Putting the CAR-T Before the Horse: How Much Disclosure is Required Under Section 112(a) for Biotechnological Inventions?

I. OVERVIEW

Chimeric Antigen Receptor T Cell (CAR-T) therapy harnesses a patient's immune response, reprogramming the patient's cells to recognize and preferentially target foreign invaders like harmful cancer cells.[1] Ushering in "the birth of the CAR-T field," Juno Therapeutics (Juno) developed such a therapy.[2] Juno subsequently filed a provisional patent application on May 28, 2002, seeking protection for a three-part CAR for T cells.[3] In U.S. Patent No. 7,446,190B2 ('190 patent), Juno claimed two binding elements known as single chain antibody variable fragments (scFvs).[4] Notably, Juno did not disclose either scFvs' amino acid sequence.[5] Instead, Juno broadly claimed a "costimulatory signaling region compris[ing] the amino acid sequence encoded by SEQ ID NO:6."[6] The dependent claims further limited the claim to a "binding element" for a scFv.[7] Other dependent claims narrowed the claimed scFv to those which bind CD19.[8]

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1. Juno Therapeutics, Inc. v. Kite Pharma, Inc., 10 F.4th 1330, 1333 (Fed. Cir. 2021) (internal citations omitted).
2. *Id.*
3. *Id.*
4. Specifically, Juno claimed two scFvs, one scFv derived from the SJ24C1 antibody, which was capable of binding to CD19, and one scFv derived from the J591 antibody which was capable of binding PSMA. The CD19 antigen is commonly expressed on B-cell lymphomas and leukemias while the PSMA is commonly expressed on prostate cancer cells. *Id.*
5. *Id.* at 1337.
6. *Id.* at 1334 (citing U.S. Pat. No. 7,446,190B2 (issued Nov. 4, 2008)).
7. *Id.* (citing U.S. Pat. No. 7,446,190B2 (issued Nov. 4, 2008)).
8. *Id.* at 1333.

Following issuance of Juno's patent, Kite Pharmaceuticals (Kite) developed YESCARTA, which utilizes a three-part CAR with a scFv capable of binding to the CD19 antigen.[9] Subsequently, Juno filed suit against Kite for patent infringement and Kite counterclaimed for declaratory judgment on the issues of infringement and invalidation of the '190 patent.[10] A jury verdict in favor of Juno found that Kite was unable to prove that the '190 patent claims lacked sufficient written description or enablement, thereby awarding Juno $585 million in damages.[11] Kite appealed the district court's denial of their motion for judgment as a matter of law.[12] The Federal Circuit Court of Appeals for the United States *held* that Juno Therapeutics, Inc.'s patent for a Chimeric Antigen Receptor T Cell therapy was invalid because the patent did not disclose a representative species or common structural feature such that a person of ordinary skill in the art would be able to identify scFvs capable of the claimed function. *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, 10 F.4th 1330 (Fed. Cir. 2021).

II. BACKGROUND

A. Written Description Requirement Under 35 U.S.C. § 112(a)

Patent law seeks to incentivize scientific innovation by granting exclusionary rights for a limited period.[13] Following this period, the patent's written description serves as a mechanism to immediately relay valuable scientific information (i.e., the invention) to the public.[14] In satisfying the written description requirement, the inventor must sufficiently describe the invention to be claimed in the patent's specification.[15] Moreover, the inventor must demonstrate that they were "in possession" of the claimed invention at the time the patent was filed.[16]

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9. *Id.* at 1334.
10. *Id.*
11. *Id.*
12. *Id.*
13. U.S. CONST. art. I § 8, cl. 8.
14. Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 922 (Fed. Cir. 2004) (quoting Enzo Biochem, Inc. v. Gen-Probe Inc., 323 F.3d 956, 970 (Fed. Cir. 2002)) ("The 'written description' requirement serves a teaching function, as a 'quid pro quo' in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time."); *see* Sean B. Seymore, *Patenting the Unexplained*, 96 WASH. U. L. REV. 707, 712-13 (2019).
15. Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010).
16. Carnegie Mellon Univ. v. Hoffmann-La Roche Inc., 541 F.3d 1115, 1122 (Fed. Cir. 2008) (quoting Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991); *see also* Noelle v. Lederman, 355 F.3d 1343, 1348 (Fed. Cir. 2004) (holding that for a patent to claim an

The "possession" test is an objective inquiry, requiring that "the specification . . . describe an invention understandable to . . . [a person of ordinary skill in the art] and show that the inventor actually invented the invention claimed."[17] Thus, the written description requirement serves a vital function of defining the scope of claims to prevent an "overreach . . . of the inventor's contribution to the field of art."[18]

The level of written description required to satisfy disclosure is a factually dependent analysis and varies depending on the invention's scope.[19] The analysis remains "the same whether the claim element is essential or auxiliary to the invention."[20] Additionally, a patentee may generically claim their invention if the other requirements of Section 112 are met.[21] The genus claim, a type of generic claim, allows the inventor to claim multiple species (i.e., embodiments) based on the species' common trait.[22] Particularly in the biotechnology and pharmaceutical fields, genus claims can be useful tools, allowing inventors broad claim coverage while providing protection for a multitude of derivate species.[23] Yet, the beneficiary breadth afforded genus claims makes such claims susceptible to a later finding of invalidity, especially in more unpredictable fields of art.[24]

A genus may be claimed by disclosing representative samples or shared structural features common to the genus.[25] For a genus with substantial variation amongst the species, the requisite number of species

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earlier filing date of a prior application, the applicant must demonstrate possession of what is later claimed at "the filing date of the earlier filed application.").

17. *Ariad*, 598 F.3d at 1351; *see also Enzo*, 323 F.3d at 970 ("For biological inventions, for which providing a description in written form is not practicable, one may nevertheless comply with the written description requirement by publicly depositing the biological material, as we have held today.").

18. *Ariad*, 598 F.3d at 1353-54 (quoting *Rochester*, 358 F.3d at 920; *see generally* 35 U.S.C. § 112(a)(2012) ("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 . . . ").

19. *Ariad*, 598 F.3d at 1351; *see generally* Dmitry Karshtedt ET AL., *The Death of the Genus Claim*, 35 HARV. J. L. & TECH. 1, 71-72, 91-92 (2021); *Seymore*, *supra* note 14, at 730.

20. Bos. Sci. Corp. v. Johnson & Johnson, 647 F.3d 1353, 1365 (Fed. Cir. 2011).

21. Amgen, Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 1213 (Fed. Cir. 1991); *see* 35 U.S.C § 112(a)(2012).

22. Karshtedt, *supra* note 19, at 17, 62, 64-65; *see* Regents of the Univ. of California v. Eli Lilly & Co., 119 F.3d 1559, 1568 (Fed. Cir. 1997) (quoting Fiers v. Revel, 984 F.2d 1164, 1171 (Fed. Cir. 1993)) ("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.").

23. Karshtedt, *supra* note 19, at 17.

24. Seymore, *supra* note 14, at 730.

25. *Eli Lilly & Co.*, 119 F.3d at 1569.

disclosed must likewise "reflect the variation within the genus."[26] However, no "bright-line rule[]" exists defining the required number of species that must be disclosed to sufficiently claim a genus.[27] Because the patent specification is interpreted from the perspective of a person skilled in the art, "a patentee may rely on information that is 'well-known in the art' for purposes of meeting the written description requirement."[28]

In the seminal case for analyzing written description, *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*, the Federal Circuit provided a framework for determining the scope of a patent's claims.[29] In *Ariad*, the patent related to the regulation of gene expression using transcription factor NF-kappaB.[30] The court construed the patent's claim as encompassing "the use of all substances that achieve the desired result of reducing the binding of NF-kappaB to NF-kappaB recognition sites."[31]

Elevating the written description requirement for biotechnology cases, the Federal Circuit held that *more than* "generic language in the application" is required to satisfactorily meet the written description requirement.[32] Further, the court clarified that "merely drawing a fence around the outer limits of a purported genus" would fail to prove the invention of a genus as opposed to "just a species."[33] Lastly, the court noted that "[p]atents are not awarded for academic theories, no matter how groundbreaking or necessary to the later patentable inventions of others."[34]

Following *Ariad*, the Federal Circuit continued to address the written description requirement in various biotechnology cases.[35] A specification that conflicts with what is "well-known" in the art may indicate that the inventor was not in possession of the claimed invention at the time of filing.[36] In the event of broad disclosure (e.g., providing many examples), the disclosure would be insufficient if it failed to explain why the examples are effective.[37] Such disclosure would thereby deprive a person skilled in

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26. U.S. PAT. & TRADEMARK OFF., MANUAL OF PATENTING EXAMINER PROCEDURE § 2163.03 (9th ed., 10th Rev. July 2020) [hereinafter MPEP].

27. Ariad Pharm., Inc. v. Eli Lilly, Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010).

28. Bos. Sci. Corp. v. Johnson & Johnson, 647 F.3d 1353, 1366 (Fed. Cir. 2011).

29. *See Ariad*, 598 F.3d 1336.

30. *Id.* at 1340.

31. *Id.* at 1341.

32. *Id.* at 1351 (emphasis added).

33. *Id.* at 1350.

34. *Id.* at 1353.

35. Centocor Ortho Biotech, Inc. v. Abbott Labs, 636 F.3d 1341, 1353 (Fed. Cir. 2011) (finding lack of written description support for antibodies containing a "human variable region").

36. *Bos. Sci.*, 647 F.3d at 1366.

37. Idenix Pharm. LLC v. Gilead Scis. Inc., 941 F.3d 1149, 1164-65 (Fed. Cir. 2019), *cert. denied*, 141 S. Ct. 1234 (2021).

the art of "any meaningful guidance into what compounds beyond the examples . . . would provide the same result."[38]

B. Chimeric Antigen Receptor (CAR) T-Cell Therapy

Modernizing cancer treatment, Chimeric Antigen Receptor T cell (CAR-T) therapy utilizes a patient's own T cells and genetically modifies these cells to create ones capable of destroying cancer cells.[39] The genetically modified cells mimic the body's natural T cell immune response, in which T cells bind to harmful target cells via antigens on the target cell's outer surface.[40] CAR-T patents have increased over time, averaging 2.09 development speed compared to the general patent population's 1.05 development speed.[41] In a study analyzing CAR-T patents, the most frequently targeted antigen was CD19.[42] Due to the complexity of the CAR-T technology, non-commercial organizations (e.g., hospitals, universities, and research institutions) and pharmaceutical companies commonly collaborate to develop CAR-T patents.[43] Importantly, the partnerships between pharmaceutical companies and non-commercial organizations have shifted from the "traditional collaboration models" to models characterized by "resource sharing, collaborative [research and development] and joint patents."[44]

III. COURT'S DECISION

In the noted case, the Court of Appeals for the Federal Circuit clarified the written description necessary for functional claims, reviewing the district court's legal conclusions *de novo*.[45] The court separated its

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38. *Id.* at 164.

39. Virgínia Picanco-Castro et al., *Emerging CAR T Cell Therapies: Clinical Landscape and Patent Technological Routes*, 16 HUM. VACCINES & IMMUNOTHERAPEUTICS 1424 (2020).

40. Juno Therapeutics, Inc. v. Kite Pharma, Inc., 10 F.4th 1330, 1333 (Fed. Cir. 2021); *see also* Kento Fujiwara et al., *Impact of scFv Structure in Chimeric Antigen Receptor on Receptor Expression Efficiency and Antigen Recognition Properties*, 527 BIOCHEMICAL & BIOPHYSICAL RES. COMMS. 350, 350 (2020).

41. Liyang Lyu et al., *The Global Chimeric Antigen Receptor T (CAR-T) Cell Therapy Patent Landscape*, 38 NAT. BIOTECHNOLOGY 1387 (2020) ("[A]verage development speed is defined as the geomean of annual development speed values over the observation period, which can be calculated as the ratio of the patent count in year *n* to the patent count in year n-1.").

42. *Id.* at 1388.

43. *Id.* at 1389-90.

44. In the traditional collaboration models, the academic institutions' scientific research would be transferred to commercial companies, rather than a cooperative effort between the institutions and companies to develop therapeutic drugs. *Id.* at 1390.

45. In the '190 patent, the invention comprised three-parts: a human CD3 (zeta) chain, a costimulatory region with a specific amino acid sequence (SEQ ID NO:6) and signaling element

analyses by the breadth of the '190 patent's claims, categorizing the claims as either broad or narrow claims.[46] Utilizing the framework established in *Ariad*, the Federal Circuit held the broad claims invalid for failing to disclose either a representative species or common structural feature.[47] Likewise, the court concluded that substantial evidence did not show the inventors' possession of the more narrow claimed genus.[48] Thus, the patent did not satisfy the written description requirement necessary and the court invalidated the '190 patent. The Federal Circuit Court of Appeals for the United States reversed the district court's finding of infringement and subsequent damages.[49]

First, the court analyzed the '190 patent's "broadest asserted claims" (claims 3 and 9) under *Ariad*.[50] The court construed these claims as broad because the claims encompassed "*any* scFv for binding *any* target."[51] The court described the '190 patent's disclosure as containing "scant details about which scFvs can bind which target antigens."[52] Importantly, Juno's expert testimony did not explain the characteristics that allowed the two sample scFvs to bind to targets.[53] Therefore, a broad statement concerning the scFvs' general binding properties was insufficient to demonstrate Juno's possession of the claimed invention.[54]

Moreover, though the two scFvs were generally known in the technological field, the '190 patent failed to describe how one skilled in the art would distinguish "which scFvs will bind to which targets."[55] The Federal Circuit distinguished *Juno* from *Capon*, noting that *Capon* was remanded after critiquing the Board's "too high a standard to satisfy the written description requirement."[56] The court reiterated that *Capon* did not stand for the proposition that generally known components require less

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(i.e., backbone) of the CAR. The CD3 zeta chain activates after the T cell binds to an antigen, creating an immune killing response. As alluded to by its name, the costimulatory region signals the cells to sustain the immune response thereby encouraging the production of more T Cells (e.g., T cell replication). *Juno*, 10 F.4th at 1335.

46. *Id.* at 1340.
47. *Id.* at 1341-42.
48. *Id.* at 1342.
49. *Id.*
50. *Id.* at 1336.
51. *Id.*
52. *Id.*
53. *Id.* at 1337.
54. *Id.* at 1338; *see* Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1353-54 (Fed. Cir. 2010).
55. *Juno*, 10 F.4th at 1338.
56. *Id.*; *see* Capon v. Eshar, 418 F.3d 1349, 1361 (Fed. Cir. 2005).

specification details.[57] Rather, *Capon* was remanded with instructions for the Board to subsequently analyze the adequacy of the patent's specification.[58]

Next, the court concluded that the '190 patent failed to disclose common structural features sufficient to demonstrate possession of the claimed invention.[59] Comparing the '190 patent to *Ariad*, the court noted that Juno did not distinguish scFvs by their binding capabilities.[60] Rather, the '190 patent claimed 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."[61] The Federal Circuit viewed the '190 patent's disclosure as comparable to other patents which failed to provide meaningful guidance to a person skilled in the art.[62] Ultimately, the court concluded that the broad claims, which covered "any scFv for binding any target," did not provide "characteristics, sequences, or structures" necessary to demonstrate possession of the claimed invention.[63]

Second, the Federal Circuit analyzed the written description of the narrower claims, relating to "[c]laims 5 and 11, which are limited to scFvs that bind CD19."[64] Compared to the broader claims covering any scFvs capable of binding any target, these claims narrowly covered scFvs capable of binding to CD19, a more specific target.[65] The court rejected Juno's assertion that expert and inventor testimony sufficiently demonstrated possession of "functional CD19-specific scFvs."[66] Looking to the disclosure factors enumerated in *Ariad*, the court noted "the diversity of the functional scFv genus, the unpredictability of an scFv's binding ability," and the limited prior art references as relevant

57. *Juno*, 10 F.4th at 1338; *see Capon*, 418 F.3d at 1358-61.
58. *Juno*, 10 F.4th at 1338; *see Capon*, 418 F.3d at 1361.
59. *Juno*, 10 F.4th at 1338.
60. *Id.* at 1339; *see* Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1350 (Fed. Cir. 2010).
61. *Juno*, 10 F.4th at 1339 (quoting *Ariad*, 598 F.3d at 1353) (internal citations omitted).
62. Idenix Pharms. LLC v. Gilead Scis. Inc., 941 F.3d 1149, 1164 (Fed Cir. 2019) (concluding the disclosure as insufficient because the inventor did not provide why the disclosed lists and examples of potential nucleosides were effective); AbbVie Deutschland GmbH v. Janssen Biotech, Inc., 759 F.3d 1285, 1301 (Fed. Cir. 2014) (determining that the disclosure of structurally similar antibodies failed to demonstrate the "correlation between [the] structure and the [claimed] function" necessary for the inventor to broadly claim every antibody that would "achieve a desired result.").
63. *Juno*, 10 F.4th at 1336-39.
64. *Id.* at 1340.
65. *Id.*
66. *Id.*

considerations.[67] The court concluded that Juno's invention included "the functional scFv for binding the target;" therefore, Juno was required to disclose details sufficient to demonstrate possession for the invention's functional component.[68] Even for the more narrow claims related to CD19-binding scFvs, the '190 patent failed to distinguish scFvs capable of binding to CD19 versus those unable to bind to CD19.[69]

IV. ANALYSIS

The noted case demonstrates the Federal Circuit's continued reluctance to validate genus claims for biotechnological inventions. For both broad and narrow claims, the Federal Circuit requires a clear showing of possession and shies away from affirming claims that fail to provide meaningful guidance to a person skilled in the art.[70] Further, the court reiterated that a deficiency in disclosure will not be cured by expert or inventor testimony.[71]

Due to the complexity of CAR-T technology, Juno may have been hindered by the perceived unpredictability of biotechnological inventions.[72] One scholar posited that the patent system itself is flawed, concluding the incentives under the first to file system "encourage[] patent applicants to 'adopt several troublesome strategies,' including claiming more broadly than the experimental data warrants."[73] Similarly, another scholar viewed "[g]un jumping [as] frequently associated with functional claiming."[74] Thus, the law seeks to avoid "discourag[ing] further work by those who do actually take the time to find the solution and not just predict it."[75] However, some have hypothesized that such a stringent written disclosure requirement will result in biotechnological inventors choosing to wait until they can describe the invention in "exhausting detail,"

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67. *Id.* at 1341; *see* Ariad Pharm., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1351 (Fed. Cir. 2010).

68. *Juno*, 10 F.4th at 1341-42.

69. *Id.* at 1342.

70. *See Ariad*, 598 F.3d at 1351.

71. *See Juno*, 10 F.4th at 1337-38.

72. *Ariad*, 598 F.3d at 1354-55; *see also* Bos. Sci. Corp. v. Johnson & Johnson, 647 F.3d 1353, 1364 (Fed. Cir. 2011).

73. Seymore, *supra* note 14, at 722 (quoting Jacob S. Sherkow, *Patent Law's Reproducibility Paradox*, 66 DUKE L.J. 845, 884 (2017)).

74. Karshtedt, *supra* note 19, at 90.

75. Gun-jumping refers to identifying a problem and claiming "anything that solves that problem." *Id.*

delaying the public's access to "potentially ground-breaking and life-saving biotechnolog[ical] advances."[76]

Another type of scientific innovation facing uncertainty in the field of patent law is CRISPR-Cas9, a gene editing technology.[77] Some inventors using the CRISPR-Cas9 technology seek to broadly claim "an entire genus of Cas9 proteins without any sequence limitation."[78] However, some scholars have noted that too broad of claim coverage will likely "impede follow-on innovation that requires use of a patented product or method," an issue that may be a "very real possibility . . . for Cas-9 based technolog[y]."[79] Thus, CRISPR-Cas9 patents experience similar disclosure problems as CAR-T patents, illustrating the complexity of the adequate disclosure in biotechnological innovations.

Juno continues the troubling trend of the Federal Circuit reversing jury verdicts through invalidation of patents.[80] Though genus claims have long been susceptible to invalidation, case law in the Federal Circuit shows a shift towards invalidity for biotechnological inventions.[81] This shift suggests inventors in the biotechnology field may require "extra care for applicants seeking broad patent protection."[82] Though CAR-T patents have steadily been increasing over the years, the principles presented in *Juno* suggest it is time to reevaluate the aims of patent law.[83] Juno both illustrates the Federal Circuit's standard for written description and highlights the trend towards greater scrutiny for biotechnology patents in meeting the written description requirement for approval.

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76. Jeffie A. Kopczynski, *A New Era For § 112? Exploring Recent Developments in the Written Description Requirement as Applied to Biotechnology Inventions*, 16 HARV. J. L. & TECH. 230, 253 (2002).

77. Benjamin N. Gray & W. Murray Spruill, *CRISPR-Cas9 Claim Sets and the Potential to Stifle Innovation*, 35 NAT. BIOTECHNOLOGY 630 (2017).

78. *Id.* at 631.

79. *Id.* at 633.

80. *See* Centocor Ortho Biotech, Inc. v. Abbott Labs., 636 F.3d 1341, 1351-53 (Fed. Cir. 2011); Idenix Pharms. LLC v. Gilead Scis. Inc., 941 F.3d 1149, 1157-63 (Fed. Cir. 2019), *cert. denied*, 141 S. Ct. 1234 (2021).

81. *See generally* Juno Therapeutics, Inc. v. Kite Pharma, Inc., 10 F.4th 1330 (Fed. Cir. 2021); *Idenix Pharms.*, 941 F.3d at 1157-65.

82. Steven Carlson & Lauren Murphy Pringle, *High Hurdles for Biotechnology Patents: The Written Description Requirement*, 4 INDUST. BIOTECHNOLOGY 337, 339 (2008).

83. *See generally Juno*, 10 F.4th at 1330.

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