UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

ALLELE BIOTECHNOLOGY AND PHARMACEUTICALS, INC., Plaintiffs, v. REGENERON PHARMACEUTICALS, INC., Defendants	Case No. 7:20-cv-08255 (PMH) (AEK) **ORAL ARGUMENT REQUESTED**

MEMORANDUM OF LAW IN SUPPORT OF DEFENDANT REGENERON PHARMACEUTICALS, INC.'S MOTION TO DISMISS

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Defendant Regeneron Pharmaceuticals, Inc. ("Regeneron") moves to dismiss Plaintiff Allele Biotechnology and Pharmaceuticals, Inc.'s ("Allele") Amended Complaint pursuant to Federal Rule of Civil Procedure 12(b)(6). Because Allele's Amended Complaint alleges conduct immune from patent infringement under the statutory "safe harbor" in 35 U.S.C. § 271(e)(1), the Court should dismiss this case in its entirety. And, because it fails to plead the requisite factors, Allele's claim for willful infringement should also be dismissed.

I. INTRODUCTION

The central issue in this dispute is a legal one: whether Regeneron was protected by the safe harbor of 35 U.S.C. § 271(e)(1) when it worked tirelessly to develop its REGEN-COV antibody cocktail to treat COVID-19 patients during the height of the global pandemic. Allele claims the answer is no, despite the broad language of the relevant statute and its correspondingly broad interpretation by the Supreme Court, the Federal Circuit, and this Court—all of which firmly support application of the safe harbor. Nonetheless, Allele still claims that Regeneron's alleged use of a patented component as part of laboratory tests, called neutralization assays, that were reasonably related to the development and submission of information to the FDA should be excluded; in Allele's view, that component is a "research tool" and not the type of invention covered by the safe harbor. Allele misreads the statute and overlooks clear Congressional intent: companies making new drugs need not await expiration of relevant patents before completing the necessary testing to demonstrate safety and efficacy, and obtain FDA approval.

Regeneron scientists worked day and night to make a lifesaving therapy for patients suffering from COVID-19 in a matter of months. Allele is not arguing that Regeneron's treatment itself, its formulation, or its use infringed or will infringe Allele's patent. Rather, Allele focuses on a mere component of one of many tests performed during Regeneron's

development of REGEN-COV, and asks this Court to determine that Regeneron's scientists should have diverted time and resources to a patent freedom-to-operate analysis rather than concentrating their efforts on the global pandemic.[1] According to Allele, Regeneron's conduct falls outside the safe harbor because Allele's patent does not cover a drug product, but a "marker" protein called mNeonGreen, which would not itself be subject to FDA approval or eligible for an extended patent term in exchange for safe harbor immunity.

Allele's argument is without merit. Nothing in the Supreme Court's broad interpretation of § 271(e)(1) limits the safe harbor's application to patents covering drug products or products requiring FDA pre-market approval, and nothing in the statute defines a "research tool" patent that would be excluded from the safe harbor. Moreover, this Court already considered nearly identical circumstances in *Teva Pharms. USA, Inc. v. Sandoz Inc.* and concluded that the safe harbor applied to the use of patented laboratory "markers" to characterize a drug in generating data for the FDA, even though the markers were not themselves drug products and did not require FDA approval. Nos. 09 Civ. 10112 (KBF), 10 Civ. 7246 (KBF), 2013 WL 3732867 (S.D.N.Y. July 16, 2013). The *Teva* Court distinguished *Proveris Scientific Corp. v. Innovasystems*, 536 F.3d 1256 (Fed. Cir. 2008), noting that the Federal Circuit only declined to apply the safe harbor because the defendant was not itself generating data for FDA submission or seeking FDA approval. *See Teva*, 2013 WL 3732867, at *8. Here, unlike the *Proveris* defendant, Regeneron was developing a drug product.

[1] If Regeneron had known about Allele's patent, it could have easily used a different fluorescent protein in its neutralization assays than the one Allele accuses of infringement, as it is now doing. But the law does not require Regeneron to divert valuable time and resources during the FDA pre-approval process to focus on patents rather than patients, as explained below.

Correspondingly, Regeneron's actions to develop and submit information for its REGEN-COV antibody cocktail to the FDA fall squarely within § 271(e)(1) and cannot form the basis for allegations of patent infringement, and Allele's complaint should be dismissed.

Allele further alleges that Regeneron's infringement was willful, despite that Regeneron had no knowledge of the patent and Allele does not—and cannot—plead that Regeneron had subjective intent to infringe or that the alleged infringing activity was egregious. Because Allele failed to adequately plead the requisite factors for willful infringement, Allele's willfulness allegation should also be dismissed.

II. PROCEDURAL BACKGROUND

On October 5, 2020 Allele filed this case asserting infringement of U.S. Patent No. 10,221,221 (the "'221 patent") based on activities Regeneron undertook in relation to its FDA submission for its COVID-19 antibody cocktail, REGEN-COV. Specifically, Allele alleges that Regeneron infringed the '221 patent when it used mNeonGreen (a marker allegedly embodied by the '221 patent) in connection with one of the assays Regeneron used to identify the optimal candidates for its FDA submission.[2] *See* D.I. 29, ¶¶ 28-33. Notably, Allele does not allege that Regeneron's COVID-19 antibody cocktail itself infringes the '221 patent. Rather, its allegations are premised on a mere component of one of many tests that Regeneron allegedly conducted over the course of several months leading up to its submission to the FDA. Allele additionally alleges, based on the same conduct, that Regeneron willfully infringed the '221 patent. *See* D.I. 29, ¶ 53. On March 8, 2020, Regeneron notified Allele of its intention to file a motion to dismiss because the accused activities were immune from infringement under the

[2] Allele's Amended Complaint (D.I. 29) and its accompanying exhibits are also submitted herewith as Exhibit 1 through the Declaration of Michael A. Morin.

statutory safe harbor codified in 35 U.S.C. § 271(e)(1), and because Allele's willfulness allegation was deficient. On April 8, 2020, Allele amended its complaint to add "information and belief" allegations regarding purported "post approval" uses and uses allegedly unrelated to Regeneron's FDA submission. Allele's Amended Complaint includes new allegations that Regeneron used mNeonGreen for "commercial purposes such as validation, quality control, promotion and for regulatory submissions abroad" and to secure issuance of patents from the United States Patent and Trademark Office. D.I. 29, ¶¶ 35-38.

Following an exchange of letter briefs on the issue, this Court conducted a hearing on June 15, 2021, wherein the Court granted Regeneron permission to file this Motion.

III. FACTUAL BACKGROUND

Headquartered in Tarrytown, New York, Regeneron is a leading biotechnology company that invents life-transforming medicines for people with serious diseases. Founded and led for over 30 years by physician-scientists, the company's science-driven approach has resulted in numerous FDA-approved medicines and a robust pipeline of product candidates in development, nearly all of which were homegrown in its laboratories.

As a leader in the biotechnology space, during the early moments of the COVID-19 outbreak, Regeneron immediately started working on a treatment, and succeeded within months. Unlike vaccines, which are designed to trigger the recipient's body to generate antibodies to the virus to prevent infection, REGEN-COV contains antibodies that bind to and block the SARS-CoV-2 virus from entering the recipient's cells and is authorized for the treatment of mild-to-moderate COVID-19 in adults and certain pediatric patients with positive results of direct SARS-CoV-2 viral testing, and who are at high risk for progression to severe COVID-19, including hospitalization or death.

The development of REGEN-COV involved a multitude of tests. *See* D.I. 29, Ex. B and Ex. D. Allele alleges that Regeneron infringed its '221 patent in connection with one of the tests Regeneron used, called a neutralization assay. *See* D.I. 29, ¶ 31 (asserting that Regeneron's "anti-SARS-CoV-2 spike antibodies were tested in neutralization assays against spike protein variants coded into pVSV-SARS-CoV-2-S(mNeon) viral pseudoparticle reporter constructs detected by their expression of mNeonGreen."). Neutralization assays test the ability of antibody candidates to "neutralize" or block the SARS-CoV-2 virus from entering cells, which is the mechanism by which REGEN-COV antibodies effectively treat COVID-19.

Allele alleges that Regeneron, in its neutralization assay, used a fluorescent protein called "mNeonGreen" which is allegedly embodied by Allele's '221 patent. *See* D.I. 29, ¶¶ 28-33. It is the alleged use of this fluorescent protein in this particular assay that Allele accuses of infringement.

Regeneron's laboratory testing, including its neutralization tests, culminated in the selection of the optimal candidates for Regeneron's FDA submission. *See* D.I. 29, Ex. B at 3-4 (identifying REGN10987 and REGN10933 as "ideal partners for a therapeutic antibody cocktail" which proceeded for testing in human trials (clinicaltrials.gov NCT04426695 and NCT04425629)). On October 7, 2020, Regeneron requested an Emergency Use Authorization ("EUA") from the FDA, which the FDA granted on November 21, 2020. The EUA is not a full FDA approval of REGEN-COV, but rather, it is a temporary authorization by the FDA based on, *inter alia*, clinical trial safety and efficacy data to use the antibody cocktail in a national emergency. *See* 21 U.S.C. § 360bbb-3(c)(2).

Regeneron continues to invest substantial time and resources developing additional data for its Biologics License Application ("BLA") to obtain full regulatory approval of REGEN-

COV from the FDA. *See* 42 U.S.C. § 262(a). Both the EUA and the eventual full regulatory approval require Regeneron to show that its antibody cocktail is safe and effective in treating the SARS-CoV-2 infection. *See* 42 U.S.C. § 262(a)(2)(C) (describing FDA regulation and license of new biological drug products, including a demonstration that "the biological product that is the subject of the application is safe, pure, and potent"); 21 U.S.C. § 360bbb-3(c) (describing the criteria for issuance of EUA by the FDA, including a showing that the product is "effective in diagnosing, treating, or preventing" the emergency-causing disease "based on the totality of scientific evidence available").

IV. LEGAL STANDARD

"A complaint is subject to dismissal for failure to state a claim if the allegations, taken as true, show the plaintiff is not entitled to relief." *Jones v. Bock*, 549 U.S. 199, 215 (2007). Although the court "accepts as true all well-pleaded factual allegations," it "does not credit 'mere conclusory statements' or 'threadbare recitals of the elements of a cause of action.'" *Teva*, 2013 WL 3732867, at *2 (quoting *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009)). "If the court can infer no more than 'the mere possibility of misconduct' from the factual averments . . . dismissal is appropriate. *Id*. (quoting *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 570 (2007)). "When evaluating the sufficiency of the allegations, courts look not only to the complaint itself, but also to documents attached to it, incorporated by reference in it, or relied upon by the plaintiff in bringing suit." *Id.* (citing *Rothman v. Gregor*, 220 F.3d 81, 88 (2d Cir. 2000)).

"Courts may grant motions to dismiss based on an affirmative defense so long as the applicability of the defense is apparent on the face of the complaint or documents incorporated by reference within the complaint." *Teva*, 2013 WL 3732867, at *3; *see also Reuben v. NYC Dep't of Corr.*, No. 11 CIV. 378 RMB, 2011 WL 5022928, at *2 (S.D.N.Y. Oct. 18, 2011) ("'[A] complaint may be subject to dismissal under Rule 12(b)(6) when an affirmative defense

. . . appears on its face.'" (quoting *Jones*, 549 U.S. at 215)); *Pani v. Empire Blue Cross Blue Shield*, 152 F.3d 67, 74 (2d Cir. 1998) ("An affirmative defense may be raised by a pre-answer motion to dismiss under Rule 12(b)(6), without resort to summary judgment procedure, if the defense appears on the face of the complaint."). "[T]he safe harbor protections of § 271(e)(1) are affirmative defenses" and "Courts dismiss patent cases when it is clear that the challenged conduct is covered by the statutory safe harbor set forth in § 271(e)(1)." *Teva*, 2013 WL 3732867, at *3.

To plead a claim for willful infringement, a defendant's conduct must be "willful, wanton, malicious, bad-faith, deliberate, consciously wrongful, flagrant or—indeed—characteristic of a pirate." *Halo Elecs., Inc. v. Pulse Elecs., Inc.*, 136 S. Ct. 1923, 1932 (2016). "In order to survive a motion to dismiss a claim of willful misconduct, a complaint must plausibly plead facts sufficient to support an inference that the infringement at issue is 'egregious' in addition to pleading subjective intent." *Novartis Vaccines & Diagnostics, Inc. v. Regeneron Pharms., Inc.*, No. 18-cv-2434 (DLC), 2018 WL 5282887, at *2 (S.D.N.Y. Oct. 24, 2018).

V. ARGUMENT

Allele's Amended Complaint asserts that Regeneron infringed the '221 patent by using mNeonGreen during neutralization assays performed to obtain efficacy data and identify the optimal candidates for Regeneron's FDA submission. Even accepting these assertions as true for the purposes of this motion, Allele's complaint fails to state a claim as a matter of law because the accused conduct is protected by the "safe harbor" provision of the Hatch-Waxman Act. That provision, codified at 35 U.S.C. § 271(e)(1), provides:

> It shall not be an act of infringement to make, use, offer to sell, or sell . . . a patented invention . . . solely for uses reasonably related to the development and

> submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products.

Id. The purpose is to allow biologic drug makers like Regeneron, "prior to the expiration of a patent, to engage in otherwise infringing activities necessary to obtain regulatory approval." *Eli Lilly and Co. v. Medtronic, Inc.*, 496 U.S. 661, 671 (1990). The statute is broad and the language is clear. As long as a party is using a "patented invention"—which the Supreme Court has "defined to include all inventions"—in a manner "reasonably related" to the development and submission of information to the FDA, it is protected by the statute's safe harbor. *Eli Lilly*, 496 U.S. at 665.

Regeneron's alleged use of Allele's patented invention fits squarely within the statutory language of the safe harbor provision. Namely, Allele alleges that the fluorescent protein marker mNeonGreen was used in connection with neutralization assays to determine efficacy and help identify optimal candidates for submission to the FDA for regulatory approval—a use that is undoubtedly "reasonably related" to the development and submission of information to the FDA. Because such activities are immunized from patent infringement under 35 U.S.C. § 271(e)(1), Allele's Amended Complaint should be dismissed under Rule 12(b)(6).

A. Regeneron's Alleged Use of mNeonGreen is Reasonably Related to FDA Submission, and Therefore, Immune from Infringement Under the Statutory Safe Harbor

The broad protection offered by the safe harbor provision of § 271(e)(1) has long been recognized by the Supreme Court, deeming the immunity to have a "wide berth" and "extend[ing] to all uses of patented inventions that are reasonably related to the development and submission of any information" to the FDA. *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005); *see also Momenta Pharms., Inc. v. Amphastar Pharms., Inc.*, 686 F.3d 1348, 1356 (Fed. Cir. 2012) ("*Momenta I*") (embracing an "expansive view in explaining that

§ 271(e)(1) "applies to a broad set" of activities "[a]s long as the accused infringer 'has a reasonable basis for believing' that use of the patented invention might yield information that 'would be appropriate to include in a submission to the FDA'" (citing *Merck*, 545 U.S. at 207)). Courts have interpreted this "wide berth" to cover the use of laboratory reagents in preclinical testing for an FDA submission. *See Teva*, 2013 WL 3732867 and *Merck*, 545 U.S. 193.

1. This Court's Decision in *Teva v. Sandoz* Correctly Applied the Safe Harbor of Section 271(e)(1) Under Nearly Identical Circumstances

This Court in *Teva* already considered and correctly applied the safe harbor of § 271(e)(1) where the alleged infringement involved defendant's use of a laboratory test or reagent to generate data to obtain approval of a new drug product. *See Teva*, 2013 WL 3732867. *Teva* involved certain "markers" that the defendants were using in the process of seeking approval to market a drug. *See id.* at *1. The *Teva* Court recognized the "wide berth" pronounced by the Supreme Court "for the use of patented products in activities related to the federal regulatory process." *Id.* at *6. It further noted the "striking similarities" to the Federal Circuit's decision in *Momenta I*, which also involved a patented invention that was not a drug product, but a test used in the process of seeking drug approval. *Id.* at *5. While Allele suggests that the *Teva* court's reliance on *Momenta I* was misplaced in view of the holding of *Momenta Pharms., Inc. v. Teva Pharms USA Inc.*, 809 F.3d 610 (Fed. Cir. 2015) ("*Momenta II*"), *Momenta II* still recognizes that the safe harbor "provides a wide berth" for the use of patented inventions in activities related to the submission of information to the FDA. *Momenta II*, 809 F.3d at 619. While the *Momenta II* court ruled that the safe harbor ultimately did not apply, it was only because the accused infringing activities were not actually "reasonably related" to submitting data to seek FDA approval, unlike here. *See id.* at 620.

The Court in *Teva* also rejected any per se exemption for "research tools" under *Proveris*. *Teva*, 2013 WL 3732867, at *9. Specifically, the *Teva* court noted that *Proveris* involved an accused infringer that was not itself involved in drug development, and was seeking to protect its infringing sales on the basis of its *customer's* activities. *See id.* at *8. It was this disconnect, the *Teva* Court concluded, that provided the Federal Circuit's rationale in *Proveris*. While the safe harbor is broad, it requires that the use be "related to the development and submission of any information" to the FDA. Therefore, if a party's use is ***not*** related to FDA submission, that use falls outside the protection of the safe harbor.[3] *See Proveris*, 536 F.3d at 1265 (noting that because "Innova is not a party seeking FDA approval for a product . . . Innova is not within the category for entities for whom the safe harbor provision was designed to provide relief"). The *Teva* Court found no broad proscription in *Proveris* against applying the safe harbor to particular types of inventions, and concluded that defendants' use of the patented markers was within the scope of the safe harbor. *Teva*, 2013 WL 3732867, at *9.

The same applies to Regeneron's alleged use of Allele's patented mNeonGreen laboratory reagent. The proper analysis is not whether mNeonGreen is a "research tool," a term not found in the statute, but whether Regeneron's alleged use was for purposes "reasonably related" to generating information for submission to the FDA.

2. Allele's Pleadings are Based on Uses Related to the Generation and Submission of Information to the FDA

[3] While the Federal Circuit in *Shire* applied the safe harbor to protect an alleged infringer who did not directly submit information to FDA, it did so in finding that the provision of the active pharmaceutical ingredient ("API"), a key component of the FDA submission, to another party was "reasonably related" to FDA submission. *See Shire LLC v. Amneal Pharms. LLC*, 802 F.3d 1301 (Fed. Cir. 2015).

Allele's pleadings demonstrate that Regeneron's accused use of its patented invention cannot be anything other than "reasonably related" to the generation and submission of information to the FDA. Allele asserts that Regeneron's "anti-SARS-CoV-2 spike antibodies were tested in neutralization assays . . . detected by their expression of mNeonGreen." D.I. 29, ¶ 31; *see also id.* ¶¶ 29, 30, 32, 33 (referencing additional scientific publications and supplementary materials describing the neutralization assays). Aside from the allegations properly discounted in Section V.C *infra*, Allele does not, and cannot, allege that Regeneron used its patented invention for any purpose other than these neutralization assays. These assays were performed for the sole purpose of identifying and characterizing the optimal anti-SARS-CoV-2 spike antibody candidates, based on neutralizing efficacy, for Regeneron's submission to the FDA to obtain an EUA and eventual BLA approval. Without data to show that the antibody cocktail is effective in neutralizing COVID-19, the FDA would be unable to grant an EUA or final approval for REGEN-COV. *See* 42 U.S.C. § 262(a)(2)(C); 21 U.S.C. § 360bbb-3(c).

Further, Regeneron need not show that all the information it generated from the accused tests was submitted to the FDA for the safe harbor to apply, nor does it matter that the tests were preclinical efforts to identify optimal antibodies rather than trials in patients. The Supreme Court has determined that safe harbor protection extends to uses generating data independent of the "phase of research in which it is developed," or whether it is "ultimately submitted to the FDA." *Merck*, 545 U.S. at 202, 206. As such, multiple courts—including this Court—have held that screening multiple drug candidates to identify the optimal candidate for FDA submission is protected under the safe harbor.

"In *Merck*, the Supreme Court held that use of patented peptides to conduct research not ultimately submitted to the FDA, but which furthered research and led to the development of

testing for another drug, fell within the safe harbor." *Teva*, 2013 WL 3732867, at *7 (citing Merck, 545 U.S. at 208). As the Federal Circuit explained on remand, "[a]ll of the experiments charged with infringement were conducted for the purposes of determining the optimum candidate angiogenesis inhibitor and proceeding with commercial development of the selected candidate in compliance with regulatory procedures . . . ." *Integra Lifesciences I, Ltd. v. Merck KGaA*, 496 F.3d. 1334, 1340 (Fed. Cir. 2007). Likewise, in *Katz v. Avanir Pharmaceuticals*, defendant's use of a patented assay "to screen compounds as part of [defendant's] IgE drug development program" through which "[o]ne of these compounds was ultimately selected" for preclinical studies forming the basis for an IND was covered by § 271(e)(1). No. 06-cv-0496 DMS (LSP), 2007 WL 9776599, at *2, *6 (S.D. Cal. Aug. 21, 2007). Similarly, in *Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, use of patented compound intermediates to run "hundreds of experiments for purposes of possibly identifying a drug candidate" was within the safe harbor. No. 95 Civ. 8833 (RPP), 2001 WL 1512597, at *4, *7-8 (S.D.N.Y. Nov. 28, 2001).

Regeneron's accused use of the patented invention is analogous to the uses protected by the safe harbor in *Merck*, *Katz*, and *Bristol-Myers Squibb*, as Allele's patented invention was allegedly used as one part of the process to identify the optimal COVID-19 treatment candidate for clinical studies and submission to FDA. Indeed, Regeneron had been diligently preparing its FDA submission when Allele filed suit.

B. Allele's Argument that mNeonGreen is a "Research Tool" Excepted from the "Patented Inventions" Covered by the Safe Harbor is Incorrect

1. Section 271(e)(1) Covers "All Inventions" and Does not Require "Symmetry"

Allele's attempt to characterize its patented invention as a "research tool" does not shield it from the plain language of the safe harbor provision. The Supreme Court has made clear that the safe harbor covers "all inventions." *See Eli Lilly*, 496 U.S. at 665 ("The phrase 'patented

invention' in § 271(e)(1) is defined to include **all inventions**, not drug-related inventions alone" (emphasis added)). And this Court in *Teva* recognized that "[i]mportant for the issue before this Court is the definition of the phrase "patented invention" in the statute." *Teva*, 2013 WL 3732867, at *5. Referencing the Supreme Court in *Eli Lilly*, this Court explained: "[i]t is defined in 35 U.S.C. § 100(a): 'When used in this title, unless the context otherwise indicates . . . **[t]he term 'invention' means invention or discovery**." *Id.* (citing *Eli Lilly*, 496 U.S. at 665) (emphasis added). Nothing in the statutory language limits the safe harbor to patents covering drug products or excludes patents on "research tools."

Faced with resounding authority interpreting the plain language of the statute to encompass all inventions within the definition of "patented invention," Allele attempts to rely on legislative history and Congressional intent to read in a requirement of statutory symmetry between § 271(e)(1) and § 156 (covering Patent Term Extension ("PTE")). However, it has been long established that "[s]tatutory interpretation begins with the language of the statute, the plain meaning of which [the court] derive[s] from its text and its structure. If the statutory language is clear and unambiguous, the inquiry ends with the plain meaning." *Myore v. Nicholson*, 489 F.3d 1207, 1211 (Fed. Cir. 2007) (internal quotations and citations omitted); *see also In re WorldCom, Inc. Sec. Litig.*, 308 F. Supp. 2d 236, 244 (S.D.N.Y. 2004) ("It is well established that statutory construction must begin with 'the plain text, and, where the statutory language provides a clear answer, it ends there as well.'" (citing *Raila v. United States*, 355 F.3d 118, 120 (2d Cir. 2004))).

Indeed, the plain language of the provision does not require any statutory symmetry or "perfect product fit" between § 271(e)(1) and § 156. *See* 35 U.S.C. § 271(e)(1) (containing no reference to § 156, nor any requirement that the "patented inventions" covered must also be eligible for PTE); *see also Momenta I*, 686 F.3d at 1361 (stating that it is "not correct" that "[the

Court] must reject any disequilibrium between sections 201 and 202 of the Hatch-Waxman Act . . . . '[S]tatutory symmetry is preferable, but not required'"); *Abtox v. Exitron*, 122 F.3d 1019, 1029 (Fed. Cir. 1997) ("statutory symmetry is preferable but not required" as "the Supreme Court commands" in *Eli Lilly*); *Eli Lilly*, 496 U.S. at 671-72 ("Under respondent's interpretation, there may be some relatively rare situations in which a patentee will obtain the advantage of the § 201 extension but not suffer the disadvantage of the § 202 noninfringement provision, and others in which he will suffer the disadvantage without the benefit.").

Courts have understood this to mean that an invention need not be a drug product eligible for PTE or be subject to FDA pre-market approval to be considered a "patented invention." This Court in *Bristol-Myers Squibb* held that under the "plain meaning" of § 271(e)(1), a process for preparing the drug taxol and four intermediates used in the process were "patented inventions." *Bristol-Myers Squibb*, 2001 WL 1512597, at *3. Judge Patterson directly rejected the argument that "Congress intended [Section 271(e)(1) and Section 156] to be construed in a complementary fashion such that only products covered under Section 156 should be considered 'patented inventions' within the scope of Section 271(e)(1)." *Id.* at *2. Instead, he noted that "[n]othing in the text of Section 271(e)(1) indicates that Congress intended to restrict the scope of the term 'patented invention' to those products covered by Section 156" and followed "clear Federal Circuit precedent that the term 'patented invention' means all patented inventions or discoveries and not merely those that are covered by Section 156." *Id.* at *2, *3.

Likewise, in *Teva*, this Court held that defendants' use of peptide markers to characterize the drug's active ingredient in generating data for FDA submission was protected by the safe harbor even though "[t]he claimed markers are not themselves drug products, nor do they need approval from the FDA." *Teva*, 2013 WL 3732867, at *2. The Federal Circuit also found

recently in *Classen Immunotherapies, Inc. v. Elan Pharm., Inc.*, 786 F.3d 892 (Fed. Cir. 2015)—a case following *Proveris*—that "a method for accessing and analyzing data on a commercially available drug to identify a new use, and then commercialize that new use" was considered a "patented invention." *Classen*, 786 F.3d at 894. *See also Momenta I*, 686 F.3d at 1361 (rejecting the proposition that "the safe harbor should not be available unless a patent term extension is also available"); *Katz*, 2007 WL 9776599, at *7 (ruling that "patented inventions" included screening assays for the identification of IgE antibody suppressors and expressly rejecting the argument that § 271(e)(1) does not apply because the screening assays are "research tool[s] rather than a patented compound"). [4]

By characterizing mNeonGreen as a "research tool," Allele attempts to carve out an exception from the broad protection offered by the safe harbor provision. D.I. 29, ¶¶ 39-40. But nothing in § 271(e)(1) defines a "research tool." What is clear is that the safe harbor is applicable to patents that do not cover drug products or qualify for PTE under § 156, so neither characteristic can be used to define so-called "research tools" or limit the scope of the safe harbor. *See e.g.*, *Eli Lilly*, 496 U.S. at 665; *Momenta I*, 686 F.3d at 1361; *Teva*, 2013 WL 3732867, at *2.

Even accepting that mNeonGreen may be characterized as a "research tool," Allele cannot escape that it is still a "patented invention"—an invention or discovery that is patented—under the plain meaning of § 271(e)(1). Allele relies on *Proveris* to argue that "research tools" are not protected by the safe harbor. That reliance is misplaced. *Proveris* did not create a "research tool" exception. Rather, it followed the clear language of § 271(e)(1) and found that

[4] While *Katz* predates *Proveris*, it is consistent with the other cases recognizing that patented inventions not subject to FDA approval or eligible for PTE are properly protected under the safe harbor.

the safe harbor did not apply to the specific optical spray analyzer at issue because the alleged infringer was not generating information to submit to the FDA. *See Proveris*, 536 F.3d at 1265 (noting that "insofar as its OSA device is concerned, Innova is not within the category for entities for whom the safe harbor provision was designed to provide relief" because "Innova is not a party seeking FDA approval").

This Court in *Teva* correctly rejected the notion that *Proveris* "created some sort of opening through which ["research tools"] squeezes: that [they] do not fall within the definition of 'patented invention' under the meaning of the statute."[5] *Teva*, 2013 WL 3732867, at *9. In doing so, the Court found that the safe harbor protects the use of peptide markers as research tools to characterize the drug's active ingredient in generating data for FDA submission. *Id.* at *2. Judge Forrest recognized that *Proveris* is not "relevant" and "is a case which cannot be separated from its factual context—as noted by the Federal Circuit itself." *Id.* at *8. The Court reasoned that *Proveris* simply recognizes that the safe harbor may not apply where a third party's use is unrelated to FDA submission as there was a "blatant commercial use of a patented product by a **party not itself engaged in development and submission of information**."[6] *Id*. (emphasis added).

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[5] Allele criticizes *Teva* as being decided before *Momenta II*. However, *Momenta II* does not affect the ruling of *Teva*. As noted above, *Momenta II* still recognizes the "wide berth" provided by the safe harbor provision and was ultimately decided on the "reasonably related" prong, leaving undisturbed the *Momenta I* holding concerning the "patented invention" prong of § 271(e)(1). *Momenta II*, 809 F.3d at 619, 620.

[6] In addition to the *Pfizer* decision, discussed below, two other district court cases have misinterpreted *Proveris*'s narrow holding. The court in *PSN Ill., LLC v. Abbott Labs.*, No. 09 C 5879, 2011 WL 4442825 (N.D. Ill. Sept. 20, 2011) interpreted *Proveris* as holding that "only 'patented inventions' for which regulatory approval is required fall within the scope of the safe harbor exemption." *PSN Illinois*, 2011 WL 4442825, at *5. This interpretation contradicts the clear language of the statute and the Supreme Court's interpretation (*see e.g.*, *Eli Lilly*, 496 U.S. at 665), and is also inconsistent with how the Federal Circuit has applied the safe harbor. Indeed,

2. The *Pfizer* Court Improperly Imported a Symmetry Requirement to Section 271(e)(1) Contrary to this Court's Decision in *Teva*

Contrary to this Court's interpretation in *Teva*, the California court in *Allele Biotechnology and Pharms., Inc. v. Pfizer, Inc.* found that *Proveris* precludes safe harbor protection premised on its interpretation of *Eli Lilly* requiring a "perfect product fit" and not extending the safe harbor protections to patents that are not subject to pre-market FDA approval. No. 20-CV-01958, 2021 WL 1749903, at *7 (S.D. Cal. May 4, 2021). Respectfully, the California court decided the issue incorrectly, and its decision is not binding on this Court, which has well-established precedent correctly interpreting the statute, and the relevant Supreme Court and Federal Circuit decisions.

As explained above, the Federal Circuit in *Abtox* and numerous other courts have recognized that *Eli Lilly* did not require symmetry, or a "perfect product fit" between § 271(e)(1) and § 156. *Abtox*, 122 F.3d at 1029 (recognizing that the court "must follow the Supreme Court's broader holding, which remains in force despite a potential conflict with its own narrower [justification of statutory symmetry]" and "the Supreme Court commands that statutory symmetry is preferable **but not required**") (emphasis added). Even *Proveris* itself acknowledged this, explaining that when the *Abtox* Court was "[f]aced with a tension between the Supreme Court's broader holding in *Eli Lilly* that 'patented invention' means 'all inventions' within section 156 and the Court's narrower focus on statutory symmetry between the two provisions, [the Court] adopted the broader holding that the phrase 'patented invention' of

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this Court expressly declined to follow *PSN Illinois*, characterizing it as "either wrong or irrelevant." *Teva* 2013 WL 3732867, at *8. Relying on *PSN Illinois*, the court in *Isis Pharms., Inc. v. Santaris Pharma A/S Corp.*, No. 11-cv-2214, 2014 WL 794811 (S.D. Cal. Feb. 27, 2014) found that there were disputes of material fact with regard to whether the inventions are "patented inventions" for purposes of § 271(e)(1) because they may not be subject to regulatory approval, similarly contrary to the noted precedent. *Isis Pharmaceuticals*, 2014 WL 794811, at *13.

section 271(e)(1) includes any medical device, regardless of its eligibility for patent term extension under section 156." *Proveris*, 536 F.3d at 1263. The court in *Pfizer* also cited *Momenta II* as support for the required "perfect product fit." *Pfizer*, 2021 WL 1749903, at *5. However, *Momenta II* simply states that "research tools or devices that are not themselves subject to FDA approval **may not** be covered" by § 271(e)(1). *Momenta II*, 809 F.3d at 619 (emphasis added). *Momenta II* does not say that research tools/devices not subject to FDA approval **are not** covered by § 271(e)(1), but that they "**may not be**" covered. *Proveris* is one such example of where they "may not be" covered: where the use is not related to FDA submission.

The California court was presented with another instance in which a "perfect product fit" was not achieved in *Classen*, but discounted it because it "contains no discussion or analysis of whether the patent at issue constituted a research tool," did not cite to *Eli Lilly* or *Proveris*, and was premised on whether the safe harbor applied to "routine post-approval reporting to FDA." *Pfizer*, 2021 WL 1749903, at *6. However, the *Pfizer* court overlooked that *Classen* is a post-*Proveris* case that recognizes safe harbor protection for a (method) patent not subject to FDA approval or eligible for PTE. *See Classen*, at 786 F.3d at 894. The absence of an express mention of a "research tool" characterization does not change the holding. Even if the focus of the decision was whether the "routine post-approval reporting to FDA" was "reasonably related" to FDA submission, the Federal Circuit necessarily must have determined that the patent—which was not subject to FDA approval or eligible for PTE—was a "patented invention," or else it would not be deserving of safe harbor protection.

The *Pfizer* court also discounted *Abtox* as issued prior to *Proveris* and distinguishable because though the patent was not eligible for PTE, it was still subject to an FDA approval

process. *Pfizer*, 2021 WL 1749903, at *6. Although the court was correct in that the invention in *Abtox* was subject to an abbreviated FDA approval process, *Abtox* still demonstrates that PTE eligibility is not a prerequisite for safe harbor protection, and a "perfect product fit" is not required. Additionally, as this Court recognized in *Teva*, *Abtox* predates *Proveris* and controls: "the Federal Circuit has instructed that when two cases from the Federal Circuit conflict, the earlier precedent controls until overruled or an en banc decision issues." *Teva*, 2013 WL 3732867, at *7, n.10 (citing *Newell Cos. v. Kenney Mfg. Co.*, 864 F.2d 757, 765 (Fed. Cir. 1988)). Finally, the California court did not find this Court's *Teva* decision as "persuasive" and dismissed it as a "non-binding district court case." *Pfizer*, 2021 WL 1749903, at *6. However, as noted above, *Teva* was decided correctly and is a decision from this district court.

3. Allele's Other Assertions Regarding a "Competitor" Requirement and Its Inability to Commercialize are Incorrect

Allele's argument that the safe harbor is limited to competitors, and thus, does not apply here because Regeneron is not seeking approval for a competing fluorescent protein product is contrary to controlling law. The Federal Circuit has expressly determined that § 271(e)(1) does not "limit the safe harbor only to those activities necessary for seeking approval of a generic version of a brand-name drug product." *See Classen*, 786 F.3d at 897. In addition, Allele's intimated parade of horribles about the inability to commercialize its invention through application of the safe harbor in this context is also incorrect. By its own admission, Allele is presently commercializing its invention through a robust licensing program. *See* D.I. 29 at ¶ 26 ("[h]undreds of organizations and universities have active licenses to use Allele's mNeonGreen technology"). Further, § 271(e)(1) recognizes that the use of a patented invention for basic research unrelated to generating information for the FDA is not immune from infringement. *See Merck*, 545 U.S. at 206-07.

In sum, the statutory language of § 271(e)(1) is clear—all inventions and discoveries are "patented inventions." There is no requirement that the invention be subject to FDA approval or eligible for PTE, *i.e.*, there is no need for statutory symmetry or "perfect product fit." Allele may try to poke holes through the broad protection offered by the safe harbor by characterizing its invention as a "research tool," but the statute and case law make clear that no such exception exists. To the extent Allele alleges that mNeonGreen is covered by the '221 patent, whether called a "research tool" or not, it is a "patented invention" under the terms of the Amended Complaint. Because mNeonGreen is allegedly a "patented invention" and Regeneron's accused use was "reasonably related" to the development and submission of information to the FDA, Allele's Amended Complaint fails to state a claim as a matter of law under the safe harbor provision of § 271(e)(1).

C. Allele's Allegations of "Post-Approval" Uses and Uses Unrelated to FDA Submission are Unsupported and Should be Properly Dismissed

Recognizing that the allegations in its original complaint would not survive a motion to dismiss under the safe harbor of § 271(e)(1), Allele filed an amended complaint with a handful of new allegations—upon information and belief—regarding purported "post-approval" uses and uses allegedly unrelated to FDA submission. *See* D.I. 29, ¶¶ 34-38. Specifically, Allele alleges—upon information and belief—that Regeneron has made "post-approval marketing uses of Allele's mNeonGreen . . . including but not limited to commercial purposes such as validation, quality control, promotion and for regulatory submissions abroad." D.I. 29, ¶ 35. Further, that Regeneron used mNeonGreen to secure issuance of two U.S. Patents, which Allele argues is unrelated to FDA submission. *Id.* at ¶¶ 36-37.

These new allegations are conclusory and baseless and cannot save Allele's case. To begin with, notwithstanding Allele's allegations, Regeneron's product is not currently approved

by the FDA, so there can be no such post-approval uses.[7] Rather, Regeneron's product is currently being distributed pursuant to EUA, and Regeneron has confirmed that it has ceased all use of mNeonGreen. That Regeneron is now distributing its antibody cocktail to doctors and patients is irrelevant, as it is undisputed that neither the product itself, nor its manufacture, sale, or use constitutes infringement. Furthermore, controlling case law makes clear that intent and alternative uses of protected information does not remove the safe harbor immunity. In *Abtox*, the Federal Circuit made clear that the safe harbor provision "requires only that the otherwise infringing act be performed 'solely for *uses* reasonably related to' FDA approval." *Abtox*, 122 F.3d at 1030 (emphasis in original). The data obtained from the act shielded by the safe harbor can later be used "for more than FDA approval." *Id.*; *see also Telectronics Pacing Sys. v. Ventritex, Inc.*, 982 F.2d 1520, 1524 (Fed. Cir. 1992) (holding that the clear, plain meaning of § 271(e)(1) does not revoke the protections of the safe harbor "when the resulting data is later used for non-FDA reporting purposes.").

As for the disclosure in a patent application of the same data generated for FDA submission, the Federal Circuit in *Classen* directly examined this issue and rejected it, ruling that using information obtained from protected uses does not revoke the protection offered by the safe harbor. *See Classen*, 786 F.3d at 897-98. Specifically, the Court held that "the subsequent disclosure or use of *information* obtained from an exempt [study], even for purposes other than regulatory approval, does not repeal that exemption of the [study]." *Id.* at 898 (emphasis in

[7] Before Allele filed its Amended Complaint, Regeneron confirmed that it ceased using the accused technology, and will not use it in the future. Regeneron is still seeking final regulatory approval from the FDA. Pursuant to the Court's order during the June 15, 2021 hearing, Regeneron is providing Allele a sworn declaration affirming that it ceased use of mNeonGreen and commits to not using it in the future for any purpose.

original). The Court also noted that "[f]iling a patent application is generally not an infringement of a patent. . . . It is not commercializing an invention." *Id*.

As for the alleged use for regulatory submissions abroad, courts have similarly rejected the proposition that the use of the same data protected under the safe harbor for regulatory submissions outside the U.S. repeals the safe harbor protection. *See Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 3 F. Supp. 2d 104, 111 (D. Mass. 1998) (quoting *Telectronics*, 982 F.2d 1524) (rejecting plaintiff's suggestion that use of the same data for Japanese and European regulators repealed the safe harbor protection, explaining that "[t]o accept this position would require this Court 'to read into this statute an unspoken requirement that the disclosure of information obtained during clinical trials to persons other than FDA officials, although not in itself an act of infringement, somehow 'repeals' the exemption.").

Additionally, the Federal Circuit has explained that because the statute "does not look to the underlying purposes or attendant consequences" of the otherwise infringing act, the alleged infringer's "intent or alternative uses," such as the co-existence of a commercial purpose, "are irrelevant" to the application of the safe harbor. *See Abtox*, 122 F.3d at 1030; *see also Classen*, 786 F.3d at 898 ("Congress did not intend to prevent competitors 'from using, in an admittedly non-infringing manner, the derived test data for fund raising and other business purposes.'"); *Genentech, Inc. v. Insmed Inc.*, 436 F. Supp. 2d 1080, 1095 (N.D. Cal. 2006) ("The Court finds that, even if the allegedly infringing experiments were conducted, in part, for commercial reasons, the experiments would produce information that would be given to the FDA in order to get FDA approval. Thus, research conducted by Protegan would be protected under the safe harbor doctrine."). Likewise, "the breadth of the exemption extends even to activities the 'actual purpose' of which may be 'promotional' rather than regulatory, at least where those activities are

'consistent with the collection of data necessary for filing an application with the [FDA] . . . for approval.'" *Momenta II*, 809 F.3d at 619 (quoting *Abtox*, 122 F.3d at 1027). Thus, even assuming Regeneron's use had some tangential commercial or promotional purpose, the safe harbor would still apply because the use was related to generating data for FDA.

In sum, Regeneron has not engaged in any "post-approval" use of mNeonGreen, and merely included the same data it generated for its FDA submission in its patent applications and allegedly in foreign regulatory submissions. Because Regeneron's use is protected under the safe harbor, as discussed above, additional uses of the same data do not surrender safe harbor protection.

D. Allele's Willful Infringement Allegations Fail to State a Cognizable Claim

Allele's allegations that Regeneron willfully infringed the '221 patent also fail to state a claim. Allele alleges—again on information and belief—that Regeneron "has actual knowledge of the '221 patent and actual knowledge that its activities constitute direct infringement of the '221 patent, or has willfully blinded itself to the infringing nature of its activities, and yet continues its infringing activities." D.I. 29, ¶ 53. However, in order to state a claim of willful infringement, a patentee must adequately plead the following requisite factors, beyond mere conclusory allegations: (1) knowledge of the patent; (2) subjective intent to infringe; and (3) egregiousness. *See Novartis Vaccines & Diagnostics*, 2018 WL 5282887, at *2-3; *see also Halo*, 136 S. Ct. at 1933, 1935. Allele's Amended Complaint fails on all three prongs.

First, Allele's allegations regarding purported pre-suit communications fail to adequately plead knowledge by Regeneron. Allele does not allege that its communications even mentioned the '221 patent, and tellingly, did not attach them as exhibits to its Amended Complaint, even after Regeneron brought these infirmities to Allele's attention. *See, e.g., Verint Sys. Inc. v. Red Box Recorders Ltd.*, No. 14-cv-05403, D.I. 138, at 7, 9 (S.D.N.Y. Aug 10, 2016) (dismissing

willfulness allegations where complaint exhibits "contain[ed] no direct reference to [] the patent itself"). Further, Allele, a sophisticated biotechnology and pharmaceuticals company, does not allege that, when faced with potential patent infringement, it ever reached out to Regeneron's in-house legal team or outside counsel. Instead, Allele alleges that it "completed an online contact form directed to Regeneron's business development group" and called Regeneron's corporate headquarters—during the height of the pandemic when the vast majority of the workforce was working remotely—instead. D.I. 29, ¶¶ 43-46. Second, mere reference to willfulness "cannot alone state a claim for willful infringement." *Novartis*, 2018 WL 5282887, at *3. Instead, Allele is required to allege facts that could plausibly demonstrate that Regeneron not only knew of the '221 patent, but also that Regeneron had a subjective intent to infringe. *See id.* at *2. Here, Allele's Amended Complaint is entirely devoid of any factual allegations to suggest Regeneron knew or should have known that it was engaging in wrongful conduct. In addition, Allele is required to allege that Regeneron's actions were "egregious." *See id.* at *2-3. Allele's conclusory allegations entirely fail to plead that Regeneron's actions were "willful, wanton, malicious, bad-faith, deliberate, consciously wrongful, flagrant, or—indeed—characteristic of a pirate," especially where Allele fails to adequately plead that Regeneron even knew about the '221 patent. *See Halo*, 136 S. Ct. at 1932.

VI. CONCLUSION

For the reasons stated above, Regeneron respectfully requests that the Court grant Regeneron's motion to dismiss pursuant to Rule 12(b)(6).

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Respectfully Submitted,

LATHAM & WATKINS LLP

/s / Michael A. Morin___
Michael A. Morin (*pro hac vice*)
David P. Frazier (*pro hac vice*)
555 Eleventh Street, NW
Suite 1000
Washington, D.C. 20004
michael.morin@lw.com
david.frazier@lw.com
Tel: (202) 637-2200
Fax: (202) 637-2201

Arlene Lee Chow
Michelle Ernst
1271 Avenue of the Americas
New York, NY 10020
arlene.chow@lw.com
michelle.ernst@lw.com
Tel: (212) 906-1200
Fax: (212) 751-4864

Attorneys for Defendant Regeneron Pharmaceuticals, Inc.