

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

FORTE BIOSCIENCES, INC.,
Petitioner,

v.

UNIVERSITY OF MASSACHUSETTS,
Patent Owner.

Case No. PGR2023-00014
Patent No. 11,278,505

PETITIONER'S REPLY TO PATENT OWNER RESPONSE

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I. INTRODUCTION

At least two undisputable points amply demonstrate the challenged claims unpatentable: (1) the claims cover several massive genera; and (2) the specification employs only a single species that is not representative of them.

The claimed genera (any inhibitor of IL-15 or the IL-15 receptor) are, indeed, massive. Paper 10 (“ID”), 19, 24-25. They encompass any kind of inhibition of IL-15 or any subunit of the multiple versions of the IL-15 receptor, without regard to structure employed, epitope bound, extent of inhibition, nature of the signaling inhibited, or even any physical interaction with IL-15 or the IL-15 receptors. Even though the results of inhibiting one receptor subunit (e.g., γ) are different from inhibiting others (β , IL-15R α) or IL-15, and different inhibitors of even the same target (β) yield different effects in unpredictable ways, the claims encompass them all.

The second key point presents a stark contrast to the first. The broad claims depend on the most anemic disclosure. A single murine antibody of undisclosed sequence, undisclosed structure, undisclosed epitope target, undisclosed extent of inhibition, and unknown nature of inhibited signaling was employed in the only inhibitory working example in the '505 patent. The Board correctly found these deficiencies were critical. ID, 19, 25-26. Despite submitting a nearly 200-page

declaration and more than 100 exhibits, the POR disputes none of what is missing from the specification. The black-box specification is irremediable.

Unable to rewrite its specification, PO attempts to rewrite the law and the state of the art. First, PO argues the claims have §112 support because they recite no meaningful structural limitations. But the law requires exactly the opposite. The great breadth of the claims demands greater disclosure, not less. As the Board correctly found at institution, defining the claims functionally without limitation as to structure, epitope, type or extent of inhibition does not excuse PO from disclosing the details required for possession and enablement of the full breadth of the claims. ID, 18-20, 24-26.

Second, PO mischaracterizes the state of the art. PO argues incorrectly that the broad claimed genera were well established as having class-wide efficacy for treating autoimmune diseases. But the evidence does not support PO's assertion. EX1047, ¶¶9-12, 54, 14-42. To the contrary, even molecules shown to inhibit IL-15 or the IL-15 receptor in vitro lacked the desired efficacy when administered in vivo, especially in humans. The complexity of the immune system meant there was no accepted class and, after decades of research, even the most advanced candidates failed to show efficacy. The earlier references PO points to discuss, at best, potential therapeutic avenues for future research that remained unrealized at

the critical date more than a decade later. PO's attempts to mischaracterize Forte statements made *years after the critical date* cannot rewrite this history.

II. THE CLAIMS LACK §112 SUPPORT

A. The Claimed Genera Are Indisputably Broad and Unpredictable.

The Board properly found at institution that the claims are broad. ID, 19 (“all other compounds that can inhibit IL-15 or the IL-15 receptor”), 24-25 (“broad ‘genus claims’”), 25 (no “structural requirement”); *see also* Pet., 1-2, 14, 23-26, 51-52, 54-58. PO does not contest the broad scope or identify any structural limitations. ID, 25 (“encompasses a ‘large variety and number of species that ‘might be used to achieve’” vitiligo treatment. Prelim. Resp. 25”); Paper 19 (“POR”), 39 (only limitation is vitiligo). Instead, trial confirmed the scope is enormously broad, and the properties, functionality, and operability of implicated molecules varies significantly and unpredictably across that breadth.

1. Inhibiting Any of Four Targets in Any Degree.

The claims encompass every inhibitor of IL-15, IL-15R α , the β -subunit (CD122, shared with IL-2), or the γ -subunit (CD132, shared among 6 cytokines), and do not even require physical or specific interaction with the claimed targets. Pet., 2, 14, 25; EX1002, ¶¶29-33, 65, 68, 86-87. PO does not dispute this. POR, 9-11; EX1046, 170:25-173:2, 173:3-22, 174:13-175:1, 176:3-11; EX1047, ¶58. The genera of inhibition monopolized by these claims are thus extremely broad.

This great breadth is exacerbated by the absence of any limitation for the extent of inhibition. EX1047, ¶51. The claims encompass using molecules that inhibit IL-15 signaling by 1%. EX1046, 245:8-246:21. The claims thus encompass innumerable distinct inhibitory approaches, including many not yet conceived. Pet., 45-46, 56-57; EX1002, ¶91.

2. Inhibiting Diverse Versions of the IL-15 Receptor and IL-15 Signaling.

The claims also encompass inhibition of any one of the various types of IL-15 signaling and inhibition of any of the various versions of the receptor, which implicate different results. *See* Pet., 11-12, 26; EX1002, ¶¶54-55, 37, 72-77, 86. The IL-15 dimeric receptor can dispense entirely with IL-15R α , employ IL-15R α supplied by the same cell (*cis* signaling), employ IL-15R α supplied by a different cell (*trans* signaling), or employ soluble IL-15R α . EX1046, 162:12-163:25, 165:11-16. EX1047, ¶58. The claims thus encompass more than a dozen different genera of inhibition. EX1047, ¶61; EX1046, 219:24-222:8. One alone is not representative.

As Dr. Plott explains, “the effects of a given molecule varied widely depending on its target (e.g., IL-15 vs. IL-15R α vs. IL-15R β vs. IL-15R γ), the variety of IL-15 receptor(s) implicated, the location (i.e., epitope) where the molecule interacts with a given target, and the nature of the specific molecule being used.” EX1047, ¶10. For example, inhibiting IL-15R γ /CD132 can inhibit six

different cytokine pathways and implicates severe autoimmunity, while inhibiting IL-15R β /CD122 can inhibit two different cytokine pathways that have differential effects on different cells in the body. Pet., 28-29; EX1002, ¶¶65-69, 86. Both generally operate very differently from inhibiting the other two claimed targets (IL-15 and IL-15R α). Pet., 28-36; EX1002, ¶¶70-81. PO's expert disputes none of this. EX1047, ¶61; EX1046, 96:18-97:8 (six cytokines), 95:21-24 (immunostimulatory IL-4), 97:22-98:1 (IL-4 initiates JAK3), 98:2-7 (blocking γ can inhibit IL-4-induced JAK3), 222:9-25 (absence of CD132 causes SCID); *see also* EX1047, ¶18 ("highly disparate effects"); EX1046, 52:1-23, 63:23-65:13; EX1040, 2 (inhibiting receptor not representative of inhibiting IL-15); EX1048, 3 (similar).

Dr. Damsky illustrated during deposition that the effects of an implicated molecule vary with which subunit(s) are affected and how. EX1047, ¶¶59-60. EX1046, 58:5-60:13, 63:2-9, 91:25-93:10, 212:17-213:3, 214:7-215:4, 216:18-217:3 (inhibit CD122 to inhibit JAK1/STAT1; inhibit CD132 to inhibit JAK3/STAT5; unknown whether blocking just one would impair T cell survival). Even inhibitors of IL-15 or IL-15R α encompass diverse forms of inhibition having differential effects. EX1047, ¶59, ¶¶25-26 (one anti-IL-15 mAb blocked both *cis*- and *trans*-presentation but also enhanced certain IL-15 "reverse" signaling), ¶¶35-

36 (one IL-15 receptor mAb was unable to block both *cis*-presentation and *trans*-presentation).

Operational differences between IL-15-specific inhibitors also resulted in differential effects. EX1047, ¶¶21, 23; EX1018, Abstract. Some inhibited TNF α . EX1047, ¶¶21-23; EX1018, Abstract, 1576, 1579. Some inhibited angiogenesis. EX1047, ¶¶40 (discussing EX2013, 4:1-8; EX2014, 4:9-15; EX2015, ¶[0022]; EX2025, 4:34-5:2). Some operate primarily to inhibit soluble IL-15 rather than the membrane-bound IL-15/IL-15R α complexes that are assembled within the cell. EX1047, ¶71; EX1046, 166:21-24, 168:25-169:5; EX1011, 1:67-2:4 (“transported to the cell surface as a complex”). EX1046, 207:23-208:13, 208:15-209:22 (binding may occur before transport to cell surface). Soluble IL-15 can signal through $\beta\gamma$ (dimeric)-receptor without binding to IL-15R α . EX1047, ¶71; EX2005, ¶134. It also can associate with soluble IL-15R α , which can *trans*-present IL-15 to $\beta\gamma$ -receptors on immune cells. EX1047, ¶71; EX2005, ¶116; EX1046, 210:4-17. Molecules that block IL-15/IL-15R α binding thus operate differently, and produce differential effects, from other implicated molecules. EX1047, ¶71; EX1046, 210:24-211:6; EX1047, ¶¶21, 23 (404E4 vs HuMax-IL-15 anti-IL-15 antibodies).

Because of the complicated interplay of the multiple receptor versions, molecules identified by the patent, PO, or Dr. Damsky *as inhibitors* also were capable of *enhancing* certain forms of IL-15 signaling. For example, HuMax-IL-

IL-15 inhibited IL-15 signaling in vitro but *stimulated IL-15* “reverse signaling” when used in vivo in humans. EX1047, ¶¶25-26 (EX2013, 2:10-18; EX2014, 2:12-20; EX2015, ¶[0003]; EX2025, 2:10-18; EX2078, 267). Soluble IL-15R α molecules that can inhibit IL-15 signaling also form complexes with IL-15 and *enhance IL-15 signaling* by improving half-life and *trans*-presenting IL-15 to $\beta\gamma$ -receptors. EX1047, ¶30; EX1046, 256:15-258:4, 258:9-16; EX2005, ¶163; EX2079, 1, 5-6, 8. Additional anti-IL-15 antibodies inhibited IL-15 signaling in vitro but enhanced IL-15 signaling in vivo, including by *trans*-presenting IL-15 to $\beta\gamma$ -receptors. EX1047, ¶¶29-30; EX1054, Abstract. The unpredictability across the breadth of the massive claimed genera was significant.

It was also known that implicated molecules¹ will have different effects depending on where they bind a particular target. EX1047, ¶¶19-23; EX1018, Abstract, 1575-77, 1579; EX1046, 207:11-14, 203:3-10, 207:15-21. Some anti-CD122 antibodies thus do not block IL-15 signaling at all, whereas others block only *cis*-presentation, only *trans*-presentation, or both. EX1047 ¶52 (citing

¹ To be clear, there was no recognized, discrete class of inhibitors of IL-15 or the IL-15 receptor. *See* Section II.A.4 *infra*. This Reply may refer to Dr. Damsky’s identification of molecules as inhibitors for rebuttal purposes; this is not a concession of any kind.

EX1011, 2:35-48, 2:61-3:2, 9:27-38; EX1012, 481-82), ¶¶35-36 (Mikβ1 blocks only *trans*-presentation).

Some implicated molecules may inhibit only IL-15 signaling whereas others may inhibit both IL-15 and IL-2 signaling or just IL-2 signaling. Pet., 55; EX1002, ¶86; EX1047, ¶36 (Hu-Mikβ1 inhibits both), ¶78 (HuABC2 and ABC101 antibodies inhibit both); EX2005, ¶¶155-56 (asserting ChMBC7 selectively inhibits IL-15 (and not IL-2)). Anti-CD122 antibodies that inhibit IL-2 signaling may decrease proliferation of regulatory T cells, though this confounding variable was unexamined in the Harris mouse model where the native immune system (e.g., CD4⁺ Treg cells) had been replaced with overwhelming amounts of CD8⁺ T cells. EX1047, ¶45; EX1006, 1870; EX1046, 169:25-170:8 (CD8⁺ T cells not Treg cells). Accordingly, even for a particular target (IL-15, α , β , γ), there was no expectation of class-wide efficacy. EX1047, ¶¶10, 50.

In summary, the effects of using the implicated molecules were complicated and unpredictable. *See, e.g.*, EX1047, ¶¶54-55; EX2015, ¶[0020] (“immune mediators” present a “complex network”); EX2025, 4:5-24 (similar); EX2078, 267 (“complex immunomodulatory function of these cells”); EX1046, 94:7-8 (“it is more complicated than that”), 121:7-16 (“I think it is complicated...I think it’s complicated.”), 158:16-23 (whether tofacitinib is within claim 1 “is really

complicated”), 118:25-119:5 (“I wouldn’t say that the mechanism is known to be that simple”), 209:1-12 (blocking IL-15 from α , “It is not as simple as that”).

Because this was so complicated and unpredictable, even *years after the critical date*,² attempting to determine whether a particular molecule (e.g., an anti-CD122 antibody) was effective for treating vitiligo was an uncertain and burdensome trial-and-error process. EX1047, ¶11. Indeed, Dr. Damsky admitted in 2021 that researchers were only then conducting a proof-of-concept study for IL-15 blockade in patients with vitiligo using the anti-CD122 antibody Auremolimab, and all he could do was keep his “fingers crossed” that it might turn “off that memory response” and “maybe” thereby provide long-lasting treatment for vitiligo “if” it works. EX1046, 88:17-22, 232:1-235:7, 235:14-236:9; EX2005, ¶106; *see also* EX1048, 14. (Dr. Harris in 2020: “this type of research takes a lot of time and resources”).

3. Inhibiting Upstream or Downstream.

The claims are broader than just physical interaction with IL-15 or the IL-15 receptor. For example, claim 2 recites nucleic acids that target nucleic acids coding

² April 2017 was the date of “invention.” EX2005, ¶¶94, 110-11, 141; EX1046, 12:7-9.

for IL-15 or IL-15 receptor peptides, and claim 1 is even broader and does not require targeting nucleic acids coding for IL-15 or the IL-15 receptor. EX1046, 174:13-175:1, 176:3-11; EX1047, ¶¶58. In either scenario, the molecular interaction takes place upstream of the cytokine/receptor.

The claims also encompass downstream inhibition. EX1047, ¶¶65-70; EX1046, 156:9-17, 161:14-162:4 (anything that inhibits a biological effect of IL-15 or its receptor, including downstream signaling). Dr. Damsky calls them “inhibitor[s] of IL-15-induced cellular responses.” EX2005, ¶¶71; EX1047, ¶¶69. Among the downstream inhibitors of IL-15 signaling are JAK inhibitors, used in the prior art for vitiligo treatment. EX1047, ¶¶65-67; EX1046, 93:11-23, 95:1-20 (JAK/STAT downstream of IL-15), 156:19-21 (JAK is a biological effect of IL-15), 157:18-21 (not ruling out ruxolitinib as an inhibitor of IL-15), 158:1-159:6 (ruxolitinib inhibits JAK1 downstream of IL-15), 158:12-160:20 (tofacitinib inhibits JAK1/3 downstream of IL-15); EX1032; EX1033. The claims are so broad that they encompass them.

The 20 molecules relied upon by PO include those that do not interact with IL-15 or its receptor, but instead inhibit microbial activity, IL-2, IL-17, Bcl-xL, or MDM2. EX1047, ¶¶68-70; EX1001, 7:40-45 (cefazolin; Y-320), 7:60-64 (Ro26-4550, SP4206, ABT-737, Nutlin-2 compound 3); EX1046, 259:7-261:19 (ABT-737 inhibits BC1-XL; Nutlin-2 inhibits MDM2); EX2022, 36 (Ro26-4550 inhibits

IL-2:IL-2R α), 41 (SP4206 and compound 3 are IL-2 antagonists), 46-47 (ABT-737/Nutlin-2); EX1047, ¶70 (Y-320 inhibits IL-17 production by CD4⁺ Treg cells); EX1058, Title, Abstract; EX2016, 292 (Y-320 inhibits “several inflammatory mediators including IL-6, IL-8,” and TNF α); EX1046, 98:9-18, 95:10-20 (IL-15 can activate IL-17). The claims are thus so broad that they encompass upstream and downstream inhibitors of any of the many differential effects of IL-15.

4. Not A Recognized Genus

PO argues the claim breadth should be ignored because the claims allegedly recite a “well-known” and discrete class of molecules with class-wide efficacy. *E.g.*, POR, 2, 27-28, 36, 39, 46-47, 51, 56. But trial rebutted this argument. First, Dr. Damsky admitted he cannot recognize from the structure of a compound whether it is an inhibitor of IL-15 or the IL-15 receptor and he wasn’t confident whether a pharmaceutical scientist could either. EX1047, ¶85; EX1046, 236:12-24; EX1047, ¶¶56, 80-85. He repeatedly confused reagents as inhibitors and counted the same inhibitors more than once. EX1047, ¶¶56, 80-85 (discussing EX2005, ¶¶70, 81, Appendix A at pgs. 4-10; EX2024, 19:15-16, 22:8, 24:19-25:15, 28:15-29:4.

Second, Dr. Damsky testified repeatedly that the available assays were inadequate to identify conclusively whether implicated molecules were

encompassed by the claims. EX1046, 189:4-19, 192:6-15 (whether IL-15 binding inhibitor is within the claim scope “would depend on the specific compound”); *see also* EX1046, 193:18-195:18 (“sometimes there is just a one-off example that doesn’t reflect”); 189:20-191:13 (one possibility), 191:15-192:4 (not definitive); EX1047, ¶63. Dr. Damsky initially identified proliferation assay as a second analytic approach, but ultimately concluded that assay also would not be conclusive. EX1046, 195:20-196:22, 181:8-186:6; EX1047, ¶64. He eventually admitted there is no “absolute standard” for identifying whether an implicated molecule is encompassed by the claims and that he could not name anything specific to conclusively make that determination. EX1046, 198:21-199:21, 197:12-198:19, 200:1-8. EX1047, ¶64. Though the patent expressly identifies the antibiotic cefazolin and Y-320 (EX1001, 7:40-45), Dr. Damsky was unsure whether cefazolin satisfies the claims and left Y-320 off his list of inhibitors. EX1047, ¶69; EX1046, 253:9-255:11; EX2005, ¶¶71, 99. Dr. Damsky’s testimony undermines PO’s assertions of a well-known or discrete genus.

B. The Specification’s Deficiencies Are Undisputed and Irremediable

1. The Black Box Disclosure Is Too Limited.

Unlike the broad claims, the specification’s sole inhibition working example is very narrow: using ChMBC7 in Harris mice. Pet., 57-58; EX1002, ¶85. The specification never evaluated any other antibody, small molecule, fusion protein,

nucleic acid, or non-antibody peptide inhibitor. EX2007, 93:16-97:25 (Dr. Abbas: “we have no idea whether they’ll have the same effects or not”; small molecules recited in patent “inhibit downstream signaling pathways”). The specification never evaluated any kind of IL-15-specific inhibition or any inhibitor of CD132/γ.

At institution, the Board properly rejected PO’s arguments that naked recitation of twenty molecules somehow conveyed possession or enablement of the full breadth of these broad claims. The Board explained that PO’s fatal written description problem is *deficiencies in the specification’s disclosure*, which fails to demonstrate its sole inhibitory working example is representative of the entire breadth. Reciting additional molecules was inadequate because: (1) the specification failed to show that ChMBC7-inhibition was representative of all claimed inhibition; and (2) the specification failed to demonstrate what structural features are necessary and sufficient to perform the claimed method. ID, 19.

The Board similarly explained that the existence of additional inhibitors was inadequate to demonstrate enablement under §112 because the specification fails to disclose:

- (1) Any structural requirement for the claimed inhibitors;
- (2) The sequence or structure that corresponds to the exemplary inhibitor;
- (3) The binding site for the exemplary inhibitor;
- (4) How the way the exemplary inhibitor binds to/blocks IL-15 receptors is representative of the remaining inhibitors;

(5) How the exemplary antibody targets only IL-15 signaling.

ID, 25-26. The POR disputes none of these inadequacies.

Instead, trial has established conclusively the irremediable inadequacies of the specification. EX1047, ¶12. Dr. Damsky admitted ChMBC7 was the only inhibitor tested, but the patent does not disclose its primary sequence, secondary structure, or binding epitope. EX1047, ¶43; EX1046, 224:18-225:12, 225:25-226:8, 230:3-5, 230:6-13. It never discloses what type of inhibition ChMBC7 employed (*cis* only, *trans* only, or both; dimeric; IL-2 only, IL-15 only, both; etc.). EX1047, ¶52; EX1011, 2:35-48, 2:61-3:2, 9:27-38; *see also* EX1012, 481-82. It provides no direction regarding the extent of inhibition. EX1047, ¶51. The specification is thus a black box that leaves “the reader to guess through trial and error which molecules might operate similarly to ChMBC7 and which do not.” EX1047, ¶53. This is inadequate under §112. ID, 14-16, 18-27.

2. The Appendix Highlights the Specification’s Inadequacies.

Because the specification essentially discloses ChMBC7 as a black box, enumerating 20 molecules that inhibit IL-2, IL-17, IL-15, or other pathways does nothing to remedy the lack of §112 support. Dr. Damsky’s attempts to identify hundreds more not mentioned in the specification similarly fails. Indeed, the Appendix merely demonstrates how limited the specification is. EX1047, ¶¶72-79. It fails to describe the vast majority of molecules in the Appendix. EX1047, ¶73

(~26 of 32 references not incorporated); EX1046, 261:22-262:2, 267:1-7; EX1047, ¶84 n.3. The Appendix identifies entire inhibition sub-classes for which it exclusively relies on references *not cited* in the patent. EX1047, ¶¶74-76; EX1059. It cites new references because the specification's recitation was not representative. EX1047, ¶77 (IL-15R α -binding peptides not representative (discussing EX2005, ¶71; EX2019, Abstract)), ¶78 (CD122 antibodies that inhibit *trans*-presentation of IL-15 and IL-2 signaling not representative (discussing EX2005, ¶67, Appendix A at 10; EX1011, 21:54-23:15 (Examples 2-3); EX2005, ¶¶155-56)). Post-hoc heaps of compounds the specification did not propose do not remedy the specification's deficiencies. EX1047, ¶79.

3. The Harris Mice Are Not Representative of Vitiligo.

The specification never evaluated the effects of any inhibitor of IL-15 or IL-15 receptor in natural or spontaneous vitiligo and the Harris model is too narrow a subset to represent the disease as a whole. Pet., 2-4, 39-41; EX1002, ¶¶35-36. By relying on a small, contrived subset to the exclusion of the condition of main concern, PO inverts the holding of *United Therapeutics Corp. v. Liquidia Techs.* 74 F.4th 1360, 1370-71 (Fed. Cir. 2023) (small subsets of patients do not represent treatment genus).

PO argues that mouse studies play a role in drug development. POR, 8-9, 48, 72-73. But PO misses the point. This particular mouse model is not representative,

but instead produces vitiligo lesions using a simplified pathogenesis. Because the immune system of the mice is depleted by radiation and replaced with melanocyte-targeting, activated CD8+ T cells, the cause of the lesions is straightforward and predictable. EX1002, ¶¶35-36 (“Such contrived mice models are useful for exploring the mechanisms of injury...but are not representative of the complexity of the natural disease.”); EX1001, 31:19-23; EX2007, 90:1-91:8, 91:23-93:14 (Harris mice not representative because their endogenous immune system is “significantly eliminated” and replaced with activated T cells having “a single specificity” for melanocytes); EX2007, 33:9-36:9 (Harris mouse model “does not recapitulate how [depigmentation] was achieved” in natural vitiligo and is instead “completely different from what you would expect to see in the human”); EX2007, 38:2-8 (“It’s improper to extrapolate from this [Harris] mouse model to the human situation—to the human disease.”); EX2009, 8-11. The replacement of the natural immune system (including CD4+ T cells) in the Harris mice with overwhelming concentrations of CD8+ T cells makes the working example unrepresentative of using any CD122 antibody in a human having other immune cells (e.g., CD4+ Treg cells) that express CD122. EX1047, ¶45; EX1006, 1870; EX1046, 169:25-170:8 (CD8+ T Cells are not Treg cells); EX1047, ¶12.

The mismatch between the Harris mice and vitiligo generally was only reinforced during trial. EX1047, ¶¶46-53. The literature identified multiple causes

of vitiligo, explained there was no singularly true mechanism behind the disease, and its pathogenesis was elusive. EX1047, ¶47; EX1057, Abstract, 153, 169. Among these causes was oxidative stress, neural interactions, dysregulations involving up to seven or more immune mediators, and melanocytorrhagy. EX1047, ¶48; EX1057, 157-160, 162-69; EX1046, 223:2-25 (claim encompasses all types of vitiligo, including segmental, chemically-induced, oxidative stress-induced). Whether and how a given molecule would treat the disease thus depended significantly on its cause(s). EX1047, ¶48. The specification fails to demonstrate the simplified form of vitiligo in the Harris mice is representative of vitiligo generally. EX1047, ¶¶12, 50.

C. PO's Attempts to Rewrite the Law Should Be Rejected

Because it cannot rewrite its specification and chose not to narrow its claims, PO instead attempts to rewrite the law. Specifically, PO turns §112 law on its head by arguing that the massive claim breadth (with no structural limitations and various claimed targets) somehow reduces the amount of disclosure required to provide §112 support. POR, 39-43, 52-56. But the law requires exactly the opposite. The more a party claims the more it must support under §112. ID, 25, 19. For written description, the specification must reasonably convey that *the inventors* were in possession of the *entire breadth* of the claim. For enablement, the specification must convey *to a POSA* how to make and use that *entire claim*

breadth without undue experimentation. Avoiding recitations of structure does not lower the bar under §112. Binding precedent (including *Rochester* and *Amgen*) confirm the claims are unpatentable, just as the Board found at institution. ID, 18-21, 24-27.

D. PO's Attempts to Rewrite History Should Be Rejected.

Unable to rewrite the law, PO is left to try to rewrite history, arguing that class-wide efficacy for treating immune diseases was established at the critical date. But the evidence does not support PO's arguments. EX1047, ¶10.

PO points to aspirational statements made years or more than a decade before the critical date that targeting IL-15 "might" be able to treat certain autoimmune diseases. POR, 6; EX2005, ¶65; EX1016, 600. But optimistic plans to test individual inhibitors for efficacy, cited by PO, do not assert class-wide efficacy had been established. EX1047, ¶19. Even Dr. Damsky admitted these references merely "suggest[]" IL-15 inhibition "*could* have a therapeutic *potential*." EX2005, ¶82 (quoting EX2019, 2:1-6; citing EX2028, 1:18-29; EX2029, [0009]); EX2005, ¶53 (gene overexpression does "*not mean* that inhibiting it will result in improvement of the disease"), ¶64 (arguing that "*potential clinical utility* as a therapeutic target have been extensively studied" (citing EX2010, 1, 10-13 (2001 reference); EX1022, 1 (2004 reference))). As Dr. Plott explains, "the references at best teach that there was interest in identifying inhibitors of IL-15 or the IL-15

receptor to potentially treat autoimmune diseases but that their ability to actually address autoimmune disease was highly variable and unpredictable.” EX1047, ¶42. Indeed, the hope for an efficacious inhibitor remained unfulfilled at the critical date because of repeated failure and great unpredictability, despite Dr. Damsky’s mischaracterizations of the references. EX1047, ¶¶14-15.

Dr. Damsky’s mischaracterizations of the references begin with the basic and advance far beyond. In one example, he couldn’t keep straight when the references were discussing anti-IL-15 antibodies vs. anti-CD122 antibody. EX1047, ¶¶16-17, 20; EX2005, ¶65; EX1016, 600; EX1018, 1571-72, 1574; EX1049, Abstract. In another example, Dr. Damsky argues that targeting IL-15 “always resulted in the alleviation of the disease symptoms.” EX2005, ¶82 (quoting EX2025, 1-2). But the reference really teaches that the tested compounds alleviated disease symptoms in specific animal models, “but none of them has been approved for clinical use so far.” EX2013, 1:31-2:18; EX2014, 1:30-2-20; EX2015, ¶[0003]; EX2025, 1:31-2:18; *see also* EX2013, 3:32-37; EX2014, 4:4-8; EX2015, ¶[0018]; EX2025, 3:33-4:2 (“To date the efficacy of these new compounds has not been proved in clinical studies.”); EX1047, ¶¶31. Dr. Damsky thus reads these references glaringly out of context.

These same references teach that the clinical trials of HuMax-IL-15 were the most advanced attempting therapeutic IL-15 blockage, but that it was ineffective in

vivo because it unpredictably *enhanced* IL-15-stimulated inflammatory responses. EX1047, ¶¶24-26; EX2013, 2:10-18; EX2014, 2:12-20; EX2015, ¶[0003]; EX2025, 2:10-18; EX2078, 267. Though HuMax-IL-15/AMG714 was well tolerated and worked in vitro, several clinical trials for treating human autoimmune diseases were abandoned, and it had not been approved to treat any autoimmune disease before the critical date. EX1047, ¶¶27-28; EX1049, Abstract (“no significant effects on T lymphocyte subset and natural killer cell number”); EX1050-EX1053. IL-15 inhibition not only lacked PO’s asserted class-wide efficacy; it failed. EX1047, ¶28.

Other inhibitors of IL-15 or the IL-15 receptor produced the opposite of the intended effect in vivo. EX1047, ¶¶29-30. For example, an anti-IL-15 antibody that inhibited IL-15 signaling in vitro ultimately served as a substitute for endogenous IL-15R α and *facilitated* IL-15 signaling in vivo. EX1047, ¶¶29-30; EX1054, Abstract. Soluble IL-15R α also facilitated IL-15 signaling in vivo despite inhibiting it in vitro. EX1047, ¶30; EX2005, ¶71 (citing EX2017), Appendix A at pg. 41-42; EX2005, ¶163 (increased vivo half-life and efficacy); EX2079, 1, 5-6, 8. The CD122 antibody Dr. Damsky relied upon as being involved in a clinical study failed to demonstrate efficacy. EX1047, ¶¶32-36; EX1012, 477 (Mik β 1 blockade of IL-15 signaling showed “no efficacy”); EX1012, Abstract, 479 & Fig. 2 (Hu-Mik β 1 was *unable* to inhibit proliferation of cells expressing the trimeric

IL-15 receptor); EX1012, 477-79 & Figs. 1-2 (“no major clinical responses were observed” with Hu-Mik β 1 treatment); EX1012, 482 (in vitro effects “not sufficient to yield a meaningful reduction in the number of circulating leukemic cells”). Subsequent studies also failed. EX1047, ¶37; EX1055; EX1012, 483. Hu-Mik β 1’s ability to block IL-15 action still has not been shown to translate into an effective therapy for humans for any autoimmune disease. EX1047, ¶37. Repeated failures undermine PO’s assertion of class-wide efficacy.

The literature teaches that new inhibitors with different effects were sought *because* the earlier molecules failed to satisfy in vivo needs. EX1047, ¶39; EX2024, 28:15-29:7. EX1047, ¶¶40-41; EX2013, 4:1-8; EX2014, 4:9-15; EX2015, ¶[0022]; EX2025, 4:34-5:2. But these new molecules also had no demonstrated efficacy in vivo. EX1046, 243:4-12, 249:5-10, 252:6-25, 253:1-8, 256:1-9 (no in vivo testing). Dr. Damsky testified that the PBMC’s used for the in vitro tests might or might not reliably predict their effect on CD8+ T cells. EX1047, ¶41; EX1046, 243:11-244:11. PO’s assertions of class wide efficacy must therefore be rejected.

PO repeatedly invokes post-critical date statements by Forte regarding Forte’s specific antibody. POR, 4, 33-34, 58, 67, 72-73. Forte’s statements that further study of FB-102 is justified by the specific data known to Forte *after the critical date* do not mean there is class-wide efficacy for the challenged claims.

Forte announced advancement into clinic for GvHD based on post-critical date, head-to-head comparisons with FDA-approved ruxolitinib in acute and chronic GvHD mice, as validated by post-critical date ruxolitinib clinical studies of GvHD in humans. EX2009, 3-6 (90% survival on FB-102 vs. 0% on vehicle control and 60% on ruxolitinib). Based on FB-102's very powerful results and other post-critical date information and pre-clinical data, Forte disclosed that there was "therapeutic potential" in other autoimmune diseases. EX2009, 6-12. None of these statements assert class-wide efficacy for the challenged claims, certainly not in 2017. Being a rational pursuit or worthy of investment does not mean class-wide results were expected, much less demonstrated. EX1047, ¶38.

III. THE ONLY WORKING EXAMPLE WAS OBVIOUS

A. Motivation to Administer TM-β1 to Harris Mice to Treat Their Vitiligo Lesions With a Reasonable Expectation of Success.

Despite PO's assertions of recognized, class-wide efficacy, PO argues that a POSA would have thought TM-β1 would not work in the Harris mice. POR, 76-77, 79-81. The known pathogenesis in the Harris mice was straightforward: their natural immune systems were replaced with overwhelming numbers of melanocyte-targeting, activated, CD8⁺ T cells. *See* Section II.B.3 above; EX1002, ¶¶35-36; EX1006, 1869-70; EX1008, 786-87. Eliminating CD8⁺ T cells in the skin would thus predictably treat the Harris lesions. EX1002, ¶¶35-36, 48, 52, 97-104. Prior art TM-β1 eliminated CD8⁺ T cells in mouse skin, and was reasonably

expected to remove the sole cause of melanocyte destruction in the Harris mice. *Id.*; EX2007, 85:21-91:8, 92:3-94:14; EX1047, ¶¶44-46; EX1007; EX1027, 291, 297; *see also* EX2012, 15851 (TM-β1 profoundly reversed existing CD8+ T cell populations); *see also* EX1046, 248:15-249:1 (proliferation assay using CD8+NKG2D+ T cells could show molecule inhibits IL-15). Dr. Damsky confirmed repigmentation was the natural and expected result of ending melanocyte destruction. EX1046, 121:17-125:6, 125:8-12, 126:23-128:2; EX1023, 1081-1082. Administering TM-β1 to Harris mice was thus reasonably expected to treat vitiligo lesions and durably reverse them. EX2009, 8-11; EX2007, 92:25-93:14; *see also id.*, 90:22-25, 98:2-99:17, 100:23-101:5, 101:25-103:23.

PO fails to reconcile its argument against TM-β1 with its argument that there was class-wide efficacy. ID, 30-32. Dr. Damsky relied on successful TM-β1 use for class-wide efficacy. EX2005, ¶¶53, 65; EX1047, ¶¶44-46; EX1007; EX2012. But prior art success of TM-β1 does not demonstrate class-wide efficacy in the face of other failed inhibitors. *See* Section II.D above. TM-β1's ability to eliminate CD8+ T cell from mouse skin supports reasonable expectation of success *in the Harris mice* even though the antibody was unable to penetrate into the bulb of the hair follicle (the situs of alopecia) in Xing. EX2005, ¶¶51, 194.

B. No Objective Indicia of Non-Obviousness

1. No Unexpected Results

PO argues durable repigmentation was unexpected because JAK inhibitors eliminated vitiligo lesions *in natural or spontaneous vitiligo* for only 2-3 months. POR, 82-84. But Harris mice did not have natural or spontaneous vitiligo. Section II.B.3 *supra*. The cause of the Harris lesions was straightforward, so durably reversing those lesions using TM- β 1 was reasonably expected. Section III.A *supra*; Pet., 4-5, 76-78; EX1002, ¶¶95-103. The results in the Harris mice were *not* unexpected.

Even if the result had been unexpected, the result is not commensurate in scope with the claims. The claims *do not* recite durable repigmentation. POR, 38. Also, the claims cover natural and spontaneous vitiligo, whereas the patent only demonstrates results in lesions caused by the specific transgenic/transplant approach taken in the Harris mice. Pet., 3-4, 62-65, 75-77; EX1002, ¶¶36, 42.

2. No Long-Felt Need, Commercial Success, Copying

PO argues (POR, 84-86) there is long-felt need for therapy to repigment vitiligo lesions. The identified need, however, is to reverse depigmentation lesions arising from natural or spontaneous vitiligo rather than the simplified Harris mice vitiligo, which are not representative of natural or spontaneous vitiligo. Section II.B.3 *supra*. Once the cause(s) of depigmentation were eliminated, prior art

methods for achieving repigmentation were known. EX1046, 121:17-125:12, 126:23-128:2; EX1047, ¶46; EX1048, 6; EX1056, 3.

PO argues recognized “commercial potential” for an as-yet-undiscovered-cure for natural or spontaneous vitiligo equates to commercial success for PO’s “invention.” POR, 85. But PO did not demonstrate a cure for natural or spontaneous vitiligo; just for the contrived Harris mouse model. Forte’s statements about untapped market potential *years after the critical date* indicate that the need for a cure for natural or spontaneous vitiligo was not met by PO. PO cites no case holding that the complete absence of any sales is evidence of non-obviousness.

PO similarly argues Forte copied the patent, but Forte could not have copied the patent because it is a black box. Section II.B *supra*. Forte’s desire to study the activity of its FB-102 antibody, which Forte developed for GvHD completely independently of PO, merely reflects years after the critical date that the challenged patent did not fill the still unmet need.

IV. DR. DAMSKY’S TESTIMONY SHOULD BE AFFORDED NO OR LITTLE WEIGHT

Dr. Damsky’s declaration merits little or no weight. First, it is not clear he possessed the knowledge of a POSA *at the time of the invention*. See *Kyocera Senco Indus. Tools Inc. v. ITC*, 22 F.4th 1369, 1376-77 (Fed. Cir. 2022). The parties agree that a POSA would have had, *inter alia*, a least 3-5 years of experience in treating autoimmune diseases or researching cytokine signaling

pathways relevant to treating autoimmune diseases. Pet., 18; EX1002, ¶¶39-40; EX1004, ¶¶31-32; EX1047, ¶13 *accord* POR, 26; EX2005, ¶94. In April 2017, Dr. Damsky was still a medical resident and was not board-certified. EX1046, 109:22-110:2, 112:18-22. He was unfamiliar with details of vitiligo’s various causes. EX1047, ¶¶47-49; EX1046, 138:6-144:3, 117:13-119:17. He does not claim in his declaration to be an immunologist himself and did not consult one. EX1046, 128:14-129:6, 131:2-23; *id.*, 106:3-22, 108:7-14. Cancer was the focus of his Ph.D. EX1046, 108:16-23. Even his study of “basic immunology” during the fellowship he completed in 2023 is all *post-critical date* experience. EX2005, ¶6; EX2006, 1; EX1046, 128:14-129:16. He has no publications providing direct research on vitiligo and no pre-critical date publications doing direct research on IL-15 or IL-2. EX1046, 134:4-10, 136:20-137:2, 137:13-15.

Second, he falsely represented himself as an “independent expert” (EX2005, ¶1), but failed to disclose his long and extensive relationship with both the inventors and Incyte. He began collaborating with the inventors in 2019. EX1046, 39:7-41:4; EX1037. In 2021, he started a lecture series with Dr. Richmond where they invited Dr. Harris to speak. EX1046, 38:15-23, 44:9-45:12, 45:24-46:2, 48:17-23; *see also* EX1046, 72:13-73:10, 101:2-102:22; EX1041; EX1044; EX1038. In other forums, they disclosed the conflict of interest for this patent. EX1046, 29:3-30:11, 31:23-32:18; 35:22-36:3; 37:5-19, 38:21-39:3; 41:5-23, 49:7-

23, 49:25-50:9, 52:1-53:19; EX1039; EX1040. Likewise, Dr. Damsky elsewhere disclosed his conflict of interest regarding Incyte, which he acknowledges had a relationship with Villarís related to the challenged patent, but camouflaged his Incyte relationship in his declaration. EX1046, 76:7-10; 74:11-75:8, 75:21-76:1, 88:17-89:4; EX1042; EX1046, 104:18-105:22; EX1045; EX1046, 90:20-91:12; EX1043. Despite extensive pre-existing relationships, he still fought to downplay his long-standing relationships rather than candidly acknowledge them. EX1046, 75:9-76:23, 77:5-79:12, 81:6-82:23, 82:25-83:10, 83:12-17, 84:6-8, 84:16-24, 88:4-8. His limited experience and extensive ties to the inventors and Incyte give considerable pause against crediting his testimony.

V. CONCLUSION

All challenged claims should be canceled.

Respectfully submitted,

Dated: January 9, 2024

/Michael T. Rosato/
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Lead Counsel for Petitioner

VI. APPENDIX – LIST OF EXHIBITS

Exhibit No.	Description
1001	U.S. Patent No. 11,278,505 to Richmond et al.
1002	Declaration of Dr. Abul Abbas
1003	<i>Curriculum Vitae</i> of Dr. Abul Abbas
1004	Declaration of Dr. R. Todd Plott
1005	<i>Curriculum Vitae</i> of Dr. R. Todd Plott
1006	“A Mouse Model of Vitiligo with Focused Epidermal Depigmentation Requires IFN- γ for Autoreactive CD8 ⁺ T-Cell Accumulation in the Skin” John E. Harris, et al., <i>Journal of Investigative Dermatology</i> (2012) 132, 1869-1876
1007	“Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition” Luzhou Xing, et al., <i>Nature Medicine</i>
1008	“Vitiligo and alopecia areata: apples and oranges?,” John E. Harris, <i>Experimental Dermatology</i> , 2013, 22, 785-789
1009	International Publication No. WO 2009/002562 to Pavlakis et al.
1010	File History for Application No. 16/608,116
1011	U.S. Patent No. 9,028,830 to Tso et al.
1012	“Phase 1 trial of IL-15 trans presentation blockade using humanized Mik-Beta-1 mAb in patients with T-cell large granular lymphocytic leukemia,” Thomas A. Waldmann et al., <i>Blood, the Journal of the American Society of Hematology</i> , 121(3), 476-484
1013	DeGottardi et al., "Effect of anti-IL-15 administration on T cell and NK cell homeostasis in rhesus macaques," <i>The Journal of Immunology</i> . Aug. 15, 2016, 197(4) H83-98.

1014	“Human IL-2 Receptor α Chain Deficiency,” Chaim M. Roifman, <i>Pediatric Research</i> 48, 6-11.
1015	“IL-15 functions as a danger signal to regulate tissue-resident T cells and tissue destruction,” Bana Jabri and Valérie Abadie, <i>NATURE REVIEWS IMMUNOLOGY VOLUME 15 AUGUST 2015</i>
1016	“The biology of interleukin-2 and interleukin-15: implications for cancer therapy and vaccine design,” Thomas A Waldmann, <i>NATURE REVIEWS IMMUNOLOGY VOLUME 6 AUGUST 2006</i>
1017	“T-box Transcription Factors Combine with the Cytokines TGF- β and IL-15 to Control Tissue-Resident Memory T Cell Fate,” Laura K. Mackay, et al., <i>Immunity</i> 43, 1101-1111
1018	“Resolution of psoriasis upon blockade of IL-15 biological activity in a xenograft mouse model,” Louise S. Villadsen, et al., <i>J Clin Invest.</i> 2003;112(10):1571-1580
1019	“Understanding autoimmunity of vitiligo and alopecia areata,” Jillian F. Rork, et al., <i>Curr Opin Pediatr</i> 2016, 28:463-469
1020	CXCL10 Is Critical for the Progression and Maintenance of Depigmentation in a Mouse Model of Vitiligo,” Mehdi Rashighi, et al., <i>ScienceTranslationalMedicine.org</i> 12 February 2014 Vol 6 Issue 223 223ra23
1021	“JAK inhibitors in dermatology:The promise of a new drug class,” William Damsky and Brett A. King, <i>J AM ACAD DERMATOL</i> APRIL 2017
1022	“Targeting the interleukin-15/interleukin-15 receptor system in inflammatory autoimmune diseases,” Thomas A Waldmann, <i>Arthritis Res Ther</i> 2004, 6:174-177
1023	“Simvastatin prevents and reverses depigmentation in a mouse model of vitiligo,” Priti Agarwal et al., <i>Journal of Investigative Dermatology</i> , Volume 135, Issue 4, April 2015, 1080-1088
1024	“Reversible Defects in Natural Killer and Memory CD8 T Cell Lineages in Interleukin 15-deficient Mice,” Mary K. Kennedy, et al., <i>J. Exp. Med.</i> , Volume 191, Number 5, March 6, 2000 771-780

1025	Intentionally Left Blank
1026	“Interleukin 15 is required for proliferative renewal of virus-specific memory CD8 T cells” Todd C Becker et al., <i>Journal of Experimental Medicine</i> (2002) 195(12): 1541-8
1027	“CD49a Expression Defines Tissue-Resident CD8 ⁺ T Cells Poised for Cytotoxic Function in Human Skin,” Stanley Cheuk, et al., <i>Immunity</i> 46, 287-300
1028	Intentionally Left Blank
1029	Intentionally Left Blank
1030	“Therapeutic activity of multiple common γ -chain cytokine inhibition in acute and chronic GVHD,” Anne-Kathrin Hechinger, et al., <i>BLOOD</i> , 15 JANUARY 2015 x VOLUME 125, NUMBER 3
1031	“Alopecia areata: Animal models illuminate autoimmune pathogenesis and novel immunotherapeutic strategies,” Amos Gilhar et al, <i>Autoimmunity Reviews</i> 15 (2016) 726-735
1032	“Rapid skin repigmentation on oral Ruxolitinib in a patient with coexistent vitiligo and alopecia areata” John E. Harris et al., <i>J Am Acad Dermatol.</i> , 2016, 74(2): 370-371
1033	“Tofacitinib Citrate for the Treatment of Vitiligo: A Pathogenesis-Directed Therapy” Brittany G Craiglow and Brett A. King, <i>JAMA Dermatol.</i> (2015), 151(10):1110-2
1034	“Autoimmune disease induction in a healthy human organ: a humanized mouse model of alopecia areata”, Amos Gilhar et al., <i>J. Invest. Dermatol.</i> , 2013; 133(3); 844-847
1035	“Low-dose IL-2 for In vivo expansion of CD4 ⁺ and CD8 ⁺ regulatory T cells in nonhuman primates,” A. Aoyama et al., <i>Am J. Transplant</i> , 2012; 112(9):2532-7
1036	(Served only) “Alopecia areata is driven by cytotoxic T lymphocytes and is reversed by JAK inhibition” Luzhou Xing, et al., <i>Nature Medicine</i>

1037	“JAK Inhibition Prevents Bleomycin-Induced Fibrosis in Mice and is Effective in Patients with Morphea,” W. Damsky, et al., <i>J. of Inventigative Dermatology</i> , 2020(140): 1446-1449
1038	Tweet from William Damsky MD, PhD., re Global Derm Talks, Sep. 22, 2020
1039	“Global Dermatology Talks is a Virtual Lecture Series for Equitable Dissemination of Dermatologic Information”, S. Ederain, et al., <i>JAAD Int.</i> , 2022(9):116-118
1040	“Translational Research in Vitiligo; Launching a New Era of Targeted Treatments,” John E. Harris, MD, PhD, <i>Global Dermatology Talks</i> , Feb. 22, 2021
1041	Tweet from William Damsky MD, PhD to Dr. Jill Richmond, PhD, Mar. 22, 2021
1042	“Dramatic Responses in Cutaneous Sarcoidosis With JAK Inhibitor, Charles Bankhead, <i>MedPage Today</i> (Nov. 7, 2021)
1043	“JAK Inhibitors in Dermatology: What to Know About These “New” Kids on the Block”, William Damsky M.D. Ph.D., <i>Medical Dermatology Society Annual Meeting</i> (Mar. 24, 2022)
1044	Tweet from William Damsky to John E. Harris, MD, PhD., re Skin of Color Society Meeting (Mar. 16, 2023)
1045	“Dermatology Meeting News 2023: A Personalized Approach to Treating Inflammatory Skin Diseases,” William Damsky (Mar. 23, 2023)
1046	Transcript of Nov. 20, 2023 Deposition of William Damsky, M.D., Ph.D
1047	Reply Declaration of R. Todd Plott
1048	“Update on IL-15 vitiligo treatment,” John E. Harris, <i>UMass Chan Medical School Vitiligo Clinic & Research Center Vitiligo Blog</i> , (Jan. 13, 2020), available at https://www.umassmed.edu/vitiligo/blog/blog-posts/1/2020/01/update-on-il-15-vitiligo-treatment/ (last visited Dec. 5, 2023)

1049	“Tareting Interluekin-15 in Patients with Rheumatoid Arthritis,” Bo Baslund et al., <i>Arthritis & Rheumatism</i> (2005) 52(9):2686-2692
1050	ClinicalTrial.Gov Study Details for NCT00433875, Phase 2 AMG714 in Rheumatoid Arthritis, available at https://clinicaltrials.gov/study/NCT00433875?intr=AMG714&limit=100&rank=3 (last visited Dec. 5, 2023)
1051	ClinicalTrial.Gov Study Details for NCT00443326, AMG714 20060349 Multiple Dose Study in Moderate to Severe Psoriasis Subjects, available at https://clinicaltrials.gov/study/NCT00443326?intr=AMG714&limit=100&rank=1 (last visited Dec. 5, 2023)
1052	Abstract of “Safety and efficacy of AMG714 in adults with coeliac disease exposed to gluten challenge: a phase 2a, randomised, double-blind, placebo-controlled study,” Marja-Leena Lahdeaho, et al., <i>Lancet Gastroenterol. Hepatol.</i> (2019) 4(12):948-959, available at https://pubmed.ncbi.nlm.nih.gov (last visited Dec. 5, 2023)
1053	Abstract of “Safety and efficacy of AMG714 in patients with type 2 refractory coeliac disease: a phase 2a, randomised, double-blind, placebo-controlled, parallel-group study,” Christophe Cellier, et al., <i>Lancet Gastroenterol. Hepatol.</i> (2019) 4(12):960-970, available at https://pubmed.ncbi.nlm.nih.gov (last visited Dec. 5, 2023)
1054	“Identification of a potent anti-IL-15 antibody with opposing mechanisms of action <i>in vitro</i> and <i>in vivo</i> ,” DK Finch, et al., <i>British Journal of Pharmacology</i> (2011) 162:480-490
1055	ClinicalTrial.Gov Search Results for Hu-Mikb1, available at https://clinicaltrials.gov/search?intr=Hu MiK-Beta-1 (last visited Dec. 5, 2023)
1056	“Diagnosing Vitiligo and Improving Care Provider Awareness,” Seemal Desai and William Damsky, <i>DermView Innovations in the Treatment of Vitiligo: Episode 4</i> (Nov. 30, 2021), available at https://www.dermatologytimes.com/view/diagnosing-vitiligo-and-improving-care-provider-awareness (last visited Nov. 19. 2023)
1057	“The pathogenesis of Vitiligo,” Neel Malhotra and Marlene Dytoc, <i>J. Cutaneous Med. & Surgery</i> (2013) 17(3):153-172

1058	“A New Phenylpyrazoleanilide, Y-320, Inhibits Interleukin 17 Production and Ameliorates Collagen-Induced Arthritis in Mice and Cynomolgus Monkeys,” Ushio et al., <i>Pharmaceuticals</i> (2014) 7:1-17
1059	Paragraph 70 of Damsky Declaration from Damsky Deposition

CERTIFICATE OF COMPLIANCE

37 CFR §42.24(d)

I certify that this paper contains 5,595 words, excluding the portions of the paper that §42.24(c) exempts, according to the word-processing system used to prepare this paper.

Respectfully submitted,

Dated: January 9, 2024

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CERTIFICATE OF SERVICE

I certify that today this paper and EX1037–EX1059 were served by email on

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