Nos. 2024-1094, -1149

IN THE

UNITED STATES COURT OF APPEALS

FOR THE FEDERAL CIRCUIT

TEVA PHARMACEUTICALS INTERNATIONAL GMBH,
TEVA PHARMACEUTICALS USA, INC.,

Plaintiffs-Appellants

v.

ELI LILLY AND COMPANY,

Defendant-Cross-Appellant

On Appeal from the U.S. District Court for the District of Massachusetts, The Honorable Allison D. Burroughs, Case No. 1:18-cv-12029-ADB

PRINCIPAL AND RESPONSE BRIEF OF ELI LILLY AND COMPANY

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EXEMPLARY CLAIM FROM U.S. PATENT NO. 8,586,045

17. A method for reducing incidence of or treating headache in a human, comprising administering to the human an effective amount of an anti-CGRP antagonist antibody, wherein said anti-CGRP antagonist antibody is a human monoclonal antibody or a humanized monoclonal antibody.

30. The method of claim 17, wherein said anti-CGRP antagonist antibody is a humanized monoclonal antibody.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

CERTIFICATE OF INTEREST

Case Number: 2024-1094, 1149

Short Case Caption: Teva Pharmaceuticals International GmbH v. Eli Lilly and Company

Filing Party/Entity: Eli Lilly and Company

Instructions:

1. Complete each section of the form and select none or N/A if appropriate.
2. Please enter only one item per box; attach additional pages as needed, and check the box to indicate such pages are attached.
3. In answering Sections 2 and 3, be specific as to which represented entities the answers apply; lack of specificity may result in non-compliance.
4. Please do not duplicate entries within Section 5.
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I certify the following information and any attached sheets are accurate and complete to the best of my knowledge.

Date: April 19, 2024

Signature: /s/ J. Michael Jakes

Name: J. Michael Jakes

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

☐ Additional pages attached

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

☐ None/Not Applicable ☐ Additional pages attached

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5. Related Cases. Other than the originating case(s) for this case, are there related or prior cases that meet the criteria under Fed. Cir. R. 47.5(a)?

☐ Yes (file separate notice; see below) ☒ No ☐ N/A (amicus/movant)

If yes, concurrently file a separate Notice of Related Case Information that complies with Fed. Cir. R. 47.5(b). **Please do not duplicate information.** This separate Notice must only be filed with the first Certificate of Interest or, subsequently, if information changes during the pendency of the appeal. Fed. Cir. R. 47.5(b).

6. Organizational Victims and Bankruptcy Cases. Provide any information required under Fed. R. App. P. 26.1(b) (organizational victims in criminal cases) and 26.1(c) (bankruptcy case debtors and trustees). Fed. Cir. R. 47.4(a)(6). ☒ None/Not Applicable ☐ Additional pages attached		

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STATEMENT OF RELATED CASES

No other appeal in or from the same district court case, No. 1:18-cv-12029-ADB (D. Mass.), was previously before this or any other appellate court.

This Court previously decided Appeal Nos. 20-1876, -1877, and -1878 from the U.S. Patent and Trademark Office's Patent Trial and Appeal Board involving the same patents-in-suit in this appeal: Patent Nos. 8,586,045; 9,884,907; and 9,884,908. The decision is dated August 16, 2021, the composition of the panel was Circuit Judges Lourie, Bryson, and O'Malley, and the decision is reported at *Eli Lilly & Co. v. Teva Pharmaceuticals International GmbH*, 8 F.4th 1331 (Fed. Cir. 2021). This Court also decided six other appeals between the parties originating at the Patent Trial and Appeal Board involving related patents: Appeal Nos. 2020-1747, -1748, -1749, -1750, -1751, and -1752. *Teva Pharms. Int'l GmbH v. Eli Lilly & Co.*, 8 F.4th 1349 (Fed. Cir. 2021).

Counsel for cross-appellant Eli Lilly and Company is unaware of any case pending in this or any other court or agency that will directly affect or be directly affected by the Court's decision in this appeal.

STATEMENT OF JURISDICTION

The U.S. District Court for the District of Massachusetts (Judge Allison D. Burroughs) had jurisdiction over the patent-infringement action giving rise to this appeal pursuant to 28 U.S.C. §§ 1331 and 1338(a). This Court has jurisdiction under 28 U.S.C. § 1295(a)(1).

Lilly's notice of cross-appeal from the Final Judgment entered on September 28, 2023, was timely filed in accordance with Fed. R. App. P. 4(a)(1)(A) and 4(a)(3) on November 7, 2023, within 14 days of Teva's notice of appeal filed October 24, 2023.

COUNTERSTATEMENT OF THE ISSUES ON TEVA'S APPEAL

1. For claims reciting methods of treating headache using an effective amount of *any* humanized anti-CGRP antagonist antibody, where the patent specification discloses only *one* humanized anti-CGRP antibody within the broad genus in the claims and no common structural features of such antibodies, did the district court correctly grant judgment as a matter of law that the claims are invalid under 35 U.S.C. § 112 for lack of written description?

2. Where a skilled artisan would have to conduct a lengthy and expensive research project to make and test each antibody to determine whether it performed the claimed functions of binding to and antagonizing CGRP, did the district court correctly grant judgment as a matter of law that Teva's claims are invalid under 35 U.S.C. § 112 for lack of enablement?

STATEMENT OF THE ISSUE ON LILLY'S CONDITIONAL CROSS-APPEAL

3. Did the district court err by denying judgment as a matter of law that the jury lacked evidence to support its award of $49.8 million in future lost profits where uncertainty in the relevant market forced Teva's damages expert to make a "dramatic change" to his initial forecast (decreasing it by nearly $200 million) and where he could not commit to whether his new forecast would change by a similar magnitude, showing the unreliability of his analysis?

INTRODUCTION

Teva's patents claim—by function—*every humanized antibody* that binds to and antagonizes CGRP to treat migraine and other types of headache. Yet, the specification only discloses *a single antibody* that falls within the scope of the claims, which was later shown to treat *a single type of headache*: migraine. This disclosure falls far short of what § 112 requires.

For a functionally defined genus like Teva's, this Court's precedents require disclosure of either a sufficient number of *representative* antibodies or common structural features that *correlate to the claimed function*. Teva's specification discloses neither. Instead, Teva's specification discloses only *a single humanized anti-CGRP antagonist antibody*, which is not representative of the claimed genus. Likewise, the specification only discloses structural features (e.g., the antibodies' "Y" shape) that are shared by all antibodies, regardless of whether they bind to or antagonize CGRP. The specification's failure to disclose more is not surprising—the named inventors tried but failed to make other antibodies that would fall within the claimed genus. Nevertheless, Teva claimed them.

Faced with expansive claims and scant disclosure, Teva points to antibody fragments and rodent ("murine") antibodies, glossing over the fact that neither falls within the scope of the claims, so they cannot be "representative" of what is claimed. Teva also argues that it should be exempt from disclosing representative species or

common structural features because the claimed antibodies were allegedly "well-known" and because it purportedly would have been "routine" for a skilled artisan to humanize the rodent antibodies that were known in the art. Teva's arguments fail on both the facts and the law.

On the facts, the claimed antibodies were not "well-known." To the contrary, it is undisputed that *no* humanized anti-CGRP antagonist antibody was known as of Teva's priority date. Teva attempts to sidestep this case-dispositive fact by focusing instead on several rodent antibodies. But even if those disclosures were relevant, they lack key information—the amino acid sequences or structures that would have allowed a skilled artisan to humanize and use them as claimed.

On the law, Teva's arguments are foreclosed by this Court's precedents. While Teva argues that humanizing rodent antibodies would be "routine," a description that might render a claim obvious is insufficient to provide written description. And this Court has been clear: whether a skilled artisan could make and use the claimed subject matter is irrelevant to written description if the specification does not contain sufficient disclosure showing that the inventors possessed what they claimed.

Based on the undisputed law and facts, the district court correctly found that no reasonable jury could conclude that Teva's specification sufficiently describes the broad genus claimed. This Court should affirm.

The district court also correctly granted judgment as a matter of law of no enablement. Teva's patents provide nothing more than a roadmap instructing a skilled artisan to conduct a lengthy, trial-and-error research process to generate humanized anti-CGRP antagonist antibodies that can be used in the claimed methods. As the district court found, a skilled artisan would need to synthesize each potential antibody and screen it for effectiveness, that is: engage in a "trial-and-error process of discovery" to "see what works." As the Supreme Court confirmed in *Amgen*, that is not enablement, but "little more than [a] research assignment[]." Likewise here, a reasonable jury could *only* have found that practicing Teva's claimed methods of using humanized anti-CGRP antagonist antibodies to treat migraine and other headache conditions requires undue experimentation.

Lilly filed a conditional cross-appeal challenging the district court's decision declining to overturn the jury's verdict on future lost profits. The Court need not reach this conditional cross-appeal if it affirms either the district court's written description or enablement rulings. The jury's verdict on future lost profits was based solely on speculative testimony by Teva's damages expert, Dr. Berkman. He initially forecast $343.7 million in future lost profits over the course of eight years. But just one year after this initial forecast, instability in the market for migraine drugs forced Dr. Berkman to decrease his estimate to $158.3 million—what he acknowledged was "a pretty dramatic change." Even after reducing his estimate by more than 50%,

Dr. Berkman could not rule out the potential that ongoing market uncertainty might require him to change even his revised forecast by a similar amount within six to 12 months.

Because the jury had no nonspeculative evidence from which to award future lost profits, the Court should reverse the district court's decision declining to grant Lilly's motion for judgment as a matter of law.

COUNTERSTATEMENT OF THE CASE

I. Technical Background

Antibodies are specialized proteins produced by the immune system that can recognize and bind to foreign substances. Appx7. Immunoglobulin G (IgG) antibodies, the most common antibodies in humans, are made up of two heavy and two light chains of amino acids. Appx7. The linear sequence and identity of those amino acids dictate how the chains fold, which is critical to an antibody's binding to a target. Appx3111-3112 at 48:23-49:10; Appx7. Put simply, an antibody's amino acid sequence determines how it functions.

Each antibody has two regions—a constant region and a variable region. Appx7. As the name suggests, the variable region varies from one antibody to another. Appx7; Appx3115-3116 at 52:25-53:22. It is formed by the variable domains of the heavy and light chains. Appx3115-3116 at 52:25-53:22. Within the variable domains, areas called complementarity determining regions (CDRs) are

particularly variable and are crucial to the antibody's binding. Appx8. The three-dimensional shape of the CDRs, determined by their amino acid sequence, dictates whether, where, and how strongly an antibody binds to a target molecule (here, CGRP). Appx1476 at 104:4-8; Appx3118 at 55:9-17.

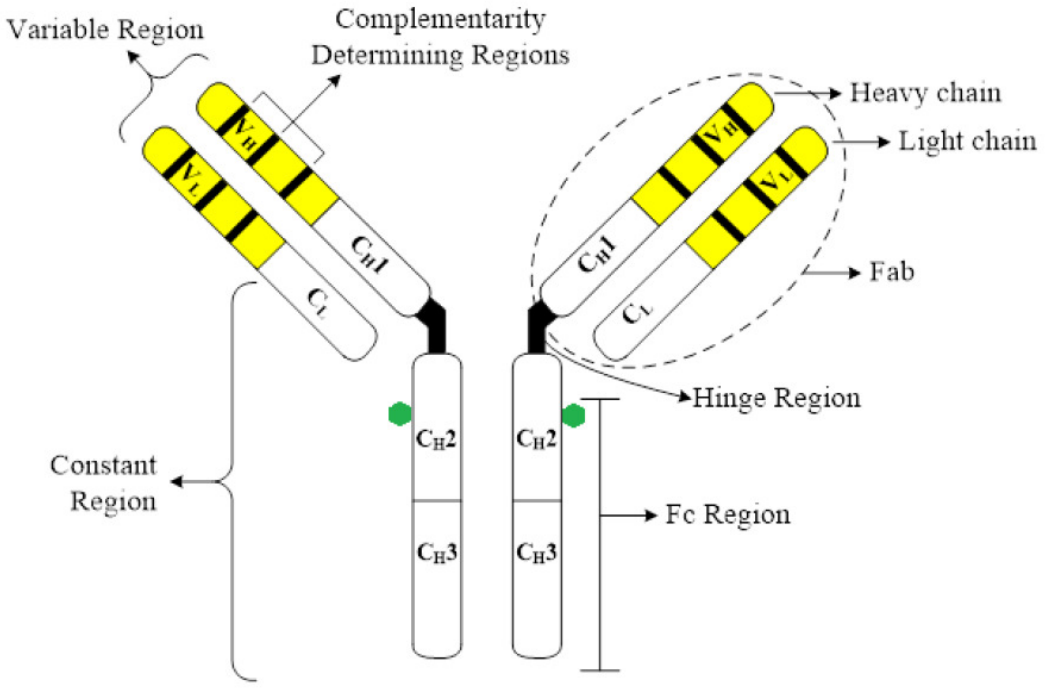

Figure 1: Exemplary Antibody Structure.

Appx21658-21569.

The three CDRs on each light and heavy chain are interspersed among "framework regions" that structurally support the CDRs. These framework regions (shown in yellow above) are also important to how antibodies function. Appx21659-21660.

Anti-CGRP antagonist antibodies are antibodies that bind to and antagonize (or inhibit) CGRP. Appx8 n.4. When an anti-CGRP antagonist antibody binds to CGRP, it disrupts CGRP's interaction with CGRP receptors and can potentially prevent CGRP from causing migraine or other types of headache.

CGRP has three portions: the N-terminal, mid-, and C-terminal regions. Appx17; Appx1401 at 29:14-23. Anti-CGRP antagonist antibodies include antibodies that bind at any of these three locations.

II. State of the Art as of the Priority Date

A. No Humanized Anti-CGRP Antagonist Antibodies Had Been Made or Tested

The asserted claims require use of *humanized* anti-CGRP antibodies to treat headache. Appx273; Appx353; Appx429-430. Unlike naturally occurring antibodies, "humanized" antibodies are engineered in a laboratory and comprise both non-human and human antibody amino acid sequences. Appx7; Appx3122-3123 at 59:13-60:1; Appx3134 at 71:3-12.

As of the 2006 priority date of Teva's patents, *no* humanized anti-CGRP antagonist antibodies were known in the art. Appx11; Appx27; Appx1400 at 28:6-9; Appx3200 at 137:4-6; Appx3390-3391 at 148:23-149:2; Appx4177-4178 at 67:25-68:5; Appx4254 at 144:17-24. Such antibodies did not exist and were unknown to skilled artisans. Teva's named inventors and experts confirmed this in their testimony. For example, Dr. Zeller confirmed that "humanized anti-CGRP

antibodies were not a previously known class of compound." Appx1400 at 28:6-9. Dr. Pons similarly confirmed that, at the time of invention, "there were no humanized monoclonal antibodies against CGRP described in the literature." Appx3390-3391 at 148:23-149:2. And Teva's experts Dr. Hill and Dr. Hale admitted that they had not identified any humanized anti-CGRP antagonist antibody in the prior art. Appx4177-4178 at 67:25-68:5; Appx4254 at 144:17-24.

At most, the prior art disclosed a handful of rodent ("murine") anti-CGRP antibodies. Even for those rodent antibodies, however, little information was reported. Significantly, the prior art did not disclose the amino acid sequence of any anti-CGRP antibody, which is vital information for a skilled artisan seeking to humanize that antibody. Appx30-31; Appx3132-3133 at 69:24-70:19; Appx4177 at 67:16-24. Nor did the prior art disclose the structure of the disclosed rodent antibodies. Appx3132-3134 at 69:24-71:12.

Further, the prior art showed that not all rodent antibodies that bind to CGRP could antagonize CGRP. Appx30-31; Appx3134-3135 at 71:15-72:9; Appx4177 at 67:16-24; Appx51990-51994. Some anti-CGRP antibodies had no effect on the biological function of CGRP while some even *agonized* (i.e., enhanced) it. Appx3134-3135 at 71:18-72:4; Appx51990-51994. The only way to know whether an anti-CGRP antibody would antagonize CGRP was to make and test it. Appx4256-

4257 at 146:23-147:7; Appx3391 at 149:17-21; Appx1407 at 35:10-18; Appx3142 at 79:2-7.

B. Humanized Antibodies Were Known to Be Unpredictable and Costly and Time-Consuming to Make

Making a humanized antibody involves stitching the CDRs of a non-human antibody (e.g., a rodent antibody) into the framework sequences from a human antibody. Appx3122-3123 at 59:13-60:1. It is impossible to humanize a non-human antibody if its sequence is not known. Appx3134 at 71:3-12; Appx3183-3184 at 120:21-121:12. Because the sequences of the disclosed prior-art rodent anti-CGRP antagonist antibodies were not known, a skilled artisan could not have made or humanized any of these. Appx3134 at 71:3-12.

As of the priority date, it was known that making humanized antibodies was a costly and time-consuming process. Appx19. At that time, making a single humanized antibody could take several months, costing half a million dollars. Appx19; Appx3213-3214 at 150:25-151:8; Appx4261-4266 at 151:21-156:18.

Furthermore, the humanization process was unpredictable. Appx3203-3210 at 140:7-147:13. Humanizing antibodies required "case-by-case design and engineering for each individual antibody," which did not work for every non-human antibody. *Id*. Because it was known that "some of them are going to fail," the processes often required humanizing multiple antibodies. *Id*. Thus, a skilled artisan could not have predicted the amino acid sequence or function of humanized

antibodies before completing this unpredictable process. Appx3209-3210 at 146:16-147:13.

C. The Ability of Anti-CGRP Antagonist Antibodies to Treat Headache (Including Migraine) in Humans Was Also Unknown

It was likewise unknown as of the priority date whether anti-CGRP antagonist antibodies could treat migraine. There was skepticism about whether an antibody could cross the blood-brain barrier ("BBB"), Appx19211; Appx19263-19265, and researchers heatedly debated where CGRP acts, i.e., outside or behind the BBB. Teva Br. 7; Appx3046-3048 at 171:22-173:6; Appx226 at 3:14-29. Thus, while it was postulated that CGRP plays a causal role in migraine many researchers were skeptical that anti-CGRP antibodies could be used to treat migraine because they could not cross the BBB to CGRP's suspected site of action. Appx225 at 2:14-22; Appx51070-51073, ¶¶ 6-14; Teva Br. 7.

Yet, Teva's specification does not address this issue. Appx4028-4029 at 250:25-251:3; Appx3560 at 72:7-10. Debate and skepticism regarding the ability of antibodies to cross the BBB continued well after Teva's patents were filed. Appx3050 at 175:14-23; Appx51073, ¶ 14; Appx4144-4145 at 34:9-35:16. Teva only became interested in its G1 antibody after Lilly's galcanezumab clinical trials showed efficacy in treating migraine. Appx4366-4368 at 31:18-33:18. Indeed, Teva argued in a prior appeal that a skilled artisan at the time of invention *would not* have had a reasonable expectation of success in using anti-CGRP antagonist antibodies to

treat migraine based on this skepticism. Appx19211; Appx19263-19265; *see also Eli Lilly & Co. v. Teva Pharms. Int'l GmbH*, 8 F.4th 1331, 1348-49 (Fed. Cir. 2021).

III. Teva's Patents

A. Teva's Claims Broadly Recite Methods of Treating Headache or Migraine Using Any Humanized Anti-CGRP Antagonist Antibody

The asserted claims recite methods of treating headache, including migraine, using any humanized anti-CGRP antagonist antibody. Appx273 (claim 30); Appx353 (claims 5-6); Appx429-430 (claims 5-6). Teva's claims are purely functional—they describe the claimed humanized antibodies solely by what they do (i.e., bind to and antagonize CGRP) instead of by identifying the structure of antibodies that can perform the desired function. Appx14-15; Appx3141 at 78:7-21; Appx3199-3201 at 136:20-138:6; Appx3409-3410 at 167:6-168:5; Appx3422 at 180:12-20.

Claim 17 of U.S. Patent No. 8,586,045 recites:

> A method for reducing incidence of or treating headache in a human, comprising administering to the human an effective amount of an *anti-CGRP antagonist antibody*, wherein said anti-CGRP antagonist antibody is a human monoclonal antibody or a humanized monoclonal antibody.

Appx273 (emphasis added). Claim 30, which depends from claim 17, recites that the "anti-CGRP antagonist antibody is a *humanized* monoclonal antibody." Appx273 (emphasis added).

Teva's patents claim *all* humanized anti-CGRP antagonist antibodies that can be used to treat headache such as migraine, regardless of their structure, the portion of CGRP where they bind, their binding affinity, or their relative efficacy for treating migraine or other types of headache. Appx1424 at 52:5-12; Appx1522 at 150:13-18; Appx4267 at 157:1-4. This Court previously decided an appeal from *inter partes* review ("IPR") proceedings involving related patents, which claimed a class of antibodies that Teva concedes is "*identical* to the class of antibodies at issue in this case." Teva Br. 27; *Teva Pharms. Int'l GmbH v. Eli Lilly & Co.*, 8 F.4th 1349, 1363 (Fed. Cir. 2021). The Court confirmed the "extremely broad scope of the functionally claimed antibodies" and reiterated the well-known principle that "functional claim language can lead to broad claims, especially when there are no structural limitations to clearly define the scope." *Teva*, 8 F.4th at 1362 (citing *Amgen Inc. v. Sanofi*, 987 F.3d 1080, 1087 (Fed. Cir. 2021)).

Likewise here, Teva's claimed genus includes antibodies that have disparate amino acid sequences and lack any common structural features.

As Lilly's expert Dr. McDonnell explained, the number of candidate antibodies that could potentially fall within the broad genus recited in Teva's claims is "mind-bogglingly" large, and the exact number of antibodies that satisfy the claimed functional requirements is unknowable. Appx18; Appx3142-3145 at 79:2-82:21; Appx3199-3201 at 136:20-138:13; *see also* Appx3409-3411 at 167:4-169:19;

Appx3422 at 180:15-20. The named inventor of the Teva patents, Dr. Abdiche, contemporaneously illustrated this problem, recognizing both the enormous number of candidate antibodies that may need to be screened and the fact that even minute changes to CDR sequence could eliminate CGRP binding. Appx18012; Appx17999-18029. Tellingly, none of Teva's experts identified or even attempted to estimate the number of antibodies that fall within the scope of the Teva patents, which Dr. McDonnell explained is "unknowable." *See* Appx3145 at 82:9-12.

B. Teva's Specification Discloses Only One Humanized Anti-CGRP Antagonist Antibody (G1)

Teva's patents disclose a single antibody (G1) within the genus recited in the claims. Appx27; Appx254-257 (Table 6); Appx3147 at 84:3-8. G1 binds to one of three known portions of CGRP—the C-terminal region. Appx3160 at 97:1-11.

Teva's specification also discloses 84 close variants of G1, but these are only antibody fragments (i.e., not full-length antibodies). Appx27. Teva's specification does not disclose whether these variants function as CGRP antagonists, as required by Teva's claims, Appx3147 at 84:9-14; Appx3211 at 148:2-8; Appx4273-4274 at 163:15-164:21, and they additionally fall outside the scope of Teva's claims limited to full-length antibodies, Appx3147 at 84:3-14; Appx3211 at 148:2-8; Appx4273-4274 at 163:20-164:8; Appx27.

These variants are structurally similar to G1, sharing more than 95% sequence identity in the variable region. They also have three of six identical CDRs and share

the same CDR lengths and V gene families (the genes encoding the variable region). Appx3149-3151 at 86:21-88:16; Appx3153-3154 at 90:15-91:8; Appx4273 at 163:20-23. Thus, these variants add very little to the diversity of disclosed species. Appx27-28.

Beyond the disclosure of G1 and its structurally similar fragments, Teva's specification discloses only 12 rodent anti-CGRP antibodies. Appx250 (Tables 2, 3). Because these antibodies come from mice and are not humanized, they fall outside Teva's claims and are not "representative species," as Teva's expert Dr. Hale acknowledged. Appx4273 at 163:2-14; Appx28; Appx3183 at 120:15-20; Appx3211 at 148:9-12. Further, Teva's specification fails to disclose important information about the 12 rodent antibodies. Most critically, the specification does not disclose the sequences of these antibodies. Appx3183 at 120:21-23. A skilled artisan therefore could not make those antibodies, let alone humanize them. Appx3183-3184 at 120:24-121:12.

G1 and Teva's rodent antibodies all bind to the C-terminal region of CGRP. Appx3183 at 120:12-14. Thus, none of Teva's disclosed antibodies bind to the N-terminal or mid-region of CGRP. Appx3184-3185 at 121:22-122:6; Appx4274 at 164:22-25.

Beyond disclosing a single species that falls within a claimed genus of "unknowable" scope, Teva's specification discloses only a roadmap for a trial-and-

error process to make additional species either by modifying G1 (i.e., substituting one or more of G1's amino acids) or de novo. Appx3211-3213 at 148:17-149:24; Appx238 at 28:16-62; Appx243 at 37:29-34; Appx18-19. The district court found that the process would require (1) in vitro testing, (2) in vivo animal testing, (3), receiving an actual antibody, and (4) humanizing the animal antibody. Appx49-50 (citing Appx1344 at 161:2-15; Appx4173 at 63:6-14; Appx4215-4216 at 105:1-106:13; Appx4227-4228 at 117:11-118:2; Appx4260-4261 at 150:25-151:12; Appx4262 at 152:11-19; Appx4266 at 156:19-22).

Teva's specification also does not disclose any particular modifications that a skilled artisan should make to G1 or how any such modifications would affect the antibody's ability to bind and antagonize CGRP or treat headache. The specification merely suggests that a skilled artisan could conduct additional research to attempt to make other antibodies that bind to and antagonize CGRP and test them to determine whether they treat migraine and other headache conditions. *See* Appx3212 at 149:4-24.

IV. Teva Tried but Failed to Make Other Antibodies Within the Recited Genus

A. Teva Failed to Make Other Humanized Anti-CGRP Antagonist Antibodies

The inventors of Teva's patents did not disclose any humanized anti-CGRP antagonist antibody other than G1 for a simple reason: they were unable to make

any. Named inventor Dr. Abdiche "attempted to humanize three," including a rodent antibody called 6H2. Appx1486-1487 at 114:20-115:3. While Dr. Abdiche contended that she "dropped" 6H2 because "it was less interesting for various reasons," *id.*, the contemporaneous documents showed that humanization of 6H2 was unsuccessful: after humanization, it "[l]ost CGRP-binding affinity to undetectable levels." Appx18026-18027; Appx3207-3208 at 144:23-145:12.

Similarly, the inventors tried and failed to make even *rodent* antagonist antibodies that bound to the mid-region of CGRP. Appx31-33; Appx1402-1405 at 30:15-33:13; Appx51968-51969 (discussing a plan in 2004 to generate antibodies to the "N-terminal and middle part of CGRP"); Appx52043-52073 ("All our mAbs are C-terminal"); Appx1410-1411 at 38:19-39:16; Appx24062 ("[F]urther functional characterization of linker [mid]-region antibodies did not confirm binding."); Appx16687-16689.

As a result, making humanized antagonist antibodies that bind to other regions of CGRP remained an unrealized goal as of the priority date (and for many years after). Appx1388-1389 at 16:14-17:17; Appx1391-1392 at 19:3-20:15; Appx24062; Appx4258 at 148:11-21; Appx51285-51294 (named inventor Poulson, in 2014, questioning: "How to do this?").

B. Teva's G1 Antibody Failed to Treat Cluster Headache

Teva broadly claims treating *all* headache disorders and includes specific claims to cluster headache, *see* Appx273 (claim 30); Appx353 (claim 5); Appx430 (claim 5), but has failed to show that *any* of its antibodies treat *anything* other than migraine. Despite the inventors' efforts, G1 failed to treat cluster headache in clinical trials and Teva has abandoned any plan to pursue FDA approval for that indication. Appx50434-50435; Appx3402-3404 at 160:21-162:8; Appx3431-3432 at 189:6-190:15; Appx3339-3340 at 97:25-98:3.

V. Lilly's Anti-CGRP Antagonist Antibody Is Structurally and Functionally Distinct from Teva's G1 Antibody

Lilly independently developed its own anti-CGRP antagonist antibody, called galcanezumab, and markets it under the name Emgality®. Appx16-17. While both Lilly's and Teva's antibody drugs bind to CGRP and inhibit its biological activity by blocking its interaction with CGRP receptors (i.e., they act as antagonists), their respective antibodies differ in several important, clinically relevant ways.

First, Teva's and Lilly's antibodies have substantial structural differences in their amino acid sequences. *See, e.g.*, Appx3151-3152 at 88:17-89:23. Whereas Teva's G1 antibody and its 84 variants share 95% sequence identity in their variable domains and have variable domains from the same V gene family, Lilly's galcanezumab and Teva's G1 have far lower sequence identity (50.8% and 64.5% for the heavy- and light-chain variable domains, respectively), and derive from

different V gene families. Appx3149-3157 at 86:21-94:16; Appx4273 at 163:15-23. Further, whereas Teva's G1 and its variants share three identical CDRs out of six and have the same CDR lengths, Lilly's galcanezumab and Teva's G1 have CDRs of different lengths and sequences. Appx3151-3157 at 88:17-94:16.

Lilly's expert Dr. McDonnell testified that Teva's specification does not disclose any antibodies similar to galcanezumab. Appx3174-3175 at 111:14-112:15. Teva's expert Dr. Hale did not dispute Dr. McDonnell's conclusion that galcanezumab is structurally distinct from G1. Appx4255 at 145:8-15; Appx4211 at 101:15-20.

Second, these structural differences result in important functional differences between G1 and Lilly's galcanezumab. Lilly's and Teva's antibodies bind to different locations on CGRP. Whereas G1 binds to the C-terminal end of CGRP, Lilly's galcanezumab binds to the mid-region of CGRP. Appx3159-3160 at 96:11-97:11; Appx3168-3170 at 105:18-107:8. Galcanezumab also binds to CGRP faster than G1 and blocks CGRP's biological activity more potently in a cellular assay. Appx3170-3173 at 107:9-110:20.

Third, the functional differences between galcanezumab and G1 extend to differences in their clinical use and efficacy. Galcanezumab is more potent than G1 in treating migraine patients, as evidenced by its lower monthly dose and higher responder rates. Appx3448-3452 at 206:12-210:16; Appx16410; Appx16415-

16416; Appx16448; Appx16454-16455. Galcanezumab also succeeded in treating episodic cluster headache, where G1 failed. Appx3339-3340 at 97:25-98:7; Appx4022 at 244:1-12; Appx16410; Appx16420-16422; Appx52120-52129; Appx50434-50435. Thus, Lilly's Emgality® product is FDA approved for both preventive treatment of migraine and treatment of episodic cluster headache, whereas Teva's AJOVY® product is approved only for the preventive treatment of migraine. Teva's witnesses, including its expert Dr. Hale, confirmed these functional differences. Appx4211 at 101:15-20 (confirming the different binding sites of galcanezumab and G1); Appx3379-3380 at 137:24-138:19 (Teva's Chief Medical Officer confirming the potency differences between galcanezumab and G1).

VI. The District Court's Ruling on Lilly's Motion for Judgment as a Matter of Law

A. The District Court Granted Judgment as a Matter of Law That Teva's Claims Lack Written Description

In its detailed decision, the district court granted Lilly's motion for judgment as a matter of law, holding that a reasonable jury could only have found that clear and convincing evidence confirms that Teva's specification failed to show sufficient written description of the claimed methods. Appx42; Appx58.

The district court first determined that, even viewing the evidence in the light most favorable to the jury's verdict, Teva's claims broadly cover a genus of any humanized antibody that performs the function of antagonizing CGRP. Appx23-24.

The court then analyzed whether Teva's specification describes representative species sufficient to describe the entire genus recited in the claims. Appx25-42. The court concluded that, even characterizing the evidence in the light most favorable to the jury's verdict, the jury could *only* have found that "there are a very large number of antibodies that would need to be screened in order to identify those that could antagonize CGRP," and that the size of the genus of possible antibodies was "unknowable." Appx27 (quoting Appx3145 at 82:9-18).

The district court further concluded that a reasonable jury could *not* have found that the patents-in-suit disclosed more than one humanized anti-CGRP antagonist antibody. Appx27. Specifically, the court concluded that the 84 closely related variants of G1 are not representative species because they fall outside the scope of the claims. Those 84 variants are fragments rather than full-length antibodies and, moreover, they had not been shown to be CGRP antagonists. Appx27.

The district court also determined that the rodent antibodies that Teva points to fall outside the claims, and thus are not representative species of the claimed humanized antibodies. Appx28-29. The court further noted the acknowledgements by Teva's expert that "none of the rodent antibodies referenced in his report disclosed an amino acid sequence, and not all rodent antibodies identified in his

report were shown to antagonize CGRP." Appx30-31 (citing Appx4177 at 67:16-24).

The district court additionally determined that the jury could *not* have found that Teva had possession of anti-CGRP antagonist antibodies that could bind to all three regions of CGRP, while acknowledging that the jury *could have* credited testimony that a skilled artisan would have known that anti-CGRP antagonist antibodies could bind to different regions of CGRP and still treat headache. Appx33.

Next, the district court determined that Teva's specification failed to disclose structural features common to the antibodies within the recited genus. The court rejected Teva's arguments that all the antibodies within the recited genus: (1) have a Y-shaped structure; (2) have structural complementarity with CGRP (i.e., are paratopes); and (3) are humanized. Appx43. The court noted that the Y-shaped structure is generic to any full-length IgG antibody. Appx43. As to paratopes, the court reasoned that the mere existence of structural complementarity with CGRP "does not describe what structure, for example an amino acid sequence, in an antibody allows for such structural complementarity." Appx43 (citing Appx1306 at 123:7-13; Appx3180-3182 at 117:9-119:24). Finally, the court explained that humanization is not specific to anti-CGRP antagonist antibodies and is not a structure that determines whether an antibody falls within the scope of the asserted claims. Appx43-44.

The district court thoroughly addressed (and rejected) Teva's other arguments in support of written description. Notably, the court rejected Teva's argument that the specification provides written description support because a skilled artisan would have been able to make antibodies within the genus in the claims by first making rodent anti-CGRP antibodies and then humanizing them. As the court noted, rodent antibodies falling outside the scope of the claims and whose structure has not been disclosed cannot provide written description support for the humanized antibodies recited in the claims. Appx30-31; Appx33-34. The court also applied this Court's precedents holding that "a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement of that invention." Appx30 (quoting *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1567 (Fed. Cir. 1997)).

B. The District Court Granted Judgment as a Matter of Law That Teva's Claims Are Not Enabled

The district court held that, even viewing the evidence in the light most favorable to the jury's verdict, making humanized anti-CGRP antagonist antibodies within the genus recited in the claims would require undue experimentation. The court determined that, based on the evidence, a reasonable jury could only have found that identifying potential antibodies and making them required four steps: (1) in vitro testing; (2) in vivo animal testing; (3) receiving an actual antibody; and (4) humanizing the animal antibody. Appx49-50 (citing Appx1344 at 161:2-15;

Appx4173 at 63:6-14; Appx4215-4216 at 105:1-106:13; Appx4227-4228 at 117:11-118:2; Appx4260-4261 at 150:25-151:12; Appx4262 at 152:11-19; Appx4266 at 156:19-22). The court further explained that, for each antibody, a reasonable jury could only have found that this process would take months and cost at least tens of thousands of dollars. Appx49-50.

The district court likened this case to *Amgen Inc. v. Sanofi*, 598 U.S. 594 (2023), where the claims covered all antibodies that bind to specific amino acids on a specific protein and block it from performing a deleterious function. Appx47 (citing *Amgen*, 598 U.S. at 599). But whereas the specification in *Amgen* disclosed amino acid sequences and three-dimensional structures for 26 antibodies that performed the required binding and blocking function, Teva's specification discloses only one humanized anti-CGRP antagonist antibody. Appx47 (citing *Amgen*, 598 U.S. at 602-03).

The district court noted the Supreme Court's statement that, although the 26 *disclosed* antibodies were enabled, the claims "swe[pt] much broader" and attempted to claim "an entire class of things defined by their function." Appx48 (alteration in original) (quoting *Amgen*, 598 U.S. at 612-13). The court concluded that, as in *Amgen*, Teva's disclosure of a process for making additional antibodies within the claims amounted to "nothing more than a 'roadmap' for a 'trial and error' process to identify and make antibodies within the scope of the Asserted Claims." Appx50

(quoting *Amgen*, 598 U.S. at 612-15) (citing *Wyeth & Cordis Corp. v. Abbott Lab'ys*, 720 F.3d 1380, 1385 (Fed. Cir. 2013)).

The district court further reasoned that the process to make other humanized anti-CGRP antagonist antibodies would require undue experimentation *even if* the jury may have concluded that the state of the art was generally predictable, because "each potential antibody would have to be synthesized and screened for effectiveness." Appx51 (citing *Idenix Pharms. LLC v. Gilead Scis. Inc.*, 941 F.3d 1149, 1163 (Fed. Cir. 2019)).

The district court also analogized this case to *Baxalta Inc. v. Genentech, Inc.*, 81 F.4th 1362 (Fed. Cir. 2023), where obtaining "undisclosed but claimed antibodies" required a multi-step, trial-and-error process involving immunizing mice and testing antibodies to determine whether they bind to a protein and have the desired effect. Appx48-49 (citing *Baxalta*, 81 F.4th at 1366). In response to Teva's argument that a skilled artisan could obtain the claimed antibodies by generating rodent antibodies and humanizing them, the court noted the explanation in *Baxalta* that even a process that "predictably and reliably generat[ed] new claimed antibodies every time it [was] performed" still required impermissible trial and error because a skilled artisan would have to "make candidate antibodies and screen them to determine which ones perform[ed] the claimed function[]." Appx49 (alterations in original) (quoting *Baxalta*, 81 F.4th at 1367).

C. The District Court Declined to Overturn the Jury's Verdict That Teva Would Be Entitled to $49.8 Million in Speculative Future Lost Profits

The district court denied Lilly's motion for judgment as a matter of law that the evidence does not support the jury's award of $49.8 million in future lost-profit damages. Appx53-58. Lilly argued that the analysis by Teva's damages expert, Dr. Berkman, was too speculative to support the jury's award. These arguments followed Lilly's earlier *Daubert* motion seeking to exclude his testimony regarding future lost profits as speculative and unreliable. *See* Appx8518-8522; Appx8501. The court denied Lilly's *Daubert* motion, stating that Lilly's arguments "largely go to the weight rather than the admissibility of the opinions sought to be offered." Appx2.

Lilly's motion for judgment as a matter of law again pointed to the speculative nature of Dr. Berkman's testimony, Appx56, as evidenced by what even Dr. Berkman conceded was "a pretty dramatic change" to his initial forecast of future lost profits, Appx2505-2506 at 85:24-86:10. Dr. Berkman initially opined that Teva should receive $343.7 million in future lost profits over the course of eight years, but he was forced to substantially lower his estimate just one year later, decreasing it by nearly $200 million to $158.3 million. Appx2488 at 68:6-9; Appx2503-2505 at 83:18-85:3. Lilly's motion argued that the fact that Dr. Berkman was forced to make such a "dramatic change" so soon after making his initial forecast revealed the

inaccuracy and unreliability of market share and sales predictions in the unstable migraine drug market.

The large decrease in Dr. Berkman's estimate resulted from decreases in the estimated number of lost sales of Teva's AJOVY® product. For example, Dr. Berkman revised his estimate of Teva's 2023 lost sales down by roughly 69% and Teva's 2025 lost sales down by roughly 82%. Appx2505-2506 at 85:4-14, 85:24-86:10. Dr. Berkman also revised his estimated price of Teva's AJOVY® product in his forecast—down more than 50% in 2023 and down roughly 45% in 2025, for example. Appx2506-2507 at 86:22-87:13.

Lilly's damages expert, Dr. Vellturo, testified that the large decreases in Dr. Berkman's estimates in the span of just one year demonstrate the unreliability and speculative nature of Dr. Berkman's analysis. Dr. Vellturo testified, for example, that "if [Dr. Berkman's] results were reliable, he should have gotten numbers in the two reports that were at least somewhere near each other," but that the numbers were instead "wildly different." Appx3906-3907 at 128:20-129-4. Dr. Vellturo testified that Dr. Berkman's numbers "were so far apart" that they could not be reliable. Appx3907 at 129:5-10.

Dr. Berkman's future lost-profits estimate decreased so substantially and so quickly because the market data on which he based his analysis (from Lilly's 2021 strategic plan) failed to accurately predict the market, including the effect of the

introduction of new oral migraine treatments (drugs called gepants), which drove down market share of both Teva's and Lilly's products. Appx2476-2477 at 56:19-57:4. Because Lilly's 2021 strategic plan had proven inaccurate and overly optimistic, Dr. Berkman revised his forecast using information from Lilly's 2022 strategic plan. But he was unable to update one of the key inputs to his forecast—market share figures—because the 2022 document did not include them. Appx2477 at 57:15-22. Instead, Dr. Berkman's revised forecast continued to rely on data from a document that had been proven inaccurate. Dr. Berkman also lacked updated full-year data for Teva's future costs, so he had to extrapolate from first-half-2022 data. Appx2479 at 59:6-22.

Dr. Berkman acknowledged that "the market has become more crowded" with the introduction of orally available, small-molecule gepants, and with more competitors in the marketplace, the incumbents "have now all seen their market shares decline." Appx2476-2477 at 56:13-57:4. He attributed the large decrease in his estimate to "forecasting error that comes about by perhaps a more sizable shift in the market than was anticipated in prior forecasts." Appx2506 at 86:17-21. Dr. Vellturo testified that "you have a lot of new entrants coming in and you never know what impact they're going to have. It just creates a lot of uncertainty, and [Dr. Berkman's] numbers reflect that." Appx3907 at 129:11-17.

Both Lilly's and Teva's witnesses and documents confirmed that the entry of oral small-molecule gepants "changed the dynamic of the marketplace and continues to change it today." Appx2675 at 23:6-14. Teva's witness Mr. Rainey, for example, testified that introduction of the gepants affected sales of Teva's AJOVY® product, which had not performed the way Teva wanted and expected. Appx1945 at 150:12-21. A Lilly Strategic Plan further confirms that, due to the market entry of the gepants, "[m]argins will continue to decrease as payers look to drive down net cost." Appx21295.

Dr. Berkman was unable to state that his revised estimate would be more accurate given the uncertain market for migraine drugs. Instead, he acknowledged that his revised estimate could change by a similar amount in the ensuing months and years. He testified: "I can't commit to whether they'll go up or down if I did this again in a month or several months," and that the same was true 12 months in the future or three years in the future. Appx2507 at 87:14-24.

Dr. Berkman conceded that "a number of the key variables in this forecast are subject to variation over time. I can't be prescient to know what the right numbers are." Appx2507 at 87:21-24; Appx2511-2512 at 91:20-92:3; *see also* Appx2509 at 89:7-10 ("[T]hese numbers are going to change over time because we don't have perfect foresight."); Appx2502 at 82:17-19. Yet he acknowledged that even in his revised estimate, he was not able to fully update his analysis with more current

market data. Dr. Berkman updated most of his analysis to reflect market data from Lilly's 2022 strategic plan, but he continued to rely on Lilly's 2021 strategic plan for market share because 2022 data were not available. Appx2477 at 57:15-22. Dr. Berkman also extrapolated from first-half-2022 data for future costs of Teva's AJOVY® product because full-year data were not yet available. Appx2479 at 59:6-21.

Given the speculative nature of Dr. Berkman's analysis, Lilly's motion for judgment as a matter of law argued that no nonspeculative evidence of future lost profits existed to support the jury's $49.8 million award. Yet, despite the lack of any nonspeculative evidence, the district court denied Lilly's motion and upheld the jury's award. The court stated that Dr. Berkman based his calculations on actual data and Lilly's projections, and that he explained his projections and the adjustments he made between 2021 and 2022. Appx58. Thus, despite the large difference between Dr. Berkman's projections and his continued reliance on forecasts that were proven to be incorrect, the court concluded that the jury was free to weigh whether his projections "were overly speculative in light of market dynamics (e.g., a market with more than two participants)" and found that the jury heard substantial evidence sufficient to support their award. Appx57-58. The court did not address Dr. Berkman's concessions that he could not say whether his revised forecast that

he revised downwards would need to be further revised down in a matter of months or years.

SUMMARY OF ARGUMENT IN RESPONSE TO TEVA'S APPEAL

1. Teva's broad, functionally defined claims lack written description.

It is undisputed that Teva's claims cover methods of treating migraine or other types of headache using *any and every* humanized anti-CGRP antagonist antibody. For a broad, functionally defined genus like Teva's, a patent specification must disclose either a representative number of species within the genus or common structural features correlated to the claimed function. Teva's specification does neither.

Teva's specification discloses *only one* humanized anti-CGRP antagonist antibody (G1) and no common structural features that correlate to CGRP binding or antagonism. The district court correctly determined that the antibody fragments not reported to antagonize CGRP and rodent antibodies disclosed in the specification cannot be "representative" of the claimed humanized anti-CGRP antagonist antibodies.

Disclosing a single antibody within the claims falls far short of what is required to provide written description support for Teva's expansive claims, particularly as G1 is far from representative. That G1 is not "representative" is evidenced by the fact that the genus encompasses antibodies like Lilly's

galcanezumab, which bears no meaningful structural or functional resemblance to G1. Indeed, while G1 binds CGRP at the C-terminal end, galcanezumab binds to the mid-region. Further, whereas G1 failed to treat a claimed headache condition (episodic cluster headache), Lilly's galcanezumab received FDA approval for that indication.

Teva argues that it need not disclose representative species or common structural features because its claims recite methods of using a purportedly "well-known" class of antibodies. This attempt to bypass the disclosure requirements for a functionally defined genus fails because it is undisputed that the claimed *humanized* antibodies were not known *at all* as of the priority date.

In an effort to overcome this defect, Teva relies on *rodent* anti-CGRP antagonist antibodies. But this reliance is misplaced for several reasons. First, rodent antibodies are not within the scope of the claims, and thus cannot be "representative." Second, neither Teva's patent nor the prior art discloses the amino acid sequences or structures of these rodent antibodies, without which a skilled artisan could not humanize and use them. Third, Teva's argument that it would have been "routine" to make and use the rodent anti-CGRP antagonist antibodies asks the Court to hold that, because the prior art renders making a humanized antibody obvious, the claimed genus of antibodies is sufficiently described. This Court has repeatedly held otherwise: even a description that might render a claim obvious is

insufficient to provide written description if the specification does not show that the inventors actually invented what they claimed.

Based on this evidence, even when viewed in the light most favorable to Teva and the jury's verdict, a reasonable jury could *only* have concluded that Teva's claims lack written description. This Court therefore should affirm the district court's grant of judgment as a matter of law that the claims are invalid for lack of written description.

2. Teva's claims are not enabled.

No reasonable jury could conclude that Teva's claims are enabled. As the district court correctly noted, Teva's specification discloses no more than a "roadmap" for a lengthy and expensive "trial and error" process to identify additional antibodies within the scope of Teva's claims. The court explained that a reasonable jury could only conclude that a very large number of candidate antibodies would need to be screened to identify those within the genus recited in Teva's claims. As a named inventor confirmed, identifying such antibodies could only be done by empirically testing each one to determine whether it binds and antagonizes CGRP. As the Supreme Court stated in *Amgen*, a "roadmap" to conduct trial-and-error research is little more than a "research assignment[]" insufficient to enable the claims. The Court therefore should affirm the district court's grant of judgment as a matter of law that Teva's claims are invalid for lack of enablement.

ARGUMENT IN RESPONSE TO TEVA'S APPEAL

VII. Standard of Review

This Court reviews a district court's grant of judgment as a matter of law under the law of the regional circuit. *Novozymes A/S v. DuPont Nutrition Bioscis. APS*, 723 F.3d 1336, 1343-44 (Fed. Cir. 2013). The First Circuit reviews the grant or denial of judgment as a matter of law de novo. *Segrets, Inc. v. Gillman Knitwear Co.*, 207 F.3d 56, 61 (1st Cir. 2000).

Judgment as a matter of law is warranted when "a reasonable jury would not have a legally sufficient evidentiary basis to find for the [non-moving] party." Fed. R. Civ. P. 50(a)(1); *see also Guilloty Perez v. Pierluisi*, 339 F.3d 43, 50 (1st Cir. 2003). Although the Court must draw "all reasonable inferences in favor of the nonmoving party," it should also credit "evidence supporting the moving party that is uncontradicted and unimpeached." *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 150-51 (2000) (citation omitted). Further, the nonmoving party "must provide 'more than a scintilla of evidence and may not rely on conjecture or speculation.'" *Segrets*, 207 F.3d at 65 (citation omitted).

The nonmoving party cannot sustain a jury verdict based on either conclusory testimony or testimony premised on an erroneous legal standard. *See, e.g.*, *InTouch Techs., Inc. v. VGO Commc'ns, Inc.*, 751 F.3d 1327, 1352-53 (Fed. Cir. 2014); *Trs. of Bos. Univ. v. Everlight Elecs. Co.*, 896 F.3d 1357, 1362-64 (Fed. Cir. 2018).

VIII. The District Court Correctly Granted Judgment as a Matter of Law of No Written Description

Section 112 requires that a patent specification contain a written description of the claimed invention sufficient to "show that the inventor actually invented the invention claimed." *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (2010) (en banc); 35 U.S.C. § 112.

When a patent claims methods of using a functionally defined genus of compounds, the specification must describe the genus by disclosing either (1) a representative number of species within the claimed genus that reflects the structural diversity of the genus, or (2) structural features common to the members of the genus and correlated to the claimed functions. *Ariad*, 598 F.3d at 1350.

The Court has reiterated this principle many times. In *Regents of the University of Minnesota v. Gilead Sciences, Inc.*, for example, the Court stated that written description of a genus requires description "of either a representative number of members of the genus or structural features common to the members of the genus, in either case with enough precision that a relevant artisan can visualize or recognize the members of the genus." 61 F.4th 1350, 1356 (Fed. Cir. 2023) (citing *Ariad*, 598 F.3d at 1350-52). The Court has also recognized that claims reciting a genus described solely by its function can be "inherently vulnerable" to a written description challenge, "especially in technology fields that are highly unpredictable, where it is difficult to establish a correlation between structure and function for the

whole genus or to predict what would be covered by the functionally claimed genus." *AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc.*, 759 F.3d 1285, 1301 (Fed. Cir. 2014) (citing *Ariad*, 598 F.3d at 1351).

Here, Teva's disclosure of only a *single* species within the broad, functionally defined genus recited in the claims cannot meet the "representative species" standard. Teva's specification also fails to disclose *any* common structural features correlated to the claimed function of binding and antagonizing CGRP. The district court therefore correctly concluded that a reasonable jury could only conclude that Teva's claims lacked written description support.

A. No Reasonable Jury Could Find That Teva's Specification Discloses a Representative Number of Species Within the Genus Recited in Teva's Claims

1. It Is Undisputed That Teva's Broad Claims Cover Using *Any* Humanized Anti-CGRP Antagonist Antibody

Because Teva's claims recite methods of treating headache using a genus of antibodies defined based solely on function—the ability to bind to and antagonize CGRP—Teva's claims broadly cover methods of treating headache using *any* humanized anti-CGRP antagonist antibody. Named inventor Dr. Abdiche confirmed that there is not "any anti-CGRP antagonist antibody that binds to CGRP and blocks CGRP's effects that would not be covered" by the claims. Appx1522 at 150:13-22. Dr. Zeller similarly acknowledged that the claims cover "all antibodies, all function blocking antibodies." Appx1424 at 52:5-12. And Teva's expert Dr. Hale stated that

"you could use any of those antibodies, any antibody." Appx4267 at 157:1-4. Accordingly, Lilly's expert Dr. McDonnell testified that the claims are "extraordinarily broad." Appx3145 at 82:19-21.

Based on this evidence, the district court correctly concluded that, even viewing the evidence in the light most favorable to the verdict, Teva's broad claims would cover use of any humanized anti-CGRP antagonist antibody. Appx23. This is consistent with this Court's prior decision addressing the same antibody genus recited here, which noted "the extremely broad scope of the functionally claimed antibodies." *See, e.g.*, *Teva*, 8 F.4th at 1362; *see also* Teva Br. 27 (describing the genus at issue in the prior IPR appeal as "*identical* to the class of antibodies at issue in this case").

Teva's attempt to impugn Lilly's expert Dr. McDonnell and his testimony about the breadth of the genus in Teva's claims, *see* Teva Br. 34-35, is unavailing. First, additional evidence beyond Dr. McDonnell's testimony supports the district court's conclusion that the jury could *only* have found that Teva's genus is broad. As discussed above, the court noted testimony by both parties' witnesses that the claims cover *any* humanized anti-CGRP antagonist antibody. Appx23. The court also pointed to testimony that the asserted claims do not include any structural limitations that would narrow the broad scope of the functionally defined genus. Appx23-24.

Second, the district court addressed Teva's critique of Dr. McDonnell's testimony, disagreeing with Teva's characterization that Dr. McDonnell "admitted" that the claims may actually cover only a small number of antibodies. Appx26-27. The court noted that the testimony, accurately recounted, was that *even if* the number of antibodies covered by the claims were small, you would still have to search through a large number of candidate antibodies to find those within the claims. Appx26-27. Dr. McDonnell's testimony was consistent with that of Teva's witnesses. Dr. Zeller, for example, acknowledged that "you would have to evaluate each anti-CGRP antibody empirically to determine whether or not it [could] inhibit CGRP." Appx1407 at 35:10-15.

The district court thus concluded that, even viewing the evidence in the light most favorable to the jury's verdict, the jury could only have found that (1) a very large number of antibodies would need to be screened to identify those that can antagonize CGRP and (2) because trial-and-error testing was required, the size of the genus "was 'unknowable.'" Appx27 (quoting Appx3145 at 82:9-18).

2. Disclosure of a Single Humanized Anti-CGRP Antagonist Antibody That Is Not "Representative" of the Recited Genus Is Insufficient

It is undisputed that the specification discloses only one *humanized* anti-CGRP antagonist antibody within the scope of the claims. Appx27. No reasonable jury could have found otherwise. As this Court has recognized, "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." *Ariad*, 598 F.3d at 1351. Here, a skilled artisan reading Teva's specification would be "deprived of any meaningful guidance into what compounds beyond" the G1 humanized antibody "would provide the same result." *Idenix*, 941 F.3d at 1164. This is fatal to Teva's "representative species" arguments.

Beyond G1, Teva's specification discloses only (1) rodent antibodies and (2) antibody fragments that are highly similar to G1. But the district court correctly determined that the variants and rodent antibodies are not "representative" because they do not "fall[] within the scope of the genus." *Juno Therapeutics, Inc. v. Kite Pharma, Inc.*, 10 F.4th 1330, 1335 (Fed. Cir. 2021) (quoting *Ariad*, 598 F.3d at 1350), *cert. denied*, 143 S. Ct. 402 (2022). The rodent antibodies are not humanized, as required by the claims. Appx27-29; Appx35 n.18. And both sides' experts testified that the antibody fragments were not shown to be CGRP antagonists, as claimed. Appx4274 at 164:17-19; Appx3146-3147 at 83:20-84:14. The fragments additionally fall outside Teva's claims requiring full-length antibodies. Appx27.

Regardless, as the district court determined, no reasonable jury could have found that these 84 variants meaningfully broadened the disclosure because they all shared 95% sequence identity with G1, had the same length of CDRs as G1, and were derived from the same V genes as G1 (i.e., genes encoding the variable region).

Appx27-28. Here, G1 and its variants "are all of the similar type and do not qualitatively represent other types of antibodies encompassed by the genus." *AbbVie*, 759 F.3d at 1300-01 (citing *Ariad*, 598 F.3d at 1351).

Lilly's galcanezumab antibody additionally confirms that G1 and its close variants are not "representative" of Teva's broad genus. Galcanezumab falls within Teva's functionally defined genus even though it differs substantially from G1 both structurally and functionally. Uncontroverted testimony established that galcanezumab has a sequence identity to G1 of only 50.8% and 64.5% for the heavy and light chain variable domains (respectively), binds to different regions (mid-region versus C-terminal), has CDRs of different sequences and lengths, and derives from different V gene families. Appx34 (citing Appx3151-3153 at 88:17-90:10; Appx3154-3155 at 91:9-92:10; Appx3156-3157 at 93:4-94:8; Appx3159-3160 at 96:11-97:11; Appx3168-3170 at 105:18-107:8; Appx4211 at 101:15-20; Appx4255 at 145:8-15; Appx4256 at 146:5-8). These structural differences make galcanezumab functionally different—it is more potent than G1, has a lower monthly dose for preventive treatment of migraine, and, unlike G1, it can treat episodic cluster headache. Appx3448-3452 at 206:12-210:16; Appx16410; Appx16415-16416; Appx16420-16422; Appx16448; Appx16454-16455; Appx3339-3340 at 97:25-98:7; Appx52120-52129; Appx50434-50435.

Given these differences, the district court correctly determined that, even viewing the evidence in the light most favorable to the verdict, no reasonable jury could conclude that G1 and its variants are *representative* of a genus that covers such structurally and functionally different antibodies. Appx35-38. This conclusion comports with this Court's reasoning in *AbbVie* that, where the "claimed genus covers structurally diverse antibodies," the specification must disclose representative species sufficient to cover that structural breadth. Appx38 (citing *AbbVie*, 759 F.3d at 1300-01). Like Teva's claims, the claims in *AbbVie* defined antibodies functionally based on "binding and neutralizing characteristics, rather than by structure." 759 F.3d at 1292. And like Teva's patents, the specification in *AbbVie* disclosed a limited number of structurally similar antibodies, all derived from an antibody that had minimal sequence identity with the accused antibody product. *Id*. at 1291, 1298. This Court held the claims invalid because there was "no evidence to show any described antibody to be structurally similar to, and thus representative of," the accused antibody. *Id.* at 1301. The same is true here.

Teva incorrectly argues that *AbbVie* is no longer good law, even though this Court continues to cite its reasoning approvingly. Teva Br. 38-39. In *Juno*, for example, the Court endorsed *AbbVie*'s finding of no written description where a patent described only one species of structurally similar antibodies and no structure-function correlation but claimed "every fully human IL-12 [targeted] antibody that

would achieve a desired result." 10 F.4th at 1339 (alteration in original) (quoting *AbbVie*, 759 F.3d at 1301-02). The Court also recently reaffirmed *AbbVie*'s rationale in *PureCircle USA Inc. v. SweeGen, Inc.*, finding no written description where "the one enzyme disclosed in the patents here has not been shown to be typical of the entire genus . . . claimed." No. 2022-1946, 2024 WL 20567, at *4 (Fed. Cir. Jan. 2, 2024) (citing *AbbVie*, 759 F.3d at 1300).

Teva also contends that the district court erred by "treat[ing] antibody G1 as the *only* [representative] species" and "disregard[ing] . . . the known murine antibodies because they had not been humanized." Teva Br. 29. Not so. The district court considered the disclosed rodent antibodies and correctly applied this Court's precedents to conclude they do not provide written description support. To be "representative," disclosed species must fall *inside* the claimed genus. Appx29-30 (citing *Eli Lilly*, 119 F.3d at 1566-67 (finding no written description because rat cDNA was not representative of genus of human cDNA)); *see also Juno*, 10 F.4th at 1335; *Ariad*, 598 F.3d at 1350 (requiring disclosure of species "falling within the scope of the genus"). Teva's attempt to sidestep the insufficiency of the sole humanized anti-CGRP antagonist antibody disclosed in the specification by relying on the rodent antibodies therefore also fails.

3. The Inventors' Unsuccessful Efforts to Make Other Humanized Anti-CGRP Antagonist Antibodies Further Confirm That the Claims Lack Written Description

The "essence" of written description is that a patent applicant must describe the invention "so that the public will know what it is and that he or she has truly made the claimed invention." *AbbVie*, 759 F.3d at 1298. Here, the inventors' failure to make other species within the genus further confirms the lack of written description. *See, e.g.*, *Idenix*, 941 F.3d at 1165.

The inventors did not disclose humanized antibodies that bind to other regions on CGRP because their efforts to make such antibodies were unsuccessful. For example, inventor Dr. Abdiche testified that she attempted to humanize three antibodies but did not complete the process. At trial, Dr. Abdiche attempted to rationalize this failure, testifying that she "dropped" one of the antibodies because "it was less interesting for various reasons." Appx1486-1487 at 114:20-115:3. But the contemporaneous documents show that her efforts were simply unsuccessful. Appx18026-18027 (after humanization, the antibody lost "CGRP-binding affinity to undetectable levels"); Appx3207-3208 at 144:23-145:12.

Further, despite a multi-year effort, the inventors could not make even *rodent* anti-CGRP antagonist antibodies, much less humanized ones, that bind to CGRP's mid-region. Appx31-33; Appx1399 at 27:21-24; Appx24062 (Dr. Zeller confirming his mid-region-binding rodent antibodies "did not confirm binding"); Appx16687-

16689; Appx51995; Appx51990-51994; Appx1402-1405 at 30:15-33:13; Appx51968-51969; Appx52043-52073; Appx1410-1411 at 38:19-39:16; Appx16687-16689. As a result, making humanized antagonist antibodies that bind to other regions of CGRP remained an unmet goal. Appx1388-1389 at 16:14-17:17; Appx1391-1392 at 19:3-20:15; Appx24062; Appx4258 at 148:11-21; Appx51285-51294.

Teva's experts downplayed these failures, describing the inventors' work as an ongoing research plan requiring additional efforts. *See, e.g.*, Appx4258 at 148:11-21 ("[I]t was a *plan* that [Dr. Zeller] was contemplating, but whether he was going to go ahead and do it, you know, I don't know." (emphasis added)); Appx1388-1389 at 16:24-17:4; Appx1391-1392 at 19:3-20:22 (acknowledging that "further efforts" and "resources" would be required); Appx24062 (same). But mere research plans are legally insufficient to provide written description support. As this Court has held, a "'mere wish or plan' for obtaining the claimed invention is not adequate written description." *Juno*, 10 F.4th at 1335 (quoting *Centocor Ortho Biotech, Inc. v. Abbott Lab'ys*, 636 F.3d 1341, 1348 (Fed. Cir. 2011)); *see also Ariad*, 598 F.3d at 1353. Teva's patents, which claim methods of using a broad, functionally defined genus but disclose only *one* species within that genus, provide a textbook example of claims that are no more than a research plan or an invitation for scientists to engage

in the trial-and-error process of discovery that Teva's inventors failed to carry out themselves.

Teva does not dispute that it failed to make or identify any humanized anti-CGRP antibodies that could bind to the N-terminal or mid-region of CGRP. Appx33. Instead, Teva wrongly contends that these failures are irrelevant because the jury *could* have credited testimony that an anti-CGRP antagonist antibody could bind to different regions of CGRP and still treat headache. Teva Br. 32 (citing Appx33). Yet, regardless of whether a skilled artisan would have known that a humanized antibody binding anywhere on CGRP could potentially treat headaches, the inventors did not *possess* any such antibodies besides G1.

In addition to failing to create other humanized antibodies within the claims, Teva also failed to create any antibody that could treat episodic cluster headache, even though this headache disorder was specifically claimed. *See* Appx273 (claim 30); Appx353 (claim 5); Appx430 (claim 5). Rather, Teva's clinical trials with G1 for this condition failed and were subsequently discontinued. Appx50434-50435; Appx3402-3404 at 160:21-162:8; Appx3431-3432 at 189:6-190:15; Appx3339-3340 at 97:25-98:3.

Teva's failures are similar to *Idenix*, where the patentee tried and failed to make certain species within the recited genus and thus did not disclose such species in the specification. 941 F.3d at 1160, 1164-65. The Court held the patent invalid for

lack of written description. Here, Teva's failures to develop an antagonist antibody that binds to other locations on CGRP or treats episodic cluster headache only underscores Teva's failure to disclose representative species. This further supports the district court's decision that Teva failed to adequately describe its broad genus.

B. No Reasonable Jury Could Find That Teva's Specification Discloses Common Structure of the Recited Genus of Antibodies That Correlates to the Claimed Functions

The district court correctly concluded that Teva's specification fails to describe any common structure of anti-CGRP antagonist antibodies. Appx44. Both parties' experts testified that there is no structural feature, such as a particular amino acid sequence, that confers ability to bind to and antagonize CGRP and is common to antibodies in the recited genus. Appx3178 at 115:1-17; Appx3182-3183 at 119:25-120:4. Teva's expert Dr. Hale, for example, confirmed that one "couldn't predict based on the sequence whether or not [antibodies] bind to an[d] antagonize[] CGRP." Appx4257 at 147:8-11.

Teva raised two arguments at trial regarding common structural features, arguing that the specification discloses the claimed antibodies as having: (1) a Y-shaped structure; and (2) binding sites that are complementary to CGRP (i.e., "paratopes"). Appx43. Both arguments fail.

This Court has held that structures common to all members of a genus but *unrelated* to binding to a given antigen are insufficient to provide written description

support. In *Juno*, for example, the Court held that the general structure common to any scFv did not provide written description support because an scFv having that structure may or may not bind the claimed antigen. 10 F.4th at 1339; *see also Idenix*, 941 F.3d at 1164. Likewise here, named inventor Dr. Rosenthal acknowledged that a Y-shaped structure is common to all IgG antibodies, regardless of whether they bind to and antagonize CGRP. Appx1306 at 123:4-13; *see also* Appx3180-3182 at 117:9-119:24; *In re Alonso*, 545 F.3d 1015, 1017 (Fed. Cir. 2008) ("Antibodies are large, Y-shaped molecules . . . ."). This structure therefore cannot provide written description support.

As to Teva's arguments about paratopes, Lilly's expert Dr. McDonnell testified that the mere fact that an antibody has a pocket for binding CGRP does not identify a common structure that a skilled artisan could use to recognize other antibodies that bind to and antagonize CGRP. Appx3182 at 119:6-16. Teva presented no contrary testimony. Moreover, a paratope refers only to a *desired* function of binding CGRP and fails to identify any actual structure or sequence that confers the ability to perform that function. The district court thus correctly concluded that neither of these arguments was sufficient to show that the required common structure correlated to the claimed function. Appx43-44.

C. Humanized Anti-CGRP Antagonist Antibodies Were Not "Well-Known," as Teva Contends

Given the lack of representative species or common structure in the specification, the core of Teva's written description argument is that such disclosure is unnecessary because "what is claimed is not a novel genus or method of using a novel genus, but a novel method of using a well-known genus." Teva Br. 44, 27. Teva is again wrong on the facts and the law.

There is no genuine dispute that the claimed genus of humanized antibodies was not known *at all*, much less "well-known," and the district court correctly concluded that no reasonable jury could have found otherwise. *See, e.g.*, Appx27; Appx35 n.18; Appx37 n.20. Indeed, Teva's own experts and the named inventors acknowledged that no humanized anti-CGRP antagonist antibodies were disclosed in the prior art. Named inventors Dr. Zeller and Dr. Pons, for example, acknowledged that as of the priority date, humanized anti-CGRP antibodies were not a previously known class of compound and were not described in the literature. Appx1400 at 28:6-9; Appx3390-3391 at 148:23-149:2. Similarly, Teva's experts Dr. Hill and Dr. Hale conceded that they did not identify *any* humanized anti-CGRP antagonist antibody in the prior art. Appx4177-4178 at 67:25-68:5; Appx4254 at 144:17-24. Lilly's expert Dr. McDonnell likewise confirmed that humanized anti-CGRP antagonist antibodies were not known in the prior art. Appx3200 at 137:4-6.

Citing these same admissions, the district court noted the "uncontroverted evidence that no humanized anti-CGRP antagonist antibodies were known in the prior art." Appx27. The court further noted that "the evidence does not support a sufficiently known correlation between the structure of anti-CGRP antagonist antibodies and their ability to accomplish the claimed function." Appx37 n.20. Based on this evidence, no reasonable jury could have found that the claimed genus of *humanized* anti-CGRP antagonist antibodies was well known, as Teva contends. As a result, Teva is not excused from disclosing either representative species or common structure sufficient to describe the genus recited in the claims.

Because the claimed *humanized* antibodies were not known at all, Teva's written description argument hinges on the contention that *rodent* anti-CGRP antagonist antibodies were "well-known."[1] Teva argues, for example, that "the underlying class of murine antibodies was well known" and "there was evidence from which the jury reasonably could have found that a representative number of such antibodies already were known, including . . . antibody G1." Teva Br. 27-28.

But Teva's arguments fail even as to rodent anti-CGRP antagonist antibodies. Dr. McDonnell confirmed that no sequence or structure was known for the rodent

[1] While Teva blurs the line between humanized and rodent antibodies, its assertions that the "entire class of anti-CGRP antagonist antibodies" was "already well-known" or "available commercially" necessarily refer to rodent antibodies because no humanized antibodies were known. *See, e.g.*, Teva Br. 1-2, 6-7, 21-22, 31, 39, 41-42.

antibodies disclosed in Teva's specification or the prior art. Appx3132-3134 at 69:4-71:12. Teva's expert Dr. Hale similarly acknowledged that "none of the rodent antibodies referenced in his report disclosed an amino acid sequence, and not all rodent antibodies identified in his report were shown to antagonize CGRP." Appx30-31 (citing Appx4177 at 67:16-24).

For these reasons, Teva's contention that it need not disclose "what already is known" to a skilled artisan fails. Teva Br. 30-31, 41-47. Indeed, in the cases relied on by Teva, the component used in the claim was ubiquitous and well-understood in the art. In *Ajinomoto Co. v. International Trade Commission*, the genus of more potent promoters in the claim "was already well explored in the relevant art," including in an article disclosing examples of such promoters, their relative strengths, and a methodology for evaluating promoter strength. 932 F.3d 1342, 1359 (Fed. Cir. 2019). In *Streck, Inc. v. Research & Diagnostic Systems, Inc.*, the Court determined that the claims covered the use of naturally-occurring reticulocytes as controls, which were both described in the specification and whose use as "stand-alone controls was well-known in the prior art." 665 F.3d 1269, 1285-87 (Fed. Cir. 2012) (citation omitted). In *Herschler*, the claims were "drawn to the Use of *Known* chemical compounds in a manner *auxiliary* to the invention." *In re Herschler*, 591 F.2d 693, 702 (CCPA 1979) (emphases added). And even those "known" compounds needed to be described sufficiently "to lead one having ordinary skill in

the art to that class of compounds." *Id.* In *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, the claim terms "mammalian" and "vertebrate" simply referred to types of cells that could be used in the claims and not to "new or unknown biological materials." 314 F.3d 1313, 1332 (Fed. Cir. 2003). Here, by contrast, the prior art disclosed *none* of the *humanized* anti-CGRP antagonist antibodies that Teva claimed, and the disclosures of the handful of unclaimed *rodent* antibodies lacked sequence and structure information, making it impossible for skilled artisans to make, humanize, and use them in the claimed method. Neither were therefore "well-known" within the meaning of *Ajinomoto*, *Streck*, *Herschler*, and *Hoechst*.

D. It Is Irrelevant for Written Description Whether a Skilled Artisan Could Make and Use the Claimed Anti-CGRP Antibodies or Whether It Would Be "Routine" to Do So

Teva argues that it need not disclose more than one humanized antibody within the broad claimed genus (or, alternatively, that unclaimed rodent antibodies are representative) because it would have been obvious and "routine" to humanize prior-art rodent anti-CGRP antibodies. *See, e.g.*, Teva Br. 2, 11, 28. These arguments are foreclosed by this Court's precedents.

This Court has repeatedly rejected attempts to replace the written description framework with an obviousness analysis. As this Court has recognized, obviousness and written description are analyzed under different standards—prior-art disclosures that would have motivated a skilled artisan to make a single species within a claimed

genus does not mean that the entire genus is adequately described. Put simply, "a description that merely renders the invention obvious does not satisfy the [written description] requirement." *Ariad*, 598 F.3d at 1352.

Teva nonetheless attempts to characterize Lilly's statements about obviousness in IPR proceedings as admissions for written description purposes. *See, e.g.*, Teva Br. 2, 12-13, 26. But Lilly did not argue that *humanized* anti-CGRP antagonist antibodies were well known or that the *sequence* of any *rodent* anti-CGRP antagonist antibodies was well known, because they were not. Lilly merely pointed out that a skilled artisan would have been motivated and had a reasonable expectation of making *one* humanized antibody within the claimed genus, rendering the genus obvious. *See, e.g.*, *Teva*, 8 F.4th at 1357, 1359. That the claimed genus may have been obvious does not absolve Teva from § 112's requirement to describe the full scope of what it claims. Teva's citations to obviousness arguments from the earlier IPR proceedings thus miss the point.

This Court has also held that, for written description, "it is not enough for the specification to show how to make and use the invention." *Amgen Inc. v. Sanofi*, 872 F.3d 1367, 1377 (Fed. Cir. 2017) (citing *Ariad*, 598 F.3d at 1345-46, 1347-48). Indeed, the Court has described this as "the core ruling of *Ariad*." *Id.* at 1378. The ability to make a claimed compound "is beside the point" because the relevant question is "whether the specification discloses the compound . . . , specifically, as

something [the inventors] actually invented." *In re Ruschig*, 379 F.2d 990, 995 (CCPA 1967); *see also Novozymes*, 723 F.3d at 1350-51 (affirming judgment as a matter of law because the patentee's make-and-use argument "misses the point" of the written description requirement).

The district court's decision is fully consistent with these holdings. Citing this Court's *Eli Lilly* decision, the court stated that the specification's disclosure of rodent anti-CGRP antagonist antibodies and prior-art knowledge of humanization techniques "does not make [the rodent antibodies] representative species, and is not enough on its own to adequately describe the claimed invention." Appx30. In *Eli Lilly*, disclosure of rat cDNA was insufficient to provide written description support for the claimed human cDNA. 119 F.3d at 1568-69. This Court explained that "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Appx29 (quoting *Eli Lilly*, 119 F.3d at 1566-67). Teva attempts to distinguish *Eli Lilly*, arguing that, while going from rat cDNA to human cDNA was nonobvious, humanizing rodent anti-CGRP antagonist antibodies was allegedly "routine." Teva Br. 33. Even if this were true, it misses the point—written description and obviousness are distinct inquiries, and a skilled artisan's ability to combine or modify a patent's disclosure to obtain a species within a claimed genus is insufficient to show possession of that genus. *Eli Lilly*, 119 F.3d

at 1566-67; *Novartis Pharms. Corp. v. Accord Healthcare, Inc.*, 38 F.4th 1013, 1017 n.2 (Fed. Cir. 2022) ("It is not enough that a claimed invention is 'an obvious variant of that which is disclosed in the specification.'"); *Purdue Pharma L.P. v. Recro Tech., LLC*, 694 F. App'x 794, 797-98 (Fed. Cir. 2017).

Here, the district court correctly applied these precedents and held that, even if humanization were "routine" or a skilled artisan could make and use the antibodies recited in the claims, that cannot establish written description because the specification does not describe a sufficient number of representative species or common structural features correlated to function. Appx32-33. Both here and in the district court, Teva failed to directly address this fatal flaw. Appx33; Teva Br. 33.

IX. The District Court Correctly Granted Judgment as a Matter of Law of No Enablement

A patent specification "'must enable the full scope of the invention as defined by its claims,' allowing for 'a reasonable amount of experimentation.'" *Baxalta*, 81 F.4th at 1364-65 (quoting *Amgen*, 598 U.S. at 610, 612). Where a patent claims an entire class of compositions, "the patent's specification must enable a person skilled in the art to make and use the entire class." *Amgen*, 598 U.S. at 610. "The more one claims, the more one must enable." *Id.* (citing *Cont'l Paper Bag Co. v. E. Paper Bag Co.*, 210 U.S. 405, 419 (1908) ("[T]he claims measure the invention." (alteration in original))).

Here, the district court correctly determined that a reasonable jury could *only* have found that identifying potential antibodies and making them required undue experimentation. The court explained that a reasonable jury could only have found that the four-step process required to screen antibodies would take months and cost tens of thousands of dollars *per antibody*. Appx49-50 (citing Appx1344 at 161:2-15; Appx4173 at 63:6-14; Appx4215-4216 at 105:1-106:13; Appx4227-4228 at 117:11-118:2; Appx4260-4261 at 150:25-151:12; Appx4262 at 152:11-19; Appx4266 at 156:19-22). That process would necessitate (1) in vitro testing; (2) in vivo animal testing; (3) receiving an actual antibody; and (4) humanizing the animal antibody. As the district court stated, this process is "nothing more than a 'roadmap' for a 'trial and error' process to identify and make antibodies within the scope of the Asserted Claims." Appx50 (citing *Amgen*, 598 U.S. at 612-15).

This roadmap is similar to *Amgen*, where the Supreme Court found that disclosing the structure of 26 antibodies within a genus was insufficient to enable the broad claims. As in *Amgen*, the processes that a skilled artisan would have to use to create additional antibodies within the recited genus amounted to "little more than two research assignments." 598 U.S. at 614. Without corresponding disclosure of "a quality common to every functional embodiment," disclosure of such "research assignments" does not enable the claims, instead leaving it to skilled artisans to

"engage in 'painstaking experimentation' to see what works." *Baxalta*, 81 F.4th at 1365-66 (quoting *Amgen*, 598 U.S. at 614).

Teva's patent also resembles the patent in *Baxalta*, where the claims covered all antibodies that performed specific functions (binding to an enzyme and increasing its procoagulant activity). 81 F.4th at 1366. While there were millions of potential candidate antibodies, the specification disclosed only eleven antibodies with the claimed functions and no common structural features correlated to the recited function. *Id.* The specification directed skilled artisans to (1) immunize mice with the enzyme; (2) form hybridomas to obtain antibodies; (3) test those antibodies to determine whether they bind to the enzyme; and (4) test antibodies that bind to determine whether they increase procoagulant activity. *Id.* This Court held the claims invalid for lack of enablement, reasoning that this "roadmap simply directs skilled artisans to engage in the same iterative, trial-and-error process the inventors followed to discover the eleven antibodies they elected to disclose." *Id.* The roadmap the Court held insufficient in *Baxalta* is strikingly similar to the process Teva outlines in its brief for obtaining additional humanized anti-CGRP antagonist antibodies. *See, e.g.*, Teva Br. 49.

Here, the mere invitation to conduct research constitutes undue experimentation, even if the jury may have concluded that some or all of the steps were routine. Appx51 (citing *Idenix*, 941 F.3d at 1163). Regardless of whether the

jury concluded that an antibody known to be an anti-CGRP antagonist would treat headache, that does not change the fact that "each potential antibody would have to be synthesized and screened for effectiveness," including determining whether it is actually a CGRP antagonist. Appx51 (citing *Idenix*, 941 F.3d at 1163). In *Idenix*, the Court affirmed judgment as a matter of law because making and screening thousands of compounds would have required "excessive experimentation, even if routine." 941 F.3d at 1163, 1165 (citation omitted). So too here.

Teva's arguments on appeal fail to show any error in the district court's conclusion or explain why this Court's reasoning in *Idenix* and other cases regarding undue experimentation should not apply equally here. Teva incorrectly contends that the district court did not consider rodent antibodies in its enablement analysis. Teva Br. 51-52. On the contrary, the court considered creation of rodent anti-CGRP antagonist antibodies as a step in the four-step process required to create humanized antibodies within the claims and rejected the assertion that the invitation to conduct research and development to generate each antibody within the claimed genus constitutes enabling disclosure. Appx49-51.

Teva also reprises its legally incorrect argument that the specification reflects a constructive reduction to practice of the entire genus of humanized anti-CGRP antagonist antibodies based on the existence of a limited number of rodent antibodies

that had not been humanized and whose sequences were not even disclosed. This argument fails for the same reasons discussed above. *See supra* Section VIII.C.

And Teva's attempt to distinguish this Court's enablement precedents, including *Baxalta*, *Amgen*, and *Wyeth*, falls short. Teva argues that those cases involved a "vast" number of compounds that would need to be tested, whereas here, Teva contends that Lilly failed to show that the recited genus would be large. Teva Br. 53-54 (quoting *Amgen*, 598 U.S. at 613). Not so. The district court correctly concluded that a reasonable jury could only conclude that a very large number of candidate antibodies would need to be screened to identify those within the recited genus, which contains an "unknowable" number of antibodies. Appx27 (quoting Appx3145 at 82:9-18); *see supra* Section III.A. Named inventor Dr. Zeller similarly confirmed that the only way to identify whether a given antibody could antagonize CGRP would be to test each antibody empirically. Appx1407 at 35:10-18. The facts closely resemble *Idenix*, where undue experimentation was required for a skilled artisan to search a large number of candidate compounds to identify the species within the recited genus. 941 F.3d at 1162 (finding undue experimentation where the patent leaves a skilled artisan "searching for a needle in a haystack" to determine which of the "large number" of species falls within the claimed genus). The district court thus correctly concluded that no reasonable jury could find that Teva's claims are enabled. Appx51-53.

X. Teva's Policy Arguments for Weakening Disclosure Requirements for Claims Reciting a Functionally Defined Genus Contravene Established Precedent and Would Upend § 112

Teva contends that the district court's decision fails to advance the purposes of § 112. Teva Br. 57-58. Teva is wrong.

The district court's decision dutifully follows the numerous precedents embodying the principle that inventors must adequately disclose and enable what is covered by their claims. A patent "is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." *Ariad*, 598 F.3d at 1353 (quoting *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 930 n.10 (Fed. Cir. 2004)). As the Supreme Court explained, § 112 "reflects Congress's judgment that if an inventor claims a lot, but enables only a little, the public does not receive its benefit of the bargain." *Amgen*, 598 U.S. at 616. In short, "the more a party claims, the broader the monopoly it demands, the more it must enable." *Id.* at 613. Here, Teva claimed the use of any and all humanized anti-CGRP antagonist antibodies, regardless of sequence, to treat any type of headache. The disclosure of a single humanized antibody in its specification cannot support these broad claims.

Similarly, the written description requirement "ensure[s] 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." *Ariad*, 598 F.3d at 1353-54 (quoting *Rochester*, 358 F.3d at 920). For claims reciting

a genus defined only by its function, the patent specification "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." *Juno*, 10 F.4th at 1335 (quoting *Ariad*, 598 F.3d at 1349). It can do so by disclosing either a representative number of species within the recited genus or structural features common to the members of the genus such that a skilled artisan can "'visualize or recognize' the members of the genus." *Id.* (quoting *Ariad*, 598 F.3d at 1350).

Here, Teva's arguments would turn these principles on their head, eliminating the requirement to disclose a representative number of species that work in a claimed method or some common structural features of those species connected to their claimed function. The result would be to allow parties to claim "any compound later actually invented and determined to fall within the claim's functional boundaries—leaving it to the pharmaceutical industry to complete an unfinished invention." *Ariad*, 598 F.3d at 1353. The Court should reject Teva's invitation to depart from the well-settled rule that a "'mere wish or plan' for obtaining the claimed invention is not adequate written description." *Juno*, 10 F.4th at 1335 (quoting *Centocor Ortho Biotech, Inc. v. Abbott Lab'ys*, 636 F.3d 1341, 1348 (Fed. Cir. 2011)).

Teva's arguments would also apply a lower disclosure requirement to a method claim reciting use of a functionally defined genus than for a composition

claim covering the genus itself. This would elevate form over substance, and this Court has already rejected this "semantic distinction without a difference." *Rochester*, 358 F.3d at 926 (citation omitted). In *Ariad*, for example, the Court explained that "the specification must demonstrate that Ariad possessed *the claimed methods* by *sufficiently disclosing molecules* capable of" performing the claimed function. 598 F.3d at 1355 (emphases added). Further, the Court stated that the patent "must adequately describe the claimed methods," "including *adequate description of the molecules*" that are necessary to perform the methods. *Id.* (emphasis added).

"Regardless [of] whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to that subject matter unless he can provide a [sufficient] description of the compound . . . ." *Rochester*, 358 F.3d at 926. Here, without disclosure of the genus of compounds recited in the claims, "it is impossible to practice the claimed method of treatment." *Id*. (citation omitted).

Finally, Teva's policy argument that patenting novel methods of treatment "may be impossible" is based on Teva's erroneous assertion that anti-CGRP antagonist antibodies were well known as of the priority date. Teva Br. 59. Teva argues that its claims are not to a novel genus but to "a novel method of using a well-known genus." Teva Br. 44. But, as detailed above, the genus of humanized anti-

CGRP antagonist antibodies recited in Teva's claims was anything but "well known." Indeed, Teva obtained (and argued the nonobviousness of) patents covering the very genus it now argues was "well-known." *Teva*, 8 F.4th at 1353. The fact that the genus was held invalid as obvious in no way suggests it was "well-known" such that Teva need not adequately disclose it. Barring Teva from broadly claiming the use of antibodies it did not disclose and failed to make is precisely what § 112 demands.

SUMMARY OF ARGUMENT IN SUPPORT OF LILLY'S CROSS-APPEAL

If the Court addresses Lilly's conditional cross-appeal, it should hold that the district court erred by declining to grant Lilly's motion for judgment as a matter of law that Teva is not entitled to any future lost profits. The speculative testimony by Teva's damages expert, Dr. Berkman, is too unreliable to support such an award. The district court thus also erred when it denied Lilly's earlier *Daubert* motion seeking to preclude Dr. Berkman's speculative testimony on future lost profits.

Dr. Berkman initially estimated $343.7 million in future lost profits over eight years, but just one year later, he was forced to revise his estimate down substantially to $158.3 million. Appx2503-2504 at 83:22-84:2; Appx2504-2505 at 84:25-85:3. This revision, which Dr. Berkman called "pretty dramatic," was necessary due to the unpredictability of the market for migraine drugs. Appx2505-2506 at 85:24-86:9. After Dr. Berkman did his initial analysis, new oral migraine drugs (gepants) entered

that market and drastically altered the market share, sales, and price of Teva's and Lilly's intravenously administered antibody drugs. For example, Dr. Berkman's decreased estimate corresponds to a 69% decrease in estimated lost sales in 2023 and an 82% decrease in estimated lost sales in 2025. Appx2505-2506 at 85:4-14, 85:24-86:10. As Lilly's damages expert, Dr. Vellturo, testified, the fact that Dr. Berkman needed to revise his estimate so substantially and so soon after he performed his initial analysis reflects the instability in the market and the unreliability of his methodology.

This revision did not resolve the speculative nature of Dr. Berkman's analysis. Indeed, he was unable to say whether his revised forecast could more reliably predict the turbulent market for migraine drugs and acknowledged that even the revised forecast could change by a similar magnitude within six to 12 months. Appx2507 at 87:14-24; Appx2509 at 89:7-10; Appx2511-2512 at 91:23-92:3. The migraine drug market is not a simple, two-supplier market, where evidence of pre- and post-infringement growth could be sufficient to establish any future lost profits. Rather, it is a complex, crowded market including several recent entrants who are continuing to change the market dynamics on which Dr. Berkman's estimates hinge. Thus, Dr. Berkman's revised forecast remains speculative and unreliable.

The jury heard no nonspeculative evidence regarding future lost profits. The Court should therefore reverse the district court's decision declining to grant Lilly's motion for judgment as a matter of law that Teva is not entitled to future lost profits.

ARGUMENT IN SUPPORT OF LILLY'S CROSS-APPEAL

XI. Standard of Review

"The burden of proving damages falls on the patentee." *Lucent Techs., Inc. v. Gateway, Inc.*, 580 F.3d 1301, 1324 (Fed. Cir. 2009). For a patentee to recover projected future losses, the "projections must not be speculative." *Oiness v. Walgreen Co.*, 88 F.3d 1025, 1031 (Fed. Cir. 1996). "The burden of proving future injury is commensurately greater than that for damages already incurred, for the future always harbors unknowns." *Id*. (quoting *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1581 (Fed. Cir. 1992)). The "factfinder must have before it 'such facts and circumstances to enable it to make an estimate of damage based upon judgment, not guesswork.'" *Id.* (quoting *Malloy v. Monahan*, 73 F.3d 1012, 1016 (10th Cir. 1996)). When the evidence demonstrates "uncertainties of future pricing, future competition, and future markets, in [a] fast-moving field," an award of future lost profits cannot be sustained. *Brooktree*, 977 F.2d at 1581.

XII. The District Court Erred in Upholding the Jury's Award of $49.8 Million in Speculative Future Lost Profits

Lilly's conditional cross-appeal involves the district court's denial of judgment as a matter of law that Teva was not entitled to speculative lost profits of

$49.8 million and earlier denial of Lilly's *Daubert* motion seeking to exclude Dr. Berkman's speculative testimony on future lost profits. Because the district court granted judgment as a matter of law of no written description or enablement, the Court only needs to reach Lilly's conditional cross-appeal if it does not affirm the judgment of invalidity on either written description or enablement.

The district court should have granted Lilly's motion for judgment as a matter of law because the record contains no nonspeculative evidence to support the jury's verdict that Teva is entitled to future lost profits. Attempts by Teva's damages expert, Dr. Berkman, to forecast future lost profits over eight years were not sufficiently reliable to predict the CGRP market even *one year* out. Indeed, after Dr. Berkman's initial estimate in 2021, he was forced to revise his analysis just a year later in 2022 to account for the market entry of new competitors (oral migraine drugs called gepants). These new drugs upended the market and dramatically decreased forecasts of Lilly's future sales. Appx2476-2477 at 56:19-57:4. Dr. Berkman's failure to account for this in his initial forecast demonstrates the uncertainty of this market and the speculative nature of any forecasts of Lilly's or Teva's future sales. Dr. Berkman's analysis violates this Court's requirement that future lost-profit "projections must not be speculative." *Oiness*, 88 F.3d at 1031.

Dr. Berkman revised his 2021 future lost-profits estimate of $343.7 million downward to $158.3 million when he revised his opinion in 2022. Appx2503-2504

at 83:22-84:2; Appx2504-2505 at 84:25-85:3. This represents a decrease of nearly $200 million and more than 50% in less than one year. Appx2504-2505 at 84:25-85:3. Dr. Berkman's future lost-profits estimate went down so substantially based on decreases in his estimates of Teva's lost sales and product price. Specifically, Dr. Berkman decreased his estimate of Teva's 2023 lost sales down by roughly 69% and Teva's 2025 lost sales down by roughly 82%. Appx2505-2506 at 85:4-14, 85:24-86:10. He also decreased his estimated price of Teva's AJOVY® product by more than 50% in 2023 and roughly 45% in 2025. Appx2506-2507 at 86:22-87:13.

The reason for the substantial decreases in Dr. Berkman's estimates was that his initial forecast failed to adequately account for the enormous effects of the oral gepants migraine drugs entering the market. As Dr. Vellturo testified, "you have a lot of new entrants coming in and you never know what impact they're going to have. It just creates a lot of uncertainty, and [Dr. Berkman's] numbers reflect that." Appx3907 at 129:11-17. Dr. Berkman himself acknowledged that "the market has become more crowded" with the introduction of the gepants, and with more competitors in the marketplace, the incumbents "have now all seen their market shares decline." Appx2476-2477 at 56:13-57:4.

As a result, Lilly's initial sales forecasts were revised downward. As Teva's witness Mr. Rainey acknowledged, "there were higher expectations for the CGRP [antibodies], and I think that the [recent] orals have had some impact, yes."

Appx1945 at 150:12-21. And these new competitor drugs are an ongoing source of uncertainty today. *See, e.g.*, Appx2675 at 23:6-14 (testifying that entry of oral CGRP drugs "changed the dynamic of the marketplace and continues to change it today"); Appx21295 (stating that, due to market entry of the gepants, "[m]argins will continue to decrease as payers look to drive down net cost").

The fact that Dr. Berkman revised his initial forecast in no way means that his new estimate is more reliable or that the relevant market is now more stable than it was when he did his initial analysis. Indeed, Dr. Berkman expressly conceded that he had no way of knowing whether his revised estimate would again need to change by a similar amount. He testified that "I can't commit to whether they'll go up or down if I did this again in a month or several months," and that the same was true 12 months in the future or three years in the future. Appx2507 at 87:14-24. Dr. Berkman similarly conceded that "a number of the key variables in this forecast are subject to variation over time. I can't be prescient to know what the right numbers are." Appx2511-2512 at 91:23-92:3; *see also* Appx2509 at 89:7-10 ("[T]hese numbers are going to change over time because we don't have perfect foresight.").

Further, even Dr. Berkman's revised estimate still used some of the same data from the 2021 Lilly strategic plan that formed the basis of his original estimate. After the predictions in that 2021 document proved to be wrong, Dr. Berkman revised his estimate using data from Lilly's 2022 strategic plan. But that document did not have

updated market share numbers. Thus, as Dr. Berkman acknowledged, his revised estimate continued using the market share numbers from Lilly's 2021 strategic plan, even though that document had already proven inaccurate. Appx2477 at 57:19-22; Appx2481 at 61:9-13. Dr. Berkman also lacked future costs for Teva's AJOVY® product from all of 2022, so his revised forecast estimated such costs by extrapolating from first-half-2022 data. Accordingly, even Dr. Berkman's revised forecast that sought to include data from 2022, following the introduction of the oral gepants drugs, still relied on data from a Lilly forecast that had already been proven to be extremely optimistic and out of sync with the current market.

The jury heard not only Dr. Berkman's acknowledgment that even his revised forecast reflected substantial uncertainty, but also Dr. Vellturo's testimony that Dr. Berkman's forecasts were not reliable. Dr. Vellturo testified that the large decrease in Dr. Berkman's estimate in just one year showed the speculative nature of Dr. Berkman's analysis, testifying that Dr. Berkman's numbers "were so far apart" that they could not be reliable. Appx3907 at 129:5-10. Dr. Vellturo testified, for example, that "if [Dr. Berkman's] results were reliable, he should have gotten numbers in the two reports that were at least somewhere near each other," but that the numbers were instead "wildly different." Appx3906-3907 at 128:20-129:4.

Dr. Berkman sought to downplay the "dramatic" change in his forecast, stating that "[f]orecasts are not certain" and "[f]uture forecasts always suffer from

uncertainty." Appx2507 at 87:21-24; Appx2502 at 82:17-19. He attributed the large decrease in his estimate to "forecasting error that comes about by perhaps a more sizable shift in the market than was anticipated in prior forecasts." Appx2506 at 86:17-21. But, while some amount uncertainty is inherent in any attempt to forecast the future, that is different from the substantial uncertainty shown in Dr. Berkman's forecasts.

Here, the magnitude of the changes between Dr. Berkman's two forecasts shows that his analysis was simply too speculative to warrant the jury's award of future lost-profits damages. The evidence here reflects precisely the kinds of "uncertainties of future pricing, future competition, and future markets, in [a] fast-moving field" that this Court has held precludes an award of future lost profits. *Brooktree*, 977 F.2d at 1581.

The district court also erred by allowing the jury to hear Dr. Berkman's unreliable testimony and decide whether his calculations "were too speculative" to be entitled to any weight. Appx58. The court reasoned that, because Dr. Berkman's calculations were based on Lilly's projections, the jury was free to weigh whether his projections were "overly speculative in light of market dynamics (e.g., a market with more than two participants)." Appx57-58. This was improper.

It is the role of the court to determine whether an expert's testimony is sufficiently reliable to be admitted. *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S.

579, 589 (1993); *see also MicroStrategy Inc. v. Bus. Objects, S.A.*, 429 F.3d 1344, 1355 (Fed. Cir. 2005). District courts, as "gatekeepers," must "ensure that all expert testimony is rooted in firm scientific or technical ground. *Power Integrations, Inc. v. Fairchild Semiconductor Int'l, Inc.*, 711 F.3d 1348, 1373 (Fed. Cir. 2013), *abrogated on other grounds by Brumfield v. IBG LLC*, 97 F.4th 854 (Fed. Cir. 2024). Where, as here, an expert's opinion is "derived from unreliable data and built on speculation," it "frustrates a primary goal of expert testimony" by "muddl[ing] the jury's fact-finding with unreliability and speculation." *Id.* at 1374. Dr. Berkman's testimony was based on unreliable data in a volatile marketplace, as he himself essentially conceded when he was forced to revise his initial forecast so substantially shortly after he rendered it and was unable to say that his revised forecast would be any more reliable. Appx2507 at 87:14-24; Appx2509 at 89:7-10; Appx2511-2512 at 91:23-92:3. The district court therefore should have excluded his testimony rather than allow the jury to take on the gatekeeper role and determine whether it was "overly speculative."

The district court sought to distinguish the evidence here from the facts in *Oiness*, Appx56-57, but that case further shows that the court erred in declining to grant judgment as a matter of law that the jury's verdict on future lost profits lacked any nonspeculative evidence to support it. In *Oiness*, the patentee failed to establish reliable sales-growth-rate estimates because the expert based his analysis on an

"initial burst in product sales" to forecast future sales. 88 F.3d at 1031. This Court rejected the expert's erroneous premise that initial sales support an extrapolation of demand over future years. *Id.*

That is precisely what Dr. Berkman did here. His 2021 forecast relied on what Teva's witness called "higher expectations for the CGRP" antibody drugs. Appx1945 at 150:12-21. This initial forecast, though based on "actual sales data" and "Lilly's projections," undisputedly failed to reliably predict the market, as evidenced by Dr. Berkman's substantially lower revised forecast in 2022. But even after Dr. Berkman revised his forecast to try to account for market entry of the gepants, he was unable to say whether the revised forecast was any more reliable than the first. Appx2507 at 87:14-24. The district court therefore was wrong when it concluded that reliance on sales data and Lilly's projections somehow distinguished this case from *Oiness*. Appx56-57.

The district court was also wrong when it sought to liken this case to *Lam, Inc. v. Johns-Manville Corp.*, 718 F.2d 1056, 1068 (Fed. Cir. 1983). Appx57-58. There, the Court affirmed a damages award because the two-supplier nature of the market meant that evidence of pre- and post-infringement growth rates were sufficient to "illustrate[] the proven detriments suffered by the patent owner" and were not "mere speculation." *Lam*, 718 F.2d at 1068.

Here, by contrast, the entry of additional competitors to the market was precisely the reason that Dr. Berkman's initial forecast had to be revised so substantially. The district court therefore erred by concluding that Dr. Berkman's reliance on initial sales data in a complex and changing market, which is nothing like the two-competitor market in *Lam*, nonetheless had the same level of reliability. Appx57-58.

The fact that Dr. Berkman's 2021 forecast was so "wildly different" from his revised 2022 forecast reveals that the methodology that he used in *both forecasts* is unreliable and speculative. As Dr. Berkman himself admitted, he had no ability to say whether his second attempt at forecasting future sales and pricing would be any less inaccurate than his first effort. Appx2507 at 87:14-24; Appx2511-2512 at 91:23-92:3. This is the type of uncertainty that the Court in *Oiness* and *Brooktree* concluded should bar an award of future lost profits.

Given the lack of nonspeculative evidence, if the Court reaches this cross-appeal issue, it should reverse the district court's denial of judgment as a matter of law on future lost-profit damages. The jury should never have heard Dr. Berkman's testimony because it was so speculative as to be unreliable, and therefore should have been precluded under *Daubert*.

CONCLUSION

For the reasons above, Lilly respectfully asks the Court to affirm the district court's grant of judgment as a matter of law of no written description and no enablement. If the Court reaches Lilly's conditional cross-appeal, it should reverse the district court's denial of Lilly's motion for judgment as a matter of law as to the jury's award of speculative future lost profits.

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Respectfully submitted,

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

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