the legal standard for written description of genus claims. (JMOL 43.) Although the Court followed a model instruction for written description, the instruction was inadequate because it referred to the invention in the singular, did not include the word genus, or explain that the specification must enable the full scope of the claims. The instruction also did not lay out the *Ariad* standard that "a sufficient description of a genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can visualize or recognize the members of the genus." (JMOL 44 (citing *Ariad*, 598 F.3d at 1350).) Defendant argues it presented clear and convincing evidence that the patent does not meet the legal standard for genus claims, but the jury was free to forgo the required analysis. (JMOL 45.)

Plaintiffs respond that Defendant cannot show, as it must, that the written description jury instruction was erroneous and prejudicial. (Opp. 44.) The instruction tracked the N.D. Cal. model patent instruction, updated in 2019. (*Id.*) There is no special instruction for what Defendant labels the *Ariad* standard, thus Defendant's objection amounts to nothing more than a complaint that the Court did not charge the jury in the particular way Defendant wanted. (*Id.*) 35 U.S.C. § 112(a) presents a single written description test, and *Ariad*'s discussion of genus claims makes clear that the description requirement does not demand any particular form of disclosure. (*Id.*) Defendant's proffered instruction would have confused the jury, where no witness ever discussed genus claims. (Opp. 45.) Defendant's objections regarding invention in the singular and omission of the term genus were likewise never raised, and the presented instruction clearly and correctly stated disclosure must show possession of the invention. (*Id.*)

Defendant replies that Plaintiffs mischaracterize the genus requirement, disclosed in *Ariad*. (Reply 22.) *Ariad* specifies what is required to show possession for a genus claim. (Reply 23.) Although the term genus was used only once, witnesses testified that the claims included millions of billions of different CARs. (*Id.*) Defendant's use of the term genus only once was unsurprising, given the Court did not rule on jury instructions until after the close of the evidence. (*Id.*)

The Court finds that Defendant cannot demonstrate the written description instruction provided by the Court was erroneous and prejudicial. First, the instruction, from the N.D. Cal. Model Patent Instructions (last updated in Oct. 2019), was not erroneous where the written description instruction mirrored statutory requirements for written description. 35 U.S.C. § 112(a). The statute requires a written description of the invention so as to enable any person skilled in the art to make and use the same. (*Id.*) The instruction stated, *inter alia*, that "[a] patent claim is invalid if the patent does not contain an adequate written description of the claimed invention." (ECF No. 591, at Instruction No. 17.) Despite Defendant's assertion that the instruction should

have set forth the specific requirements for a genus claim as set forth in *Ariad*, if true, Defendant offers no explanation for why the model instruction has not been modified in the nine years following *Ariad*'s issuance. Nor did Defendant present a model instruction from ***any*** authority for genus claims, instead drafting from scratch a two-part written description jury instruction, where the second part cherry-picked language from various decisions. (ECF No. 372, at 90-93.) Defendant's instruction was confusing, where the term "genus" was only used at trial once during Defendant's opening, and the jury did not hear the term referenced by any of the witnesses. Defendant's instruction was also argumentative and improper, for example because it used language improperly shifting the burden: "the specification needs to show that the inventors had truly invented the claimed genus." (*Id.* at 91.) In light of these factors, the Court cannot conclude that providing Plaintiffs' instruction rather than Defendant's was erroneous.

Second, even if it was, the Court finds that Defendant cannot demonstrate the instruction was prejudicial. As *Ariad* states, the inquiry of whether a written description is sufficient is a question of fact that "will necessarily vary depending on the context," specifically "the nature and scope of the claims and . . . the complexity and predictability of the relevant technology." Both sides presented conflicting evidence regarding whether the three-part CAR structure, including the description of scFvs for use with the Sadelain backbone, was adequately described. Defendant had the opportunity to, and indeed did, argue that the claimed invention included millions and billions of potential scFvs, and that the patent did not contain an adequate written description describing which scFvs would create working CARs. If the jury agreed with Defendant's argument, based on the instruction provided to the jury, it could not have found the written description adequate. Based on this, Defendant cannot demonstrate the requisite prejudice warranting a new trial.[9]

Thus, the Court denies Defendant's motion for a new trial based on the written description jury instruction.

5. Plaintiffs' IPR Arguments

Defendant argues Plaintiffs misled the jury about the IPR for the '190 Patent when they questioned Dr. Belldegrun about the fact that none of the challenged claims was invalidated during IPR, and during closing arguments referenced Defendant having lost all challenges raised before the PTO. (JMOL 46.) The curative instructions could not dispel Plaintiffs' persistent misdirection. (JMOL 47.)

[9] The Court also notes that in its view, even if Defendant's two-part instruction had been read, the jury's finding of adequate written description would not have been in contravention of the clear weight of the evidence. (*See supra*, Section III.A.); *see also Ariad*, 598 F.3d at 1352 (stating in part that "written description and enablement often rise and fall together . . .").

Plaintiffs respond that it was Defendant who offered the Final Written Decision ("FWD") from the IPR into evidence. (Opp. 46.) Once Defendant offered the patent prosecution history, including the FWD, into evidence, Plaintiffs were entitled to explain the FWD and place it in context. (*Id.*) Additionally, the IPR was relevant following Dr. Belldegrun's testimony that the '190 Patent was not important to Defendant. (*Id.*) Plaintiffs further respond that their IPR statements were accurate and proper, where they stated Defendant made arguments on a separate issue than the one the jury was asked to decide, three patent judges reviewed the IPR, and Defendant could have raised claim construction arguments on the SEQ ID NO:6 term. (Opp. 47.) Plaintiffs further respond Defendant was not prejudiced, where the Court provided a limiting instruction multiple times, and Defendant's counsel highlighted the instruction during closing argument. (*Id*.)

Defendant replies that Plaintiffs' misuse of the IPR was prejudicial where the Court admitted testimony regarding the filing of the IPR. (Reply 23.) Defendant used the patent prosecution history only to cross-examine Dr. Sadelain regarding the CoC, and never mentioned anything related to the IPR. (Reply 23-24.) Plaintiffs' references to Defendant's CoC defense in the IPR were prejudicial and erroneous, and the curative instruction did not resolve the issue where the Court never specifically instructed the jury to disregard Plaintiffs' statements. (Reply 24.)

As a preliminary matter, the Court notes it already ruled on the record regarding Defendant's oral motion for a mistrial based on Plaintiffs' IPR arguments. During closing argument, counsel for Plaintiffs argued that "either party in an IPR proceeding can make arguments about claim construction . . . . [I]t's apparent that Kite made no argument before the three patent judges, who really know the technology and the law, that the '190 patent sequence for SEQ ID:6 started at 113." (Tr. 1532:1-8.) The Court subsequently issued a written Order:

> The Court understands Plaintiffs' argument to be that Defendant, while asserting some claim construction arguments during the IPR, did not ask PTAB to construe whether the sequence in claim 1 should start at 113 or 114. The Court is not persuaded that this comprises a misstatement of law. The Court already granted Defendant's request to instruct the jury during trial that a patent can only be challenged during IPR on grounds of anticipation or obviousness, not for a certificate of correction, inadequate written description, or enablement. The Court again included the instruction as Closing Instruction No. 15(a). Given the limited nature of Plaintiffs' remark during closing, the Court's multiple IPR instructions to the jury, and the Court's instruction to the jury that attorney argument is not evidence, the Court decides a mistrial is not appropriate.

(Order, ECF No. 584 at 3.)

Nevertheless, the Court again addresses Defendant's argument. Defendant made the decision

to admit the entire prosecution history into evidence, including the FWD. If Defendant believed the FWD to be prejudicial, Defendant had the option of admitting an excerpted version of the prosecution history. Based on its failure to do so, Plaintiffs were entitled to utilize the FWD once admitted. The Court further notes that the IPR became relevant when Dr. Belldegrun testified that the '190 Patent was not important to Plaintiffs, as his testimony was contradicted by Defendant's decision to file the IPR to attempt to invalidate the '190 Patent. As the Court noted throughout trial, it did not view Plaintiffs' statements regarding the IPR as inaccurate, and moreover, the Court provided multiple limiting instructions regarding the IPR. The Court's view is thus that Plaintiffs' arguments did not misstate the law, the Court cured whatever prejudice may have resulted, and any prejudice was not so pervasive that a new trial is warranted.

Thus, the Court denies Defendant's motion for a new trial based on Plaintiffs' IPR arguments.

6. Good-Faith Evidence

Defendant argues that because it maintained privilege in this case, 35 U.S.C. § 298 precluded Plaintiffs from using Defendant's failure to present such advice to prove willful infringement. (JMOL 47.) Defendant further argues it should have been permitted to offer Dr. Bot's homology analysis as non-attorney evidence of good faith. (*Id.*) Plaintiffs should not have been permitted to reference Defendant's lack of evidence, and Defendant should have been granted a curative instruction. (JMOL 47-48.)

Plaintiffs respond that Defendant, in its opening statement, promised the jury that Defendant had "very, very good reasons" for believing it did not infringe. (Opp. 48.) Plaintiffs' closing argument noted Defendant failed to fulfill its promise of showing those very, very good reasons. (*Id.*) Plaintiffs further respond Defendant was precluded from introducing Dr. Bot's homology analysis because it was outdated, irrelevant, and unfairly prejudicial, not because Defendant asserted privilege. (*Id.*) Plaintiffs further respond that their comment that Defendant presented no fact witness who reviewed the patent for non-infringement or invalidity did not violate 35 U.S.C. § 298 because Plaintiffs did not reference any failure to obtain advice from counsel, or choice to obtain advice of counsel but not present it. (Opp. 48-49.)

Defendant replies that Plaintiffs previously persuaded the Court that good faith evidence was inadmissible because Defendant elected to withhold the advice of counsel. (Reply 24-25.) Having been successful, Plaintiffs could not rely on the absence of such evidence at trial. (Reply 25.)

Regarding Dr. Bot's homology analysis, as noted above, the testimony was excluded for reasons other than Defendant's assertion of privilege. (*See supra*, Section III.D.) However, unlike for a JMOL, for a motion for new trial, the Court may weigh the evidence to determine whether the

jury verdict is contrary to the clear weight of the evidence. *DSPT Int'l*, 624 F.3d at 1218. Under this standard for a motion for a new trial, the Court finds that even if Dr. Bot's testimony had been permitted, the clear weight of the evidence would still support the jury's verdict.

Regarding Plaintiffs' reference to Defendant's lack of testimony of good-faith evidence, the Court finds that Plaintiffs' arguments were not improper, where Defendant promised during opening that it had very, very good reasons for believing it did not infringe. Given Defendant's statements, Plaintiffs were permitted to point out any purported failure by Defendant to satisfy its promise, particularly where the reference was to the lack of any fact witness, not advice of counsel.

Regarding the curative instruction, the Court notes it already ruled on Defendant's request on the record. (Tr. 1537:5-14.) Specifically, the Court stated that "the Court would conclude that it cannot be inferred from [Plaintiffs' counsel's] statements that he was suggesting to the jury that Kite should be found to have willfully infringed because it did not present advice of its lawyers that it had defenses under section 112 or 255." (*Id.*) Defendant's motion now does not change the Court's prior ruling.

For these reasons, the Court denies Defendant's motion for a new trial based on good-faith evidence.

7. Time Limit

Defendant argues it was prejudiced by insufficient time, where it was given only 11.7 hours to present evidence on a wide range of issues, and where it bore the burden on three liability defenses. (JMOL 48.) Defendant argues the time limit forced it to drop or truncate the testimony of numerous witnesses and could not develop key aspects of its case. (JMOL 49.)

Plaintiffs respond that the Court imposed no rigid time limits, and Defendant was ultimately satisfied with its time. (Opp. 49.) The Court noted from the beginning that time limits were subject to adjustment during trial, and in fact expanded time to allow for interim summation (which neither party utilized). (*Id.*) Throughout trial, the Court noted its flexibility and willingness to add time. (Opp. 49-50.)

Defendant requested more than one time for additional time, and the Court denied those requests. (Reply 25.) Only on the last day of testimony did the Court allow Defendant extra time for cross-examination, which did not undo the prejudice of having to drop or truncate every witness in its case. (*Id.*)

As an initial matter, the Court has already considered and ruled upon Defendant's request for additional time. ***First***, the Court stated on the record, "I have always made it clear that the Court

would reconsider in terms of the time. The defendant asked for 40 minutes. They were given an additional 40 minutes. The plaintiff asked for an additional 40 minutes, they were given 40 minutes. And there was no request for more time. So that should be clear in the record also." (Tr. 1314:22-1315:3.) ***Second***, following trial, the Court issued an Order noting that: (1) at the parties' Scheduling Conference in March 2018, the Court contemplated a five or six day trial, as only one patent was at issue (ECF No. 92 at 54); (2) after the Scheduling Conference, the disputed issues narrowed significantly, as literal infringement and infringement under the doctrine of equivalents were no longer at issue; (3) at the parties' November 26, 2019 Pretrial Conference, the Court initially allotted 10 hours for each side for witness testimony; (4) at the parties' unopposed request, the Court expanded the time limit to 11 hours for each side to permit witness summation, "subject to adjustment" (Order, ECF No. 530, at 1); (5) after trial began, Defendant requested an extra forty minutes for witness testimony, which based on the stage of trial and stage of examination, the Court granted; and (6) Defendant did not utilize the full amount of its requested extension. (Order, ECF No. 584, at 2.) The Court further noted that for its closing argument, Defendant initially requested and was granted 1.5 hours, then requested and was granted 2 hours, then requested and was granted 2.25 hours, and still exceeded its time allotment. (*Id.*) Because the Court disclosed as early as eighteen months before trial the trial would be allotted five to six days,[10] the case subsequently narrowed, the Court adjusted the time limits for trial based on a demonstrated need, and Defendant did not utilize its full time on the record, the Court found Defendant was allotted sufficient time at trial.

Defendant's current arguments largely mirror its previous arguments. Nevertheless, the Court addresses them again. The Court's view is that the scope of this patent case, although dealing with complex technology, was not large. There was one asserted patent, with essentially two asserted claims (four claims, broken into pairs, with limitations common to all four claims). This was an untraditional patent case in the sense that infringement (neither literal nor under the doctrine of equivalents) was at issue for trial. Nor were there common invalidity issues, such as invalidity or anticipation. The Court's view is that neither party bore a substantially heavier burden, where Plaintiffs bore the burden of introducing the technology, proving willful infringement, and proving damages in the amount of $752 million, and where Defendant bore the burden of proving the Certificate of Correction invalid and proving its written description and enablement defenses.[11]

Trial spanned eight days, during which the jury heard from 23 total witnesses,[12] twelve for

[10] In the Court's view, a six-day trial estimate, expecting 5.5 hours of witness testimony per day, would break down to one day for jury selection and opening statements, four days of witness testimony (11 hours per side), and one day for closing arguments.
[11] The Court's view is that there was significant overlap between Defendant's written description and enablement defenses at trial.
[12] The testimony of five witnesses was by deposition designation.

Plaintiffs and eleven for Defendant. The Court repeatedly maintained flexibility and accommodated the parties where a need was demonstrated. For example, the Court permitted Defendant to put up two of its own witnesses out of order. Dr. Bot testified on December 5 in order to allow him to attend a conference, and Dr. Schuetz was permitted to testify on December 6, during the middle of Plaintiffs' expert's testimony. The Court further accommodated Defendant by keeping the jury late on December 5 for Dr. Bot to complete his testimony. With regard to the time limit, the Court granted Defendant's request for time when Defendant demonstrated a need, for example by granting an extra forty minutes during a cross-examination when Defendant was nearing the end of its allotted time. The Court further granted Defendant's two requests to extend its time allotted for closing argument.

Defendant's argument that it was forced to drop or truncate the testimony of numerous witnesses due to its 11.7-hour allotment is not persuasive. Before trial, Defendant itself requested 12.5 hours of witness testimony (ECF No. 531, at 1), yet filed an order of proof on the evening before the last day of witness testimony containing nine pages of testimony and exhibits that it was supposedly precluded from presenting (ECF No. 543, at 2-10). The Court is doubtful that all of Defendant's arguments and exhibits could have been introduced in an additional 48 minutes. Nor is Defendant's authority persuasive. Defendant cites a "similarly meager 10-hour time allotment in a 'complex' copyright case" as grounds for a new trial, but the district court's time limit in that case has since been affirmed by the Ninth Circuit, sitting *en banc*. *Skidmore v. Led Zeppelin*, No. 16-56057, at 49-50 (9th Cir. 2020) (*en banc*) (finding trial time limit was not an abuse of discretion where the district court was "up front about the limits and then . . . flexible at counsel's request").

Thus, the Court denies Defendant's request for a new trial based on time limits.

8. Cumulative Prejudice

Defendant argues the cumulative prejudice of multiple errors requires the Court to grant a new trial. (JMOL 49.) Defendant alleges that misconduct and error pervaded the trial, and each error affected a central component of the case. (*Id.*) The errors were not harmless because the Federal Circuit has invalidated analogous antibody claims, Plaintiffs offered no new evidence demonstrating the CoC's error and correction were clearly evident, and Plaintiffs' damages vastly exceeded comparable licenses. (JMOL 49-50.)

Plaintiffs respond that all of their previous arguments address why there was no prejudice to Defendant, and thus why no errors could have accumulated. (Opp. 50.) Even if errors had occurred, they would have been harmless, especially given Defendant's new trial arguments largely address different legal issues and discrete evidentiary issues. (*Id.*)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: March 24, 2020**

Based on the Court's analysis above, and based on the Court's observations having presided over the entirety of trial, the Court finds that prejudice for each of Defendant's issues (if any exists) did not accumulate to a level such that the jury's verdict was against the clear weight of the evidence. *DSPT Int'l*, 624 F.3d at 1218.

IV. RULING

For the foregoing reasons, the Court **DENIES** Defendant's Motion for Judgment as a Matter of Law Pursuant to Fed. R. Civ. P. 50(b) and/or a New Trial Pursuant to Fed. R. Civ. P. 59 [ECF No. 659].

IT IS SO ORDERED.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

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CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

TITLE: Juno Therapeutics, Inc., et al. v. Kite Pharma, Inc.

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PRESENT: THE HONORABLE S. JAMES OTERO, UNITED STATES DISTRICT JUDGE

Victor Paul Cruz	Not Present
Courtroom Clerk	Court Reporter

COUNSEL PRESENT FOR PLAINTIFFS:	**COUNSEL PRESENT FOR DEFENDANTS:**
Not Present	Not Present

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PROCEEDINGS (in chambers): ORDER RE: DAUBERT MOTIONS [ECF Nos. 270, 271, and 274]; **DEFENDANT'S EX PARTE APPLICATION TO STRIKE SUPPLEMENTAL COMPLAINT** [ECF No. 395]; **DEFENDANT'S EX PARTE APPLICATION TO STRIKE UNTIMELY AND UNRELIABLE OPINIONS OF DR. SULLIVAN** [ECF No. 428]

This matter comes before the Court on the following motions:

(1) Defendant Kite Pharma, Inc.'s ("Kite" or "Defendant") Motion in Limine (No. 1) to Exclude Damages Opinions of Ryan Sullivan, Ph.D. ("Sullivan Motion") filed October 29, 2019 (ECF No. 309; Opposition at ECF No. 321; Reply at ECF No. 363-1; Defendant's Supplemental Memorandum at ECF No. 378; Plaintiffs' Supplemental Memorandum at ECF No. 388; Plaintiffs' Second Supplemental Opposition at ECF No. 433; Defendant's Objection to Unauthorized Surreply at ECF No. 435);
(2) Defendant's Motion in Limine (No. 2) to Exclude Expert Testimony of Mark Gilbert, M.D. ("Gilbert Motion") filed October 29, 2019 (ECF No. 271; Opposition at ECF No. 322; Reply at ECF No. 453);
(3) Plaintiffs Juno Therapeutics, Inc.'s ("Juno") and Sloan Kettering Institute for Cancer Research's ("SKI") (collectively, "Plaintiffs") Motion to Exclude Dr. Mohan Rao's Testimony Regarding Damages ("Rao Motion") filed October 29, 2019 (ECF No. 274; Opposition at ECF No. 377; Reply at ECF No. 368-1);
(4) Defendant's Ex Parte Application to Strike Supplemental Complaint ("Motion to Strike Complaint") filed November 22, 2019 (ECF No. 395; Opposition at ECF No. 408; Reply at ECF No. 420); and
(5) Defendant's Ex Parte Application to Strike Untimely and Unreliable Opinions of Dr. Sullivan ("Motion to Strike Sullivan's Amended Report") filed on November 29, 2019 (ECF No. 428; Opposition at ECF No. 440).

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

Regarding the Daubert motions, the parties filed respective Oppositions on November 12, 2019 and respective Replies on November 19, 2019. Additionally, the Court permitted each party to submit a supplemental filing on the Sullivan Motion. Plaintiffs filed a second supplemental response regarding the same, and Defendant responded thereto. For the following reasons, the Court:

(1) **GRANTS-IN-PART** and **DENIES-IN-PART** the Sullivan Motion;
(2) **GRANTS-IN-PART** and **DENIES-IN-PART** the Gilbert Motion;
(3) **GRANTS-IN-PART** and **DENIES-IN-PART** the Rao Motion;
(4) **GRANTS** the Motion to Strike Complaint. Plaintiffs are ordered to file a supplemental Complaint within 24 hours of entry of this Order; and
(5) **GRANTS** the Motion to Strike Sullivan's Amended Report.

I. BACKGROUND

A. General Overview

This is a patent infringement action involving U.S. Patent No. 7,446,190 (the "'190 Patent"), titled "Nucleic Acids Encoding Chimeric T Cell Receptors." The '190 Patent issued on November 4, 2008 and incorporates a provisional application filed on May 28, 2002. ('190 Patent Caption.) The claimed invention provides "nucleic acid polymer encoding [] chimeric TCR's [T Cell Receptors] . . . ." ('190 Patent, col. 2:11-14.) The chimeric TCRs encoded by the claimed invention "combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain ("zeta chain portion"), a signaling region from a costimulatory protein such as CD28 with a binding element that specifically interacts with a selected target." ('190 Patent, col. 2:14-18.) These TCRs are designed to "specifically interact[] with a cellular marker associated with target cells," resulting in the stimulation of a T cell immune response to the target cells. ('190 Patent, col. 2:30-36.)

Plaintiffs initiated this action on October 18, 2017, alleging that Defendant infringes the '190 Patent through the use, sale, offer for sale, or importation of one of Kite's immunotherapy treatments, Yescarta. Yescarta is described as 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." (Compl. ¶ 18, ECF No. 1.) Plaintiffs assert that Yescarta infringes on the '190 Patent by utilizing nucleic acid polymers encoding chimeric TCRs within the scope of the '190 Patent claims. (Compl. ¶ 24.) Defendant, in turn, filed counterclaims seeking declaratory judgments of non-infringement and invalidity of the '190 Patent. (*See generally*, Amended Answer and Counterclaims, ECF No. 66.)

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

B. Expert Opinions

1. Plaintiffs' Expert, Ryan Sullivan

Dr. Sullivan opines that the parties would have agreed to a license totaling $1.245 billion, based on three components. First, Dr. Sullivan calculates a royalty rate, for use in determining the running royalties on Yescarta's sales through August 2019. He begins with the parties' 2013 Exclusive License Agreement, under which he opines Juno would have owed a 7.25% running royalty on Kite's net sales to SKI. (Sullivan Opp. 3.) Dr. Sullivan then makes two adjustments to the 7.25% royalty rate, one to adjust for Kite being a commercial competitor (for this, Dr. Sullivan references a Juno-Novartis settlement for a different patent), the second to adjust for the hypothetical negotiation in 2017, during which he opines Juno would have viewed Kite as a greater competitive threat than Novartis. (Sullivan Opp. 3.) From these adjustments, Dr. Sullivan presents a 27.6% royalty rate, amounting to $155.6 million on Yescarta's sales through August 2019.

Second, Dr. Sullivan opines that the parties would have agreed to a $930 million upfront payment. (Sullivan Opp. 4.) The 2013 Exclusive License Agreement transferred 500,000 shares of Juno stock, with a $150 million bonus if Juno's stock increased thirtyfold. Dr. Sullivan substituted 500,000 shares of Juno's stock in 2013, with 500,000 shares of Kite's stock in 2017, and added the $150 million bonus for stock increase, to reach $240 million. Dr. Sullivan then applied the same two adjustments that he applied to his royalty rate, to opine that the parties would have agreed to a $930 million upfront payment.

Third, Dr. Sullivan calculates a $159.7 million launch delay consideration. Dr. Sullivan opines that Kite's first-to-market entry would cause regulatory delay and hurdles for Juno's CAR-T therapy. (Sullivan Opp. 4.)

2. Plaintiffs' Expert, Mark Gilbert

Dr. Gilbert, Juno's Chief Medical Officer, opines on technical issues relating to damages. Specifically, he: (1) rebuts Defendant's contention that its manufacturing process and lymphodepletion regime add value to Yescarta by making it safer and more effective, and (2) compares Yescarta to JCAR017, to opine JCAR017 is safer/more effective. Dr. Sullivan then relies on Dr. Gilbert's opinion to compare the parties' relative bargaining strengths.

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

3. Defendant's Expert, Mohan Rao

Dr. Rao opines that the parties would have agreed to a 6.715% running royalty, with an $88M upfront payment, prorated to the term of the hypothetical license here. He starts with the MSKCC/Juno license, apportions as it covers 5 patents and know-how, and adjusts the 7.25% rate to 3.625% by opining half the value transferred by the agreement comprises know-how, and the other half of value transferred comprises the '190 patent. Then based on a separate agreement with Novartis, he adjusts the royalty rate to 6.715%. He then considers another license between St. Jude and Juno and opines that the parties here would have adopted the same $88M upfront payment in that agreement, prorated for the licensing term of the hypothetical negotiation here.

C. Order re Standing

On November 6, 2019, the Court granted-in-part and denied-in-part Defendant's Motion to Dismiss Memorial Sloan Kettering Cancer Center and Juno Therapeutics, Inc. as Plaintiffs for Lack of Standing ("Order re Standing"). (Order re Standing, ECF No. 304.) The Court held that the 2013 Exclusive License Agreement executed between MSK and Juno did not confer upon Juno constitutional rights to enforce the '190 patent against third parties, because SKI, not MSK, was the owner of the '190 patent. The Court noted that no evidence was presented by either party to undermine the rational purpose of the Exclusive License Agreement as transferring rights to the '190 patent. The Court also noted that this rational purpose would be relevant in the context of a breach of contract claim between the parties. The Court directed Plaintiffs to file an amended Complaint by November 20, 2019 and plead allegations regarding the October 2018 agreement's subsequent conferral of standing upon Juno, for the purpose of conducting a proper hypothetical negotiation.

On November 20, 2019 and November 21, 2019, Plaintiffs filed their application to seal Supplemental Complaint. (Application to Seal, ECF Nos. 384, 392-1.)

II. DISCUSSION

A. Legal Standards

1. Motions in limine

Motions in limine are "important tool[s] available to the trial judge to ensure the expeditious and evenhanded management of the trial proceedings." *Jonasson v. Lutheran Child & Family Servs.*, 115 F.3d 436, 440 (9th Cir. 1997). "A party may use a motion in limine to exclude inadmissible or prejudicial evidence before it is actually introduced at trial." *Barnett v. Gamboa,* No. CV 05-01022 BAM, 2013 WL 174077, at *1 (E.D. Cal. Jan. 16, 2013) (citing *Luce v. United States*, 469

U.S. 38, 40 n.2 (1984)). Regardless of a court's initial decision on a motion in limine, however, it may revisit the issue at trial. *See Luce*, 469 U.S. at 41-42 ("[E]ven if nothing unexpected happens at trial, the district judge is free, in the exercise of sound judicial discretion, to alter a previous *in limine* ruling."). "The Supreme Court has recognized that a ruling on a motion in limine is essentially a preliminary opinion that falls entirely within the discretion of the district court." *United States v. Bensimon*, 172 F.3d 1121, 1127 (9th Cir. 1999) (citing *Luce*, 469 U.S. at 41-42).

2. Relevance and unfair prejudice

Under the Federal Rules of Evidence ("FRE"), all relevant evidence is admissible. Fed. R. Evid. 402. Evidence is relevant if it has "any tendency to make a fact [that is of consequence in determining the action] more or less probable than it would be without the evidence." Fed. R. Evid. 401. Evidence that cannot meet this standard is inadmissible. *See* Fed. R. Evid. 402.

Even if relevant, evidence may be excluded "if its probative value is substantially outweighed by a danger of . . . unfair prejudice, confusing the issues, misleading the jury, undue delay, wasting time, or needlessly presenting cumulative evidence." Fed. R. Evid. 403. "A district court is accorded a wide discretion in determining the admissibility of evidence under the Federal Rules." *United States v. Abel*, 469 U.S. 45, 54 (1984). Nevertheless, "[i]n making a determination under [FRE] 403, the balance in close cases is struck in favor of admission" of the evidence. *United States v. Crosby*, 75 F.3d 1343, 1347 (9th Cir. 1996) (quoting *United States v. Payne*, 805 F.2d 1062, 1066 (D.C. Cir. 1986)) (internal quotation marks omitted).

3. Expert testimony

The Federal Rules of Evidence "assign to the trial judge the task of ensuring that an expert's testimony both rests on a reliable foundation, and is relevant to the task at hand." *Daubert v. Merrell Dow Pharms.*, 509 U.S. 579, 597(1993). In serving this "gatekeeper" function, a district court performs a two-part analysis. *Domingo v. T.K.*, 289 F.3d 600, 605 (9th Cir. 2002). First, a district court "must determine nothing less than whether the experts' testimony reflects scientific knowledge, whether their findings are derived by the scientific method, and whether their work product amounts to good science." *Daubert v. Merrell Dow Pharms.* (*Daubert II*), 43 F.3d 1311, 1315 (9th Cir. 1995) (internal quotations and citations omitted). "*Daubert*'s general holding—setting forth the trial judge's general 'gatekeeping' obligation—applies not only to testimony based on 'scientific' knowledge, but also to testimony based on 'technical' and 'other specialized' knowledge." *Kumho Tire v. Carmichael*, 526 U.S. 137, 141 (1999). Second, the court "must ensure that the proposed expert testimony is relevant to the task at hand . . . *i.e.*, that it logically advances a material aspect of the proposing party's case." *Daubert II*, 43 F.3d at 1315.

When considering whether expert testimony is reliable, a trial court should consider the factors laid out by the United States Supreme Court in *Daubert*, 509 U.S. at 593-95, including:

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

(1) "whether the theory or technique employed by the expert is generally accepted in the scientific community;" (2) whether "it's been subjected to peer review and publication;" (3) "whether it can be and has been tested;" and (4) "whether the known or potential rate of error is acceptable." *Daubert II*, 43 F.3d at 1316-17 (citing *Daubert*, 509 U.S. at 593-595). The Supreme Court acknowledged in *Daubert* that the trial judge's reliability inquiry is "flexible," and therefore trial courts are encouraged to consider other factors not specifically mentioned by the Supreme Court in *Daubert*. *Daubert*, 509 U.S. at 594. To that end, trial courts have also considered other potentially relevant factors, including (1) "whether the expert is proposing to testify about matters growing directly out of independent research he or she has conducted or whether the opinion was developed expressly for the purposes of testifying;" (2) whether the expert has "unjustifiably extrapolated from an accepted premise to an unfounded conclusion;" (3) "whether the expert has adequately accounted for obvious alternative explanations;" (4) "whether the expert is being as careful as he would be in his regular professional work;" and (5) "whether the field of expertise claimed by the expert is known to reach reliable results for the type of opinion offered." *In re Silicone Gel Breast Implants Litig.*, 318 F. Supp. 2d 879, 890 (C.D. Cal. 2004) (citing Fed. R. Evid. 702 Advisory Committee's Notes).

B. Dauberts

1. Dr. Sullivan

a. 27.6% license rate

Both damages experts use the Exclusive License Agreement as a starting point, as it is the only license agreement covering the '190 patent. Dr. Sullivan then makes two adjustments to the 7.25% royalty rate from the Exclusive License Agreement, one in reliance on the 2015 Novartis license agreement (to account for the hypothetical agreement being between competitors), and the second to adjust for Kite's status as a competitive threat in 2017. While the Court notes that Dr. Sullivan's royalty rate of 27.6% is significantly higher than the comparable licenses relied upon by either expert, Dr. Sullivan's adjustments to account for the circumstances of the hypothetical negotiation are sufficiently reliable to be admitted. Defendants' arguments can be addressed through the testimony of Dr. Rao and through vigorous cross-examination of Dr. Sullivan. The Court **DENIES** this part of Defendant's Sullivan Motion.

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

b. $930 million up-front payment

The Court is troubled by the obviously large amount of the $930 million up-front payment.[1] As an initial matter, this award exceeds Defendant's projected and actual revenues through trial, and other courts have excluded opinions not presenting reasonable conclusions about that to which the parties to the hypothetical negotiation would have agreed. (Sullivan Motion 3.) Dr. Sullivan relies on two agreements to reach his large figure—the Exclusive License Agreement and Novartis license—but both provide royalty rates between 4.75% - 7.25%, with $8.9 million cash and stock initial payments, and up to $150 million extra in potential milestone payments. (Sullivan Motion 4.) Conversely here, Dr. Sullivan provides an up-front payment of $930 million. Defendant objects to several factors leading to Dr. Sullivan's up-front payment.

Improper term. Dr. Sullivan's report clearly states that the term covered by his upfront payment is compensation for harms "realized at the hypothetical negotiation." (Sullivan Reply 1; *id.* (also stating Dr. Sullivan's opinion that his upfront payment "does not include compensation for any type of future anticipated harm").) He testified at deposition that Plaintiffs would not be seeking double recovery if they sought both his upfront fee, ***and*** future equitable relief (or lost profits). (Sullivan Reply 1.) However, Defendant states that Plaintiffs, for the first time, argued otherwise in their Opposition to Defendant's Sullivan Motion. There, Plaintiffs asserted the term for Dr. Sullivan's upfront payment was through the life of the patent, i.e., 2024. At the parties' December 2, 2019 hearing, when asked where Dr. Sullivan disclosed in his report that the term of the patent was through 2024, Plaintiffs' counsel asserted that the term was "built into" Dr. Sullivan's analysis, by virtue of having relied on the MSK/Juno Exclusive License Agreement, which provided a license for the duration of the patent term. But such an assumption cannot stand, in light of Dr. Sullivan's express disclosures to the otherwise (Sullivan Reply 1 (nothing Dr. Sullivan's statement that his upfront payment "does not include compensation for any type of future anticipated harm.") Plaintiffs' late attempt to rewrite Dr. Sullivan's report on the eve of trial is prejudicial to Defendant. Dr. Sullivan's upfront payment is thus limited to his disclosure of the term in his expert report, i.e., for harms realized at the hypothetical negotiation, not compensation for any type of future anticipated harm.

Adjustments. Dr. Sullivan utilizes the same two adjustments that he did in reaching his 27.6% royalty rate. For the reasons discussed above, the adjustments—while high—are sufficiently reliable to be presented to a jury.

//

[1] The Court has read and considered Plaintiffs' Second Supplemental Brief (ECF No. 433), which provides the testifying history of Dr. Sullivan. However, the Court draws its own conclusions regarding Dr. Sullivan based solely on the merits of his opinion in this case.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

Stock swap. Dr. Sullivan carries over Juno's grant of 500,000 shares of Juno stock in 2013 to 500,000 shares of Kite in 2017. (Sullivan Motion 5.) In 2013, Juno's stock was valued at $2 million, whereas Kite's stock in 2017 was valued at $90 million. Dr. Sullivan then adds $150 million, because Kite's stock increased over 30 times its initial price (a provision of the Exclusive License Agreement). Thus, Dr. Sullivan opines the upfront equivalent stock grant should be $240 million. With the two adjustments, this figure becomes $930 million.

At the December 2, 2019 hearing, Plaintiffs' counsel argued that the stock swap was valid because of the similarities between Juno and Kite. He stated both were CAR-T companies, had similar valuations when going public, focused on CAR-T technology, and sold for reasonably similar amounts. Be that as it may, Dr. Sullivan's report did not disclose this reasoning. Instead, Dr. Sullivan broadly opined that the '190 patent's benefits to Defendant would result in an increase in company value and stock price. (Sullivan Report ¶ 162.) Dr. Sullivan also states that Yescarta contributed significant value to Gilead's acquisition price of Kite (Sullivan Report ¶ 76); states that he accounts for differences in marketplace risk and uncertainty associated with CAR-T technology by using stock price (Sullivan Report ¶ 204); and opines that the MSKCC-Juno agreement uses a royalty rate reasonably reflecting apportionment (Sullivan Report ¶ 264).

In fact, Dr. Sullivan's cited documents show that uncertainty surrounding CAR-T technology can result in volatile stock prices: "[Kite's] stock can and may be highly volatile." (Sullivan Report ¶ 203 (as of May 2015).) Dr. Sullivan's report does not account for this volatility. While the stock price of a company *may* be used in a comparable license analysis, a company's stock price must be shown to have some tie to the accused product, in order to be reliable enough to be admitted. Here, Dr. Sullivan draws inference upon inference to reach an unreliable conclusion. He infers Yescarta drives Kite's stock price, infers marketplace risk can be reflected in a stock price without having made any adjustments, and based on these inferences (without any further reasoning), simply substitutes the stock price of a de-risked, late-stage cancer company in 2017 in place of a different cancer company's stock price in 2013. Such wholesale adoption of a stock price, without accounting for other factors such as business decisions (for example, issuing double the number of shares at half the price), effect of other offerings of a company independent of those relating to accused technology, stage of the company, and comparability of the company, does not merit inclusion of a damages figure for the jury to consider. On the first point alone, because Dr. Sullivan's analysis does not account for business decisions, Kite's decision to issue half the number of shares at double the price would have doubled Dr. Sullivan's $240 million payment to $480 million, without any difference in the parties' bargaining positions. Such an outcome is not reliable.

The fact that Dr. Sullivan's $930 million upfront payment (not meant to compensate for future infringing acts) exceeds Defendant's revenues through trial does not comport with the common

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

sense approach required for a hypothetical negotiation. Moreover, Plaintiffs' counsel's statements at the December 2, 2019 hearing likewise demonstrate the ambiguity of Dr. Sullivan's upfront award. When asked whether Plaintiffs would seek injunctive relief if awarded only a portion of Dr. Sullivan's upfront payment, counsel could not definitively provide a response without knowing how much of the payment was awarded. This uncertainty further illustrates Dr. Sullivan's upfront payment is not sufficiently reliable for the jury to hear.

For these reasons, the Sullivan Motion as to Dr. Sullivan's upfront payment depending on the stock swap is **GRANTED**. If Plaintiffs can identify a different disclosed initial amount in Dr. Sullivan's report, the alternative amount may be introduced with Dr. Sullivan's enhancement factors.

c. $159.7 million launch consideration

Dr. Sullivan calculates launch consideration as the royalty percentage multiplied by six months projected profits, to account for an estimated six-month delay to Juno due to Kite's Yescarta therapy. Given Plaintiffs' representation at the December 2, 2019 hearing that they withdraw this portion of Dr. Sullivan's report, the Court **DENIES AS MOOT**.

d. Other figures referenced by Dr. Sullivan

Dr. Sullivan does not use any of these figures in his damages calculations, but claims they validate his conclusions.

- Gilead's acquisition price of Kite ($11.9 billion): The Court **GRANTS** as irrelevant and confusing, given the lack of nexus to the accused product.
- Gilead's values assigned to CAR-T therapies ($8.13 billion): The Court **GRANTS** as irrelevant and confusing, given the minimal nexus to the accused product.
- Gilead's values assigned to Yescarta ($6.2 billion): The Court **DENIES**, because the amount has a nexus to the accused product. Defendant may cross-examine to the extent the revenue extends beyond the term of the hypothetical license or patent term.
- [redacted]
- [redacted]

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

- Value of first-mover advantage to Kite ($620 million): The Court **GRANTS**, as the value of a first-mover is self-evident, and the prejudice of introducing this number outweighs any probative value.

2. Dr. Gilbert

Defendant moves to exclude Dr. Gilbert's opinions as irrelevant, because Juno's JCAR017 therapy is not FDA approved and does not utilize the '190 patent. Defendant further argues that Dr. Gilbert's comparison is unreliable (single arm study, no adjustment for known differences in the study populations, no adjustment for known differences in how trial measure safety events).

Plaintiffs respond that Dr. Gilbert's opinion is relevant because he responds to Kite's expert opining that Kite's manufacturing and lymphodepletion regimes contributed to the success of Yescarta, that despite no FDA approval of JCAR017, the parties would have been aware of its development and safety profile, and Defendant would have been even more motivated to get a license from Plaintiffs and be first to market (with its alleged inferior product). Plaintiffs further respond that Defendant's complaints merit cross-examination, not exclusion (especially because no head-to-head studies exist for this treatment—that would be inhumane).

There is no dispute that Dr. Gilbert is qualified as an expert on CAR-T therapies, as he has treated cancer patients for decades. However, the Court strains to follow Plaintiffs' theories of relevance as to Dr. Gilbert's safety/efficacy comparison of JCAR017 to Yescarta. JCAR017 does not utilize the '190 patent. It is neither FDA approved nor available on the market. Plaintiffs contend the comparison between JCAR017 and Yescarta would have been considered during the hypothetical negotiation, but the safety and efficacy test results for JCAR017 were not released until March 2019, a year and a half after the hypothetical negation. At the December 2, 2019 hearing, counsel for Plaintiffs stated that the 2019 test results showed testing occurred during 2017, but Dr. Gilbert's deposition testimony does not indicate that in 2017, the test results were reliable, or that the 2017 test results were known to Defendant at that time. Plaintiffs have thus not shown how they could have known they had an allegedly safer product, or that Defendant would be motivated get a license to get first to market status with an allegedly inferior product. Dr. Gilbert may thus present his rebuttal opinion as to why Kite's manufacturing and lymphodepletion regimes did not contribute substantially to the success of Yescarta. He may not present any expert opinion comparing Yescarta and JCAR017, but may provide lay witness testimony regarding JCAR017 to the extent he has personal knowledge.[2] The Court **DENIES-IN-PART**.

[2] At the December 2, 2019 hearing, counsel for Defendant alleged that Plaintiffs have not complied with discovery obligations regarding their BLA submissions to the FDA, and that Dr. Gilbert should not be permitted to testify at all.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

3. Dr. Rao

Plaintiffs argue Dr. Rao's opinion should be excluded for three independent reasons: (1) Dr. Rao opines that Juno would have sublicensed the '190 patent to Kite for less than the rate Juno must pay to MSK, (2) Dr. Rao's hypothetical negotiation is not based on the parties' bargaining positions as of October 2017, and (3) Dr. Rao relies on settlement ranges prepared in connection with Celgene's acquisition of Juno, which bear no relationship to the hypothetical negotiation.

Defendant responds that: (1) Dr. Rao's licensing rate is properly apportioned to the value of the '190 patent itself (with half the royalty rate attributed to know-how); (2) Dr. Rao did account for the parties' respective bargaining positions because he opined Plaintiffs could not ask for the entire value of Yescarta simply because the hypothetical negotiation occurred on the eve of launch; and (3) Celgene's and Juno's financial models projecting '190 patent royalties are data points that reflect the perceived value of the '190 patent at the time of the hypothetical negotiation.

As to the first point (Juno's sublicense rate), Juno pays to MSK a running royalty of 7.25% of worldwide, annual net sales sold by Juno, its affiliates, and sublicensees. Dr. Rao argues the royalty covers five patents and knowhow. He adjusts for the fact that only the '190 patent is at issue here, and that valuable know-how would also have been transferred. He thus adjusts to 3.625%, then based on the Novartis agreement, adjusts to 6.715%. Plaintiffs argue it is improper to set a royalty below what Juno would have to pay to MSKCC (7.25%), because this leads to the absurd result that Juno would be losing money by licensing to a competitor. Defendant disagrees because it asserts the Exclusive License Agreement is invalid based on the Court's Order re Standing. But the Court's Order re Standing clarified that while MSK and Juno did not have *constitutional standing* to enforce patent rights against a third party under the Exclusive License Agreement, there was no evidence that as of October 2017, the parties did not intend the '190 patent to be included in the Exclusive License Agreement, that the parties did not intend to be bound by the Excusive License Agreement, or that the Exclusive License Agreement was a sham. (*See also infra*, Section II.C.) The hypothetical negotiation must be evaluated on the basis of what the parties to the hypothetical negotiation would have considered at the time of the negotiation. Based on the parties' knowledge as of October 2017, there is no evidence that the parties would have acted to negotiate with SKI, not Juno. Thus, Dr. Rao's 6.715% license rate does lead to the illogical conclusion that Juno would lose money every time Kite made a sale. The Court **GRANTS**.[3]

Because the BLA submissions relate to the now-withdrawn launch delay portion of Dr. Sullivan's opinion, and because Dr. Gilbert may not present an expert opinion comparing JCAR017 and Yescarta, the Court deems the issue resolved.

[3] At the parties' December 2, 2019 hearing, Defendant stated Dr. Rao has provided an alternative 10.34% licensing rate.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

As to the second point (bargaining positions), Plaintiffs argue that Dr. Rao does not consider the actual circumstances of the parties, *i.e.*, that Yescarta was on the eve of launch without a noninfringing alternative. Plaintiffs further argue that Dr. Rao improperly prorates the upfront payment for the hypothetical negotiation, rather than running through the expiration of the '190 patent. Defendant rebuts that accounting for the entire value of Yescarta would not properly apportion for the '190 patent, and that any failure to weigh more heavily bargaining leverage is appropriate for cross-examination, not exclusion. The Court agrees with Defendant and finds that Dr. Rao's adjustments for the actual circumstances (including Plaintiffs' complaints about Dr. Rao's decision not to make certain adjustments) weigh in favor of cross-examination, not exclusion. The Court **DENIES**.

As to the third point (settlement ranges), the parties dispute [redacted] the Court finds that the maximum contemplated [redacted] is not probative. Neither expert relies on the figure in calculating his upfront payment award. It is unclear whether the amount was contemplated assuming the '190 patent was valid and infringed. The other circumstances surrounding the estimate are likewise uncertain (whether they accounted for factors irrelevant to damages, including propensity to avoid litigation, mitigate risk, and/or divert resources elsewhere). Given the low probative value in light of neither expert's reliance, and the high 403 concerns given the circumstances surrounding the estimate, the Court **GRANTS**.

C. Motion to Strike Complaint

Defendant argues the Supplemental Complaint exceeds the scope of the Court's Order re Standing. Specifically, instead of pleading allegations specific to the October 2018 Agreement, Plaintiffs allege a new 2013 verbal license agreement, and SKI's hypothetical contract liabilities under that verbal agreement. (Motion to Strike Complaint 1.) Plaintiffs' only allegation regarding the October 2018 agreement is that it "reaffirmed" the parties' Exclusive License Agreement. (Motion to Strike Complaint 1.) The new 2013 verbal license agreement allegations contradict the Order re Standing, are irrelevant, and highly prejudicial at this stage. (Motion to Strike Complaint 2.) Moreover, Plaintiffs did not allege the oral agreement in response to interrogatories. (Motion to Strike Complaint 4.)

Plaintiffs respond that the Supplemental Complaint is proper. First, their re-pleading of allegations regarding Juno's constitutional standing prior to 2018 was to preserve their rights for appeal. (Opp. to Motion to Strike Complaint 1.) Second, the new allegations regarding the 2013 verbal or implied agreement "naturally follow[]" from the Order re Standing, given the facts of this case. (Opp. to Motion to Strike Complaint 2.) The Supplemental Complaint requires no new discovery, because Plaintiffs have maintained that the 2017 hypothetical negotiation would take Juno's interests into account. (Opp. to Motion to Strike Complaint 4.)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

Defendant replies that the Supplemental Complaint exceeds the scope of the Order re Standing. (Reply in Support of Motion to Strike Complaint 1-2.) Defendant further replies that although the oral license theory was not previously disclosed, the theory cannot stand, given the 2013 Exclusive License Agreement does not grant rights to the '190 patent to Juno, and even if it did, the integration clause expressly states it supersedes prior oral arguments. (Reply in Support of Motion to Strike Complaint 2-3.)

The Court finds that the new allegations regarding the alleged 2013 oral or implied license are improper. These allegations pose a new legal theory, and is improper to be disclosed in the month before trial.

The Court also finds that Plaintiffs' allegation that the October 2018 agreement "reaffirmed" Juno's exclusive rights to the '190 patent is improper. The Court's Order re Standing clearly found that the October 2018 agreement conferred standing upon Juno in the first instance—not that it affirmed any prior rights.

For these reasons, the Court **GRANTS** Defendant's Motion to Strike Complaint. Given that trial has started, Plaintiffs are re-instructed to file an amended Complaint within 24 hours of entry of this Order with allegations directed to the October 2018 agreement, consistent with the Court's Order re Standing. The Court clarifies that granting this motion does not preclude either party's damages expert from opining that Juno's interests would have been represented at the hypothetical negotiation, as neither party has provided evidence that Plaintiffs were not acting as if the Exclusive License Agreement conveyed rights to the '190 patent, or that the Exclusive License Agreement was a sham executed in an attempt to drive up sublicensing royalty rates.

D. Motion to Strike Dr. Sullivan's Amended Report

Defendant moves to strike the second supplemental Sullivan report, served one court day before trial. Dr. Sullivan provides two supplemental opinions. First, he opines that even if SKI is the sole licensor, economic evidence (*i.e.*, $149 million of consideration provided from Juno to SKI) supports Juno's interests being represented at the hypothetical negotiation. (Motion to Strike Sullivan's Amended Report 4.) Second, Dr. Sullivan opines that SKI would have sought to resolve issues with Juno's rights with regard to the '190 patent prior to the hypothetical negotiation. (Motion to Strike Sullivan's Amended Report 4.) Third, Dr. Sullivan offers a prorated calculation of his upfront payment through trial, *i.e.*, $243 million rather than $930 million. Dr. Sullivan does so for the purpose of opining that his total damages award, now prorated through the end of trial to $230 million, is comparable in magnitude to Dr. Rao's $70 million. (Motion to Strike Sullivan's Amended Report 8.)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES – GENERAL

CASE NO.: 2:17-cv-07639 SJO-KS **DATE: December 3, 2019**

Plaintiffs respond that Dr. Sullivan has not served any new opinions. First, Dr. Sullivan has already opined that if SKI, rather than Juno, was the hypothetical negotiator, his opinion would remain unchanged. (Opp. to Motion to Strike Sullivan's Amended Report i.) Dr. Sullivan's approach is consistent with Dr. Rao's approach, in that Dr. Rao similarly supplemented his hypothetical negotiation in light of the Court's Order re standing.[4] (Opp. to Motion to Strike Sullivan's Amended Report ii.) Second, it would be irrational to determine that SKI, without Juno, would enter into a hypothetical agreement given the Exclusive License Agreement and the parties' behavior surrounding the agreement. (Opp. to Motion to Strike Sullivan's Amended Report iii.) Third, although Dr. Sullivan maintains pro-rating is improper, he provides a pro-rated number for purposes of comparing the magnitude of his damages calculation with Dr. Rao.

The Court finds Defendant's arguments persuasive. First, Dr. Sullivan has already opined that his position would not change if SKI, not Juno, was the hypothetical negotiator. The Court sees no reason for him to supplement his opinion on this point. Second, Dr. Sullivan's new opinion that SKI would have sought to resolve standing issues with Juno prior to the hypothetical negotiation is likewise improper. Third, Dr. Sullivan presents no reason why he could not have pro-rated his damages opinion in the first instance, or sought to supplement to pro-rate his opinion any time after service. Dr. Sullivan's supplementation is further improper because of the Court's determination as to the appropriate time period for his original opinion. *See supra*, Section II.B.1.b. For these reasons, the Court **GRANTS** the Motion to Strike Sullivan's Amended Report.

III. RULING

For the foregoing reasons, the Court:

(1) **GRANTS-IN-PART** and **DENIES-IN-PART** the Sullivan Motion;
(2) **GRANTS-IN-PART** and **DENIES-IN-PART** the Gilbert Motion;
(3) **GRANTS-IN-PART** and **DENIES-IN-PART** the Rao Motion;
(4) **GRANTS** the Motion to Strike Complaint. Plaintiffs are ordered to file a supplemental Complaint within 24 hours; and
(5) **GRANTS** the Motion to Strike Sullivan's Amended Report.

IT IS SO ORDERED.

[4] In light of its ruling on Plaintiffs' Motion in Limine No. 3, the Court granted Plaintiffs' ex parte application to exclude Dr. Rao's supplemental report. (Text Order, ECF No. 424.)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

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CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE:** October 9, 2018

TITLE: Juno Therapeutics, Inc., et al. v. Kite Pharma, Inc.

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PRESENT: THE HONORABLE S. JAMES OTERO, UNITED STATES DISTRICT JUDGE

Victor Paul Cruz Courtroom Clerk	Not Present Court Reporter
COUNSEL PRESENT FOR PLAINTIFF:	**COUNSEL PRESENT FOR DEFENDANT:**
Not Present	Not Present

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PROCEEDINGS (in chambers): CLAIM CONSTRUCTION ORDER

Plaintiffs and Counter-defendants Juno Therapeutics, Inc. ("Juno"), Memorial Sloan Kettering Cancer Center, and Sloan Kettering Institute for Cancer Research (together, "MSKCC") (collectively, "Plaintiffs") and Defendant and Counter-claimant Kite Pharma, Inc. ("Kite" or "Defendant") have filed claim construction briefs in which they ask the Court to construe two (2) disputed phrases found in the sole patent asserted in this litigation, U.S. Patent No. 7,446,190 ("the '190 Patent"). Plaintiffs filed their Opening Claim Construction Brief ("Pl.'s Brief") on August 13, 2018. Defendant filed its Responsive Claim Construction Brief ("Def.'s Brief") on August 27, 2018. Plaintiffs filed a reply ("Pl.'s Reply") on September 3, 2018. The Court heard argument from counsel on September 18, 2018.

I. FACTUAL AND PROCEDURAL BACKGROUND

Plaintiffs initiated the instant action on October 18, 2017, alleging that Defendant infringes the '190 Patent through the use, sale, offer for sale, or importation of one of Kite's immunotherapy treatments, Yescarta. Yescarta is described as 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." (Compl. ¶ 18.) Plaintiffs assert that Yescarta infringes on the '190 Patent by utilizing nucleic acid polymers encoding chimeric TCRs within the scope of the '190 Patent claims. (Compl. ¶ 24.) Defendant, in turn, filed counterclaims seeking declaratory judgments of non-infringement and invalidity of the '190 Patent. (*See generally*, Amended Answer and Counterclaims, ECF No. 66.) On March 2, 2018, the Court held a scheduling conference in which it ordered that the Northern District of California's Patent Local Rules will govern the case and set a claim construction ("Markman") hearing for September 17, 2018. (Minutes of Sched. Conf., ECF No. 71.)

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

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JS-5/JS-6	____
Scan Only	____

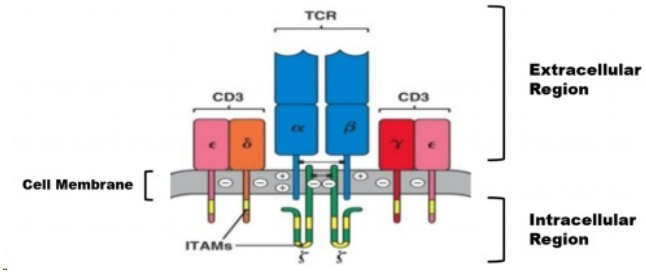
CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

II. TECHNOLOGICAL SUMMARY

The '190 Patent issued on November 4, 2008 and incorporates a provisional application filed on May 28, 2002. ('190 Patent Caption.) The claimed invention provides a "nucleic acid polymer encoding [] chimeric TCR's [T Cell Receptors]." ('190 Patent, col. 2:11-14.) The chimeric TCRs encoded by the claimed invention "combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain ('zeta chain portion'), a signaling region from a costimulatory protein such as CD28 with a binding element that specifically interacts with a selected target." ('190 Patent, col. 2:14-18.) These TCRs are designed to "specifically interact[] with a cellular marker associated with target cells," resulting in the stimulation of a T cell immune response to the target cells. ('190 Patent, col. 2:30-36.)

A. T-Cell and Targeted Immune Response

T cells, also known as T lymphocytes, are a form of white blood cell that plays a critical role in the body's cell-mediated immunity. (Declaration of Dr. Richard P Junghans, Ph.D., M.D. ("Junghans Decl.") ¶ 40, ECF No. 87-1; Declaration of Dr. Thomas Brocker, Ph.D. ("Brocker Decl.") ¶ 46, ECF No. 85-2.) The primary role of T cells is to detect and respond to "antigens"—molecules capable of producing an immune response. (Junghans Decl. ¶ 40.) They detect the presence of antigens through the use of T cell receptors ("TCRs"), which are polypeptide chains appearing on the surface of the T cell. (Junghans Decl. ¶ 40; Brocker Decl. ¶ 47.) Within the cell, TCRs typically form a complex with another protein, CD3ζ, and the two work together to create an immune activation signal upon encountering an antigen. (Junghans Decl. ¶ 40; Brocker Decl. ¶ 47.) An illustration of this TCR/CD3ζ complex can be seen below:



(Junghans Decl., Fig. 5.) TCRs are able to detect antigens by binding to particular, identifying protein fragments that appear on the surface of each antigen. (Brocker Decl. ¶ 49.) This is accomplished through the TCR's "variable" region, which allows it to bind with specificity to a particular antigen. (Brocker Decl. ¶ 22.) Because there are a diverse range of TCRs that appear on a given T cell, each cell is able to recognize and respond to a number of antigens. (Brocker Decl. ¶ 50.) Once a TCR binds with a known antigen, it prompts an immune response from the T cell that is specifically targeted at cells displaying that particular antigen. (Brocker Decl. ¶ 50.)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
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Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE:** October 9, 2018

It is the distinct, variable antigen binding domain that permits a TCR to recognize a particular antigen. (Brocker Decl. ¶ 54.) Recognizing that the binding domain presented an opportunity to harness the body's immune response, researchers developed ways of creating "chimeric" TCRs, that is, TCRs that are made by fusing different protein chains together to create a single receptor. (Junghans Decl. ¶ 43.) One of the ways this was accomplished was by linking the variable regions of an antibody—another naturally occurring antigen-receptive element—into a single chain. (Brocker Decl. ¶ 55.) The resulting antigen-specific "single chain antibody fragment" ("scFv") can then be grafted onto other signaling proteins, such as TCRs, permitting those proteins to recognize and respond to the target antigen. (Brocker Decl. ¶ 55.) This is accomplished through the use of recombinent DNA—a process discussed in more detail below.

T Cells utilize a dual-signaling system that combines the initial TCR signal with a second, co-stimulatory signal, reducing the likelihood of erroneous immune response. (Brocker ¶ 57.) When a TCR encounters an antigen that corresponds to its antigen-specific binding domain, it sends a "first signal" to the T Cell. (Brocker ¶ 57.) This first signal is sufficient to trigger an initial immune response. (Brocker ¶ 57.) If the antigen also interacts with the complex's costimulatory receptors, creating a "second signal," the immune response is augmented and/or prolonged. (Brocker ¶ 58.) One such costimulatory domain is CD28. (Junghans ¶ 51.)

The invention claimed in the '190 patent is a nucleotide sequence which encodes a molecule comprising three separate proteins fused into a single chimeric TCR. Specifically, Claim 1 of the '190 Patent recites in full:

> A nucleic acid polymer encoding a chimeric T cell receptor, said chimeric T cell receptor comprising:
>
> (a) a zeta chain portion comprising the intracellular domain of human CD3 ζ chain,
>
> (b) a costimulatory signaling region, and
>
> (c) a **binding element that specifically interacts with a selected target**, wherein the costimulatory signaling region comprises **the amino acid sequence encoded by SEQ ID NO:6**.

('190 Patent col. 25:30-38 [disputed claim terms in bold].) Such a molecule would theoretically be able to initiate a prolonged immune response upon encountering a specifically targeted antigen triggering both a first and second signal. The target antigen could be chosen by the researcher through the selection of the binding element.

B. Molecular Biology and the Construction of Chimeric TCRs

Because the '190 Patent claims only the nucleic acid polymer that encodes a chimeric T cell receptor, it is important to also understand how such a polymer relates to the creation of a TCR.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
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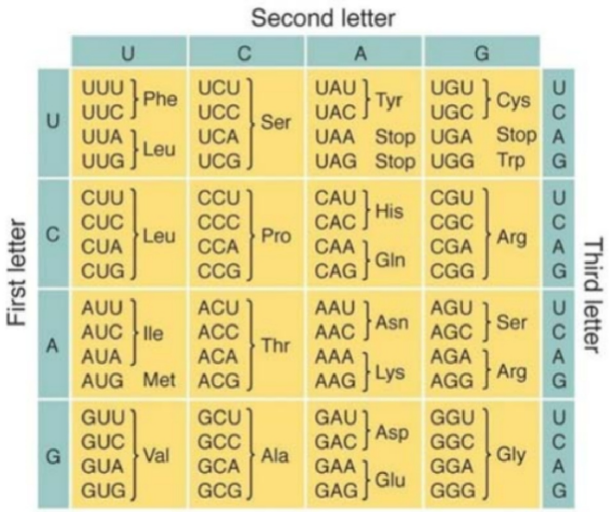
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE:** October 9, 2018

Deoxyribonucleic acids ("DNA") are molecules that contain the genetic information necessary to create the proteins that make up each of the components of chimeric TCRs. (Brocker Decl. ¶ 27; Junghans Decl. ¶ 29.) DNA is chain molecule made up of interlinking nucleotides. (Brocker Decl. ¶¶ 28-29; Junghans Decl. ¶ 29.) DNA nucleotides come in one of four flavors: adenine (A), thymine (T), cytosine (C), and guanine (G). (Brocker Decl. ¶ 28; Junghans Decl. ¶ 29.) Each nucleotide is able to form a pair with its complementary base—A with T and G with C. (Brocker Decl. ¶ 29; Junghans Decl. ¶ 29.) In DNA, nucleotides are organized into two complementary chains of nucleotides forming a double helix. (Brocker Decl. ¶ 29; Junghans Decl. ¶ 29.)

Proteins are manufactured from DNA using a two-step process: transcription and translation. During transcription, the DNA is used as a template to produce a strand of messenger ribonucleic acid ("mRNA"). (Brocker Decl. ¶ 31; Junghans Decl. ¶ 31.) This is accomplished by splitting apart or "denaturing" the DNA double helix and allowing a naturally-occuring enzyme, RNA polymerase, to create a complementary mRNA strand from the denatured DNA. mRNA is very similar to single strand DNA, but substitutes uracil (U) in place of thymine (T). (Brocker Decl. ¶ 31; Junghans Decl. ¶ 31.) Following the transcription process, the mRNA strand undergoes translation, whereby the mRNA is used to synthesize proteins from amino acids. (Brocker Decl. ¶ 32; Junghans Decl. ¶ 31.) This is accomplished by translating the sequence of nucleotides contained in the mRNA into a corresponding sequence of amino acids. (Brocker Decl. ¶ 32; Junghans Decl. ¶ 34.) Each group of three nucleotides, referred to as "codons," correlates to one of approximately 20 amino acids. (Brocker Decl. ¶¶ 32-33; Junghans Decl. ¶ 34.) For example, the nucleotide sequence "GCA" is the codon that results in the amino acid alanine, while "GGC" would code for glycine. (Brocker Decl. ¶ 33.) A full chart of RNA codons and their corresponding amino acids is reproduced below:



(Brocker Decl. ¶ 33.)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE:** October 9, 2018

Thus, the DNA sequence CAAAACCGATGG would translate to glutamine, asparagine, arginine, and tryptophan. In addition to codons that correspond to amino acids, there are several codons that indicate when to stop or start a coding sequence. (Brocker Decl. ¶ 34; Junghans Decl. ¶ 35.) The starting codon is "ATG" and the stop codons are "TGA," "TAA," and "TAG." (Brocker Decl. ¶ 34; Junghans Decl. ¶ 35.) Using this two-step transcription and translation process, a polymeric strand of nucleotides can encode entire complex protein structures.

Using these principles, researchers are able to create chimeric or "recombinant" proteins by fusing together two or more nucleotide sequences that originally coded for wholly separate proteins. (Brocker Decl. ¶ 35; Junghans Decl. ¶ 39.) One method of creating such a protein is through the use of "restriction enzyme cloning." (Brocker Decl. ¶ 36; Junghans Decl. ¶ 39.) This process uses a set of specialized proteins, or "primers," to target and amplify a particular portion of a longer DNA sequence. (Brocker Decl. ¶¶ 36, 38; Junghans Decl. ¶ 38.) Primers are short single-strand nucleotide sequences (typically 18-22 nucleotides in length) that are complementary to the nucleotides found at a specific site ("restriction site") of the target DNA sequence. (Brocker Decl. ¶ 36; Junghans Decl. ¶ 38.) The primer that is complementary to the front end of the target sequence is known as the "upstream" primer. (Junghans Decl. ¶ 38.) The primer that is complementary to the rear end of the DNA sequence is known as the "downstream" primer. (Junghans Decl. ¶ 38.) Once the primers have attached to each of the targeted restriction cites, a "restriction enzyme" is used to cut or "cleave" the target sequence from the larger DNA chain. (Brocker Decl. ¶ 36.) One example of restriction enzyme is Not1, which is used to cleave DNA segments at the sequence GCGGCCGC:

(Junghans Decl., Fig. 4.) The process of cleaving a DNA sequence creates a "sticky end" or a complementary overhang which can be used to join DNA segments to one another. (Brocker Decl. ¶ 37; Junghans Decl. ¶ 39.) In this manner, researchers are able to target particular portions of a longer DNA chain using primers, cut them using restriction enzymes, and attach them to one another using the resulting complementary overhangs, creating a combined DNA sequence encoding a chimeric protein.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

III. LEGAL STANDARDS

A. Principles of Claim Construction

Before a jury can determine if any of the asserted claims are invalid or if the defendant's technology infringes one or more asserted claims, the court must determine the meaning and scope of the asserted claims through the process of "claim construction." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 976 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370, 116 S. Ct. 1384 (1996). Only after the claims have been construed can the jury compare the allegedly infringing device against the claims. *Id.*

In *Phillips v. AWH Corp.*, 415 F.3d 1303, 1311-24 (Fed. Cir. 2005) (en banc), the en banc Federal Circuit set forth a number of principles to guide lower courts through the claim construction process. The general rule is that the words of a claim "are generally given their ordinary and customary meaning," which is "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application" *Id.* 1312-13 (citations omitted). "[T]he person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification." *Id.* at 1313.

"In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words." *Id.* at 1314. "In such circumstances, general purpose dictionaries may be helpful." *Id.* Where, however, "determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art," courts look to other sources, including "the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art." *Id.* (quoting *Innova/Pure Water, Inc. v. Safari Water Filtration Sys., Inc.*, 381 F.3d 1111, 1116 (Fed. Cir. 2004)).

Moreover, "[t]he claims themselves provide substantial guidance as to the meaning of particular claim terms," for example by observing "the context in which a term is used in the asserted claim." *Id.* Comparing the usage of a term across different claims and examining difference among claims can also provide valuable insight into the meaning of claim terms. *Id.*

"The claims, of course, do not stand alone," and the specification provides "the single best guide to the meaning of a disputed term." *Id.* at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). One reason the specification is of paramount importance is that it "may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess." *Id.* at 1316; *see also Markman*, 52 F.3d at 980 ("[A]

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

patentee is free to be his own lexicographer"). That said, "[t]hough understanding the claim language may be aided by explanations contained in the written description, it is important not to import into a claim, limitations that are not part of the claim. For example, a particular embodiment appearing in the written description may not be read into a claim when the claim language is broader than the embodiment." *Superguide Corp. v. DirecTV Enters., Inc.*, 358 F.3d 870, 875 (Fed. Cir. 2004). Moreover, the prosecution history, which consists of the complete record of the proceedings before the PTO and includes the prior art cited during the examination of the patent, may also shed "decisive light" on the proper construction of a claim term, particularly where an applicant limits her invention to overcome prior art. *Regents of Univ. of Cal. v. Dakocytomation Cal., Inc.*, 517 F.3d 1364, 1372-73 (Fed. Cir. 2008); *Phillips*, 415 F.3d at 1316-17; *N. Am. Container, Inc. v. Plastipak Packaging, Inc.*, 415 F.3d 1335, 1345 (Fed. Cir. 2005); *Seachange Int'l, Inc. v. C-Cor Inc.*, 413 F.3d 1361, 1372-73 (Fed. Cir. 2005).

District courts may also rely on extrinsic evidence, which "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises," in construing claims, although such evidence is afforded less significance than the intrinsic record. *Phillips*, 415 F.3d at 1317 (citations omitted). "[W]hile extrinsic evidence 'can shed useful light on the relevant art,' we have explained that it is 'less significant than the intrinsic record in determining "the legally operative meaning of claim language."'" *Id.* (citations omitted).

In summation, although "there is no magic formula or catechism for conducting claim construction . . . . certain types of evidence are more valuable than others," and "what matters is for the court to attach the appropriate weight" to each piece of evidence. *Phillips*, 415 F.3d at 1324.

B. Means-Plus-Function Claiming

In its opinion in *Williamson v. Citrix Online, LLC*, 792 F.3d 1339 (Fed. Cir. 2015), the Federal Circuit modified the standard for determining whether a claim element is governed by 35 U.S.C. § 112, para. 6, which provides that

> [a]n element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

35 U.S.C. § 112(f). The Federal Circuit majority began by observing that its "precedent has long recognized the importance of the presence or absence of the word 'means'" in determining whether § 112, para. 6 applies, and that a "strong" but rebuttable presumption had arisen that was tethered to the inclusion of the word "means." 792 F.3d at 1348-49. The majority found this "heightened burden [to be] unjustified," and accordingly "abandon[ed] characterizing as 'strong' the presumption that a limitation lacking the word 'means' is not subject to § 112, para.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

6." *Id.* at 1349. The majority clarified that "[t]he standard is whether the words of the claim are understood by persons of ordinary skill in the art to have a sufficiently definite meaning as the name for structure." *Id.* (citing *Greenberg v. Ethicon Endo-Surgery, Inc.*, 91 F.3d 1580, 1583 (Fed. Cir. 1996)). Thus, "[w]hen a claim term lacks the word 'means,' the presumption can be overcome and § 112, para. 6 will apply if the challenger demonstrates that the claim term fails to 'recite sufficiently definite structure' or else recites 'function without reciting sufficient structure for performing that function.'" *Id.* (quoting *Watts v. XL Sys., Inc.*, 232 F.3d 877, 880 (Fed. Cir. 2000)).

In applying these principles to the claims before it, the majority held that "[g]eneric terms such as 'mechanism,' 'element,' 'device,' and other nonce words that reflect nothing more than verbal constructs may be used in a claim in a manner that is tantamount to using the word 'means' because they 'typically do not connote sufficiently definite structure' and therefore may invoke § 112, para. 6." *Id.* at 1350 (quoting *Mass. Inst. of Tech. & Elecs. for Imaging, Inc. v. Abacus Software*, 462 F.3d 1344, 1354 (Fed. Cir. 2006)). The majority then concluded that the term "distributed learning control module" was subject to the provisions § 112, para. 6, notwithstanding the absence of the term "means." In particular, the majority noted that "[w]hile portions of the claim do describe certain inputs and outputs at a very high level (e.g., communications between the presenter and audience member computer systems), the claim does not describe how the 'distributed learning control module' interacts with other components in the distributed learning control server in a way that might inform the structural character of the limitation-in-question or otherwise impart structure to the 'distributed learning control module' as recited in the claim." *Id.* at 1351.

Where a claim element is subject to application § 112, para. 6, the court must then determine "whether the specification discloses sufficient structure that corresponds to the claimed function." *Id.* If the patentee fails to disclose adequate corresponding structure to perform all of the claimed functions, the claim is indefinite. *Id.* at 1351-52 (citing *Noah Sys., Inc. v. Intuit Inc.*, 675 F.3d 1302, 1311-12 (Fed. Cir. 2012)).

IV. ANALYSIS

A. Definition of "Person of Ordinary Skill in the Art" at the Time of the Invention

Defendant asserts that a person of ordinary skill in the art ("POSITA") at the relevant time would have had a Ph.D. or an M.D. in "immunology, biochemistry, cell biology, molecular biology, or a related discipline and at least two years of experience in conducting laboratory research on chimeric TCR therapies, TCRs, T cells or other types of immune cells, chimeric TCRs or related work." (Junghans Decl. ¶ 28.) Plaintiff generally agrees with the educational requirements (albeit considering a M.Sc. sufficient), but would only require that the POSITA have "knowledge of the scientific literature relating to T cell biology, as well as laboratory techniques and strategies in designing recombinant DNA." (Brocker Decl. ¶ 21.) The Court

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

does not find that there is any material dispute between the parties on the definition of a POSITA, and therefore adopts a definition that incorporates the characteristics proposed by both parties.

B. "the amino acid sequence encoded by SEQ ID NO:6"

The parties' first dispute centers on the meaning of the term "the amino acid sequence encoded by SEQ ID NO:6," which is recited in independent claim 1 of the '190 Patent as "the costimulatory signaling region comprising the amino acid sequence encoded by SEQ ID NO:6." ('190 Patent col. 25:36-38.) The parties' positions are provided below:

Plaintiff's Proposed Construction	Defendants' Proposed Construction
"Amino Acids 114-220 of CD28 (starting with isoleucine (I))"	**Before the Certificate of Correction:** "Amino Acids 113-220 of CD28 (starting with lysine (K))**"** **After the Certificate of Correction:** Kite agrees with Juno's proposed construction

The parties disagreement is straightforward. Juno contends that "the amino acid sequence encoded by SEQ ID NO:6," as defined in the originally-issued patent, should be construed as beginning with Isoleucine and comprising the amino acids **114**-220 (corresponding to nucleotides **340-**660) of the CD28 protein. Kite, on the other hand, contends that the original patent defined the term as a sequence beginning with Lysine and comprising the amino acids **113**-220 (corresponding to nucleotides **337**-660) of the CD28 protein.

At the center of the parties' dispute is the 2012 Certificate of Correction to the '190 Patent. In the specification as issued in 2008, SEQ ID NO:6 is described as having a length of 328 nucleotides and beginning with nucleotide 336 of the CD28 protein. ('190 Patent col. 15.) The Certificate of Correction alters the definition of this sequence, such that it has a length of 321 nucleotides and begins with nucleotide 340 of the CD28 protein. ('190 Patent, Certificate of Correction.) Defendant claims that this alteration materially changes the scope of the claim terms and intends to challenge the issuance of the Certificate of Correction on these grounds.

Plaintiff first argues that there is no reason to separately assess the scope of the original claim term as the Certificate of Correction supplants the original patent and "shall have the same effect and operation in law on the trial of actions for causes thereafter arising as if the same had been originally issue in such corrected form." 35 U.S.C. § 255. As Defendant notes, however, the

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

very validity of the CoC is at issue and "[i]nvalidating a certificate of correction for impermissible broadening [] requires proof of two elements: (1) the corrected claims are broader than the original claims; and (2) the presence of the clerical or typographical error, or how to correct that error, is not clearly evident to one of skill in the art." *Central Admixture Pharmacy Services, Inc. v. Advanced Cardiac Solutions, P.C.*, 482 F.3d 1347, 1353 (Fed. Cir. 2007). Therefore, while the Court will not rule on the ultimate issue of the CoC's validity at this time, it must nevertheless interpret both the original and amended claims to determine whether they do indeed differ in scope. *Id.*

In determining the scope of a claim term, the Court ordinarily begins with the plain meaning of a claim term. However, because neither party argues that "SEQ ID NO:6" has any plain meaning, it turns instead to the specification, which provides "the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996)). In the specification of the '190 Patent, there are both explicit and implicit definitions of "the amino acid sequence encoded by SEQ ID NO:6." The Court finds that the explicit definition of SEQ ID NO: 6 is provided in the sequence list and describes a sequence beginning with the nucleotide sequence "CAAAATTGAA . . . ," corresponding to the CD28 sequence spanning nucleotides 336-660.

Plaintiffs dispute that this is an express definition, arguing that a person of skill in the art would look beyond the sequence listing to determine the definition, examining primers and other less direct clues in the specification to determine where the sequence begins and ends. (Pl.'s Brief, at 9.) The Court finds, however, that the sequence listing provides, at least in this particular instance, the explicit definition of "the amino acid sequence **encoded by SEQ ID NO:6**" because the claim term expressly points a reader—not to the other potential means of defining the sequence—but directly to the sequence listing itself. The claim term is not, for instance, "the amino acid sequence encoded by the nucleotide sequence **defined by primers SEQ ID NO:4 and SEQ ID NO:5**." Nor is it "the amino acid sequence **corresponding to amino acids 114-220 of CD28**."

While the express definition ordinarily governs the construction of a claim term, the Court nevertheless considers the remainder of the intrinsic record to determine if this definition is rebutted by conflicting definitions. Plaintiffs focus on various information contained in the specification that they assert would indicate to a personal of ordinary skill in the art that the amino acid sequence begins, not at position 113, but rather at the isoleucine found at position 114. In particular, they focus on (1) the provisional application, (2) the specification, (3) the prosecution history, and (4) Defendant's positions taken during IPR. The Court will address each in turn.

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UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

1. Provisional Application

On May 28, 2002, provisional Application No 60/383,872 was filed with the USPTO. (Heinrich Decl., Exh 4 ("Provisional Appl.").) The invention claimed in this Provisional Application was described in a journal article, written by the inventors of the '190 Patent, which was incorporated by reference. In this article, the inventors identified the set of PCR primers used to isolate and amplify the portion of the CD 28 used to construct the costimulatory region of the claimed T-Cell Receptor. The article states that "nucleotides 336-660 of CD28 were amplified using primers 1 (5'-GGCGGCCGCAATTGAAGTTATGTATC-3') and 2 (5'-TGCGCTCTCCTGCTGAACTTCACTCTGGAGCGATAGGCTGCGAAGTCGCG-3')." (Provisional Appl., at 7.) Plaintiffs contend that these primers correspond to a CD 28 domain beginning with isoleucine, and argue that a POSITA "would know to align these primers to the publicly-known sequence of CD28, and in so doing would have readily seen that the CD 28 domain of the construct begins with the isoleucine at amino acid 114 of CD28." (Pl.'s Brief, at 7.) While it is true that these definitions, one by nucleotide number and one by primer, differ from one another, there is nothing in the provisional application that would clarify which of the two definitions is correct. The Court therefore concludes that nothing in the Provisional Application rebuts the explicit definition provided in the sequence listing.

2. Specification

In arguing that the specification defines the claim term differently than does the sequence list, Plaintiffs point to the following passage from column 4 of the '190 Patent.

> In one embodiment, where CD 28 is between the zeta chain portion and csFv, the CD28 portion suitably includes the transmembrane and signaling domains of CD28,i.e., the portion of CD28 cDNA spanning nucleotides 340 to 663, including the stop codon (amino acids 114-220 of Seq. ID No. 10). This portion of CD28 can be amplified by PCR using the primers of Seq ID No. 4 and 5. The full sequence of this region is set forth in Seq ID No: 6.

('190 Patent, col. 4:21-28.) This section defines the given sequence in three ways. The first is its reference to the explicit definition in the sequence list. As discussed previously, this definition clearly defines the sequence as nucleotides 336-660 of the CD28 protein. The second definition directly contradicts this by identifying "the portion of CD28 cDNA spanning nucleotides 340 to 663, including the stop codon (amino acids 114-220 of Seq. ID No. 10)." (190 Patent, col. 4:24-26.) As provided in the sequence listing, SEQ ID NO:10 provides the amino acid sequence of CD28 wherein amino acid 114 is isoleucine, consistent with Juno's current position. Defendant notes, however, that the particular language used in this section is open-ended, stating merely that "the CD28 portion **suitably includes** . . . the portion of CD28 spanning nucleotides 340 to 663"—implying that it could encompass more than this portion. While this is admittedly a

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE:** October 9, 2018

somewhat unnatural interpretation, it is not entirely unreasonable and a POSITA might arrive at this understanding in an attempt to read the specification consistently and bring column 4 in line with the express definition found in the sequence listing.

The final definition provided in column 4—the "portion of CD 28 [that] can be amplified by PCR using the primers of Seq ID No. 4 and 5"—is also somewhat unclear. ('190 Patent, col. 4:26-27.) SEQ ID NO:4 is defined twice in the specification, once in the sequence listing and once in column 7. These definitions differ from one another in both the number of nucleotides they contain and the portion of CD28 that they amplify. (Junghans Decl. ¶ 88.) Furthermore, Defendant's expert claims, neither version of the primer would result in the sequence claimed by Plaintiffs in their CoC. (Junghans Decl. ¶ 89.) The first would amplify a nucleotide sequence beginning with nucleotide 339 of the CD28 protein,[1] while the second would amplify the sequence beginning with nucleotide 342. (Junghans Decl. ¶ 89.)

In addition to column 4, Defendant draws the Court's attention to two other portions of the specification. First is SEQ. ID NO:11, which Defendant asserts corresponds directly to the amino acid sequence encoded by SEQ. ID NO:6 and begins, not with isoleucine, but with lysine. This, it claims, is further evidence that Plaintiffs intended to claim the amino acid sequence that appeared in the original issued patent. While this is admittedly an intriguing correlation, it carries little weight as SEQ ID NO:11 is never specifically referenced in the written description and is, it seems, vestigial. The second portion of the specification to which Defendant cites is column 7, where the patent appears to pull language from the Provisional Application and states that "nucleotides 336-660 of CD28 were amplified using primers . . ." ('190 Patent, col. 7:52-53.) This nucleotide sequence maps directly onto the original SEQ. ID NO:6—including the allegedly extraneous leading cytosine. Plaintiffs contend that this is yet another clerical error and points to the fact that this same language was corrected in column 4 during the prosecution of the '190 Patent. (Pl.'s Brief, at 8-9.) "A POSA," they claim, "would clearly recognize that column 7 was merely an oversight to be corrected in the same manner." (Pl.'s Brief, at 9.) Column 7's description is, however, consistent with original SEQ ID NO:6, and could just as easily lead a POSITA to the opposite conclusion: that column 7's description is correct and that it is column 4 that is the outlier.

Plaintiffs' final contention is that a POSITA would know that the nucleotide sequence originally identified as SEQ. ID NO:6 was incorrect because the number of nucleotides was not divisible by three. Defendant offers two convincing arguments why this is not the case. First, it notes that the CD28 portion does not exist on its own, but as a single component of a three part chimeric TCR. Because the entire TCR is made up of amino acids, it is the nucleotide sequence of the entire

[1] An argument made less persuasive by Dr. Abken's position during IPR that the primer disclosed in the post-CoC SEQ ID NO:4 "align[s] perfectly with the start of SEQ ID NO: 6." (Abken Decl. ¶ 100)

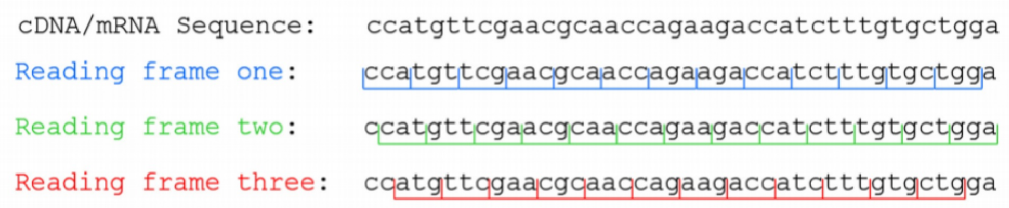
UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE:** October 9, 2018

TCR chain that must be divisible by three—not the individual components, which may contain additional nucleotides utilized during ligation. Secondly, Defendant's expert contends that a POSITA would have easily been able to determine the correct amino acid sequence by applying the correct "reading frame." (Junghans Decl. ¶ 79.) He explains that a given sequence of nucleotides can be read in one of three "frames." (Junghans Decl. ¶ 79.) The first frame assumes that a given sequence begins with a complete codon, the second that there is a single, leading nucleotide before the first codon, and the third frame includes two leading nucleotides. (Junghans Decl. ¶ 79.) Dr. Junghans provides the following example in his declaration:



(Junghans Decl., Fig 2.) In order to determine which reading frame is correct, Junghans explains, a POSITA would likely look for the longest "open reading frame"; that is, the longest amino acid sequence uninterrupted by a stop codon ("TGA", "TAA", or "TAG").[2] (Junghans Decl. ¶ 37.)

Dr. Junghans opines that examining SEQ ID NO:6 using each of the three reading frames makes readily apparent that frame 2 is the appropriate approach:

> [A] POSA would generally look for a reading frame with the longest uninterrupted sequence useful for encoding an amino acid sequence. The first reading frame includes a stop codon after just six nucleotides, followed by five other stop codons within the chain. The third reading frame begins with a slightly longer sequence, however, it still includes just 32 nucleotides prior to the initial stop codon, followed by six other stop codons within the chain. Unlike the first and third, the second reading frame includes a single stop codon at the very end of the sequence and provides the longest open reading frame.

(Junghans Decl. ¶ 79.)

In light of the above, the specification is, at best, ambiguous regarding the nucleotide sequence comprising SEQ. ID NO:6. The sequence described in column 7 and the explicit definition contained in the sequence list would indicate to a POSITA that the patent is claiming nucleotides

[2] Alternatively, a researcher could make use of the Basic Local Assignment Search Tool ("BLAST"), a free and publicly available software tool that uses a database of known DNA sequences to properly align the sequence. (Junghans Decl. ¶ 36.)

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
Send	____
Enter	____
Closed	____
JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

336-660 of CD28, a sequence that, correctly framed, would result in a leading lysine, consistent with Defendant's proposed construction. The information found in column 4 may also be interpreted in a manner consistent with this understanding due to its use of open-ended language. It is only the primers disclosed in column seven and the sequence list that would produce a sequence potentially consistent with Plaintiffs' proposed definition. Yet even here, the specification is unclear, providing two conflicting definitions for SEQ ID NO: 4.

In this way, the present case differs from *Cubist Pharms., Inc. v. Hospira, Inc.*, in which the Federal Circuit found that a claimed compound was not expressly defined by the chemical diagram in the specification. 805 F.3d 1112, 1118 (Fed. Cir. 2015). There, the inventor was granted a certificate of correction altering the structural diagram of a compound labeled "Formula 3." *Id.* at 1116. The court found that, while the alteration was material, the diagram was only one definition of the claim term and was in direct conflict with several other definitions found in the original specification, including references to compounds that were well-known in the art. *Id.* at 1115. Furthermore, the diagram represented the universal understanding of the known compound's structure at the time of filing and it was only years later that researchers discovered that this universal understanding was incorrect. *Id.* at 1116. Here, however, there is no evidence that the specific portion of CD28 referenced in the specification was well-known in the art, nor was the correction related to any new understanding on the part of the scientific community as a whole. Because the sequence listing is supported by numerous other statements found in the specification, the Court finds the disclosure of specific primers, without more, insufficient to rebut the express definition in the sequence listing.

3. Prosecution History

As an initial matter, the Court notes that, while "the prosecution history provides evidence of how the PTO and the inventor understood the patent," it "represents an ongoing negotiation between the PTO and the application, rather than the final product of that negotiation, [and] often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Phillips*, 415 F.3d at 1317. "The purpose of consulting the prosecution history in construing a claim is to 'exclude any interpretation that was disclaimed during prosecution.'" *Id.* (quoting *Chimie v. PPG Indus., Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005)).

Plaintiffs contend that the following events that occurred during the prosecution of the '190 Patent would indicate to a POSITA its intent to claim amino acids 114-220. On September 4, 2007, the applicants filed a Request for Continued Examination ("RCE") claiming that:

> In preparing to pay the issue fee for this application, it was determined that an error occurred in the presentation of Seq. ID No. 6, which is recited in the previously allowed claims. In addition, a discrepancy was noted between the bases of Seq ID No. 4 in the specification [] and the sequence listing. Finally, it was noted that the

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

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Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

> Seq ID No. 10 was not referenced in the specification and that the amino acids of the CD28 Sequence (144-220 contained a typographical error and should have been 114-220). This RCE application and amendment are filed to correct these errors.

(RCE, Sept. 4, 2007.)

Along with this request, the applicants submitted a sequence listing which amended (1) SEQ ID NO:4—the nucleotide sequence of the upstream primer—to add a single Thymine, bringing it into agreement with the primer sequence disclosed in column 7 of the specification, and (2) SEQ ID NO:6, removing the first four nucleotides, such that the first codon corresponds to isoleucine, amino acid 114 of CD28, rather than lysine, amino acid 113. This amended listing was rejected by the Patent Office as "damaged and/or unreadable," prompting the applicants to provide a new copy. This copy, too, reflected the amendments requested in the RCE. The Patent Office again rejected the filing, this time for failure to comply with the USPTO formatting requirements. The applicants reformatted the listing and, for the third time, filed an amended sequence listing with the Patent Office. This time, however, they included the original sequence listing that did not reflect the amendments originally requested in the RCE. It was this unaltered listing that was ultimately included in the patent as it was finally issued.

Plaintiffs contend that "any reasonable reader of the prosecution history would understand that the applicants inadvertently submitted the original, incorrect sequence listing in their April 16, 2008 submission." (Pl.'s Brief, at 12.) While it is true that this is one possible interpretation of the events, it is also possible for a POSITA to conclude that the applicants intentionally submitted the original sequence listing.[3] Ultimately, the ambiguity of the prosecution history would require a POSITA to guess at the applicants' intent. Such a level of uncertainty is insufficient to overcome the express definition as provided in the sequence listing and supported by numerous portions of the specification.

4. IPR History

Plaintiffs' final argument is that there are contradictions between the testimony of Dr. Junghans in this action and Kite's expert during the IPR, Dr. Abken. Specifically, they point to the fact that, during the IPR, both parties and their experts agreed that a certain prior art publication (the "Krause Paper") disclosed the same amino acid sequence as the amino acid sequence encoded by SEQ ID NO:6. (Pl.'s Brief, at 13-14.) In reaching this conclusion, Dr. Abken observed that "[b]oth Krause's forward primer and the '190 Patent's forward primer (SEQ ID NO: 4) align

[3] Or, more cynically, that the ambiguity was intentional, calculated to permit the patent-holder to determine at a later date which of the two positions was more advantageous.

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

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JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

perfectly with the start of SEQ ID NO: 6 (*i.e.*, ATTGA . . .)." (Heinrich Decl., Exh. 8 ("Abken Decl.") ¶ 100.) Plaintiffs also point to a diagram prepared by Dr. Abken which depicts SEQ ID NO:6 beginning with ATT—the codon for isoleucine. (Pl.'s Brief, at 14.) These disclosures, they claim, demonstrate that Kite's expert recognized and accepted that SEQ ID NO:6 encoded an amino acid sequence beginning at amino acid 114.

Defendant correctly observes, however, that a petitioner cannot challenge the validity of the certificate of correction during an IPR proceeding and therefore argues that Dr. Abkens statements did not relate to his understanding of SEQ ID NO:6 as disclosed in the original issuance of the '190 Patent, but rather reflected his views on the '190 Patent after the USPTO issued its Certificate of Correction. The Court finds this argument persuasive. Because a patent can only be challenged during IPR on grounds of anticipation or obviousness, Dr. Abkens statements have no bearing on the meaning of the patent as it initially appeared upon issuance. 35 U.S.C. § 311.

5. Conclusion

In a sense, this dispute strikes at the heart of the policy undergirding patent law. Patents are, at their core, a "carefully crafted bargain that encourages both the creation and the public disclosure of new and useful advances in technology." *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 63 (1998). They "grant[] inventors 'the right to exclude others from making, using, offering for sale, selling, or importing the patented invention,' in exchange for full disclosure of [the] invention." *Markman,* 517 U.S. at 373 quoting H. Schwartz, Patent Law and Practice 1, 33 (2d ed. 1995). In order to serve this function, "it has long been understood that a patent must describe the exact scope of an invention and its manufacture to 'secure to [the patentee] all to which he is entitled, [and] to apprise the public of what is still open to them.'" *Markman,* 517 U.S. at 373 (quoting *McClain v. Ortmayer*, 141 U.S. 419, 424 (1891)). For this reason, claim terms are interpreted—not based on the intent of the patentee—but based on the understanding of POSITA as members of the public.

In order for a POSITA to arrive at Plaintiffs' proposed construction, she must first determine that (1) the provisional application incorrectly identified the claimed sequence, (2) the originally submitted patent application incorrectly identified the claimed sequence in three separate locations, (3) the applicants attempted to correct the mistakes in column 4, but failed to do so in column 7, and (4) in their attempt to correct the sequence listing, the applicants accidentally submitted the incorrect sequence listing on their third attempt to file corrections. While it is possible that each of these mistakes did occur and that the patentee's intent was to claim the sequence beginning with nucleotide 340 of the CD28 protein, it is unreasonable to expect a POSITA to make each of these assumptions despite (1) the '190 Patent's express definition of SEQ ID NO:6 in the sequence listing, (2) the support for this definition within the specification, and (3) the fact that the other purported definition as provided in the amended column 4 is open-

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

Priority	____
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JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE:** October 9, 2018

ended and may be read in a manner consistent with the sequence listing. Accordingly, the Court concludes that the '190 Patent explicitly defined the claim term "the amino acid encoded by SEQ ID NO:6" by way of the sequence listing and that nothing in the intrinsic record is sufficient to overcome this express definition.

For this reason, the Court finds that a POSITA encountering the '190 Patent prior to the CoC would have understood SEQ ID NO:6 to begin with nucleotide 336 of the CD28 protein. It further finds that, when SEQ ID NO:6 is proper framed, it encodes an amino acid sequence corresponding to "amino acids 113-220 of CD28 (starting with lysine (K))." For this reason, the Court construes the term as follows:

Claim Term	Court's Construction
"the amino acid sequence encoded by SEQ ID NO:6"	**Before the Certificate of Correction:** Amino Acids 113-220 of CD28 (starting with lysine (K)) **After the Certificate of Correction:** Amino Acids 114-220 of CD28 (starting with isoleucine (I))

C. "nucleic acid polymer encoding . . . a binding element that specifically interacts with a selected target"

The parties next dispute whether the term "nucleic acid polymer encoding . . . a binding element that specifically interacts with a selected target," found in claim 1, is a means plus function term governed by 35 U.S.C. § 112(6). The parties' positions are provided below:

Plaintiff's Proposed Construction	Defendants' Proposed Construction
Plain and ordinary meaning	Term "binding element" is governed by 35 U.S.C. § 112(6).

When a limitation "recit[es] a function be performed rather than . . . reciting structure for performing that function," the scope of the claim is limited "to only the structure, materials, or acts described in the specification as corresponding to the claimed function and equivalents." *Williamson v. Citrix Online LLC,* 792 F.3d 1339, 1347-48 (Fed. Cir. 2015). While this restriction ordinarily applies only to those claim terms utilizing the word "means," 35 U.S.C. § 112(6) may also apply to certain "nonce words" if "the claim term fails to 'recite sufficiently definite structure' or else recites 'function without reciting sufficient structure for performing that function.'" *Williamson*, 792 F.3d at 1349. Claims that do not explicitly use the term "means" are entitled to

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

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JS-5/JS-6	____
Scan Only	____

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

a rebuttable presumption that they are not implicated by § 112(6). *Id.* at 1348; *EnOcean GbH v. Face Int'l Corp.*, 742 F.3d 955, 959 (Fed. Cir. 2014).

Here, Defendant contends that the use of the term "binding element" in Claim 1 of the '190 Patent is just such a nonce word and that the scope of the claim term should therefore be limited only to SJ25C1-derived scFv and J591-derived scFv—the specific embodiments disclosed in the specification. (Def.'s Brief, at 17-20.) Plaintiffs respond that (1) "binding element" is not a nonce word, and (2) the preamble defines the binding element as part of a CAR-T encoded by a nucleic acid polymer and must therefore be a polypeptide. (Pl.'s Brief, at 15-19.) Before determining whether the specification provides sufficient structure, the Court must first decide whether "binding element" is, in fact, a word that is "tantamount to using the word 'means.'" *Williamson*, 792 F.3d at 1350.

Defendant's expert claims that "a POSA would have understood the term [binding element] to convey a purely functional meaning, *i.e.*, a means for binding and specifically interacting with a selected target." (Junghans Decl. ¶ 100.) This very statement, however, undermines his argument that the term is a nonce word; the fact that he reads the term to describe an element that binds to and specifically interacts with a selected target reveals that he does have an understanding of the term's scope. Constrained by the biochemistry required to "bind" to a potential antigen, there is a limited universe of appropriate "binding element[s] that specifically interact[] with a particular target." Defendant admits as much in its invalidity contentions, stating that "[a] person of ordinary skill in the art would understand that the term 'binding element' could include any polypeptide, including for example, receptors, receptor ligands, antibodies, and single chain antibodies." (Heinrich Decl., Exh. 11 ("Invalidity Contentions"), ECF No. 85-11; Abken Decl. ¶ 45 (Defendant's IPR expert stating that researchers were aware of the use of "binding elements" to target antigens at the time of invention of the '190 Patent and that "[t]ypically, the binding element was an antibody or an antibody fragment, with single chain antibody fragments ("scFv") being preferred . . .")).

The disagreement between the parties, then, is not whether a POSITA would have known the class of elements being claimed, but whether narrowing the possible choices to a particular set of polypeptides is sufficient. On this, the Federal Circuit has been clear. A claim term "need not connote a single specific structure; rather it may describe a class of structures." *Apple v. Motorola, Inc.*, 757 F.3d 1286, 1301 (Fed. Cir. 2014), *overruled on other grounds by Williamson*, 792 F.3d at 1349. "To determine whether a claim recites sufficient structure, 'it is sufficient if the claim term is used in common parlance or by persons of skill in the pertinent art to designate structure, even if the term covers a broad class of structures and even if the term identifies the structures by their function.'" *Skyy, Inc. v. MINDGEEK, S.A.R.L.*, 859 F.3d 1014, 1019 (Fed. Cir. 2017) (quoting *TecSec, Inc. v. Int'l Bus. Machs. Corp.*, 731 F.3d 1336, 1347 (Fed. Cir. 2013)). Such is the case here. As evidenced by Defendant's own expert witnesses, a POSITA encountering the disputed claim term would understand it to denote

UNITED STATES DISTRICT COURT
CENTRAL DISTRICT OF CALIFORNIA

CIVIL MINUTES - GENERAL

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Closed	___
JS-5/JS-6	___
Scan Only	___

CASE NO.: 2:17-cv-07639 SJO (RAOx) **DATE: October 9, 2018**

a particular class of structures—namely polypeptides capable of specifically interacting (*i.e.*, binding) with a particular antigen target. For this reason, the Court finds that § 112(6) is not implicated in this instance. To the extent that Defendant argues that the patent claims too wide a range of species, this is not an argument properly grounded in §112(6), but rather in written description or enablement—claims properly brought upon summary judgment, not at claim construction.

Claim Term	Court's Construction
"nucleic acid polymer encoding . . . a binding element that specifically interacts with a selected target"	Plain and ordinary meaning

V. CONCLUSION

For the foregoing reasons, the Court construes the disputed claim terms as follows:

1. **"the amino acid sequence encoded by SEQ ID NO:6"** before the Certificate of Correction means **"Amino Acids 113-220 of CD28 (starting with lysine (K))"** and after the Certificate of Correction means **"Amino Acids 114-220 of CD28 (starting with isoleucine (I))"**
2. **"nucleic acid polymer encoding . . . a binding element that specifically interacts with a selected target"** is given its **plain and ordinary meaning**.

IT IS SO ORDERED.

The United States of America

The Director of the United States Patent and Trademark Office

Has received an application for a patent for a new and useful invention. The title and description of the invention are enclosed. The requirements of law have been complied with, and it has been determined that a patent on the invention shall be granted under the law.

Therefore, this

United States Patent

Grants to the person(s) having title to this patent the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States of America or importing the invention into the United States of America for the term set forth below, subject to the payment of maintenance fees as provided by law.

If this application was filed prior to June 8, 1995, the term of this patent is the longer of seventeen years from the date of grant of this patent or twenty years from the earliest effective U.S. filing date of the application, subject to any statutory extension.

If this application was filed on or after June 8, 1995, the term of this patent is twenty years from the U.S. filing date, subject to any statutory extension. If the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121 or 365(c), the term of the patent is twenty years from the date on which the earliest application was filed, subject to any statutory extensions.

Jon W. Dudas

Director of the United States Patent and Trademark Office

Plaintiffs' Trial Exhibit

PX0001

Case No. 2:17-cv-07639 SJO-KS

PX0001.1

(12) **United States Patent**
Sadelain et al.

(10) **Patent No.: US 7,446,190 B2**
(45) **Date of Patent: Nov. 4, 2008**

(54) **NUCLEIC ACIDS ENCODING CHIMERIC T CELL RECEPTORS**

(75) Inventors: **Michel Sadelain**, New York, NY (US); **Renier Brentjens**, Maplewood, NJ (US); **John Maher**, Surrey (GB)

(73) Assignee: **Sloan-Kettering Institute for Cancer Research**, New York, NY (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 458 days.

(21) Appl. No.: **10/448,256**

(22) Filed: **May 28, 2003**

(65) **Prior Publication Data**

US 2004/0043401 A1 Mar. 4, 2004

Related U.S. Application Data

(60) Provisional application No. 60/383,872, filed on May 28, 2002.

(51) **Int. Cl.**
C07H 21/04 (2006.01)

(52) **U.S. Cl.** **536/23.4**; 536/23.53

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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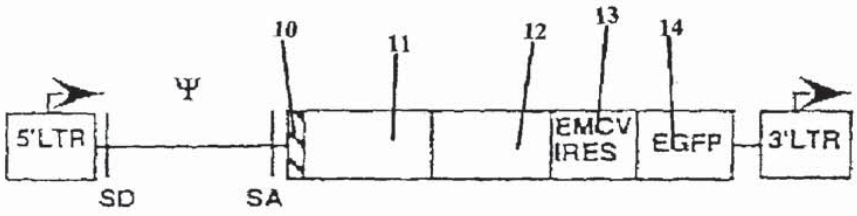
Primary Examiner—Ilia Ouspenski
(74) *Attorney, Agent, or Firm*—Marina Larson & Associates, LLC

(57) **ABSTRACT**

Chimeric T cell receptors (TCR) are provided that combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain, a signaling region from a costimulatory protein such as CD28, and a binding element that specifically interacts with a selected target. When expressed, for example in T-lymphocytes from the individual to be treated for a condition associated with the selected target, a T cell immune response is stimulated in the individual to the target cells. The chimeric TCR's are able to provide both the activation and the co-stimulation signals from a single molecule to more effectively direct T-lymphocyte cytotoxicity against the selected target and T-lymphocyte proliferation.

13 Claims, 8 Drawing Sheets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Ψ
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SD
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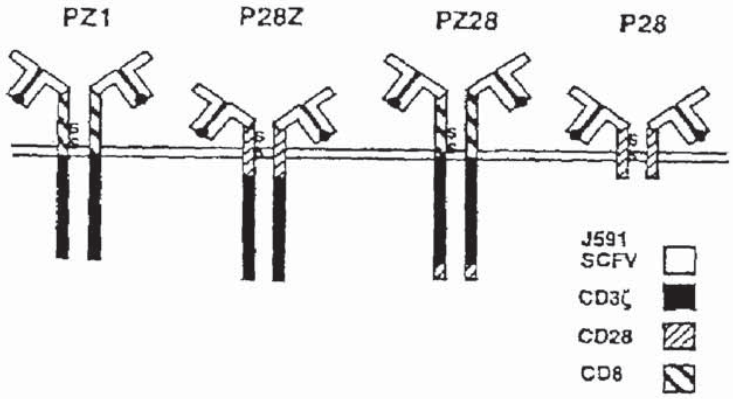
Fig. 1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J591
SCFV
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CD28
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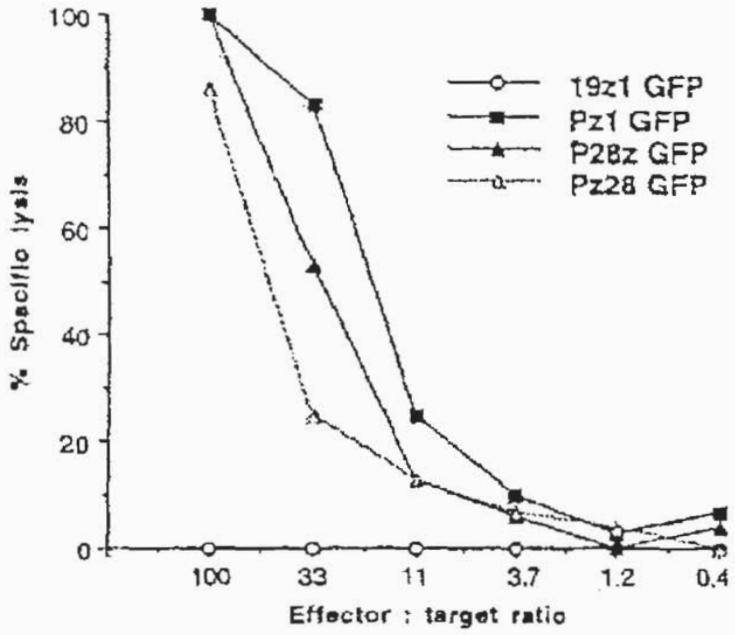
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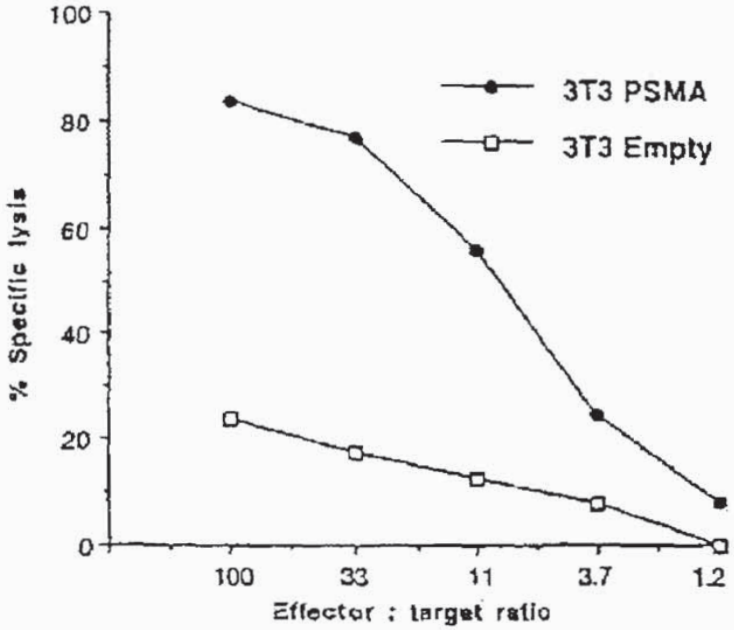
0.4
Effector : target ratio

Fig. 3A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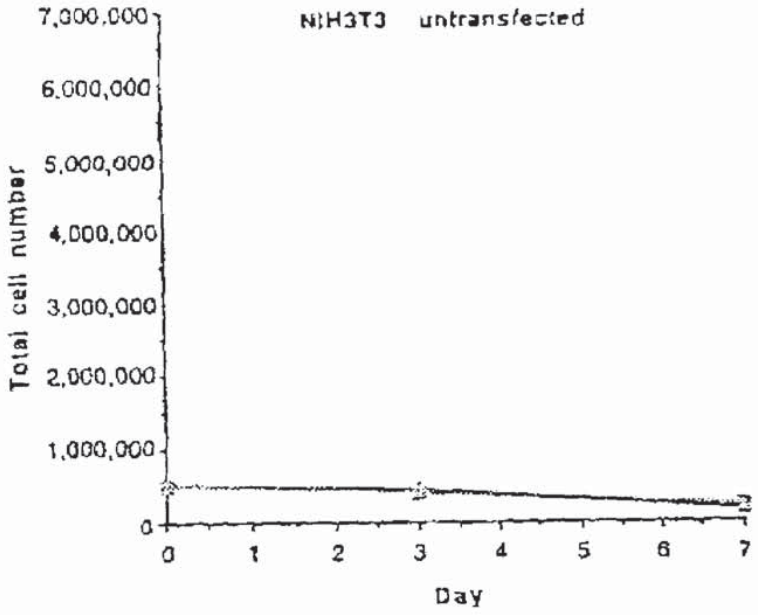
3.7
1.2
Effector : target ratio

Fig. 3B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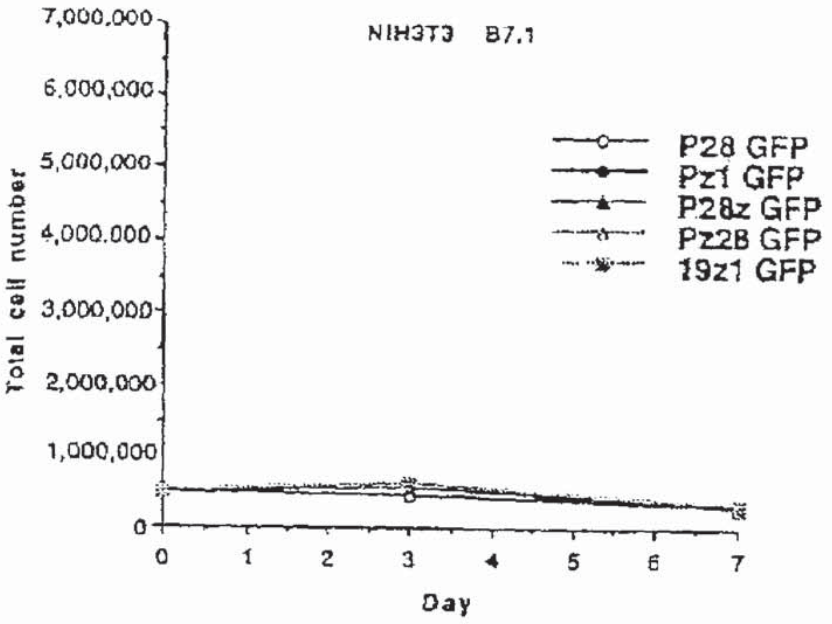
0 1 2 3 4 5 6 7
Day

Fig. 4A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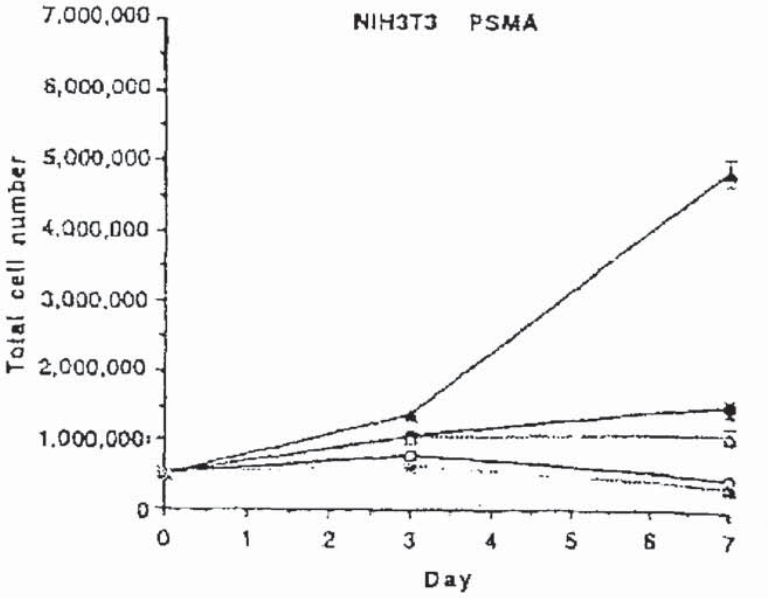
Day

Fig. 4B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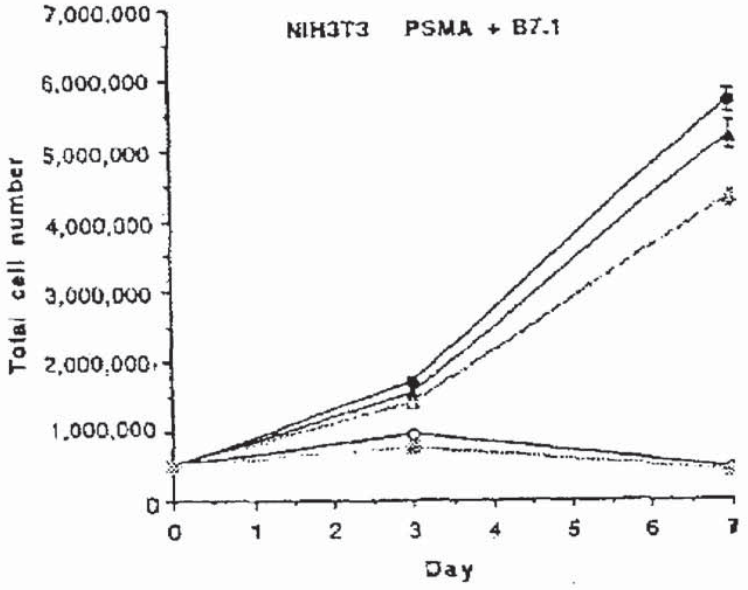
Day

Fig. 4C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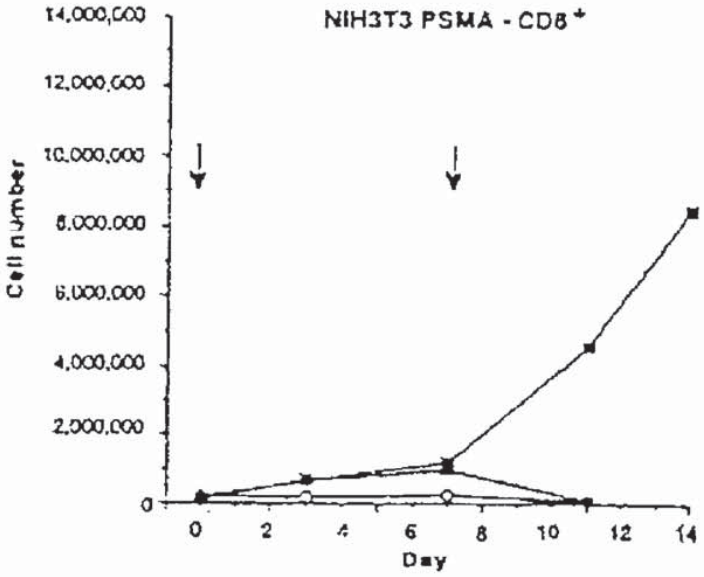
0 1 2 3 4 5 6 7
Day

Fig. 4D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6,000,000
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Cell number
0
2
4
6
8
10
12
14
Day

Fig. 5A

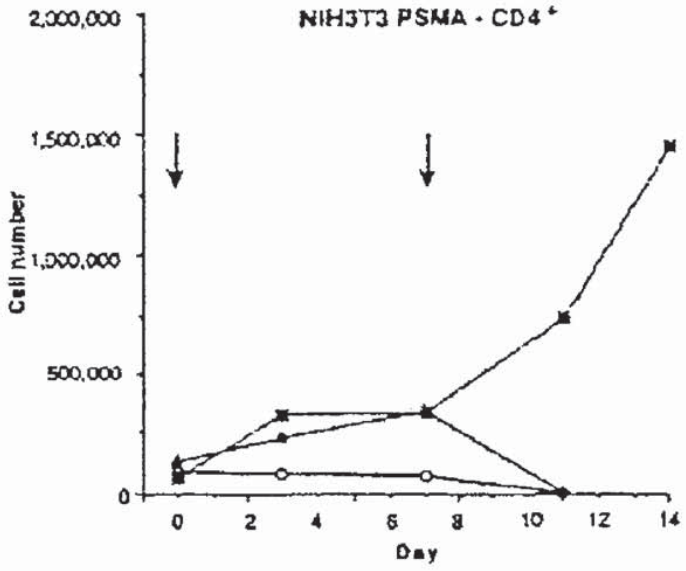

NIH3T3 PSMA - CD4+
2,000,000
1,500,000
1,000,000
500,000
0
Cell number
0
2
4
6
8
10
12
14
Day

Fig. 5B

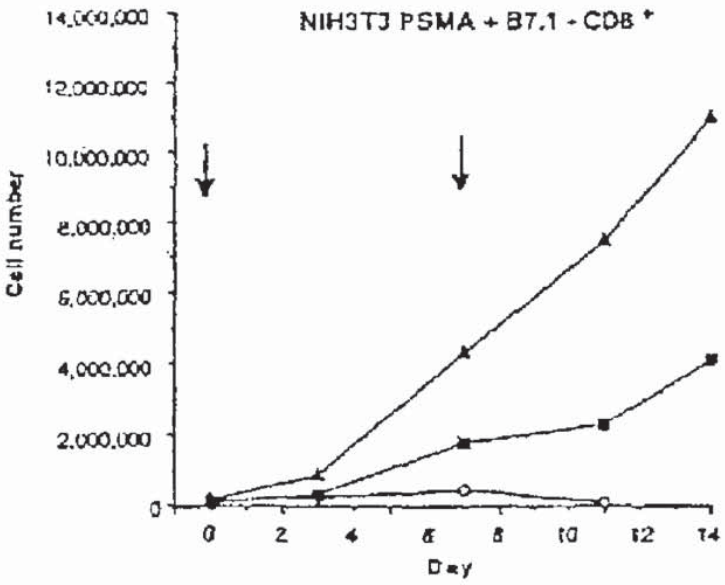

NIH3T3 PSMA + B7.1 - CD8 +
Cell number
14,000,000
12,000,000
10,000,000
8,000,000
6,000,000
4,000,000
2,000,000
0
0
2
4
6
8
10
12
14
Day

Fig. 5C

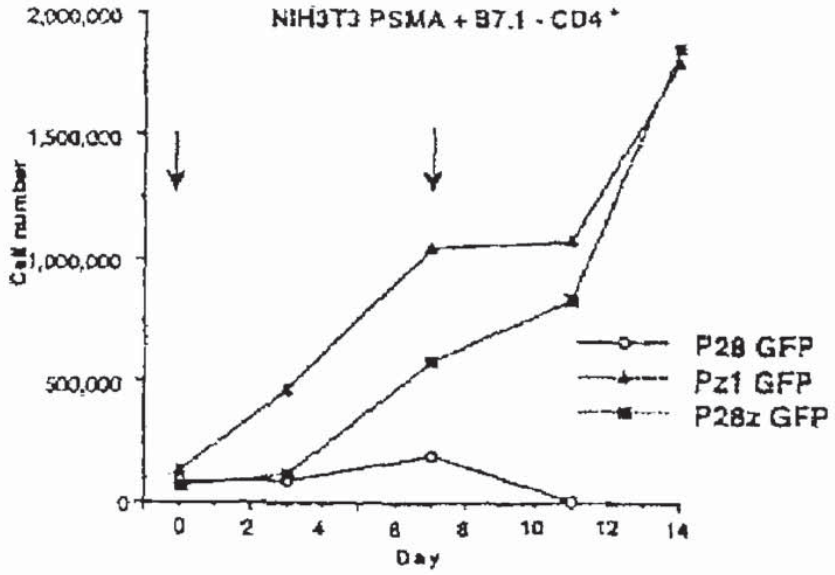
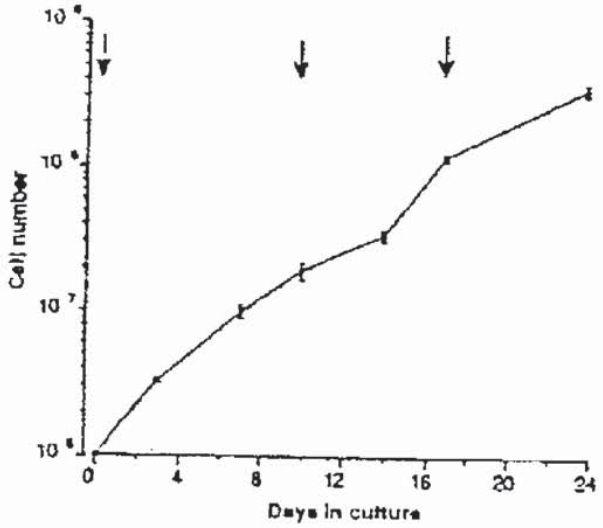

NIH3T3 PSMA + B7.1 - CD4 +
Cell number
2,000,000
1,500,000
1,000,000
500,000
0
0
2
4
6
8
10
12
14
Day
P28 GFP
Pz1 GFP
P28z GFP

Fig. 5D


Cell number
Days in culture
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4
8
12
16
20
24

Fig. 5E

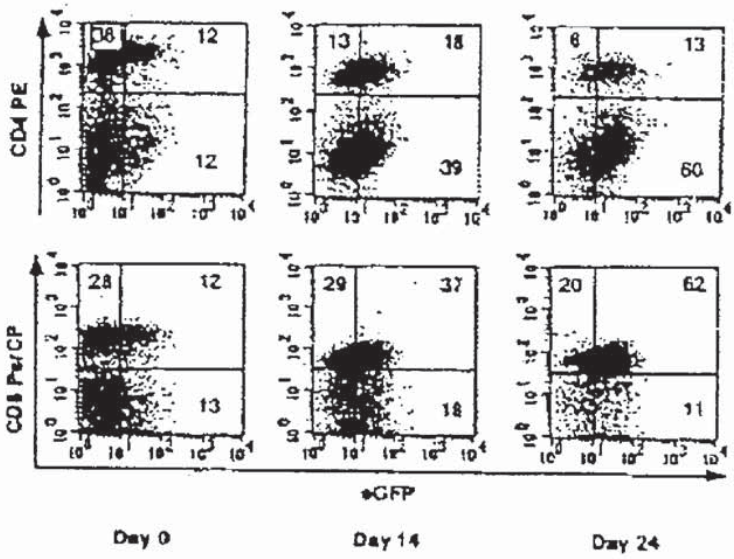
CD4 PE
CD8 PerCP
•GFP
38
12
12
13
18
39
6
13
60
28
12
13
29
37
18
20
62
11
Day 0
Day 14
Day 24

Fig. 5F

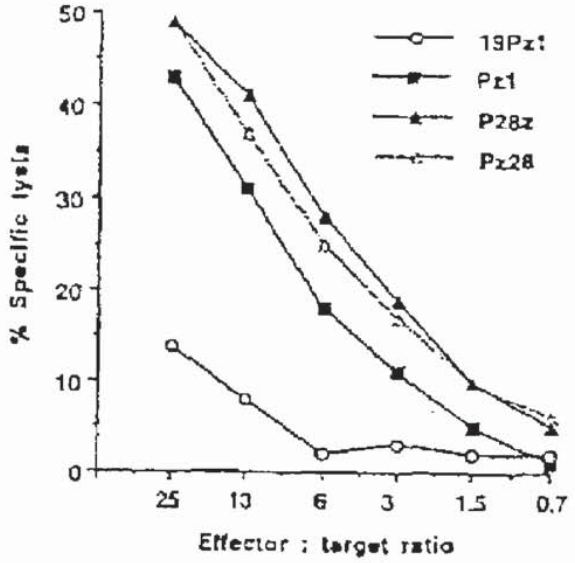
19Pz1
Pz1
P28z
Pz28
% Specific lysis
50
40
30
20
10
0
25
13
6
3
1.5
0.7
Effector : target ratio

Fig. 6A

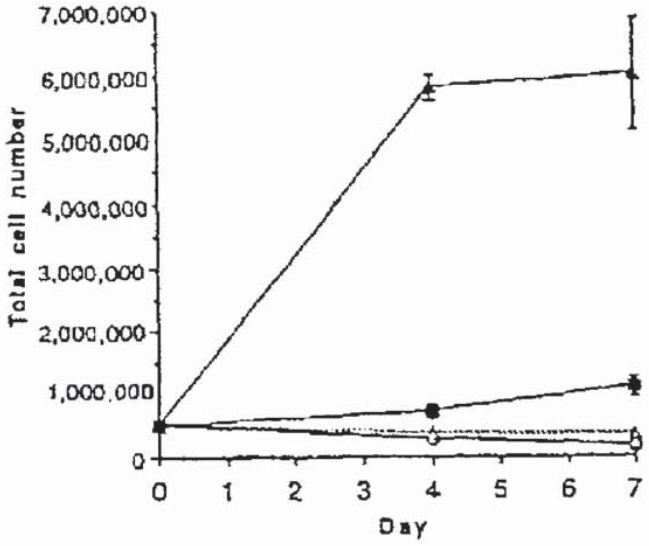
Total cell number
7,000,000
6,000,000
5,000,000
4,000,000
3,000,000
2,000,000
1,000,000
0
0
1
2
3
4
5
6
7
Day

Fig. 6B

NUCLEIC ACIDS ENCODING CHIMERIC T CELL RECEPTORS

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application No. 60/383,872, filed May 28, 2002, which is incorporated herein by reference.

BACKGROUND OF INVENTION

This application relates to nucleic acid polymers encoding chimeric T cell receptors (TCRs), to the chimeric TCRs, and to methods of using same to facilitate a T cell response to a selected target.

The induction of potent tumor immunity presents a major challenge for cancer immunotherapy. Tumor cells have many properties that facilitate immune evasion 1-3. Most tumor antigens characterized to date are self-antigens and are thus poorly immunogenic 4,5. The paucity of target antigens, the difficulty of overcoming tolerance to self-antigens, and impaired antigen presentation also contribute to compromise T-cell priming in cancer-bearing hosts 1-3,6-10. Furthermore, malignant cells may escape from tumor-specific effector T cells by downregulating major histocompatibility complex (MHC) and/or antigen expression, or by establishing an immunosuppressive microenvironment 1-3,11.

Genetic approaches offer a potential means to enhance immune recognition and elimination of cancer cells. One promising strategy is to genetically engineer T lymphocytes to express artificial TCRs that direct cytotoxicity toward tumor cells 12,13. Artificial receptors typically comprise a tumor antigen-specific recognition element derived from a single-chain antibody variable fragment (scFv). When used to reprogram T-cell specificity, such fusion receptors permit MHC-independent recognition of native rather than processed antigen 12-14. ScFv-based TCRs are engineered to contain a signaling domain that delivers an activation stimulus (signal **1**) only 12-14. The TCR-ζ cytoplasmic domain, which delivers a potent signal **1** in the absence of the remaining components of the TCR-CD3 complex 15,16, is well suited for activating cytolytic functions. The potential clinical utility of this strategy is supported by the demonstration that, despite fears about defective signaling in lymphocytes of tumor-bearing subjects 17, ζ-chain fusion receptors retain potent activity in cancer patent cytotoxic T cells 18.

However, while sufficient to elicit tumoricidal functions, the engagement of ζ-chain fusion receptors may not suffice to elicit substantial IL-2 secretion in the absence of a concomitant co-stimulatory signal 18. In physiological T-cell responses, optimal lymphocyte activation requires the engagement of one or more co-stimulatory receptors (signal **2**), the best characterized of which is CD28 19-22. Provision of signal **1** in the absence of CD28 signaling can result in a very poor T-cell proliferative response or in the induction of anergy or apoptosis 19-22. Consequently, it may be extremely valuable to engineer human T cells so that they receive a co-stimulatory signal in a tumor antigen-dependent manner. An important development in this regard has been the successful design of scFv-CD28 fusion receptors that transduce a functional antigen-dependent co-stimulatory signal in human primary T cells, permitting sustained T-cell proliferation when both the endogenous TCR and the chimeric CD28 receptor are engaged 23. See U.S. patent application Ser. No. 08/940,544.

Notwithstanding the foregoing efforts, there remains a continuing need for more effective chimeric TCRs. The present invention offers chimeric TCRs that are able to provide both the activation and the co-stimulation signals from a single molecule to more effectively direct T-lymphocyte cytotoxicity against a defined target and T-lymphocyte proliferation. ζ

SUMMARY OF INVENTION

The present invention provides chimeric TCR's, nucleic acid polymer encoding the chimeric TCR's and methods of using the chimeric TCR's to facilitate T cell response to a specific target. The chimeric TCR's of the invention combine, in a single chimeric species, the intracellular domain of CD3 ζ-chain ("zeta chain portion"), a signaling region from a costimulatory protein such as CD28 and a binding element that specifically interacts with a selected target. Thus, in accordance with a first aspect of the invention, there is provided a nucleic acid encoding a chimeric T cell receptor, said chimeric T cell receptor comprising a zeta chain, a CD28 signaling region and a binding element that specifically interacts with a selected target. In accordance with a second aspect of the invention, there is provided a chimeric T cell receptor comprising a zeta chain portion, a CD28 signaling region and a binding element.

In accordance with the method of the invention a chimeric TCR is provided which comprises a zeta chain portion, a co-stimulatory signaling element and a binding element which specifically interacts with a cellular marker associated with target cells. T-lymphocytes from the individual to be treated, for example a human individual, are transduced with the chimeric TCR. This transduction may occur ex vivo, after which the transduced cells are reintroduced into the individual. As a result, T cell immune response is stimulated in the individual to the target cells.

BRIEF DESCRIPTION OF DRAWINGS

FIG. **1** shows a schematic of a nucleic acid polymer within the scope of the invention.

FIG. **2** shows a series of chimeric TCR's.

FIGS. **3** A and B show specific target lysis by PSMA redirected T cells.

FIGS. **4** A-D. The P28z fusion receptor renders human T lymphocytes capable of PSMA-dependent expansion. Human T cells were transduced with the following retroviral constructs (gene transfer efficiency indicated in parentheses): SFG 19z1 (60%), SFG P28 (53%), SFG PZ1 (68%), SFG P28z (23%), and SFG Pz28 (32%). Three days later, 5×105 transduced T cells were co-cultured in 20 U/ml IL-2 with irradiated NIH3T3 feeder cells as follows: (A) unmodified (B) NIH3T3-B7.1 (C) NIH3T3-PSMA, or (D) NIH3T3-PSMA+B7.1. Cell numbers were counted on days 3 and 7, and data presented are mean±s.d. of triplicate evaluations. Similar results were obtained in three experiments.

FIGS. **5** A-F. Primary and secondary stimulation of transduced T cells in response to PSMA. Peripheral blood T cells were transduced with the following retroviral constructs (gene transfer efficiency indicated in parentheses); P28 (27%), Pz1 (36%), or P28z (17%). Then the cells were subjected to two rounds of stimulation on NIH3T3 fibroblast feeder layers (indicated by arrows). For the primary stimulation, 1×106 transduced T cells were co-cultured in IL-2 (20 U/ml) with irradiated NIH3T3 cells expressing PSMA (panels A and B) or PSMA+B7.1 (panels C and D). On day 7, cultures were re-stimulated by co-culture with a similar

monolayer. Absolute numbers of transduced CD8+ (panels A and C) and CD4+ T cells (panels B and D) were calculated as the product of percentage transduced (determined by flow cytometry)×total cell count. Co-culture of all transduced PBL populations with B7.1 expressing or unmodified NIH3T3 cells resulted in a progressive decline in total cell number and content of transduced T cells (data not shown). (E) P28z-transduced T cells were expanded by sequential re-stimulation on NIH3T3 PSMA fibroblast feeder layers, is indicated by the arrows. Cultures were maintained in IL-2 (20 U/ml), which was added every three days. The data represent the mean±s.d. of six data points (triplicate cell counts from two separate cultures). These cultures were subjected to three-color flow cytometry at intervals to detect transduced (eGFP+) cells of the CD4+ and CD8+ subsets. Similar data were obtained upon analysis of both cultures, and data shown are from one representative example (F).

FIGS. **6**A and B. PSMA+ tumor cells activate cytolytic and proliferative responses in P28z-transduced PBLs. (A) Specific tumor cell lysis by PSMA-redirected T cells. T cells were transduced with 19z1 (control), Pz1, P28z GFP, and Pz28 GFP. Four days after completion of gene transfer, equivalent numbers of transduced T cells were added to LNCaP human prostate cells. All PSMA-specific T cells (Pz1, P28z, and Pz28) demonstrated cytotoxic activity similar to that demonstrated against NIH3T3 PSMA+ fibroblasts. Background cytotoxic activity seen with 19z1 control T cells may be due to alloreactivity (which is not seen with the murine NIH3T3 fibroblasts: FIG. **3**). (B) The P28z fusion receptor renders T lymphocytes capable of PSMA-dependent, B7.1-independent expansion following co-cultivation with LNCaP tumor calls. 19z1-, Pz1-, and Pz28-transduced T cells did not expand.

DETAILED DESCRIPTION

In accordance with the present invention, activation and co-stimulation are provided by a single chimeric T cell receptor comprising a zeta chain portion, a costimulatory signaling region and a target-specific binding element. The T cell receptor is suitably generated in situ in T lymphocytes by expression of a nucleic acid polymer encoding the three portions of the chimeric T cell receptor.

As used in the specification and claims of this application, the term "costimulatory signaling region" refers to it portion of the chimeric T cell receptor comprising the intracellular domain of a costimulatory molecule. Costimulatory molecules are cell surface molecules other than antigen receptors or their ligands that are required for an efficient response of lymphocytes to antigen. Examples of such molecules include CD28, 4-1BB, DAP-10 and ICOS. Thus, while the invention in exemplified primarily with CD28 as the co-stimulatory signaling element, other costimulatory elements are within the scope of the invention. For example, chimeric TCR containing the intracellular domain of 4-1BB (full sequence given in Seq ID No: 15), ICOS (full sequence given in Seq ID No: 16) and DAP-10 (full sequence given by Seq. ID No: 17) are also suitably employed in the invention.

FIG. **1** shows a schematic of a nucleic acid polymer within the scope of the invention in which the T cell receptor is positioned within an SFG onco-retroviral vector. As shown, the nucleic acid polymer comprises the 5'-long terminal repeat (LTR) and the packaging signal ψ portion of the vector, followed by the CD8 α-hinge **10** and the binding element **11**. SD and SA represent the splice donor and splice acceptor, respectively. The next region **12** encodes the zeta chain portion and CD28 sequences, and may additionally include transmembrane sequences from other sources, for example from CD8. The zeta and CD28 may be disposed in the nucleic acid polymer is either order. Next in order comes an EMCV IRES **13**, followed by a sequence **14** encoding a marker protein, such as enhanced green fluorescent protein (EGFP). At the 3' end of the nucleic acid polymer as illustrated in FIG. **1** is a 3'-LTR from the SFG onco-retroviral vector. While the structure in FIG. **1** reflects the vector which was used in the examples described below, other vectors which result in expression of the chimeric TCR of the invention may also be employed.

The zeta chain portion sequence employed in the present application includes the intracellular domain. This domain, which spans amino acid residues 52-163 (Seq. ID No: 14 (nucleotides 154-489, Seq. ID No. 3) of the human CD3 zeta chain, can be amplified using the primers of Seq. ID Nos. 1 and 2.

CD28 sequences can be found in the present application on either side of the zeta chain portion sequence. In either case, the CD28 sequences include the signaling elements from CD28. In one embodiment, where CD 28 is between the zeta chain portion and the scFv, the CD28 portion suitably includes the transmembrane and signaling domains of CD28, i.e., the portion of CD28 cDNA spanning nucleotides 340 to 663, including the stop codon (amino acids 114-220 of Seq. ID No. 10). This portion of CD28 can be amplified by PCR using the primers of Seq. ID NO. 4 and 5. The full sequence of this region is set forth in Seq. ID No: 6. Alternatively, when the zeta sequence lies between the CD28 sequence and the binding element, the 41 amino acid intracellular domain of CD28 (amino acid residues given by Seq. ID No. 9) is suitably used alone. This fragment of CD28 cDNA can be amplified using primers of Seq. ID. Nos. 7 and 8.

Binding elements used in the invention are selected to provide the chimeric TCR with the ability to recognize a target of interest. The target to which the chimeric T cell receptors of the invention are directed can be any target of clinical interest to which it would be desirable to induce a T cell response. This would include markers associated with cancers of various types, including without limitation prostate cancer (for example using a binding element that binds to PSMA), breast cancer (for example using a binding element that targets Her-2) and neuroblastomas, melanomas, small cell lung carcinoma, sarcomas and brain tumors (for example using a binding element that targets GD 2). Known binding elements used in chimeric TCR's are generally useful in the present invention, and include without limitation those described in commonly assigned PCT Publication 97/36434 and U.S. patent application Ser. Nos. 08/940,544 and 09/786,502 which are incorporated herein by reference in their entirety.

The binding elements used in the invention are suitably antibodies that recognize a selected target. For convenience, the antibody used as the binding element is preferably a single chain antibody (scFv). Single chain antibodies may be cloned from the V region genes of a hybridoma specific for a desired target. The production of such hybridomas has become routine, and the procedure will not be repeated here. A technique which can be used for cloning the variable region heavy chain (V-H-) and variable region light chain (V-L-) has been described in Orlandi et al., Proc. Natl. Acad. Sci. (USA) 86: 3833-3837 (1989). Briefly, mRNA is isolated from the hybridoma cell line, and reverse transcribed into complementary DNA (cDNA), for example using a reverse transcriptase polymerase chain reaction (RT-PCR) kit. Sequence-specific primers corresponding to the sequence of the V-H- and V-L-genes are used. Sequence analysis of the cloned products and com-

parison to the known sequence for the V-H- and V-L-genes can be used to show that the cloned V-H-gene matched expectations. The V-H- and V-L-genes are then attached together, for example using an oligonucleotide encoding a (gly-ser-2-)-5-linker.

As is reflected in the examples below, the transmembrane domain does not need to be the CD28 transmembrane domain, and indeed is CD28 in the embodiment with the centrally-positioned largely as a matter of convenience to minimize the number of amplification/cloning steps that need to be performed. Other transmembrane domains that may be employed include the CD8 and CD3 zeta transmembrane domains.

In addition to the zeta chain portion, CD28 and binding elements, the chimeric TCR may include a selection element. For example, dihydrofolate reductase (DHFR) may be included in the TCR to allow ex vivo or in vivo selection for transduced cells using methotrexate. (See commonly-assigned PCT Publication 97/33988, which is incorporated herein by reference).

FIG. **2** shows a series of chimeric TCR's specific for PSMA that were prepared in order to evaluate the efficacy of the invention. TCR PZ1, a control species, contains a PSMA-specific scFV, the α hinge and transmembrane portions from CD8, and the intracellular domain of CD3 zeta. P28, the other control species contains a P3MA-specific scFV and the intracellular, transmembrane and much of the extracellular portions of CD28. P28Z and PZ28 represent TCR's in accordance with the invention. In P28Z, the intracellular zeta chain portion is joined to the C-terminus of P28. In PZ28, the intracellular 41 amino acids (SEQ ID NO: 9) of CD28 are joined to the C-terminus of the PZ1 receptor.

The expansion of functional tumor-specific T lymphocytes is of central importance in tumor immunity. Whether in the context of in vivo immunization or ex vivo T-cell expansion, the biological requirements for T-cell priming and amplification have to be met to attain meaningful immune responses. Co-stimulation is crucial in this process 19-22 and is thus central to the development of effective adoptive immunotherapy of cancer 19,29.

The present invention describes chimeric TCRs and in particular scFv-based chimeric receptors designed to provide both TCR-like and co-stimulatory signals upon binding of the tumor antigen PSMA. To achieve this, the intracellular domains of human TCRζ and CD28 have been fused in series within a single molecule, thereby recruiting these signaling motifs to the site of antigen engagement at a fixed stoichiometry of 1:1. Most important, our study was performed in human primary T lymphocytes—that is, in biologically and therapeutically relevant cells. The ability to sustain T-cell expansion and tumoricidal functions could therefore be evaluated, which is not possible in leukemic cells 30,31. We show here that, following contact with cell-bound PSMA, activated human PBLs engineered to express the P28z receptor produce IL-2, undergo sequential rounds of expansion, and maintain thereafter their ability to execute specific lysis of PSMA-expressing target cells.

The most important finding in this study is the demonstration that expression of P28z enables T cells to undergo repeated rounds of antigen-dependent stimulation and expansion. This process was accompanied by a progressive increase in the proportion of transduced T cells within bulk cultures, consistent with the expected selective advantage conferred by the receptor. The capacity of P28z to deliver signal **1** is demonstrated by production of IL-2 and induction of cell proliferation upon stimulation with PSMA+B7.1, which are comparable to those obtained in T cells expressing Pz1 (which contains TCRζ but no CD28 sequences). Specific lysis of PSMA+ targets also reflects functional activation through the TCR pathway. Importantly, the P28z fusion receptor can also provide potent co-stimulation (signal **2**). Thus, in the absence of exogenous B7-driven co-stimulation, engagement of PSMA elicits IL-2 production and proliferation. Under the same conditions, Pz1-transduced cells fail to secrete IL-2 and proliferate, corroborating findings by Finney et al. obtained in Jurkat cells 31.

The relative positions of the TCRζ and CD28 signaling elements within the fusion receptor proved crucial. In P28z, the hinge, transmembrane, and proximal intracellular portions of the molecule were derived from CD28, followed by the signaling domain of TCRζ. When CD28 sequences were fused to the C terminus of TCRζ, as in Pz28, the functional activity was substantially compromised relative to P28z, particularly with regard to sustaining proliferation. This occurred despite comparable cell-surface expression of the two receptors. Pz28 retained the ability to deliver a TCR-like signal upon PSMA binding, as evidenced by cytolytic activity and B7.1-dependent proliferation and IL-2 production. However the co-stimulatory potency of Pz28, as evaluated in the absence of B7.1, was no better than that of Pz1.

One potential explanation for this finding is that the conformational integrity of the fusion receptor is disrupted when the CD28 signaling domain is placed downstream of TCRζ. It is noteworthy in this regard that western blotting analysis indicated that the Pz28 receptor exhibited less homodimerization in human T cells than either P28z or Pz1. An alternative explanation is that membrane proximity is more critical for CD28 than for TCRζ. Thus, placement of the CD28 moiety distal to TCRζ might impair its ability to associate with downstream signaling molecules, such as p56-lck (ref. 32), which reside in very close proximity to the cell membrane. A third possibility is that these fusion receptors differ in their ability to interact with negative regulators, for example, MAP kinase phosphatase-6 (MKP-6) 33. It is plausible that the ability of P28z to bind MKP-6 might be impaired as a result of steric hindrance, thereby enhancing co-stimulatory activity. Conversely, in the case of Pz28, the binding of this phosphatase at the C terminus may adversely affect the signaling potency of this receptor. This hypothesis is supported by findings indicating that Pz28 was not only less active in eliciting IL-2 secretion than P28z, but also less active than Pz1. A final possible explanation for the superior function of P28z is that it contains the CD28 transmembrane domain, unlike Pz28 and Pz1. However, this is unlikely because the cytoplasmic portion of CD28 is sufficient for co-stimulatory activity 34.

How might adoptive transfer of cells expressing P28z be developed for therapy directed against PSMA-expressing tumors or tumor-associated vasculature? As this fusion receptor enables transduced T cells to proliferate in an antigen-dependent manner, this raises the prospect that these cells could be expanded both in vitro, before infusion, and, most importantly, in vivo in the tumor-bearing host. There is substantial preclinical evidence indicating that success of adoptive T-cell therapy depends largely on the relative numbers and growth kinetics of tumor cells and therapeutically administered T cells 35,36. Consequently, treatment with T cells expressing a receptor like P28z may require smaller T-cell doses (and thus shorter in vitro culture periods) and allow for T-cell expansion following infusion. As P28z-transduced T cells expanded on PSMA-positive cells retained their specific cytolytic activity, such a cell culture procedure could provide a useful means to selectively expand transduced T cells. Importantly, P28z provides a means to activate and expand T

cells upon engaging cells that lack MHC and/or co-stimulatory molecules, and may thus target the transduced lymphocytes to cells that escape immune recognition.

In summary, we have shown that artificial receptors based upon fusion of the signaling domains of TCRζ and CD28 can be used to redirect the specificity of primary human T cells to a tumor antigen. The transduced T cells undergo selective expansion following contact with cell-bound PSMA while maintaining the ability to mediate specific lysis of tumor cells. The availability of a single chimeric receptor providing both activation and co-stimulatory functions facilitates lymphocyte transduction and hence clinical applicability.

Thus, the present invention also provides a method for stimulating a T cell mediated immune response to a target cell population in a subject individual comprising the step of administering to the subject individual a chimeric T cell receptor comprising a zeta chain portion comprising the intracellular domain of human CD3 ζ chain, a CD28 signaling region and a binding element that specifically interacts with a selected target such that the chimeric T cell receptor is expressed in T lymphocytes of the subject individual, wherein the binding element is selected to specifically recognize the target cell population.

As used in the specification and claims of this application, the term "administering" includes any method which is effective to result in expression of a chimeric TCR of the invention in T lymphocytes of the subject individual. One method for administering the chimeric TCR is therefore by ex vivo transduction of peripheral blood T cells or hematopoietic progentior cells (which would eventually be allogeneic) with a nucleic acid construct in accordance with the invention and returning the transduced cells, preferably after expansion to the subject individual.

As used in the specification and claims of this application, the term "subject individual" refers to a living organism in which the immune response to the target cell population is to be induced. The subject individual is preferably mammalian, including humans, companion animals such as dogs and cats, horses, agricultural mammals such as cattle, pigs and sheep, and laboratory animals including mice and rats.

The invention will now be further described with reference to the following non-limiting examples.

Example 1 Recombinant receptors and retroviral vectors. All fusion receptors contain a scFv derived from the J591 hybridoma **25** as described[18]. To facilitate detection of transduced cells, all constructs contained the encephalomyocarditis Virus internal ribosome entry site (EMCV-IRES)[37] and the eGFP gene inserted in the SFG vector[38]. In Pz1, the J591 scFv is coupled through human CD8α hinge and transmembrane sequences to the intracellular domain of human TRCζ (ref. 18). P28 comprises a fusion of the J591 scFv to human CD28 as described[23,39]. To construct P28z, nucleotides 336-660 of CD28 were amplified using primers 5'-GGCGGCCG CAATTGAAGTTATGTATC-3' (SEQ. ID NO: 4) and 5'-TGCGCTCCTGCTGAACTTCACTCTG-GAGCGATAGGCTGCTAAGTCGCG-3 SEQ ID NO: 5). The intracellular domain of TCRζ was amplified using primers 5'-AGAGTGAAGTTCAGCAGGAGCGCA-3' (SEQ. ID NO: 1) and 5'-CTCGAGTGGCTGTTAGCCAGA-3' (SEQ ID NO: 2). The products were fused in a separate PCR reaction driven by primers of SEQ ID Nos. 4 and 2, A-tailed with Taq polymerase, and subcloned as a NotI/XhoI ligament into SFG-Pz1. To generate Pz28, the intracellular domain of CD28 was amplified using 5'-GCACTTCACATGCAGGC TCTGCCACCTCGCAGGAGTAAGAGGAGCAGG CTC-CTGCAC-3' (SEQ ID NO: 7)and 5'-CGCTCGAGTCAG-GAGCGATAGGCTGCGAAGTCGCGT-3' (SEQ ID NO: 8) (two silent mutations introduced to interrupt cytosine repeats are underlined). The resultant PCR product represents a fusion of the distal nine codons of TCRζ (minus stop codon) to the intracellular domain of CD28 and contains a convenient 5' NspI site. This fragment was subcloned, digested with NspI/XhoI, and ligated into SFG-Pz1. SFG-c-fms encodes the human macrophage colony-stimulating factor receptor. This resulted in a series of receptors that comprise a PSMA-specific scFv fragment coupled to signaling elements derived from TCRζ and/or CD28 (FIG. **2**). Pz118 and P28 are designed to respectively deliver signals **1** and **2** in a PSMA-dependent manner. In P28z, the intracellular portion of TCRζ has been joined to the C terminus of P2823, while in Pz28, the CD28 signaling domain was added at the C terminus of Pz1. All chimeric complementary DNAs (cDNAs) were cloned in bicistronic onco-retroviral vectors upstream of enhanced green fluorescent protein (eGFP; FIG. **1**).

Example 2 Culture and retroviral transduction of primary human T cells. Peripheral blood mononuclear cells from healthy donors were established in RPMI+10% (vol/vol) human serum, activated with phytohemagglutinin (2 μg/ml) for two days, and transferred to non-tissue culture-treated plates (FALCON, Becton Dickinson, Franklin Lakes, N.J.) precoated with retronectin (15 μg/ml; Takara Biomedicals, Shiga, Japan). Gibbon ape leukemia virus envelope-pseudotyped retroviral particles were generated as described[27,40]. Transduced cells were co-cultivated with NIH3T3 fibroblasts expressing PSMA and/or B7.1 as described[18,23]. For experiments with LNCaP cells, cells were admixed weekly at a T-cell: tumor cell ration of 5:1.

For protein analyses, flow cytometry was carried out using a FACScan cytometer with Cellquest software. Expression of PSMA-specific fusion receptors was directly demonstrated using phycoerythrin (PE)-conjugated goat anti-mouse antiserum 18. CD4-PE and CD8-PerCP antibodies (Becton Dickinson) were used for T-cell subset identification. For western blot analysis, transduced T-cell samples were prepared as described 41. Briefly, cells were suspended in radioimmunoprecipitation buffer at a concentration of 1×10-7 cells/ml. After 1 hour incubation on ice, cells were boiled in 2× loading buffer under nonreducing or reducing conditions with 0.1 M dithiothreitol. Samples were run on 10-20% acrylamide gradient gels and transferred to polyvinylidene fluoride transfer membrane (NEN Life Science Products, Boston, Mass.). Fusion proteins were detected using the anti-human ζ-chain monoclonal antibody 8D3 (PharMingen, San Diego, Calif.) as described 41. Immunodetection was performed using the ECL Plus western blotting detection system (Amersham, Buckinghamshire, UK).

Three days after transduction of mitogen-activated PBLs, gene transfer efficiency, as assessed by flow cytometry, ranged from 20% to 70%. CD4+ and CD8+ T-cells subsets were transduced at similar efficiencies, as reported elsewhere 18,19,27. Expression of ζ-chain containing fusion receptors was also analyzed by western blotting, confirming homodimer formation and little, if any, heterodimerization with endogenous CD8 or CD28.

To determine the percentage transduction of T-cell subsets, samples were also stained with CD4 PE and CD8 PerCP antibodies and analyzed by three-color flow cytometry, using GFP emission to identify transduced cells. Quadrants were set using control samples so that 99% of events were negative for the marker of interest. Surface expressions of Pz1 was typically greater than that of P28 or either of the TCR ζ-CD28 fusion receptors. Mean fluorescence intensity when Pz1 expression was normalized to **100** was as follows: P28=35.1∀17.8 ($P<0.05$); P28z=29.6∀12.2 ($P<0.01$);

Pz28=25.9∀6.9 (P<0.01) (n=3-4 experiments). There was no significant difference in expression intensity between P28, P28z, Pz28.

Lysates were prepared under reducing and nonreducing conditions from PBLs following transduction with Pz1 (54% GFP-expressing), P28z (21% GFP-expressing), and Pz28 (20% GFP-expressing). Untransduced PBLs were used as controls. Immunoreactive receptor hands were detected by western blotting using an anti-TCRζ monoclonal antibody. Filled arrows indicate the monomeric and dimeric forms of the endogenous TCRζ. Pz1 and Pz28 are predominantly expressed as homedimers, as would be expected from the design of the hinge regions of these molecules. However, Pz28 was found to dimeric less effectively in T-cells and in PG13 cells (data not shown). No hands indicating productive heterodimerization with CD8α, CD8β or CD28 were detected. The additional hand seen under that corresponding to dimerized ζ is likely to be a degradation product of this dimer. Empty arrows show the positions of the monomeric and dimeric PSMA-specific fusion receptors. Molecular mass markers are indicated on the left on the panel.

Example 3 Cytotoxicity assays. Cytotoxic T-lymphocyte assays were performed using a nonradioactive cytotoxicity detection kit (lactate dehydrogenase (LDH); Roche Diagnostics, Indianapolis, Ind.) as described 18.

To confirm that the TCRζ-CD28 fusion receptors specifically engaged PSMA, cytotoxicity assays were performed three days after the transduction. T-cells were transduced with 19z1GFP (control), Pz1 GFP, or Pz28 GFP. Three days after completion of gene transfer 4 h CTL assays were established at the indicated ratios using as targets NIH3T3 cells expressing PSMA. No specific lysis was observed using untransduced NIH3T3 as control targets. The greater lytic activity of Pz1-transduced cells may reflect the higher cell-surface expression of this receptor, or, more likely, the greater proportion of transduced T-cells (46% of T-cells, of which 21% are CD8+, compared with 25% P28z-transduced cells, including 12% CD8, and 20% Pz28-transduced cells, including 10% CD8+ cells). The control 19z1 receptor (specific for CD19) did not effect lysis of PSMA expressing targets, despite the presence of the same TCRζ chain in this molecule.

Both P28z and Pz28 receptors, but not P28, mediated specific lysis of fibroblasts expressing human PSMA (FIG. **3**A).

Example 4 P28z-transduced T-cells were stimulated on NIH3T3 cells expressing PSMA and, after one week, were established in 4 h CTL assays with NIH3T3 cells expressing PSMA or untransduced cells as controls. At this time, the T-cells were 62% GFP+ (of which 17% were CD8+). (FIG. **3**B) The fusion receptor P28z elicits IL-2 production upon engagement with PSMA. To assay the ability of the different receptors to signal for IL-2 production, transduced PBLs were co-cultivated with NIH3T3 cells expression PSMA and/or B7.1 (refs 18,19) in medium lacking IL-2 (Table 1). Three receptors (Pz1, P28z, and Pz28) elicited IL-2 secretion in the presence of the PSMA and B7.1. In the absence of the co-stimulatory ligand, IL-2 production was only observed in cultures of P28z-transduced T-cells. IL-2 levels were elated, ranging within 40-55% of those obtained by co-culturing the same transduced T-cells with the monolayer co-expressing PSMA and B7.1.

The P28z fusion receptor promotes proliferation of genetically modified T-cells in response to PSMA. To test if P28z could deliver combined and functional signals **1** and **2**, transduced PBLs were plated on NIH3T3 cells expressing B7.1, PSMA, PSMA+B7.1, or on unmodified NIH3T3 cells. All cultures declined over one week in the absence of PSMA (FIG. **4**A, B). When stimulated by a monolayer co-expressing PSMA+B7.1 (FIG. **4**D), Pz1-transduced PBLs underwent expansion, as did PBLs transduced with P28z or Pz28, further establishing that both TCRζ CD28 fusion receptors deliver a TCR-like signal. Control P28-transduced T cells did not expand under these conditions, indicating that neither co-stimulation alone nor adherence to the monolayer enhanced proliferation. When stimulation was provided by NIH3T3 cells expressing PSMA alone (FIG. **4**C), T-cells expressing Pz1 underwent limited expansion. Pz28-transduced cells also (grew poorly, further indicating that this fusion receptor does not deliver a meaningful co-stimulatory signal. By contrast, P28z-transduced T-cells consistently proliferated, corroborating observation by Eshhar et al. showing that immobilized hapten can induce proliferation in T-cells that express a trinitophenol-specific CD28-Fcγ fusion receptor **28**. P28z-transduced T-cells markedly expanded, showing absolute increases in cell numbers 8.6±5.2-fold over a seven-day period, n=8 experiments). Taken together, these data strengthen the argument that P28z can provide both signals **1** and **2**. Importantly, after seven days of co-culture onto a PSMA+ fibroblast monolayer, T-cells expressing the P28z fusion receptor retained the ability to specifically lyse PSMA+ targets (FIG. **3**B).

Example 5 The P28z fusion receptor permits sequential re-stimulation of transduced human PBLs in response to PSMA. If P28z can provide co-stimulation in addition to a TCR like signal, it would be expected that cells expressing the receptor should undergo further expansion upon secondary encounter with PSMA. However, if the co-stimulatory potency of this molecule is inadequate, sequential exposure to antigen could result in a poor proliferative response resulting from induction of energy and/or apoptosis[20,21]. To test this, transduced PBLs stimulated on the different NIH3T3 manslayers were subjected to secondary re-stimulation after a seven-day interval. Pz1 transduced T-cells expanded in response to primary encounter with PSMA. However, re-stimulation with PSMA resulted in a dramatic decline in the number of transduced cells (FIG. **5**A, B). Importantly, the same T-cells underwent brisk expansion after both primary and secondary stimulation if the fibroblast manslayer co-expressed PUMA and B7.1 (FIGS. **5**C and D, respectively). In contrast, the absolute number of P28z-transduced CD8+ and CD4+ T cells increased after primary stimulation and underwent further increase after re-stimulation on day 7, irrespective of the presence of B7.1. Expansion was indeed similar in response to PSMA alone or PSMA+B7.1, underscoring the relative potency of the co-stimulatory signal provided by P28z. Re-stimulation of P28z cultures with PSMA yielded a 4.0±2.4-fold expansion in total cell number over a seven-day period (n=4 experiments). Following another re-stimulation under the same conditions, the total cell number increased by more than 2 logs over a three-week interval (FIG. **5**E). In this period, a progressive enrichment of transduced over non-transduced cells was observed, in keeping with the selective advantage conferred to cells expressing p28z. (FIG. **5**F). Together, these data provide conclusive evidence that P28z delivers a functional signal **1** and **2** upon interaction with PSMA. Importantly, the same result was obtained with another receptor, 19-28z, which was modeled on P28z, 19-28z-transduced PBLs showed the same ability to be re-stimulated by CD19+ cells and to proliferate, indicating that proliferative responses were achieved with receptors recognizing unrelated antigens.

Example 6 P28z-transduced PBLs lyse PSMA+ tumor cells and proliferate in response to LNCaP cells. We had previously shown that Pz1-transduced T cells specifically lyse LNCaP cells, a PSMA+ human prostate cancer cell line,

as well as PSMA-transduced PC3 and EL4 cells, which are respectively a human prostate cancer cell line and a murine thymoma 19. Pz1, P28z, and Pz28 directed comparable and elevated cytolytic activity against LNCaP cells (FIG. **6**A). Proliferative responses elicited by LNCaP cells expressing B7.1 were also comparable for these receptors (data not shown). Of the three receptors, however, only P28z could induce sustained proliferation during co-cultivation with LNCaP cells (FIG. **6**B). The re-stimulated T cells preserved their tumoricidal activity (data not shown), corroborating findings obtained with PSMA+ fibroblasts (FIG. **3**B).

Example 7 To construct a CD19-specific scFv, we cloned the heavy (VH) and light (VL) chain variable regions from hybridoma cell line SJ25C1 derived cDNA by the polymerase chain reaction (PCR) using degenerate primers described by Orlandi et. al.[43] and fused these coding regions with a DNA fragment encoding for a $(Gly3Ser)_4$ spacer region. We ligated a costimulatory signaling element from human CD28, including transmembrane and extracellular portions SEQ ID NO: 6) to the 3' end of the resulting scFv and the cytoplasmic domain of the human-ζ SEQ ID NO: 3) to the 3' end of the CD28 portion to form fusion gene 19-28z.

The 19-28z fusion was tested for its ability to reduce tumor growth and enhance survival in mice injected with NALM6 T cells. NALM6 cells express CD19, MHC I, and MHC II but not B7.1 or B7.2. Most (~80%) untreated SCID-Beige mice develop hind-limb paralysis 4-5 weeks after tumor cell injection, remaining mice develop weight loss and/or other CNS symptoms (i.e. vestibular symptoms). When the 18-28z fusion was present, T cell stimulation was enhanced nearly ten-fold, and survival of some of the mice was greatly extended as compared to mice treated with Pz1 (a PSMA specific construct) or 19z1, a CD19-specific construct lacking the costimulatory signaling element.

Example 8 A chimeric TCR containing a CD19 binding element, 4-1BB as the costimulatory region and the intracellular domain of the CD3ζ chain in that order is prepared using the methodology of Example 1. The 4-1BB is amplified using the following primers GCGGCCGCA-CCATCTCCAGC-CGAC SEQ ID NO: 18) and CTTCACTCT-CAGTTCA-CATCCTTC SEQ ID NO: 19) to generate a 4-1BB amplicon with CD19 scFv and zeta tails with restriction cleavage sites to facilitate ligation to the CD19 scFv and zeta chain portions. The hyphen in the sequence indicates the transition from the 4-1BB sequence to the tail. The same primer can be used for other binding elements such as PSMA which end in the same sequence.

Example 9 A chimeric TCR containing a CD19 binding element, ICOS as the costimulatory region and the intracellular domain of the CD3 ζ chain in that order is prepared using the methodology of Example 1. The ICOS is amplified using the following primers GCGGCCGCA-CTAT-CAATTTTTGATCCT SEQ ID NO: 20) and CTTCACTCT-TAGGGTCACATCTGTGAG SEQ ID NO: 21) to generate a ICOS amplicon with CD19 scFv and zeta tails with restriction cleavage sites to facilitate ligation to the CD19 scFv and zeta chain portions. The hyphen in the sequence indicates the transition from the ICOS sequence to the tail. The same primer can be used for other binding elements such as PSMA which end in the same sequence.

Example 10 A chimeric TCR containing CD19 binding element, DAP-10 as the costimulatory region and the intracellular domain of the CD3 ζ chain in that order is prepared using the methodology of Example 1. The DAP-10 is amplified using the following primers GCGGCCGCA-CAGAC-GACCCCAGGA (SEQ ID NO: 22) and CTTCACTCT-GC-CCCTGCCTGGCATG (SEQ ID NO: 23) to generate a DAP-10 amplicon with CD19 scFv and zeta tails with restriction cleavage sites to facilitate ligation to the CD19 scFv and zeta chain portions. The hyphen in the sequence indicates the transition from the DAP-10 sequence to the tail. The same primer can be used for other binding elements such as PSMA which end in the same sequence.

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Asp Val Leu Asp Lys Arg Arg Gly Arg Asp Pro Glu Met Gly Gly Lys
35 40 45

Pro Arg Arg Lys Asn Pro Gln Glu Gly Leu Tyr Asn Glu Leu Gln Lys
50 55 60

Asp Lys Met Ala Glu Ala Tyr Ser Glu Ile Gly Met Lys Gly Glu Arg
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ggatgtgggt ccctctctct gccgctcctg gcaggcctcg tggctgctga tgcggtggca 180

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The invention claimed is:

1. A nucleic acid polymer encoding a chimeric T cell receptor, said chimeric T cell receptor comprising

(a) a zeta chain portion comprising the intracellular domain of human CD3 ζ chain,

(b) a costimulatory signaling region, and

(c) a binding element that specifically interacts with a selected target, wherein the costimulatory signaling region comprises the amino acid sequence encoded by SEQ ID NO:6.

2. The nucleic acid polymer of claim **1**, wherein the binding element is an antibody.

3. The nucleic acid polymer of claim **2**, wherein the antibody is a single chain antibody.

4. The nucleic acid polymer of claim **3**, wherein the single chain antibody binds to prostate specific membrane antigen.

5. The nucleic acid polymer of claim **3**, wherein the single chain antibody binds to CD19.

6. The nucleic acid polymer of claim **3**, wherein the encoded T cell receptor comprises binding element-costimulatory signaling region-zeta chain portion in that order.

7. The nucleic acid polymer of claim **1**, wherein the zeta chain portion comprises the sequence obtained by amplification of human zeta chain DNA with the primers of SEQ ID Nos 1 and 2.

8. The nucleic acid polymer of claim **7**, wherein the binding element is an antibody.

9. The nucleic acid polymer of claim **8**, wherein the antibody is a single chain antibody.

10. The nucleic acid polymer of claim **9**, wherein the single chain antibody binds to prostate specific membrane antigen.

11. The nucleic acid polymer of claim **9**, wherein the single chain antibody binds to CD19.

12. The nucleic acid polymer of claim **9**, wherein the encoded T cell receptor comprises binding element-costimulatory signaling region-zeta chain portion in that order.

13. The nucleic acid polymer of claim **1**, wherein the encoded T cell receptor comprises binding element-signaling region-zeta chain portion in that order.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,446,190 B2
APPLICATION NO. : 10/448256
DATED : November 4, 2008
INVENTOR(S) : Sadelain et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Specifications:

Column 15, Line(s) 14-19 should read

<210> 4
<211> 26
<212> DNA
<213> human

<400> 4
ggcggccgca attgaagtta tgtatc 26

Column 15, Line(s) 26-36 should read

<210> 6
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gacttcgcag cctatcgctc c321

Signed and Sealed this
Sixteenth Day of July, 2013

Teresa Stanek Rea
Acting Director of the United States Patent and Trademark Office

CERTIFICATE OF SERVICE

I hereby certify that I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the Federal Circuit by using the appellate CM/ECF system on August 31, 2020.

I hereby certify that on August 31, 2020, by agreement of the parties, the confidential version of the Opening Brief and Addendum for Kite Pharma, Inc. was served by email on the following counsel of record:

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/s/ E. Joshua Rosenkranz
E. Joshua Rosenkranz
Counsel for Defendant-Appellant

CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limitation of Fed. R. App. P. 32(a)(7)(B)(i) because this brief contains 13,991 words, including the words from the claim language on the inside cover and images in the brief and excluding the parts of the brief exempted by Fed. R. App. P. 32(f) and Fed. Cir. R. 28(a)(12)(B).

This brief complies with the typeface requirements of Fed. R. App. P. 32(a)(5) and the type style requirements of Fed. R. App. P. 32(a)(6) because this brief has been prepared in a proportionally spaced typeface using Microsoft Word 2013 in Century Schoolbook 14-point font.

ORRICK, HERRINGTON & SUTCLIFFE LLP

/s/ E. Joshua Rosenkranz
E. Joshua Rosenkranz
Counsel for Defendant-Appellant

FORM 31. Certificate of Confidential Material **Form 31**
July 2020

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

CERTIFICATE OF CONFIDENTIAL MATERIAL

Case Number: 20-1758

Short Case Caption: Juno Therapeutics, Inc. v. Kite Pharma, Inc.

Instructions: When computing a confidential word count, Fed. Cir. R. 25.1(d)(1)(C) applies the following exclusions:

- Only count each unique word or number once (repeated uses of the same word do not count more than once).
- For a responsive filing, do not count words marked confidential for the first time in the preceding filing.

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☑ This number does not exceed the maximum of 15 words permitted by Fed. Cir. R. 25.1(d)(1)(A).

☐ This number does not exceed the maximum of 50 words permitted by Fed. Cir. R. 25.1(d)(1)(B) for cases under 19 U.S.C. § 1516a or 28 U.S.C. § 1491(b).

☐ This number exceeds the maximum permitted by Federal Circuit Rule 25.1(d)(1), and the filing is accompanied by a motion to waive the confidentiality requirements.

Date: 08/31/2020

Signature: s/ E. Joshua Rosenkranz

Name: E. Joshua Rosenkranz