No. 2020-1758

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.

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

PLAINTIFFS-APPELLEES' PETITION FOR PANEL REHEARING OR REHEARING EN BANC

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CERTIFICATE OF INTEREST

Case No. 2020-1758

Juno Therapeutics, Inc. v. Kite Pharma, Inc.

Filing Party/Entity: Juno Therapeutics, Inc. and Sloan Kettering Institute for Cancer Research

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

Date: October 27, 2021 Signature: */s/ Gregory A. Castanias*

Name: Gregory A. Castanias

1. Represented Entities (Fed. Cir. R. 47.4(a)(1)) – Provide the full names of all entities represented by undersigned counsel in this case.

(a) Juno Therapeutics, Inc. & (b) Sloan Kettering Institute for Cancer Research

2. Real Party in Interest (Fed. Cir. R. 47.4(a)(2)) – 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

3. Parent Corporations and Stockholders (Fed. Cir. R. 47.4(a)(3)) – 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.

Juno Therapeutics, Inc. is a wholly owned subsidiary of Celgene Corporation. Celgene Corporation is a wholly owned subsidiary of Bristol Myers Squibb Company. Bristol Myers Squibb Company has no parent corporation, and there is no publicly held corporation that owns 10% or more of its stock.

Sloan Kettering Institute for Cancer Research: Not applicable.

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).

Jones Day: Luke Burton (no longer at firm), Sarah Geers, Christopher Harnett (no longer at firm), Kevin McCarthy, John Michalik, Emily Whitcher (no longer at firm)

Irell & Manella LLP: Rebecca Carson, Lauren Drake (no longer at firm), Moon Hee Lee (no longer at firm), Ingrid Petersen, Crawford Maclain Wells

King & Spalding LLP (representing third party Bristol Myers Squibb Company): Joseph Akrotirianakis

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

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).

Not Applicable

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STATEMENT OF COUNSEL

Based on my professional judgment, I believe this appeal requires an answer to a precedent-setting question of exceptional importance: Whether the Court's "written description" requirement is contrary to 35 U.S.C. § 112 ¶ 1 (now § 112(a)).

Based on my professional judgment, I further believe the panel decision is contrary to the Court's "written description" requirement as set forth in its precedent, including *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005).

/s/ Gregory A. Castanias, Counsel for Appellees

INTRODUCTION*

Sloan Kettering developed and claimed in the '190 patent a revolutionary cancer-fighting technology: a novel two-part backbone that, in combination with a third, well-known element (an scFv) that binds the backbone to the cancer cell, creates a chimeric antigen receptor, *i.e.*, a "CAR." Sloan Kettering's backbone—precisely identified in the patent by its amino-acid sequence—was a true, groundbreaking invention.

The panel, overturning a jury's factual finding to the contrary, held the patent invalid under § 112 as a matter of law, based solely on the *old, well-known scFv element* of the CAR. The panel applied a rigid, formalistic test demanding evidence of the inventors' "possession" of the "full scope of the invention" through "representative examples" or "common structural features."

Section 112 contains no inventor-possession requirement, nor can its text be fairly read to demand one. Yet this Court's decisions have cemented notions of inventor "possession," "representative examples," and "common structural elements" into a "written description" requirement that has no footing in the statutory text, nor in any sound policy that promotes the progress of the useful arts. The Court should correct its over-complication of the statute's straightforward, singular requirement.

* All emphasis in this petition is added.

This case is the ideal vehicle: The panel decision rested solely on this written-description test, and found only the routine, well-known binding element inadequately described. This case thus presents a narrow issue, the panel's resolution of which highlights the Court's misguided § 112 precedent.

The mischief of the Court's separate, rigid written-description inquiry is particularly devastating for pharmaceutical inventions, and especially biologics. A bright-line rule of "possession," requiring a showing of "representative examples" or "common structural features" across the "full scope" of an element, is essentially impossible to meet—as well as unnecessary—where the permutations of that element, though sharing the same function and easily made and used, will not share an entirely common structure.

Even were the Court to maintain "written description" as a separate requirement, the binding element would still satisfy any reasonable standard. The panel decision, which focused on the small number of "representative species" in the specification, completely overlooked the patent's disclosure of the Orlandi article—a decades-old "cookbook" for making and using scFvs. For well-known elements in biologics, of which the '190 patent is a classic example, disclosure of one or more examples along with a well-known, predictable method of making other permutations demonstrates "possession." Sloan Kettering possessed its inventive CAR across scFv permutations, just as the inventor of a novel electrically

powered machine would possess the invention by disclosing just one kind of power-cord connection.

Capon v. Eshhar, 418 F.3d 1349 (Fed. Cir. 2005), which also involved CAR claims reciting scFv binders, underscores the panel's misapprehension of the maturity of this science. *Capon* acknowledged that the scFv binder for CARs was already well known by 1995, years before the 2002 priority date here, and made clear there is no "requirement that these [scFv] sequences must be analyzed and reported in the specification." *Id.* at 1358. The panel decision squarely conflicts with *Capon*.

BACKGROUND

Scientists have long known that certain cells, including cancer cells, can be identified by "antigens" on their surface. Scientists have also long known that antigens have corresponding antibodies. For decades, antibodies (or antibody fragments known as scFvs) have been used to attach CARs to corresponding antigens, as in the '190 patent. CARs modify T-cells with a "signaling" domain that enhances the T-cell's natural immune response. scFvs are "antigen-specific," binding the CAR-modified T-cell ("CAR-T cell") to the scFv's corresponding antigen, which is expressed by the target cell. Appx103.

scFvs date back to the 1980s, and the earliest CARs—from the 1990s—used them. Appx33925-33928; Appx270. The trial record confirmed that scFvs in

CARs have long been "well known," "old technology"; decades of research showed CARs readily incorporating scFvs. *E.g.*, Appx33931-33935; Appx33938-33939; Appx32909; Appx33208-33209. By 1989, skilled artisans had the "cookbook" or "recipe" for generating scFvs to bind to any target antigen—the Orlandi method. Appx36185-36189 (Orlandi article); Appx33014-33015; Appx33945. Using this method, skilled artisans would inject a selected antigen into a mammal (such as a mouse). The mammal's immune system would recognize the antigen and generate corresponding antibodies, from which fragments would be collected and used to create scFvs. The scFvs could then be used to bind to the selected target in other mammals. Appx33678-33679; *see* Appx36185-36189. Generating scFvs was easy; a self-taught employee, hired as a dishwasher in a trial expert's laboratory, successfully used Orlandi's method to do so. Appx33942; Appx33966; Appx63.

Scientists at Sloan Kettering, a research arm of Memorial Sloan Kettering (the world's oldest cancer-research institution), invented and used a special CAR "backbone" consisting of *two* particular signaling domains in combination. The inventive two-part backbone can be targeted to a selected antigen using the well-known scFv element to connect to the antigen. Sloan Kettering's claims in the '190 patent recite:

- "a zeta chain portion comprising the intracellular domain of human CD3 ζ chain";
- "a costimulatory signaling region" that "comprises the amino acid sequence encoded by SEQ ID NO:6"; and
- "a binding element [further limited in claims 3 and 9 to an scFv] that specifically interacts with a selected target."

Appx282. Claims 5 and 11 are further narrowed to scFvs that bind to a specific cancer cell target, CD19. Appx282.

The '190 patent expressly details the amino-acid sequences for the two signaling domains (specific regions of CD3 ζ and CD28, respectively). Appx271. This groundbreaking "two-part backbone" both kills the cancer cell *and* allows the CAR-T cells to reproduce, "build[ing] up an army" of CAR-T cells to kill additional cancer cells. Appx32913-32914; Appx272. There was no issue as to the adequacy of the description of the two-part backbone.

The third element—the scFv—did not need much, if any, detail. As of the '190 patent's 2002 priority date, scientists regularly used scFvs; CARs routinely implemented them; and the then-13-year-old Orlandi method taught how to obtain scFvs for any given antigen. Scientists could also "just look [scFvs] up in the literature" and find "different choices" that "were decades old." Appx33209-33211. Nevertheless, the patent explicitly refers to the Orlandi method, Appx271;

Appx276, and identifies two scFvs as examples, including one targeting CD19. Appx271-275.

Sloan Kettering's groundbreaking advance of replicating the CAR-T cells within the body is heralded as the world's first "living drug." Appx32913-32914; Appx33930-33931. This was undisputed. Manufacturers flooded Sloan Kettering with license requests. Appx33028-33029; Appx33054-33055. One was Kite. Appx33032-33041; Appx33082. Kite never obtained a license, though. Nor did it otherwise succeed in avoiding infringement: It was unable to design around Sloan Kettering's two-part backbone, and lost its IPR challenge at the Patent Office and on appeal. Appx33445-33447; Appx35325-35355; Appx7791-7792. Kite nonetheless copied and commercialized Sloan Kettering's patented invention without authorization, combining Sloan Kettering's revolutionary backbone with an scFv that had been known since 1997. Appx33946-33947.

When Sloan Kettering and its licensee Juno sued for infringement, Kite raised enablement and written-description defenses centered on the scFv element. The jury rejected those defenses, found infringement, and awarded damages. The district court upheld the jury's verdict. The panel, however, overturned the verdict—on the single issue of written description. To support its conclusion, the panel cited excerpts of certain trial testimony—completely overlooking the

evidence before the jury of the patent's disclosure, and its incorporation by reference of the Orlandi article.

REASONS FOR GRANTING EN BANC OR PANEL REHEARING

The text of § 112 does not require a "written description" separate from enablement, and this Court's "inventor possession" standard for this atextual requirement cannot fairly be teased out of Congress's command.

Even under the Court's existing "written description" test, the district court's judgment upholding the jury verdict should be reinstated. In reviewing the district court's JMOL denial, the panel was required to consider *all* the evidence in the light most favorable to Plaintiffs. Instead, the panel disregarded key evidence, never once addressing teachings in the specification related to scFvs, including, especially, the Orlandi article.

I. THE EN BANC COURT SHOULD ABANDON THE ATEXTUAL "WRITTEN DESCRIPTION" REQUIREMENT

A. The Court's Separate "Written Description" Requirement Contradicts § 112's Plain Language

Section 112 states that "[t]he specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art … to make and use the same…." 35 U.S.C. § 112 ¶ 1. This language is straightforward. It requires only that the specification describe the invention in sufficient detail to enable skilled artisans to make and use it.

In *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*, however, the en banc Court imported a separate "written description" requirement, requiring inventors to show "possession" of the claimed invention. 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). Although it focused on "representative" examples or "common" "structural features," *Ariad* noted that a written-description analysis also evaluates "'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'" *Id.* (quoting *Capon*, 418 F.3d at 1359). Subsequent decisions, including the panel decision here, focus primarily upon the disclosure of sufficient "representative species" or "common structural features" for whether "the inventors possessed the full scope of the genus" of a claim element, without meaningfully analyzing the existing knowledge or the maturity of the science. Op. 8-19.

The judicially created written-description requirement contravenes the statute's plain language, violates the rules of statutory interpretation, and conflicts with Supreme Court (and other appellate-court) jurisprudence. As the Supreme Court has emphasized, it is improper to "impose limitations on the Patent Act that are inconsistent with the Act's text," *Bilski v. Kappos*, 561 U.S. 593, 612 (2010), yet this atextual "written description" requirement, and the Court's formalistic tests implementing it, do just that.

"In statutory interpretation disputes, a court's proper starting point lies in a careful examination of the ordinary meaning and structure of the law itself. Where, as here, that examination yields a clear answer, judges must stop." *Genentech, Inc. v. Immunex R.I. Corp.*, 964 F.3d 1109, 1111 (Fed. Cir. 2020). Courts "must follow the directions of the law, not [their] own conceptions of the best way to make the law achieve certain policy objectives." *Arnold P'ship v. Dudas*, 362 F.3d 1338, 1342 (Fed. Cir. 2004); *see also SAS Inst. Inc. v. Iancu*, 138 S. Ct. 1348, 1357 (2018) ("We need not and will not invent an atextual explanation for Congress's drafting choices when the statute's own terms supply an answer."). Section 112's plain language is clear—there is no separate written-description standard, and certainly no "inventor possession" standard, satisfied only by "representative species" or "common structur[e]."

This Court's interpretation conflicts not just with § 112's text, but with the Supreme Court's and other circuits' interpretations of that provision. The Supreme Court has long understood the patent laws to demand a single disclosure inquiry: whether an inventor "describes his method with sufficient clearness and precision to enable those skilled in the matter to understand what the process is, and if he points out some practicable way of putting it into operation." *The Telephone Cases*, 126 U.S. 1, 535-36 (1888); *e.g.*, *United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 187 (1933) (similar); *Universal Oil Prods. Co. v. Globe Oil & Ref.*

Co., 322 U.S. 471, 484 (1944) (similar). The Supreme Court has never asked what an inventor "possessed." Nor have any other courts of appeals, which instead asked whether "the patentee [had made] a written description of his invention or discovery, 'in such full, clear … and exact terms as to enable any person skilled in the art … to make, construct … and use the same.'" *Donner v. Am. Sheet & Tin Plate Co.*, 165 F. 199, 206 (3d Cir. 1908); *accord Philip A. Hunt Co. v. Mallinckrodt Chem. Works*, 177 F.2d 583, 585 (2d Cir. 1949); *Ill. Tool Works, Inc. v. Foster Grant Co.*, 547 F.2d 1300, 1309 (7th Cir. 1976). This Court stands alone.

The "written description" requirement also, at times, conflates patent requirements with FDA standards. At oral argument, Plaintiffs' counsel was asked why there were not more *commercially available* products, implying that a sufficient disclosure would have led to more embodiments on the market. Oral. Arg. 50:17-51:04. But while patents are an important step toward the creation and ultimate commercialization of medicines, they are not equivalent to the FDA's approval standards, *e.g.*, *In re '318 Pat. Infringement Litig.*, 583 F.3d 1317, 1324 (Fed. Cir. 2009), which "scrutinize[] everything about the drug—from the design of clinical trials to the severity of side effects to the conditions under which the drug is manufactured." FDA, *The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective* (Nov. 24, 2017), https://www.fda.gov/drugs/information-consumers-and-patients-drugs/fdas-drug-review-process-ensuring-drugs-are-safe-

and-effective. If FDA standards applied to § 112 disclosure, "the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer." *See In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995).

Because the panel decision rested *solely* on written description, including the atextual "inventor[] possess[ion]" test, Op. 11, this case presents an ideal vehicle to reconsider the Court's written-description requirement.

This case also highlights the faulty premise of the Court's "written description" standards. Requiring Sloan Kettering to show "possession" of the "full scope" (meaning all possible permutations) of well-known elements like scFvs (or CD19-specific scFvs for claims 5 and 11) is not only unmoored from the statute, but unnecessary for artisans to make and use the CAR described in the '190 patent. Demanding disclosure of well-known components does not facilitate the patent system's *quid pro quo* bargain.

B. The Court's Written-Description Requirement Impedes Rather Than Promotes The Progress Of Biologic Inventions

For claims reciting generic biological elements, the demand for disclosing "possession" via "representative species" or "common structur[e]" renders innovative patents particularly vulnerable to *post hoc* invalidation. There are well-known biologic "genera," having the same function and substantially overlapping

structure, but which ultimately do not share entirely "common" or "representative" structures because each "species" has some portion with a distinct amino-acid sequence. Yet, even where such permutations can be easily made and used, the Court's test would be satisfied only by making, characterizing, and reciting nearly every permutation. That standard is essentially impossible to meet.

scFvs offer a prime example: it is their variable regions that make each scFv unique and "antigen-specific." Appx103; Appx33938 (if scFvs shared "the same amino acid sequence," then "they would all recognize the same antigen"). In the CAR field, artisans have long taken advantage of that variability to target the CAR to the scFv's corresponding antigen. The evidence showed that for any target antigen, the Orlandi method could be used to generate millions or billions of scFvs, each of which would be expected to work with the inventive backbone. Appx36185-36189; Appx32917; Appx32923; Appx33014-33015; Appx33942-33946; Appx33966; Appx33715-33717; Appx35483-35488; Appx36283-36290; Appx37501-37508. Yet, to protect its novel invention from Kite's (and others') piracy under the panel's rubric, Sloan Kettering would have needed to devote its finite resources to the rote work of injecting mice and creating and characterizing myriad scFvs in order to recite their sequences in the patent, rather than pursuing the next revolutionary cancer treatment. And even though the process for creating such scFvs is entirely routine and predictable, creating and characterizing scFvs

takes time—Kite itself contended that "even six minutes per scFv would entail a billion-man years." KBr. 19. Even setting aside the impracticability of performing and disclosing that exercise as a precondition of patenting—with inventors all the while keeping their inventions secret—such a requirement lacks any basis in the statute. Not even *Ariad* commands such a waste of time and talent.

Besides, a scientist needs only a single scFv that binds the backbone to the selected antigen. For example, once Sloan Kettering had an scFv that binds to CD19, there was no medical reason to create another. Kite's own infringing product highlights that a skilled artisan need not spend time creating different scFvs to make and use the invention—Yescarta uses an old, off-the-shelf scFv. Appx33946-33947. Yet this Court's caselaw now demands inventors spend time and resources on the rote process of making additional scFvs.

Claiming only specific embodiments is an illusory protection, not an adequate alternative to "generic" claiming. As *Enzo Biochem, Inc. v. Gen-Probe, Inc.* recognized, if patentees could claim only the specific permutations they have themselves made and tested, copyists could "avoid infringement" by making a "minor change" while "still exploiting the benefits of [the] invention." 323 F.3d 956, 966 (Fed. Cir. 2002). Nor is the doctrine of equivalents a meaningful protection, or even reconcilable with the Court's § 112 doctrines. If a patentee may not claim a scope directly without disclosing structures for every permutation,

the doctrine of equivalents is an illogical recourse for protecting that scope—not to mention contrary to the public-notice function of patents.

The result of all of this: an atextual test, unmoored from the science, that undermines the patent laws' purpose of encouraging innovation and its dissemination to the public.

II. THE PANEL OVERLOOKED KEY EVIDENCE

Even if the separate, atextual written-description requirement remains, it is met here, as the jury found. The patent's disclosure of a well-known method for obtaining scFvs is more than enough to satisfy any conceivable "inventor possession" requirement. Even under the Court's articulations, the '190 patent adequately discloses "possession," whether by one "example" sufficiently representative of all, or by a method for obtaining scFvs for any chosen target. A wooden evaluation of percentages of either examples or structural commonality, without regard to the pertinent field, its maturity, and the patent's own disclosures, does not comport with any reasonable written-description test.

In particular, the panel ignored critical evidence showing that artisans knew exactly how to make and use the old scFv binders with the revolutionary CAR backbone. The panel decision should be corrected to account for the patent's *own disclosure* that:

- scFvs "may be cloned from the V region genes of a hybridoma *specific for a desired target*." Appx271.
- "The production of *such hybridomas* has become *routine*, and the procedure will not be repeated here." Appx271.
- "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)." Appx271.
- The specification further "incorporate[s]" the Orlandi article "by reference." Appx275-276.

These disclosures are "sufficient materials to accomplish," *Ariad*, 598 F.3d at 1352-53, the "full scope" of claimed scFvs.

Trial witnesses explained exactly how this disclosure demonstrated the applicants' possession of the invention: Skilled artisans using the Orlandi "recipe" or "cookbook" can generate scFvs that bind to any target antigen: you start with the *selected target* and reverse-engineer scFvs that bind. Appx33678-33679; Appx33014-33015; Appx33945.

Kite's own expert explained it step-by-step:

1) A skilled artisan would "immunize the mice with your target,"
2) The mouse would "make cells that that make antibodies to that target,"

3) The artisan would then "isolat[e] those cells."

Appx33678. With those isolated cells, Kite's expert continued, the artisan can create an scFv that would bind to the selected antigen. Appx33678-33679; *see* Appx36185-36189.

The evidence also showed Orlandi's method was easy to use: a self-trained employee, hired as a dishwasher in one of Plaintiffs' experts' labs, used it to make binding scFvs. Appx33942; Appx33966; Appx63. Moreover, although biologics are subject to anomalies, the evidence showed that this "recipe" for producing scFvs to bind to targeted antigens is all but certain to work. *Supra* p. 13. Kite, which bore the burden of proving invalidity by clear-and-convincing evidence, showed *no* instance of the recipe or resulting scFv failing to work. *See* Plaintiffs' Rule 28(j) Response (D.I. 56) at 2. To the contrary, articles as far back as 1993 confirmed "scFvs had been successfully used as the binding elements in [CARs]." Appx35766-35768.

The panel, however, never addressed this evidence. "Orlandi" does not appear even once in the 19-page decision.

The panel's error is underscored by its discussion of *Capon v. Eshhar*, in particular the panel's statement that "more was known in the prior art in *Capon* than here." Op. 12. This cannot be. The *Capon* facts and its CAR claims, which similarly recited scFvs for the same binding function as here (*e.g.*, an "scFv

domain [that] binds to its antigen," 418 F.3d at 1352-53), pre-date the facts and priority date here by over a decade. *See id.* at 1355-56 (surveying state of scFv field as of 1990-91). As *Capon* acknowledged: "The chimeric genes here at issue are prepared from *known DNA sequences of known function*. The Board's requirement that these sequences must be analyzed and reported in the specification does not add descriptive substance." *Id.* at 1358. This remained true years later in 2002 when the '190 patent inventors developed their CAR—and Kite, which bore all the burdens of proving invalidity, produced not a shred of contrary evidence. *Cf. Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) (rejecting § 112 enablement defense where the patent disclosed a process for obtaining antibodies that was "well known and not repeated here").

The panel decision relied instead on inapposite cases. Op. 14 (citing *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149 (Fed. Cir. 2019); *AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc.*, 759 F.3d 1285 (Fed. Cir. 2014)). In *Idenix* and *AbbVie*, the Court found the asserted patents inadequately described because skilled artisans needed iterative "trial and error" testing to identify which embodiments would actually perform the claimed newly discovered function. Op. 14. No trial-and-error testing was necessary here; the '190 patent fully disclosed that the POSITA would start with the antigen and use it to generate

a desired scFv, not start with "millions and billions" of scFvs and then try to match them to an antigen. Appx271; Appx33678-33679; Appx33014-33015; Appx33945; Op. 15-16. The specification—and the cited Orlandi article—are clear: you start with the target antigen and predictably generate binding scFvs, not vice versa.

Overturning the jury's verdict required the panel to conclude that every reasonable juror had to find that Kite showed, by clear-and-convincing evidence, the inadequacy of the patent's written description. Yet, the panel decision failed to consider Plaintiffs' key evidence—let alone in the light most favorable to the verdict. That violated basic tenets of patent law that place the burden of proving invalidity on the defendant by clear-and-convincing evidence, Kite's additional burden on JMOL after an unfavorable jury verdict, and the appellate court's limited role under Rule 50 and the Seventh Amendment in reviewing factual determinations. Patents are "born valid." *Roper Corp. v. Litton Sys.*, 757 F.2d 1266, 1270 (Fed. Cir. 1985). Where validity challenges arise, it is not a "court's role to start from scratch, as a surrogate Examiner, to referee de novo a dispute on the validity question." *Panduit Corp. v. Dennison Mfg. Co.*, 774 F.2d 1082, 1096 (Fed. Cir. 1985), *vacated on other grounds*, 475 U.S. 809 (1986).

The Court—panel or en banc—should correct the evidentiary oversight.

CONCLUSION

Panel or en banc rehearing should be granted.

Dated: October 27, 2021

Respectfully submitted,

/s/ *Gregory A. Castanias*

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CERTIFICATE OF COMPLIANCE

Pursuant to Fed. R. App. P. 32(g)(1), the undersigned hereby certifies that this petition complies with the type-volume limitation of Fed. R. App. P. 35(b)(2)(A).

1. Exclusive of the exempted portions of the petition, as provided in Fed. R. App. P. 32(f), Fed. R. App. P. 35(b)(2)(A), and Fed. Cir. R. 32(b)(2), the petition contains 3,869 words.

2. The petition has been prepared in proportionally spaced typeface using Microsoft Word 2016 in 14 point Times New Roman font. As permitted by Fed. R. App. P. 32(g)(1), the undersigned has relied upon the word count feature of this word processing system in preparing this certificate.

Dated: October 27, 2021 */s/ Gregory A. Castanias*

Statutory Addendum

35 U.S.C. § 112 ¶ 1 (pre-AIA)

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

35 U.S.C. § Section 112(a) (AIA)

In General.--The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

Panel Opinion

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

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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

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

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

binds the CD19 antigen, a CD3-zeta chain portion, and a costimulatory signaling region. J.A. 58; *see also* Kite Br. 11; J.A. 383–96 (Complaint).

Juno sued Kite, alleging infringement of various claims of the '190 patent through the use, sale, offer for sale, or importation of YESCARTA®. Kite filed counterclaims seeking declaratory judgments of noninfringement and invalidity of the '190 patent. After a two-week jury trial, the jury reached a verdict in Juno's favor, finding (1) Kite failed to prove the '190 patent's certificate of correction was invalid, (2) Kite failed to prove any of the asserted claims were invalid for lack of written description or enablement, (3) Juno proved Kite's infringement was willful, and (4) Juno proved Kite owed damages amounting to a $585 million upfront payment and a 27.6% running royalty.

The parties then filed post-trial briefs. Kite moved for judgment as a matter of law (JMOL), arguing (a) the claims were not supported by a sufficient written description, (b) the claims were not enabled, (c) Juno's certificate of correction was invalid, (d) Kite acted in good faith such that it could not be found to be a willful infringer, and (e) Juno's damages expert should have been excluded. J.A. 57, 60. Juno, for its part, moved for entry of judgment on the verdict, prejudgment interest, enhanced damages, and for the court to set an ongoing royalty rate. J.A. 38. The district court denied Kite's motions for JMOL. J.A. 86. The district court granted-in-part Juno's motion, updating the jury's award to $778,343,501 to reflect updated YESCARTA® revenues through trial, awarding prejudgment interest, enhancing damages by 50%, and awarding a 27.6% running royalty. J.A. 56.

Kite appeals, arguing the district court erred in denying JMOL on each of the above issues that Kite raised in its post-trial briefing. We have jurisdiction under 28 U.S.C. § 1295(a)(1). Because we determine that the record does not contain substantial evidence that the patent

contains written description support for the asserted claims, we hold the claims invalid and need not reach Kite's alternative arguments.

DISCUSSION

We review denial of a motion for JMOL under regional circuit law. *See Trs. of Boston Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1361 (Fed. Cir. 2018). The Ninth Circuit reviews a denial of JMOL de novo, and reversal is appropriate when "the evidence, construed in the light most favorable to the nonmoving party, permits only one reasonable conclusion, and that conclusion is contrary to that of the jury." *White v. Ford Motor Co.*, 312 F.3d 998, 1010 (9th Cir. 2002).

I

A patent's specification "shall contain a written description of the invention." 35 U.S.C. § 112 ¶ 1.[1] "[T]he hallmark of written description is disclosure." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc). A specification adequately describes an invention when it "reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Id.* at 1351. "A 'mere wish or plan' for obtaining the claimed invention is not adequate written description." *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1348 (Fed. Cir. 2011). What

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[1] Paragraph 1 of 35 U.S.C. § 112 was replaced with newly designated § 112(a) by section 4(c) of the Leahy-Smith America Invents Act ("AIA"), Pub. L. No. 112-29, sec. 4, 125 Stat. 284, 296–97 (2011). Section 4(e) of the AIA makes those changes applicable "to any patent application that is filed on or after" September 16, 2012. *Id.* Because the applications resulting in the patent at issue in this case was filed before that date, we refer to the pre-AIA version of § 112.

is required to meet the written description requirement "varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005); *see also Ariad*, 598 F.3d at 1351.

As we explained in *Ariad*, "[f]or generic claims, we have set forth a number of factors for evaluating the adequacy of the disclosure, including 'the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue.'" 598 F.3d at 1351 (citing *Capon*, 418 F.3d at 1359). For genus claims using functional language, like the binding function of the scFvs claimed here, the written description "must demonstrate that the applicant has made a generic invention that achieves the claimed result and do so by showing that the applicant has invented species sufficient to support a claim to the functionally-defined genus." *Ariad*, 598 F.3d at 1349. "The written description requirement [ ] ensures that when a patent claims a genus by its function or result, the specification recites sufficient materials to accomplish that function." *Id.* at 1352. Generally, a genus can be sufficiently disclosed by "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." *Id.* at 1350. "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997) (quoting *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993)).

Whether a patent complies with the written description requirement of § 112 ¶ 1 is a question of fact, and "we review a jury's determinations of facts relating to

compliance with the written description requirement for substantial evidence." *Ariad*, 598 F.3d at 1355 (quoting *PIN/NIP, Inc. v. Platte Chem. Co.*, 304 F.3d 1235, 1243 (Fed. Cir. 2002)).

II

Kite argues that the asserted claims are invalid for failing to satisfy the written description requirement because the '190 patent discloses neither representative species nor common structural features of the claimed scFv genus to identify which scFvs would function as claimed. Kite argues that the claims cover an enormous number (millions of billions) of scFv candidates, only a fraction of which satisfy the functional binding limitation for any given target, and that the written description does not meet the written description requirement for this functional binding limitation. It also argues that the scFv field is unpredictable since an scFv's binding ability depends on a variety of factors.

Juno responds that scFvs were well-known (as was how to make them), that multiple scFvs for specific targets were well-known, that the '190 patent describes two working scFv embodiments that are representative of all scFvs, and that scFvs had been incorporated in CARs well before the '190 patent's priority date. It also argues that scFvs are interchangeable and have common structural features.

We agree with Kite that no reasonable jury could find the '190 patent's written description sufficiently demonstrates that the inventors possessed the full scope of the claimed invention. We hold that substantial evidence does not support the jury's finding of adequate written description for any of the asserted claims.

A

The broadest asserted claims of the '190 patent, claims 3 and 9, recite that the scFv binding element "specifically interacts with a selected target." As the '190 patent

explains, "[t]he target . . . can be *any target of clinical interest* to which it would be desirable to induce a T cell response." '190 patent at 4:36–39 (emphasis added). In other words, claims 3 and 9 broadly cover, as part of the claimed nucleic acid polymer encoding for the three-part CAR, *any* scFv for binding *any* target. But the '190 patent's written description fails to provide a representative sample of species within, or defining characteristics for, that expansive genus.

1

The '190 patent's written description contains scant details about which scFvs can bind which target antigens. The '190 patent discloses two example scFvs for binding two different targets: one derived from J591, which targets a PSMA antigen on prostate cancer cells, and another derived from SJ25C1, which targets CD19. J.A. 32922–23; J.A. 32967; J.A. 33945. The '190 patent contains no details about these scFv species beyond the alphanumeric designations J591 and SJ25C1 for a skilled artisan to determine how or whether they are representative of the entire claimed genus. Juno argues these two working embodiments are representative of all scFvs in the context of a CAR. The evidence does not support Juno's argument. The claims are directed to scFvs that bind to selected targets. In claims 3 and 9 there is no limit as to the particular target. To satisfy the written description requirement, the patent needed to demonstrate to a skilled artisan that the inventors possessed and disclosed in their filing the particular species of scFvs that would bind to a representative number of targets. Kite demonstrated by clear and convincing evidence that this patent does not satisfy the written description requirement for the claims at issue and this record does not contain substantial evidence upon which a jury could have concluded otherwise. The disclosure of one scFv that binds to CD19 and one scFv that binds to a PSMA antigen on prostate cancer cells in the manner provided in this patent does not provide information sufficient to

establish that a skilled artisan would understand how to identify the species of scFvs capable of binding to the limitless number of targets as the claims require.

Juno primarily relies on the testimony of its immunological expert, Dr. Brocker, but that testimony is far too general. Dr. Brocker testified that the two exemplary scFvs are representative "because [scFvs] all do the same thing. They bind to the antigen." J.A. 33945. Nothing about that testimony explains which scFvs will bind to which target or cures the '190 patent's deficient disclosure on this score. Without more in the disclosure, such as the characteristics of the exemplary scFvs that allow them to bind to particular targets or nucleotide sequences, the mere fact that scFvs in general bind does not demonstrate that the inventors were in possession of the claimed invention.

This is not to say, however, that a patentee must in all circumstances disclose the nucleotide or amino acid sequence of the claimed scFvs to satisfy the written description requirement when such sequences are already known in the prior art. *See Capon*, 418 F.3d at 1360–61 (holding it was error for the Board of Patent Appeals and Interferences to require "recitation in the specification of the nucleotide sequence of claimed DNA, when that sequence is already known in the field"). But the written description must lead a person of ordinary skill in the art to understand that the inventors possessed the entire scope of the claimed invention. *Ariad*, 598 F.3d at 1353–54 ("[T]he purpose of the written description requirement is to ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification." (internal quotation marks omitted)). Dr. Sadelain, one of the '190 patent's inventors, testified that, at the time he filed his patent application, he had used only the SJ25C1-derived scFv and J591-derived scFv. J.A. 32965–67. Yet the '190 patent claims any scFv on its CAR that binds to any target, without disclosing details

about which scFvs bind to which target. It is not fatal that the amino acid sequences of these two scFvs were not disclosed as long as the patent provided other means of identifying which scFvs would bind to which targets, such as common structural characteristics or shared traits. But this patent provides nothing to indicate that the inventors possessed the full scope of the genus that they chose to claim. Thus, the '190 patent's disclosure does not demonstrate the inventors possessed the entire class of possible scFvs that bind to various selected targets.

Relying upon witness testimony, Juno argues that because scFvs, in general, were known, the two scFvs in the '190 patent are representative. *See, e.g.*, J.A. 32909 (Dr. Sadelain testifying that scFvs were not new in the field, and that they "had been around since the [1980s]"); J.A. 33209 (Kite's founder, Dr. Belldegrun, agreeing that "scientists knew about the scFvs that could be used with CARs going back to the 1980s"); J.A. 33932 (Juno's expert, Dr. Brocker, testifying that scFvs "were in the field for more than a decade, nearly 15 years" at the time of Dr. Sadelain's invention); J.A. 33939–40 (Dr. Brocker testifying that people knew how to make scFvs and "several of them had been described"). To satisfy written description, however, the inventors needed to convey that they possessed the claimed invention, which encompasses all scFvs, known and unknown, as part of the claimed CAR that bind to a selected target. Even accepting that scFvs were known and that they were known to bind, the specification provides no means of distinguishing which scFvs will bind to which targets. *See Eli Lilly*, 119 F.3d at 1568 ("A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." (quoting *Fiers*, 984 F.2d at 1171)). Accordingly, testimony that scFvs were generally known in the field is insufficient to satisfy the written description

requirement for the '190 patent's claims requiring scFvs that bind to a selected target.

Juno relies heavily on our decision in *Capon*, arguing that we already determined that "scFvs were well-known CAR components that did not need to be detailed in CAR patents' specifications to satisfy Section 112." Juno Br. 27. Our *Capon* decision neither made the determination Juno alleges nor determined that the inventors there satisfied the written description requirement. Instead, we vacated the Board's decision for imposing too high a standard to satisfy the written description requirement, and remanded for the Board to consider the evidence and determine whether the specification adequately supported the claims at issue. *Capon*, 418 F.3d at 1358–61; *see also id.* at 1358 ("The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization."). Also, more was known in the prior art in *Capon* than here, particularly when the inventors here used only two scFvs as of the '190 patent's priority date out of the vast number of possibilities. *See id.* at 1355, 1358; J.A. 32965–67. *Capon* does not support Juno's arguments regarding its exceedingly broad functional claim limitations.[2]

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[2] We agree with Juno that a patent specification need not redescribe known prior art concepts. Juno Br. 28 (citing *Immunex Corp. v. Sandoz Inc.*, 964 F.3d 1049, 1064 (Fed. Cir. 2020)). The problem with the '190 patent is that, although there were some scFvs known to bind some targets, the claims cover a vast number of possible scFvs and an undetermined number of targets about which much was *not* known in the prior art.

2

In addition to lacking representative species, the '190 patent does not disclose structural features common to the members of the genus to support that the inventors possessed the claimed invention. *See Ariad*, 598 F.3d at 1350. Juno argues that the '190 patent satisfies the written description requirement because scFvs are interchangeable, with a similar, common structure. It relies on Dr. Brocker's testimony that scFvs have "known structural commonalities, similarities." J.A. 33926. He explained that scFvs have the same general, common structure consisting of a variable region derived from the light chain of an antibody and a variable region derived from the heavy chain of an antibody, where these two portions are connected with a linker. J.A. 33936–38. These general assertions of structural commonalities, in the context of the technology in this case, are insufficient.

It is undisputed that scFvs generally have a common structure, as described by Dr. Brocker. But, as Dr. Brocker acknowledged, an scFv with the same general common structure but with a different amino acid sequence would recognize a different antigen. J.A. 33938. Dr. Brocker also testified that all scFvs have a common structure, regardless of whether they bind. J.A. 33959. The '190 patent not only fails to disclose structural features common to scFvs capable of binding specific targets, it also fails to disclose a way to distinguish those scFvs capable of binding from scFvs *in*capable of binding those targets. The '190 patent provides no amino acid sequences or other distinguishing characteristics of the scFvs that bind. Simply put, the '190 patent claims a "problem to be solved while claiming all solutions to it . . . cover[ing] any compound later actually invented and determined to fall within the claim's functional boundaries," *Ariad*, 598 F.3d at 1353, which fails to satisfy the written description requirement.

We have previously held similar claims invalid based on lack of written description. In *Idenix*, we held invalid claims that required nucleosides effective against hepatitis C virus, and the patent merely provided "lists or examples of supposedly effective nucleosides, but [did] not explain what makes them effective, or why." *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1164 (Fed. Cir. 2019). Without this explanation, "a [person of ordinary skill] is deprived of any meaningful guidance into what compounds beyond the examples and formulas, if any, would provide the same result." *Id.* Similarly, in *AbbVie,* we concluded that substantial evidence supported the jury's verdict of inadequate written description when the patents described one species of structurally similar antibodies derived from only one lead antibody but the asserted claims covered "every fully human IL-12 [targeted] antibody that would achieve a desired result" without an indication about an established correlation between the structure and the claimed function. *AbbVie Deutschland GmbH v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301–02 (Fed. Cir. 2014).[3] As

[3] Juno also relies on *Erfindergemeinschaft UroPep GbR v. Eli Lilly & Co.*, 276 F. Supp. 3d 629 (E.D. Tex. 2017), *aff'd*, 739 F. App'x 643 (Fed. Cir. 2018). In that case, there were hundreds of known PDE5 inhibitors, the type of compound at issue, and the patent identified the compounds by chemical name and structural drawings. *Id.* at 645–46. The compounds also shared a common physical structure to fit the active site of the PDE5 enzyme to inhibit its activity, and the evidence supported that a skilled artisan "could make modifications to increase potency and selectivity." *Id.* at 652–53. The '190 patent, in contrast, does not disclose any amino acid sequences or structures to distinguish scFvs that bind to selected targets from those that do not, and the modifications of the sequence can change the binding ability. Juno also does not dispute that very

in these two cases, the '190 patent does not provide meaningful guidance about which scFv will bind which target.

Claims 3 and 9 broadly claim all scFvs, as part of the claimed CAR, that bind to any target. But the written description of the '190 patent discloses only two scFv examples and provides no details regarding the characteristics, sequences, or structures that would allow a person of ordinary skill in the art to determine which scFvs will bind to which target. That scFvs in general were well-known or have the same general structure does not cure that deficiency. Thus, substantial evidence does not support the jury's finding that the '190 patent conveys, to a skilled artisan, that the inventors possessed the broad genus of scFvs as recited in claims 3 and 9.

B

Claims 5 and 11, which are limited to scFvs that bind CD19 (a specific target), likewise find no written description support in the '190 patent. And again, Juno's general testimony about general scFv structure does not provide substantial evidence regarding the claims containing the functional limitation that covers all scFvs that bind to CD19.

Kite argues that there were "four or five" CD19-specific scFvs "arguably known in the art" at the priority date of the '190 patent. Kite Br. 35. Kite argues that the universe of possible sequences for scFvs is in the range of "millions of billions." *Id.* at 26. Given the vast number of possible scFvs, the lack of detail in the '190 patent regarding the scFv sequences, and the few scFvs known in the art to bind CD19, Kite argues substantial evidence does not support

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few CD19-specific scFvs were known as of the priority date. *See* § II.B below.

that the '190 patent discloses species representative of the claimed genus.

Juno does not dispute Kite's characterizations regarding either the number of known CD19 scFvs at the priority date of the '190 patent or the universe of possible scFvs. Instead, it cites Dr. Brocker's general testimony that "there were several known" CD19 scFvs and publications "which have demonstrated that it's possible to make these single-chain Fvs that can bind to CD19." J.A. 33942. Juno also acknowledges that the '190 patent discloses only one CD19-specific scFv (the SJ25C1-derived scFv), but argues that a second CD19-specific scFv, the one used in YESCARTA®, was known by 1997. Juno Br. 24.

Substantial evidence does not support the jury's finding that the '190 patent disclosed sufficient information to show the inventors possessed the claimed genus of functional CD19-specific scFvs as part of their claimed CAR. The '190 patent provides no details about any CD19-specific scFv, such as an exemplary amino acid sequence, a shape, or general characteristics that would allow this target-specific scFv to bind. Instead, it provides only an alphanumeric designation, SJ25C1, as the source for the CD19-specific scFv. Without more guidance, in a vast field of possible CD19-specific scFvs with so few of them known, no reasonable jury could find the inventors satisfied the written description requirement.

Juno's reliance on a combination of expert and inventor testimony does not provide the required support. Dr. Brocker's testimony that "there were several [CD19 scFvs] known" at the priority date and that it was "possible to make these single-chain Fvs that can bind CD19," J.A. 33942, at most demonstrates a small number of CD19-specific scFvs were known and others were possible, albeit undiscovered. Indeed, Dr. Sadelain admitted that the SJ25C1-derived scFv was the only CD19-specific scFv he used at the time he filed his patent application. J.A. 32965.

And Juno's reliance on only one more CD19-specific scFv, the one used in YESCARTA®, further demonstrates that the number of known CD19-specific scFvs at the time was small. Juno again relies on Dr. Brocker, who testified that he was not "aware of any *functional* CD19 scFv that has not been shown to work with Dr. Sadelain's CAR backbone." J.A. 33943–44 (emphasis added). But that testimony presupposes an scFv already known to be functional; one that was known to bind to CD19. Such circular reasoning does not support that the inventors possessed the full scope of possible CD19-specific scFvs, particularly when the genus of possibilities is expansive with only four or five CD19 scFv species known at the time. Finally, Juno relies on Dr. Sadelain's testimony that, since he filed his patent application, he has "placed multiple scFvs" on the CAR backbone, "probably up to 30 [CD19-specific scFvs] by now." J.A. 32923.[4] But we assess whether the written description requirement is satisfied as of the filing date of the patent application. *Ariad*, 598 F.3d at 1351. Dr. Sadelain's testimony about post-priority date developments, therefore, is irrelevant to the inquiry before us. *See id.* at 1355 (post-priority date evidence "legally irrelevant to the question of whether" the disclosure conveyed possession at the time of filing).

Juno's further arguments that it would not matter to a person of ordinary skill (1) that scFvs may be highly diverse in the abstract, (2) that "millions of billions" of scFvs would need to be made and tested to ascertain their binding properties, or (3) that a skilled artisan could not predict

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[4] Fifteen years after the '190 patent's priority date, individuals from Juno published an article, J.A. 37426–34, in which they discussed having screened over a billion human scFv sequences to arrive at only 60 that "displayed elevated binding to CD19-expressing cells," J.A. 37427–28.

before testing whether an scFv would bind, Juno Br. 28–29, are contrary to our precedent. In *Ariad*, we explained 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." 598 F.3d at 1351. Some factors to consider when evaluating the adequacy of the disclosure include "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue." *Id.* (alteration in original) (citing *Capon*, 418 F.3d at 1359). Contrary to Juno's argument, the diversity of the functional scFv genus, the unpredictability of an scFv's binding ability, and that the prior art had, at most, five CD19-specific scFvs as of the priority date are all relevant to the written description inquiry.

We likewise reject Juno's argument that our decision in *Ariad* is "irrelevant" because the claims at issue here do not involve method claims reciting a "newly-identified cellular function or mechanism of action." Juno Br. 25. Juno relies on its expert's testimony that Dr. Sadelain invented the backbone, not scFvs. J.A. 33932; *see also* J.A. 33934 (Dr. Brocker testifying that scFvs were "not part of this invention. The real invention was the backbone."). But the '190 patent's claims are not limited to just the claimed backbone; they also include the functional scFv for binding the target. As we explained in *Boston Scientific Corp. v. Johnson & Johnson*, "[t]he test for written description is the same whether the claim is to a novel compound or a novel combination of known elements. The test is the same whether the claim element is essential or auxiliary to the invention." 647 F.3d 1353, 1365 (Fed. Cir. 2011). The '190 patent inventors, therefore, needed to provide a sufficient disclosure that "reasonably conveys to those skilled in the art that the inventor[s] had possession of the claimed subject matter as of the filing date," *Ariad*, 598 F.3d at 1351, including for the claimed functional binding element.

While it is true that scFvs in general were known, and even known to bind, the record demonstrates that, for even the narrowest claims at issue, the realm of possible CD19-specific scFvs was vast and the number of known CD19-specific scFvs was small (five at most). The '190 patent, however, provides no details about which scFvs bind to CD19 in a way that distinguishes them from scFvs that do not bind to CD19. Without this guidance, under our controlling *Ariad* decision, no reasonable jury could find the '190 patent satisfies the written description requirement.

CONCLUSION

Substantial evidence does not support the jury's verdict in Juno's favor on the issue of written description. For the claimed functional scFv genus, the '190 patent does not disclose representative species or common structural features to allow a person of ordinary skill in the art to distinguish between scFvs that achieve the claimed function and those that do not. Accordingly, we reverse.

REVERSED

COSTS

Costs to Kite.