APPENDIX A

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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

2020-1758

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

Decided: August 26, 2021

MORGAN CHU, Irell & Manella LLP, Los Angeles, CA, argued for plaintiffs-appellees. Also represented by ALAN J. HEINRICH, ELIZABETH C. TUAN; GREGORY A. CASTANIAS, JENNIFER L. SWIZE, Jones Day, Washington, DC; LISA LYNN FURBY, Chicago, IL; ANDREA WEISS JEFFRIES, Los Angeles, CA; MATTHEW J. RUBENSTEIN, Minneapolis, MN.

E. JOSHUA ROSENKRANZ, Orrick, Herrington & Sutcliffe LLP, New York, NY, argued for defendant-appellant. Also represented by MELANIE L. BOSTWICK, ROBBIE MANHAS, JEREMY PETERMAN, Washington, DC; GEOFFREY DONOVAN

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BIEGLER, Fish & Richardson, San Diego, CA; TED G. DANE, PETER GRATZINGER, ADAM R. LAWTON, GARTH VINCENT, JEFFREY I. WEINBERGER, Munger, Tolles & Olson LLP, Los Angeles, CA.

Before MOORE, *Chief Judge*, PROST and O'MALLEY, *Circuit Judges*.

MOORE, *Chief Judge*.

Kite Pharma, Inc. appeals a final judgment of the United States District Court for the Central District of California that (1) claims 3, 5, 9, and 11 of U.S. Patent No. 7,446,190 are not invalid for lack of written description or enablement, (2) the '190 patent's certificate of correction is not invalid, and (3) Juno Therapeutics, Inc., and Sloan Kettering Institute for Cancer Research (collectively, Juno) were entitled to $1,200,322,551.50 in damages. *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, No. 2:17-cv-07639-PSG-KS, (C.D. Cal. April 8, 2020), ECF 728. Because we conclude that the jury verdict regarding written description is not supported by substantial evidence, we reverse.

BACKGROUND

T cells are white blood cells that contribute to the body's immune response. J.A. 32906–07. They have naturally occurring receptors on their surfaces that facilitate their attack on target cells (such as cancer cells) by recognizing and binding an antigen, i.e., a structure on a target cell's surface. J.A. 32907–08.

Chimeric antigen receptor (CAR) T-cell therapy involves isolating a patient's T cells; reprogramming those T cells to produce a specific, targeted receptor (a CAR) on each T cell's surface; and infusing the patient with the reprogrammed cells. J.A. 32913; '190 patent at 2:31–36, 7:24–33. The reprogramming involves introducing genetic material containing a nucleotide sequence encoding for a

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CAR into the T cell so that the cell produces the CAR on its surface. J.A. 32913; '190 patent at 1:30–34, 2:27–36. This CAR allows the T cell to recognize the specific antigen for which it was programmed. J.A. 32913; '190 patent at 2:27–36.

The '190 patent relates to a nucleic acid polymer encoding a three-part CAR for a T cell. It claims priority to a provisional application filed May 28, 2002, a time period that one of the inventors labeled as "the birth of the CAR-T field." J.A. 32976. The first portion of the three-part CAR is called the intracellular domain of the human CD3 ζ (zeta) chain. *See, e.g.*, '190 patent at 2:14–16, 4:12–17. It is a signaling domain that, when the T cell binds to an antigen, is activated to create an initial immune response. J.A. 103. The second portion is a costimulatory region comprising a specific amino acid sequence (SEQ ID NO:6) that is part of a naturally occurring T-cell protein called CD28. '190 patent at 2:16–17, 3:44–54. When activated, the costimulatory region creates a second signal to augment or prolong the immune response by, for example, directing the T cells to multiply. J.A. 103; J.A. 32912. The CD3-zeta portion and the costimulatory region combine to make a signaling element, or backbone, of the CAR. J.A. 32906; J.A. 32912–13. This combination of the CD3-zeta and costimulatory regions allows the T cells to not only kill target cells but also to divide into more T cells. J.A. 32913–14. The third and final portion of the '190 patent's CAR is the binding element, which is the portion of the CAR that determines what target molecule or antigen the CAR can recognize and bind to. '190 patent at 4:34–45; J.A. 32912–13.

One type of binding element in the '190 patent is a single-chain antibody, i.e., a single-chain antibody variable fragment (scFv). '190 patent at 4:52–57; *see also* J.A. 32910. An scFv is made by taking two pieces of an antibody, one from the heavy chain of an antibody's variable region and one from the light chain of an antibody's variable region, and linking them together with a linker

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sequence. J.A. 32908–09; *see also* J.A. 2643–44; J.A. 103; '190 patent at 4:52–5:5. Each variable region has a unique amino acid sequence that can dictate whether and how an antibody, and thus an scFv, binds to a target. J.A. 2643; J.A. 103. The '190 patent discloses two scFvs. One of those scFvs is derived from the SJ25C1 antibody and binds CD19, a protein that appears on the surface of diffuse large B-cell lymphoma cells. '190 patent at 11:12–22; *see also* J.A. 58. The other disclosed scFv is derived from the J591 antibody and binds PSMA, a protein that appears on the surface of prostate cancer cells. '190 patent at 7:43–51, 8:5–10; *see also* J.A. 32967; J.A. 33945. The '190 patent does not disclose the amino acid sequence of either scFv.

Independent claim 1 of the '190 patent 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.

Dependent claims 3 and 9 limit the claimed "binding element" to "a single chain antibody," i.e., an scFv. Claims 5 and 11, which depend from claims 3 and 9, respectively, further specify that the claimed scFv binds to CD19.

Kite's YESCARTA® is a "therapy in which a patient's T cells are engineered to express a [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." J.A. 58; J.A. 384; Kite Br. 17. It is a treatment that uses a three-part CAR containing an scFv that

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