Nos. 22-1594 and 22-1653

In the
United States Court of Appeals
for the Federal Circuit

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, UNIVERSITY OF VIENNA, AND EMMANUELLE CHARPENTIER,

Appellants,

v.

THE BROAD INSTITUTE, INC., MASSACHUSSETS INSTITUTE OF TECHNOLOGY, PRESIDENT AND FELLOWS OF HARVARD COLLEGE,

Cross-Appellants.

Appeal and Cross-Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board, in Interference No. 106,115 (DK)

BRIEF OF REGENERON PHARMACEUTICALS, INC. AS *AMICUS CURIAE* IN SUPPORT OF APPELLANTS AND REVERSAL

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CERTIFICATE OF INTEREST

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

Regeneron Pharmaceuticals, Inc.

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/Not Applicable

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.

None/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).

None/Not Applicable

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).

The Regents of the University of California v. ToolGen, Inc., Patent Interference No. 106,127 (Patent Trial and Appeal Board)

The Regents of the University of California v. Sigma-Aldrich, Co., LLC, Patent Interference No. 106,132 (Patent Trial and Appeal Board)

CERTIFICATE OF INTEREST—Continued

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

None/Not Applicable

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

Cases

TABLE OF AUTHORITIES—Continued

Page(s)

TABLE OF AUTHORITIES—Continued

Page(s)

Statutes

Other Authorities

INTEREST OF *AMICUS CURIAE*

Regeneron Pharmaceuticals, Inc. is a leading biotechnology company that invents, develops, and commercializes life-transforming medicines for people with serious diseases. Regeneron regularly seeks and receives patent protection for its many scientific advancements. As a result, Regeneron has a strong interest in ensuring that the Patent Trial and Appeal Board ("Board") awards patent protection, under the correct understanding of patent law. Because the Board failed to do so here—confusing *conception* with *reduction to practice*—Regeneron files this brief supporting Appellants and urging reversal.[1]

INTRODUCTION

The patent system promotes new ideas. Thomas Jefferson wrote that patent protection was meant as "encouragement to men to pursue *ideas*, which may produce utility."[2] Our patent system promotes "[i]nnovation, advancement, and things which add to the sum of useful knowledge." *Graham v. John Deere Co.*, 383 U.S. 1, 6

[1] No party's counsel authored this brief either in whole or in part; no party or party's counsel contributed money that was intended to fund preparing or submitting this brief; and no person—besides *amicus curiae* Regeneron Pharmaceuticals—contributed money that was intended to fund preparing or submitting the brief.

[2] Alexander J. Kasner, *The Original Meaning of Constitutional Inventors: Resolving the Unanswered Question of the Madstad Litigation*, 68 STAN. L. REV. ONLINE 24, 29 (2015) (emphasis added) (quoting Letter from Thomas Jefferson to Isaac McPherson (Aug. 13, 1813), in 13 THE WRITINGS OF THOMAS JEFFERSON 326, 335 (Andrew A. Lipscomb & Albert Ellery Bergh eds., 1903)).

(1966). "Invention" thus "is not the work of the hands, but of the brain." *Edison v. Foote*, 1871 C.D. 80, 81 (Comm'r Pat. 1871).

And the patent system *promotes* new ideas by *protecting* them. The word *invention* under U.S. patent law "refers to the inventor's *conception* rather than to a physical embodiment of that idea." *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 60 (1998) (emphasis added). "It is well settled that an invention may be patented before it is reduced to practice." *Id.* at 61. So, under the first-to-invent rule governing this priority dispute,[3] priority of invention goes to whoever was "first to conceive the invention" and "exercised reasonable diligence in later reducing that invention to practice"—even if the inventor was last to reduce the invention to practice. *Price v. Symsek*, 988 F.2d 1187, 1190 (Fed. Cir. 1993) (citing *Lutzker v. Plet*, 843 F.2d 1364, 1366 (Fed. Cir. 1988)).

The CVC inventors had just the kind of revolutionary new idea that the patent system seeks to protect and promote. They conceived of a process—known as a CRISPR-Cas9 system—for editing DNA sequences in animal, plant, and human cells. And they were the first to do so. They described their idea in detailed,

[3] The America Invents Act replaced the first-to-invent rule with a first-to-file rule for patent applications filed after March 15, 2013. *See* Leahy–Smith America Invents Act, Pub. L. No. 112-29, § 3(n), 125 Stat. 284, 293 (2011). Because the parties' provisional applications were accorded filing dates predating March 15, 2013, *see* Appx117, the first-to-invent rule applies here.

contemporaneous notebooks. Appx142–144. They pointed out two ways in which that system might be done. Appx143. They and others ultimately showed that their idea works. *Id.*

But the Patent Trial and Appeal Board failed to protect that idea. The Board instead erroneously rejected the CVC inventors' argument that they were the first to conceive of a CRISPR-Cas9 system that works in eukaryotic cells. Appx162. In doing so, the Board conflated conception—a *mental* act that the patent system promotes and protects—with actual reduction to practice—a *physical* step. The Board's decision denying CVC's priority claim rests on fundamental errors.

First, the Board required the CVC inventors to have conceived "a system they *knew* would produce the effects on genes on a eukaryotic cell recited in Count 1." Appx162 (emphasis added). But "[a]n inventor's belief that his invention will work or his reasons for choosing a particular approach are irrelevant to conception." *Burroughs Wellcome Co. v. Barr Lab'ys, Inc.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994) (citing *MacMillan v. Moffett*, 432 F.2d 1237, 1239 (C.C.P.A. 1970)). The inventor's "discovery that an invention actually works is part of its reduction to practice." *Id.* (citing *Applegate v. Scherer*, 332 F.2d 571, 573 (C.C.P.A. 1964), and *Oka v. Youssefyeh*, 849 F.2d 581, 584 n. 1 (Fed. Cir. 1988)).

Second, the Board held that the inventors' post-conception tests, which did not all succeed, "reveal[ed]" their "uncertainty" about whether their idea would

work, making their earlier conception incomplete. Appx162. But post-conception testing is the act of discovering whether an invention will work, and so it is part of reduction to practice, not conception. For that reason, post-conception experimental failures cannot undo an earlier conception. *See, e.g.*, *In re Jolley*, 308 F.3d 1317, 1325 (Fed. Cir. 2002).

The Court should correct those errors and reinforce the vital distinction between conception and reduction to practice.

ARGUMENT

I. THIS COURT SHOULD CORRECT THE BOARD'S MISINTERPRETATION OF *CONCEPTION*.

A. The Court should reinforce the fundamental distinction between conception and reduction to practice.

Conception is the "mental part of invention." *Burroughs Wellcome*, 40 F.3d at 1227–28. It is the instant when the inventor forms "a specific, settled idea" for "a particular solution to the problem at hand." *Id.* at 1228. To show conception, the inventor must have "had an idea that was definite and permanent enough that one skilled in the art could understand the invention." *Id.*

Reduction to practice, by contrast, is the physical process of invention that "follows conception." *Mahurkar v. C.R. Bard, Inc.*, 79 F.3d 1572, 1578 (Fed. Cir. 1996). It is the process of "discover[ing] that an invention actually works." *Burroughs Wellcome*, 40 F.3d at 1228 (citing *Applegate*, 332 F.2d at 573, and *Oka*,

849 F.2d at 584 n.1). To show reduction to practice, the "inventor must have (1) constructed an embodiment or performed a process that met all the claim limitations and (2) determined that the invention would work for its intended purpose." *Fox Grp., Inc. v. Cree, Inc.*, 700 F.3d 1300, 1305 (Fed. Cir. 2012) (quoting *Teva Pharm. Indus. Ltd. v. AstraZeneca Pharms. LP*, 661 F.3d 1378, 1383 (Fed. Cir. 2011)).

Because "[c]onception defines the legally operative moment of invention," *Invitrogen Corp. v. Clontech Lab'ys, Inc.*, 429 F.3d 1052, 1063 (Fed. Cir. 2005), it is crucial to distinguish *conception* from *reduction to practice*. They "are separate and distinct concepts and tests." *Fox Grp.*, 700 F.3d at 1305. And this Court "will not combine them." *Id.*

B. The Board erroneously held that conception requires knowing that the invention will work.

The Board misunderstood a basic difference between conception and reduction to practice. Though it recited the blackletter law (*see, e.g.*, *Burroughs Wellcome*, 40 F.3d at 1228) that an "inventor need not know that the invention will work for conception to be complete," Appx138, it did not practice what it preached. It instead held that it was "not sufficient for CVC to show only that its inventors conceived of the mechanics of a CRISPR-Cas9 system." Appx161–162. It required that, "[t]o have conceived of an embodiment of Count 1," the CVC inventors must "have had a definite and permanent idea of . . . a system they *knew* would produce

the effects on genes in a eukaryotic cell recited in Count 1." Appx162 (emphasis added).

"But this is not the law." *Burroughs Wellcome*, 40 F.3d at 1228 (citing *MacMillan*, 432 F.2d at 1239). Because "the discovery that an invention actually works is part of its reduction to practice," the "inventor need not know that his invention will work for conception to be complete." *Id*. (citing *Applegate*, 332 F.2d at 573, and *Oka*, 849 F.2d at 584 n.1); *see also, e.g.*, *Dana-Farber Cancer Inst., Inc. v. Ono Pharm. Co.*, 964 F.3d 1365, 1372 (Fed. Cir. 2020); *Univ. of Pittsburgh v. Hedrick*, 573 F.3d 1290, 1298 (Fed. Cir. 2009). Nor must the inventor have even "a *reasonable expectation* that the invention will work for its intended purpose." *Burroughs Wellcome*, 40 F.3d at 1228 (emphasis added). By requiring that the CVC inventors had conceived a system they *"knew* would produce the effects on genes in a eukaryotic cell recited in Count 1," the Board got the law of conception wrong. Appx162 (emphasis added).

To be sure, conception is evaluated at the time it occurs, and so an inventor cannot retroactively establish it. *See, e.g.*, *Cooper v. Goldfarb*, 154 F.3d 1321, 1331 (Fed. Cir. 1998). But that rule is irrelevant here. It does not require—as the Board seemed to suggest (Appx162–163)—*knowledge* that the invention will *work*. Nor does it require that the inventor know whether the invention satisfies the requirements for patent protection. *Dow Chem. Co. v. Astro-Valcour, Inc.*, 267 F.3d

1334, 1341 (Fed. Cir. 2001). Rather, it requires only that, at the time of conception, the inventor "understood his creation to have the features that[] comprise the inventive subject matter at bar." *Invitrogen Corp.*, 429 F.3d at 1064. The Board nowhere suggested—nor could it—that the CVC inventors formed their idea without understanding that their invention had the features recited in Count 1. All the Board did was mangle an actual rule precluding *nunc pro tunc* conception into a non-existent rule requiring knowledge that the invention will work. *See* Appx163.

The test for conception also requires "conceiving a way to make an idea operative." *Dawson v. Dawson*, 710 F.3d 1347, 1356 (Fed. Cir. 2013). But that requirement merely distinguishes "a specific, settled idea" for "a particular solution to the problem at hand" (a conception) from "just a general goal or research plan" that the inventor "hopes to pursue" (not a conception). *Burroughs Wellcome*, 40 F.3d at 1228 (citing *Fiers v. Revel*, 984 F.2d 1164, 1169 (Fed. Cir. 1993); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991)). What the test for conception *never* requires is the "inventor's belief that his invention will work"—rather, the inventor's beliefs and "reasons for choosing a particular approach" to making the idea operative "are irrelevant to conception." *Id.* (citing *MacMillan*, 432 F.2d at 1239).

The CVC inventors easily satisfied the test. They identified a particular problem—editing genes in animal, plant, and human cells—and formed a specific

solution—a single guide RNA (sgRNA) CRISPR-Cas9 system that could target and modify DNA in prokaryotes and eukaryotes alike. The CVC inventors testified that they "had conceived of a CRISPR-Cas9 system in eukaryotic cells" and "had discussed and developed a schematic diagram" of that system. Appx140. And the Board admitted that the inventors' "notebook pages corroborate" that testimony. Appx145. The Board even accepted that the CVC's invention disclosure form—in which "the inventors assumed that what was known about other genome editing systems . . . would be applicable to a CRISPR-Cas9 system"—was correct. Appx148. "[I]n the end, only routine materials and techniques, as described by the CVC inventors, were required for" their invention to become operative. Appx161.

Even so, the Board concluded that "the inventors' *uncertainty*" about whether their ideas would work trumped that evidence and fatally undermined their conception. Appx162 (emphasis added). That was error. "The determinative inquiry" here "is not whether" the idea was "phrased certainly or tentatively." *Univ. of Pittsburgh*, 573 F.3d at 1299 (citing *In re Jolley*, 308 F.3d at 1325) (holding that idea expressed in laboratory notebooks constituted conception despite being tentative and uncertain). It is whether "the inventors embraced the invention in their minds as of the date alleged." *In re Jolley*, 308 F.3d at 1324.

C. The Board erroneously held that post-conception experimental failures preclude conception.

The Board also observed "that the CVC inventors encountered multiple experimental failures" during post-conception testing, which it held created "sufficient uncertainty" to undermine the CVC inventor's "definite and permanent idea." Appx160. But that conclusion conflates conception with reduction to practice. This Court should correct the Board's misunderstanding.

Post-conception testing determines whether an invention works and thus relates to reduction to practice. To reduce an invention to practice, the inventor must determine whether the invention works. *Fox Grp.*, 700 F.3d at 1305. And determining whether the invention works often requires post-conception testing. Though "some devices are so simple and their purposes and efficacy so obvious" that simply constructing the device is enough "to demonstrate workability," *Scott v. Finney*, 34 F.3d 1058, 1061 (Fed. Cir. 1994) (alteration marks omitted) (quoting *King Instrument Corp. v. Otari Corp.*, 767 F.2d 853, 861 (Fed. Cir. 1985)), post-conception "testing [can be] necessary to show proof of actual reduction to practice." *Id.* "Testing sufficient to show a reduction to practice has often been at issue in interference proceedings." *Id.* (citing *Newkirk v. Lulejian*, 825 F.2d 1581, 1582 (Fed. Cir. 1987)).

But—because an inventor's understanding about whether the invention will work is irrelevant to conception, *Burroughs Wellcome*, 40 F.3d at 1228—"[w]hether

or not subsequent testing succeeded or failed, or even took place, does not determine whether conception was complete as of that date," *In re Jolley*, 308 F.3d at 1325; *see also Dana-Farber*, 964 F.3d at 1372 (holding that "*in vivo* verification is not required for a conception to be definite and permanent") (citing *In re Isaacs*, 347 F.2d 887, 889 (C.C.P.A. 1965)). As Judge Lourie explained in *Burroughs Wellcome*, "[a] conception must be judged as to its completeness in relation to the invention being claimed." *Id.* at 1233 (Lourie, J., concurring-in-part and dissenting-in-part). Just because "subsequent experimentation shows that an invention that was only conceived does not work, that fact does not vitiate the earlier conception. A conception not later reduced to practice may have little significance, but it is important that we not confuse concepts. The conception was still a conception." *Id.*

In other words, the test for conception requires only that the inventor's idea for solving a particular problem encompassed the claimed invention. That the inventor had trouble reducing the invention to practice says nothing about what idea the inventor had in mind before attempting to reduce it to practice. 1 John Gladstone Mills III et al., *Patent Law Fundamentals* § 2:4 (2d ed.) ("[A]n invention is very much a mental abstraction having an existence, at least in contemplation of law, independent of and distinct from physical embodiments thereof."). In addition, "[c]orroboration must be of the date of the conception." *Burroughs Wellcome*, 40 F.3d at 1233 (separate opinion of Lourie, J.). But, by definition, post-conception

testing happens after conception. It thus reveals little or nothing about what the inventor had in mind on the conception date.

For these reasons, patent law has long recognized that a conception "need not be a 'working drawing.'" *Edison*, 1871 C.D. at 81. Instead, an inventor "may still need much patience and mechanical skill, and perhaps a *long series of experiments*, to give the conception birth in a useful, working form." *Cameron & Everett v. Brick*, 1871 C.D. 89, 90 (Comm'r Pat. 1871) (emphasis added). So a "conception may be complete" even when "further investigation, and perhaps *experiment*, may be necessary in order to embody the idea in a useful form." *Edison*, 1871 C.D. at 81 (emphasis added). And an inventor's "*bona fide* effort . . . to ascertain whether [the invention] will answer the purpose intended" does not vitiate an earlier conception. *Pfaff*, 525 U.S. at 65 (quoting *Elizabeth v. Am. Nicholson Pavement Co.*, 97 U.S. 126, 137 (1877)).

The Board ignored all of this. To hold that post-conception experimental failures negate conception, the Board instead cherrypicked a sentence from *Burroughs Wellcome*: "A conception is not complete if the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice." 40 F.3d at 1229.

But that sentence described (and thus relates only to) "the so-called doctrine of simultaneous conception and reduction to practice." *Id.* at 1228. That doctrine applies when an inventor cannot envision a thing's composition—say, a particular DNA or gene sequence—without first experimentally obtaining that thing. *See, e.g.*, *Amgen*, 927 F.2d at 1206 (DNA sequence); *Fiers*, 984 F.2d. at 1169 (same). In those "instances, an inventor is unable to 'establish a conception until he has reduced the invention to practice through a successful experiment,'" *Burroughs Wellcome*, 40 F.3d at 1229 (quoting *Amgen*, 927 F.2d at 1206), and "the event of reduction to practice in effect provides the *only* evidence to corroborate conception of the invention." *Id.* (emphasis added). The Board did not purport to apply that doctrine, and for good reason. The invention at issue here involved a gene-editing *system* with a known sequence, not an unknown chemical substance such as a novel genomic sequence. Nor did the Board suggest that reduction to practice would have provided the only evidence to corroborate conception of the invention. To the contrary, the Board acknowledged all the evidence corroborating CVC's conception, including: contemporaneous emails among the inventors; the inventors' notebook memorializing invention; and an invention disclosure form, among other evidence. Appx140–145, Appx147.

To be sure, courts have held that reduction to practice can corroborate conception. *See, e.g.*, *Burroughs Wellcome*, 40 F.3d at 1229 (noting that reduction

to practice sometimes "provides the only evidence to corroborate conception"). But that fact does not help the Board. For starters, not everyone agrees that reduction to practice corroborates conception. Judge Lourie has reasoned that, because "[c]orroboration must be of the date of the conception," when "the only 'corroboration' of the conception is its reduction to practice, corroboration has not occurred concerning the alleged date of conception." *Id.* at 1233 (Lourie, J., concurring-in-part and dissenting-in-part). In addition, "corroboration must be independent of the inventor. Corroboration is not a demonstration that the conceived invention works; it is evidentiary proof that the mental act of invention occurred on a certain date." *Id.* In all events, as the Supreme Court has pointed out, "just because reduction to practice is *sufficient* evidence of completion, it does not follow that proof of reduction to practice is *necessary* in every case." *Pfaff*, 525 U.S. at 66 (emphasis added).

Despite acknowledging CVC's other evidence corroborating conception, the Board erroneously held that CVC's initial post-conception experimental failures precluded conception. The Board thus made reduction to practice a necessary element of conception. This Court should correct that fundamental error.

CONCLUSION

The Court should reinforce two fundamental distinctions between *conception* and reduction to practice. The Court should reaffirm that the inventor's knowledge,

understanding, or belief about the invention's workability is irrelevant to conception. And the Court should clarify that post-experimental failures cannot negate an earlier conception. Because the decision below misapprehended those distinctions, the Court should reverse.

Dated: October 7, 2022

Respectfully submitted,

/s/ Irena Royzman

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This brief complies with the type-volume limitations of Federal Rule of Appellate Procedure 29(a)(5) and Federal Circuit Rule 29(b). Exclusive of the items excluded by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b)(2), this brief contains 3,100 words. It has been prepared in proportionally spaced typeface using Microsoft Word for Office 365 in 14-point Times New Roman font. I have relied on the word count feature of this word processing system in preparing this certificate.

Dated: October 7, 2022

/s/ Irena Royzman
Irena Royzman

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