Appeal No. 2019-2011

IN THE

United States Court of Appeals for the Federal Circuit

CONCERT PHARMACEUTICALS, INC.,

Appellant,

—v.—

INCYTE CORPORATION,

Appellee.

ON APPEAL FROM THE UNITED STATES PATENT AND TRADEMARK OFFICE, PATENT TRIAL AND APPEAL BOARD, IN NO. IPR2017-01256 BEFORE ERICA A. FRANKLIN, ADMINISTRATIVE PATENT JUDGE

BRIEF FOR *AMICUS CURIAE* BALD GIRLS DO LUNCH IN SUPPORT OF APPELLANT

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CERTIFICATE OF INTEREST

Counsel for *amicus curiae* Bald Girls Do Lunch certifies the following:

1. The full name of every party represented by me is:

   Bald Girls Do Lunch.

2. The name of the real party in interest represented by me is:

   None.

3. All parent corporations and any publicly held companies that own 10 percent or more of the stock in the party represented by me are:

   None.

4. The names of all law firms and the partners and associates that have appeared for the party in the trial court or are expected to appear for the party in this Court and who are not already listed on the docket for this case are:

   None.

5. The title and number of any case known to counsel to be pending in this or any other court or agency that will directly affect or be directly affected by this court's decision in the pending appeal are:

   None.

Dated: July 1, 2022

/s/ *John Kappos*
John Kappos

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Pursuant to Federal Rule of Appellate Procedure 29(a), all parties have consented to the filing of this *amicus curiae* brief.

STATEMENT OF INTEREST OF *AMICUS CURIAE*[1]

Amicus Curiae Bald Girls Do Lunch ("BGDL") is a 501(c)(3) non-profit organization dedicated to improving the quality of life for females living with alopecia areata ("AA"), an autoimmune skin disease resulting in partial to complete hair loss on all hair-bearing areas of the body, including, for example, on the face, resulting in loss of eyebrows and eyelashes. BGDL's mission is to enhance the self-esteem, self-confidence, sense of community, and capacity of AA patients to manage the various aspects of living with AA effectively, to improve the acceptance of females with AA worldwide by educating the public and increasing public awareness, knowledge, and understanding of AA, and to support research and development efforts to understand and treat the disease.

In 2012, there was a long-felt, unmet need for a treatment for AA. That need was satisfied by Appellant's innovative drug claimed in U.S. Patent No. 9,249,149 ("'149 Patent"). BGDL supports efforts by companies such as Appellant that are committed to developing and bringing to market innovative drugs to treat serious

[1] BGDL files this brief pursuant to Rule 29(a) of the Federal Rules of Appellate Procedure. Neither Appellant nor Appellant's counsel authored this brief in whole or in part, or contributed financial support intended to fund the preparation or submission of this brief. And no other individual or organization contributed financial support intended to fund the preparation or submission of this brief.

conditions and fill unmet medical needs. BGDL supports reversal of the obviousness determination by the Patent Trial and Appeal Board ("PTAB") and, more specifically, supports reversal of the determination that objective indicia of long-felt, unmet need can be ignored because the subject matter of the '149 Patent had not yet received FDA approval.

SUMMARY OF THE ARGUMENT

AA is an autoimmune skin disease that results in the loss of hair on the patient's scalp and other hair-bearing areas on the body. AA is not a simple cosmetic problem—it is a chronic, often devastating condition that has substantial and wide-ranging implications, affecting patient's physical, mental, and emotional health. Indeed, in severe cases, AA can lead to chronic depression. There is no cure for AA.

In 2012, there were over six million people in the United States with a lifetime risk of developing AA. No FDA-approved AA treatment existed, and off-label treatments were ineffective or not tolerable long-term, or both, and many caused unwanted side effects, ranging from unpleasant or undesirable to potentially serious. There was thus a critical need for a safe and effective long-term treatment for AA. The long-felt, unmet need for an AA treatment was satisfied in 2012 by the innovative CTP-543 AA treatment claimed in Appellant's '149 Patent.

ARGUMENT

I. The Obviousness Analysis Includes Consideration Of Objective Indicia Of Nonobviousness

The Supreme Court has long required the obviousness analysis to include consideration of each of the following four factors, which are critical to an obviousness determination: "(1) the scope and content of prior art, (2) differences between claims and prior art, (3) the level of ordinary skill in pertinent art, and (4) secondary considerations such as commercial success and satisfaction of a long-felt need." *Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)); *see also Apple Inc. v. Int'l Trade Comm'n*, 725 F.3d 1356, 1365 (Fed. Cir. 2013) ("We have repeatedly held that evidence relating to all four *Graham* factors—including objective evidence of secondary considerations—must be considered before determining whether the claimed invention would have been obvious to one of skill in the art at the time of invention.").

A. Objective Indicia Of Nonobviousness Are Critical To Guard Against Hindsight Bias

Evidence of objective indicia are critical to the obviousness analysis in order to prevent inappropriate use of hindsight bias. *See, e.g.*, *Apple*, 725 F.3d at 1366 ("[Secondary considerations] evidence guards against the use of hindsight because it helps 'turn back the clock and place the claims in the context that led to their invention.'" (citations omitted)); *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346,

1358 (Fed. Cir. 2013) (explaining that objective indicia should be considered "a critical piece of the obviousness analysis" because it "can be the most probative evidence of nonobviousness in the record, and enables the court to avert the trap of hindsight" (citations omitted)). Indeed, objective indicia can be "the most probative and cogent evidence" of nonobviousness in the record, and establish that "an invention appearing to have been obvious in light of the prior art," in fact is not. *Apple*, 725 F.3d at 1366 (citations omitted) (finding failure to consider objective indicia of nonobviousness was not harmless error); *see also Leo*, 726 F.3d at 1358 ("Here, the objective indicia of nonobviousness are crucial in avoiding the trap of hindsight when reviewing, what otherwise seems like, a combination of known elements." (citations omitted)).

B. Objective Indicia Of Long-Felt, Unmet Need Is Compelling Evidence Of Nonobviousness

Long-felt, unmet need is, when present, a compelling objective indicium of nonobviousness. In fact, as this Court has repeatedly explained, "[e]vidence of a long-felt but unresolved need tends to show non-obviousness because it is reasonable to infer that the need would have not persisted had the solution been obvious." *Forest Labs., LLC v. Sigmapharm Labs., LLC*, 918 F.3d 928, 936 (Fed. Cir. 2019) (quoting *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1332 (Fed. Cir. 2016)); *see also Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 364 F. Supp. 2d 820, 906 (S.D. Ind. 2005) ("Evidence of a long-felt but unsolved need in the industry

for the solution offered by the patented invention supports a finding that the invention would not have been obvious at the time the invention was made."), *aff'd*, 471 F.3d 1369 (Fed. Cir. 2006).

For example, in *Leo*, this Court reversed PTAB's conclusion that long-felt, unmet need did not support nonobviousness of the innovative treatment, explaining that, to the contrary, objective indicia evidence of long-felt, unmet need "[spoke] volumes to the nonobviousness" of the patent-at-issue. 726 F.3d at 1359 ("Here, the objective indicia—taken in sum—are the most 'probative evidence of nonobviousness . . . enabl[ing] the court to avert the trap of hindsight.'" (citations omitted)).

II. Long-Felt, Unmet Need Is Determined From The Patent Filing, Not The Marketed Product

A proper long-felt, unmet need analysis turns on the patent application filing. Courts determine the existence of a long-felt, unmet need as of the date of patent application filing, and then consider whether that long-felt, unmet need was satisfied by the innovative pharmaceutical treatment claimed in the patent application.

A. Presence Of A Long-Felt, Unmet Need Is Determined As Of The Time Of Patent Filing

The presence of a long-felt, unmet need is determined as of the filing date of the challenged patent. Indeed, courts are ***required*** to "look to the filing date of the challenged invention to assess the presence of a long-felt and unmet need." *Procter*

& Gamble, 566 F.3d at 998 (citing *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877 (Fed. Cir. 1998)); *see also Merck Sharp & Dohme Corp. v. Sandoz Inc.*, No. 3:12-CV-03289-PGS, 2015 WL 5089543, at *45 (D.N.J. Aug. 27, 2015) (explaining, "'long-felt need is analyzed as of the date of an articulated identified problem and evidence of efforts to solve that problem.' In practical terms, courts 'look to the filing date of the challenged invention to assess the presence of a long-felt and unmet need.'" (citing *Tex. Instruments, Inc. v. Int'l Trade Comm'n*, 988 F.2d 1165, 1178 (Fed. Cir. 1993); *Procter & Gamble*, 566 F.3d at 998)); *Eli Lilly*, 364 F. Supp. 2d at 852 (same).

This Court and others have long adhered to this standard when determining whether objective indicia of long-felt, unmet need supports the nonobviousness of an inventive treatment. For example, in *Procter & Gamble*, this Court found that when the challenged patent was filed "in the mid–1980s, osteoporosis was recognized as a serious disease and existing treatments were inadequate" which supported the existence of a long-felt, unmet need at the time of patent filing. 566 F.3d at 998 (holding that "it was not clear error for the district court to conclude that risedronate met such a need and that secondary considerations supported a finding of non-obviousness").

Similarly, in *Forest Laboratories*, this Court held that the district court did not clearly err in finding that objective indicia of long-felt, unmet need weighed in favor

of nonobviousness because "at the time of the invention [in 1994], there was a long-felt, but unmet, need for 'a safe, effective, and tolerable atypical antipsychotic useful to treat schizophrenia and mania'" and evidence supported that asenapine met that need. 918 F.3d at 936. The Court found that "prior to 1994" when the patent was filed, "typical antipsychotics were the primary therapeutic options for treating schizophrenia and mania," however, they "possessed debilitating side effects" and "a significant number of patients did not respond to treatment." *Id.* (citations omitted). Moreover, "there were also two atypical antipsychotics available" but "[o]ne 'require[d] constant blood monitoring' and had a 'life-threatening side effect'" and "[t]he other had a variety of side effects that resulted in a discontinuation rate of around 74%." *Id.* (citations omitted). Accordingly, agreeing with the district court, this Court held that "ordinarily skilled artisans 'recognized the need for additional antipsychotic drugs' with improved side effect profiles" in 1994 and "asenapine met this profile." *Id.* (citations omitted).

In *Bristol-Myers Squibb Co. v. Teva Pharmaceuticals USA, Inc.*, the court explained:

> The Federal Circuit has recently explicitly stated that ***a court is to assess whether a long-felt and unmet need existed as of the "filing date*** of the challenged invention," ***not as of "the time the invention becomes available on the market***, when it can actually satisfy that need." In light of this clear, recent guidance from the Federal Circuit, the court feels compelled to assess the "long-felt and unmet need" prong as of October 1990 [the patent's filing date].

923 F. Supp. 2d 602, 683 (D. Del. 2013) (citations omitted) (emphases added), *aff'd*, 752 F.3d 967 (Fed. Cir. 2014).

B. Satisfaction Of A Long-Felt, Unmet Need Is Determined Based On The Invention As Claimed In The Patent Filing

Likewise, whether the innovative treatment satisfies the long-felt, unmet need—i.e., creates the solution to the long-felt, unmet need—is determined based on the inventive treatment as claimed in the as-filed patent application. *See, e.g.*, *Eli Lilly*, 364 F. Supp. 2d at 906 ("Evidence of a long-felt but unsolved need in the industry for the solution offered by the patented invention supports a finding that the invention would not have been obvious at the time the invention was made.").

Satisfaction of a long-felt, unmet need by a claimed innovative treatment is determined as of the patent's filing date. For example, in *Leo*, this Court found that the inventive treatment claimed in the patent-at-issue satisfied a long-felt, unmet need in calendar year 2000, when the patent was filed. 726 F.3d at 1359 ("Yet, it was not until the '013 patent's filing in 2000 . . . that the solution to the long felt but unsolved need for a combined treatment of vitamin D and corticosteroid was created."). Likewise, in *Eli Lilly*, this Court upheld the district court's finding that the innovative treatment satisfied a long-felt, unmet need in 1990, when the patent was filed. 364 F. Supp. 2d at 852, 906 (finding that "there was a long-felt but unsolved need for a safe, atypical antipsychotic from 1975 until 1990" that "remained unsatisfied at the time Lilly filed the olanzapine ['382] patent application

in 1990" and holding that "[b]ecause [no other treatments were] prescribed or otherwise available to schizophrenic patients at the time the '382 patent was filed, olanzapine met the long-felt but unsolved need for a safe, atypical antipsychotic").

C. Neither FDA Approval Nor Market Availability Is Required To Show Long-Felt, Unmet Need

Neither FDA approval nor market availability is required to show nonobviousness of an innovative treatment based on objective indicia of long-felt, unmet need. To the contrary, this Court and others have properly held objective indicium of long-felt, unmet need weighed in favor of nonobviousness as of the patent's filing date based on the innovative treatment embodied in the patent filing—often years before the treatment is FDA-approved or available on the market. *See, e.g.*, *Bristol-Myers Squibb*, 923 F. Supp. 2d at 684 (finding that "there was clearly a long-felt but unmet need for an effective hepatitis B treatment as of October 1990, and entecavir theoretically satisfied that need (though BMS would not know that until four years later, in 1994, when it began testing entecavir against hepatitis B")).

There is no legal authority to support Appellee's position that FDA approval or market availability is necessary to show that an inventive treatment satisfies long-felt, unmet need. Indeed, this Court has already rejected that precise argument. *See Procter & Gamble*, 566 F.3d at 998. In *Procter & Gamble*, the accused infringer, Teva, argued that because the claimed osteoporosis treatment was not available as a marketed treatment at the time when the patent was filed in 1985, it could not have

satisfied the long-felt, unmet need. According to Teva, "long-felt need must be unmet at the time the invention becomes available on the market, when it can actually satisfy that need." *Id.* This Court expressly rejected Teva's argument. *See id.* (holding that "it was not clear error for the district court to conclude that [the claimed invention] met such a need [at the time of patent filing] and that secondary considerations supported a finding of non-obviousness").

Moreover, in *Forest Laboratories*, this Court rejected the argument that the inventive treatment did not satisfy a long-felt, unmet need, finding that the district court was not required to consider post-approval evidence in determining long-felt, unmet need. 918 F.3d at 936 (holding that the district court did not clearly err in its determination that objective indicia of long-felt, unmet need weighed in favor of the nonobviousness of the patented inventive treatment).

In *Eli Lilly*, at issue was Zyprexa® (olanzapine), Lilly's innovative schizophrenia treatment claimed in a patent application filed in 1990, which first became available on the market as a treatment for schizophrenic patients in 1996. 364 F. Supp. 2d at 852. However, by that time, a safe and effective treatment option was already available, and had been since 1994, when Risperdal® (risperidone) was first prescribed to treat schizophrenia. Nevertheless, this Court agreed with the district court's determination that "[o]lanzapine satisfied the long-felt but unsolved need for a safe, atypical antipsychotic" based on its findings that "the olanzapine

patent application was filed well before risperidone was found to be safe and effective for use by schizophrenic patients" and that, at the time the olanzapine patent was filed in 1990, "risperidone was not prescribed or otherwise available to schizophrenic patients." *Id.* at 852, 906.

Indeed, FDA approval and market availability are rarely, if ever, considered by courts in determining objective indicia of long-felt, unmet need in support of nonobviousness. In *Procter & Gamble*, neither the district court nor this Court considered the marketed product (Actonel®) or FDA approval date (1998) in determining that objective indicia of long-felt, unmet need supported nonobviousness of the claimed invention as of the effective filing date. *See generally* 566 F.3d at 998. Likewise, in *Leo*, neither this Court nor PTAB considered the marketed product (Talconex®) or its FDA approval date (2006) in determining whether objective indicia of long-felt, unmet need supported nonobviousness of the claimed inventive method of treatment as of the effective filing date. *See generally Leo*, 726 F.3d at 1359.

III. PTAB Erred In Rejecting Evidence Of Objective Indicia Of Long-Felt, Unmet Need For The Claimed Alopecia Areata Treatment And PTAB's Determination Should Not Be Given Deference

The conclusion by PTAB that objective indicia of long-felt, unmet need for the invention claimed in the '149 Patent does not support a finding of nonobviousness based solely on the fact that Concert's innovative AA treatment is

still in clinical testing is inconsistent with Supreme Court and Federal Circuit precedent. Courts have never demanded an FDA-approved or marketed product in order to establish objective indicia of long-felt, unmet need in favor of nonobviousness. There is no legal precedent to support a "marketed product" requirement, which would apply only to products that require premarket approval such as innovative pharmaceuticals, to find that objective indicia of long-felt, unmet need weighs in favor of nonobviousness of the product or treatment. Accordingly, consistent with the legal principles explained above and for the additional reasons explained below, PTAB's conclusion that objective indicia of long-felt, unmet need for the claimed invention does not support a finding of nonobviousness of the '149 Patent should be reversed.

A. In 2012, There Existed A Long-Felt, Unmet Need For An Alopecia Areata Treatment

Here, the "relevant timeframe" from which to assess evidence of long-felt, unmet need is 2012—the effective filing date of the '149 Patent. *See* Section II; '149 Patent (cover). Implicit in PTAB's determination that the '149 Patent has not satisfied a long-felt, unmet need for treating AA is the fact that, in 2012, there indeed existed a long-felt, unmet need for a treatment for AA. This need had been repeatedly identified throughout the literature before 2012 and in numerous public forums, including meetings before FDA attended by patients themselves.

It was known in 2012 that "[a]lthough diagnosing alopecia areata is usually

easy, treating it is not" because "[c]urative therapy does not exist, and there is a paucity of well-conducted, long-term, controlled trials evaluating therapy for alopecia areata and its effect on the quality of life." Amos Gilhar et al., *Medical Progress: Alopecia Areata*, 366 N. Engl. J. Med. 1515, 1518 (2012); *see also* Finola M. Delamere et al., *Interventions for Alopecia Areata*, Cochrane Database Syst. Rev. 2008, at 3-4 ("Overall, none of the interventions showed significant treatment benefit in terms of hair growth when compared with placebo. . . . There is no good trial evidence that any treatments provide long-term benefit to patients with alopecia areata, alopecia totalis and alopecia universalis."); Abdullah Alkhalifah et al., *Alopecia Areata Update: Part II. Treatment*, 62 J. Am. Acad. Derm. 191, 191 (2010) ("A Cochrane review has shown that few therapies for alopecia areata (AA) have been comprehensively evaluated in randomized controlled trials. The lack of good evidence-based data for therapeutic approaches is a challenge to the dermatologist in choosing efficacious AA treatments. Indeed, the Cochrane review concluded that there were no validated treatments for AA."); Victor M. Meidan & Elka Touitou, *Androgenetic Alopecia and Alopecia Areata*, 61 Drugs 53, 58-59 (2001) ("Alopecia areata is difficult to treat because of its chronic, inflammatory nature" and "[r]esearch has been hindered by the fact that relatively few double-blind, randomised trials on alopecia areata have been published and the results derived from uncontrolled trials are questionable because of the high rate of spontaneous

remission."). Moreover, it was known that AA "is one of the most difficult skin diseases to manage well" because the pathogenesis of the disease "is still not fully understood and clinical phenotype and disease course are variable." Taisuke Ito, *Advances in the Management of Alopecia Areata*, 39 J. Derm. 11, 11 (2012); *see also* Shabnam Madani & Jerry Shapiro, *Alopecia Areata Update*, 42 J. Am. Acad. Derm. 549, 557-58 (2000) ("The only predictable thing about the progress of the AA is that it is unpredictable.").

In 2012, there were no FDA-approved therapies for the treatment of AA in the United States. Off-label or unapproved treatment options were scarce, and for most patients, were disappointingly ineffective or not tolerable. As a whole, the options available in 2012 were of "little value" as they lacked the necessary requirements—efficacy and safety—for use by AA patients long-term. Maria K. Hordinsky, *Treatment of Alopecia Areata: "What Is New on the Horizon?"*, 24 Derm. Ther. 364, 364 (2011); *see also* Seema Garg & Andrew Messenger, *Alopecia Areata: Evidence-Based Treatments*, 28 Semin. Cutan. Med. Surg. 15, 17 (2009); Delamere, *Interventions for Alopecia Areata*, *supra*, at 14-16 ("[C]onsiderable numbers of patients withdrew [from studies] or were lost to follow up. . . . [I]t is clear that participants were disheartened by the lack of efficacy. . . . [E]vidence suggests that current treatment confers no long-term benefit."); Alkhalifah, *Alopecia Areata Update: Part II. Treatment*, *supra*, at 192 ("No treatment has been shown to

alter the course of the disease or to have a significant long-term benefit compared to placebo according to evidence-based assessment."); Madani & Shapiro, *Alopecia Areata Update*, *supra*, at 549 ("[A]ll treatments are palliative and do not change the prognosis of the disease."). Moreover, as of 2012 "assessment of each treatment [was] difficult because of a lack of controlled trials" lasting longer than 6 months and those that lasted longer showed "poor long-term benefit." Garg & Messenger, *Alopecia Areata: Evidence-Based Treatments*, *supra*, at 17.

Unfortunately, in many cases, "not treating" a patient's AA at all was determined to be "the best option." A.G. Messenger et al., *British Association of Dermatologists' Guidelines for the Management of Alopecia Areata 2012*, 166 Brit. Ass'n Derm. 916, 922 (2012); *see also* Delamere, *Interventions for Alopecia Areata*, *supra*, at 16 ("Considering the possibility of spontaneous remission and lack of efficacy of treatments, the option of not treating may be the best one for many patients."). Given the lack of available treatments that were efficacious and safe, there was, as of 2012, a critical "need for long-term therapy in AA." Madani & Shapiro, *Alopecia Areata Update*, *supra*, at 561.

Available therapies by 2012 were "disappointing and there are many unwanted results." Jan Wolf, Alopecia Areata Patient Testimony at U.S. Food & Drug Admin. Patient-Focused Drug Development Public Meeting, 70:17-19 (Oct. 25, 2012), https://www.fda.gov/media/84913/download; *see also* Gilhar, *Medical*

Progress: Alopecia Areata, *supra*, at 1515. And, for patients suffering from chronic AA, "the treatment choices [were] almost nonexistent." Alkhalifah, *Alopecia Areata Update: Part II. Treatment*, *supra*, at 199 (explaining "[t]here has been little progress in the treatment of AA in the past decade . . . . We are still in need of developing treatment options"). As one patient pleaded to FDA: "We desperately need an FDA-approved treatment." Jan Wolf, AA Patient Testimony at U.S. Food & Drug Admin. Patient-Focused Drug Development Public Meeting, *supra*, at 70:19-20 (Oct. 25, 2012).

"[M]ost of the available therapeutic options" were known to be "unsatisfactory" and there was "no good trial evidence that any treatment provide[d] long-term benefit to patients" with AA. M.J. Harries et al., *Management of Alopecia Areata*, 341 B.M.J. 3671, 3672 (2010); *see also* Nigel Hunt & Sue McHale, *Clinical Review: The Psychological Impact of Alopecia*, 331 B.M.J. 951, 951, 953 (2005) ("Medical treatment for the disorder has limited effectiveness. . . . Doctors should be aware of the psychological impact of alopecia, especially as current treatments have limited effectiveness. Providing treatment that is unlikely to be effective may do more psychological harm than medical good."). Therefore, there was a long-felt, unmet need for safe and effective treatments for AA. *See, e.g.*, Hordinsky, *Treatment of Alopecia Areata: "What Is New on the Horizon?"*, *supra*, at 366 (summarizing in Table 1 the subjects that were discussed at the Clinical

Research/Translational Summit on Alopecia Areata at Columbia University, held on October 23, 2010, including the "[n]eed for safe and effective treatments for alopecia areata" among "leaders in alopecia areata clinical research, as well as those in drug delivery, immunology drug development, and experts from the National Institutes of Health").

Patients with the most severe forms of AA involving the entire scalp (totalis) or whole body (universalis) are notoriously "difficult to treat over a short duration of time and require some additional or modified therapies" because they "often show high resistance against any treatment." Ito, *Advances in the Management of Alopecia Areata*, *supra*, at 11-12; *see also* Messenger, *British Association of Dermatologists' Guidelines for the Management of Alopecia Areata 2012*, *supra*, at 918 ("[T]hese patients tend to be resistant to all forms of treatment."). Indeed, it was well known at the time of the invention that "[a]ll treatments have a high failure rate" in AA totalis and universalis patients and that for these patients "there is no hope of recovery" as treatment with therapies for a long time tend to result in "no improvement." Ito, *Advances in the Management of Alopecia Areata*, *supra*, at 16. "[S]tudies incorporating patients with severe disease are hampered by the poor response to any form of treatment in this group of patients." Garg & Messenger, *Alopecia Areata: Evidence-Based Treatments*, *supra*, at 15. Therefore, it was widely-accepted that in 2012 AA totalis and universalis patients were "most in need

of an effective treatment." Pia Freyschmidt-Paul et al., *Alopecia Areata*, *in Autoimmune Diseases of the Skin: Pathogenesis, Diagnosis, Management* 385, 396 (Michael Hertl ed., 2d ed. 2005).

That Concert's innovative CTP-543 product, which is the undisputed embodiment of the treatment claimed in the '149 Patent, was granted "fast track" and "breakthrough therapy" status by FDA is further evidence that there was a long-felt, unmet need for treatment for AA patients. *FDA Grants Fast Track Designation to Concert Pharmaceuticals' CTP-543 for the Treatment of Alopecia Areata*, BusinessWire (Jan. 12, 2018), https://www.businesswire.com/news/home/20180112005098/en/FDA-Grants-Fast-Track-Designation-Concert-Pharmaceuticals%E2%80%99; Press Release, Concert Pharm. Inc., *Concert Pharmaceuticals Receives FDA Breakthrough Therapy Designation for CTP-543 for the Treatment of Alopecia Areata* (July 8, 2020) (https://ir.concertpharma.com/node/11441/pdf). Indeed, this Court has considered FDA's award of "fast track" status to a new drug as "supporting evidence [that] demonstrated that there was a long-felt and unmet need for a treatment." *Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1401, 1407 (Fed. Cir. 2014) (affirming district court's finding of nonobviousness and finding FDA's award of "fast track" status to Ferring's New Drug *Application*—i.e., the ***application*** filed ***seeking*** FDA approval for use as a marketed treatment—was evidence of long-felt and unmet

need). Indeed, according to FDA, its "fast track" program is specifically "designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need." U.S. Food & Drug Admin., *Fast Track*, https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track (last visited June 22, 2022) (explaining that "fast track" designated drugs are subject to expedited FDA review in order "to get important new drugs to the patient earlier"); *see also* U.S. Food & Drug Admin., *Breakthrough Therapy*, https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy (last visited June 22, 2022) ("Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).").

B. In 2012, Concert's Innovative Alopecia Areata Treatment Claimed In The '149 Patent Satisfied A Long-Felt, Unmet Need

That Concert's innovative treatment has not been approved for widespread use in AA patients does not preclude a finding that it ***satisfies*** a long-felt, unmet need in patients for whom other drugs were not effective. *See, e.g.*, *Argentum Pharm. LLC v. Research Corp. Techs., Inc.*, No. IPR2016-00204, 2017 WL 1096590, at

*17–18 (P.T.A.B. Mar. 22, 2017), *aff'd sub nom*. *Mylan Pharm. Inc. v. Research Corp. Techs., Inc.*, 914 F.3d 1366 (Fed. Cir. 2019) ("That lacosamide has not been approved for widespread use in epilepsy patients also does not persuade us that lacosamide's effectiveness failed to satisfy a long-felt need in patients for whom other drugs were not effective. As Patent Owner contends, and Petitioner does not dispute, investigators have sought, for decades at least, to uncover effective drugs for treating epilepsy. . . . Thus, that lacosamide is effective in a subset of patients for which other antiepileptic drugs are not effective, is evidence that lacosamide satisfied a long-felt, but unmet need, which is a significant objective indicium of nonobviousness." (citations omitted)).

Clinical testing results available to date, including from Concert's recently completed Phase 3 clinical trial, THRIVE-AA1, demonstrate that Concert's innovative CTP-543 AA treatment claimed in the '149 Patent ***satisfied*** the long-felt, unmet need—41.5% of patients achieved a Severity of Alopecia Tool ("SALT") score of 20 or less at week 24 of treatment (meaning that 80% or more scalp hair coverage was achieved compared to an average baseline SALT score of 85.9 (15% scalp hair coverage) at enrollment) in the 12 mg twice-daily dose group and 29% in the 8 mg twice-daily dose group, both statistically significant relative to the placebo group. Press Release, Concert Pharm. Inc., *Concert Pharmaceuticals Reports Positive Topline Results for First CTP-543 Phase 3 Clinical Trial in Alopecia Areata*

(May 23, 2022), https://ir.concertpharma.com/news-releases/news-release-details/concert-pharmaceuticals-reports-positive-topline-results-first ("With these compelling Phase 3 data, we believe that CTP-543 has the potential to be a best-in-class treatment for patients with alopecia areata, a disease that has long been ignored."); *see also* Press Release, Concert Pharm. Inc., *Concert Pharmaceuticals Presents Positive Phase 2 Data in Alopecia Areata During Late-Breaker Session at EADV Congress* (Oct. 12, 2019), https://ir.concertpharma.com/node/11046/pdf (78% of patients rated their AA was "much improved" or "very much improved" following treatment with Concert's innovative CTP-543 AA drug (12 mg dose, administered twice-daily for 24 weeks)); Press Release, Concert Pharm. Inc., *Concert Pharmaceuticals Reports Positive CTP-543 Results from Phase 2 Alopecia Areata Trial* (Sept. 3, 2019), https://ir.concertpharma.com/node/10986/pdf (patients treated with CTP-543 experienced statistically significant results in comparison to placebo and "rated significantly greater improvement in their [AA] on the Patient Global Impression of Improvement Scale"); James Cassella et al., *CTP-543, an Oral JAK Inhibitor, Achieves Primary Endpoint in Phase 2 Randomized, Placebo-Controlled Dose-Ranging Trial in Patients with Moderate-to-Severe Alopecia Areata*, Eur. Acad. Derm. & Venereology Ann. Cong. (Oct. 12, 2019), https://www.concertpharma.com/wp-content/uploads/2019/10/EADV-Late-Breaker-CTP543-Presentation-FINAL-12OCT2019.pdf.

Concert Pharm. Inc., *Creating New Possibilities for Patients to Live Their Lives*, 10 (Oct. 2019), https://ir.concertpharma.com/static-files/c5ffc32e-8fe5-41a3-aefd-cb9ece67e9e3.

Concert's statistically significant clinical study data further establish that Concert's innovative CTP-543 AA treatment claimed in the '149 Patent is safe and effective in treating AA patients, and, accordingly, support the conclusion that CTP-543 ***satisfied*** the long-felt, unmet need in 2012 for a treatment for AA.

IV. PTAB's Conclusion Regarding Long-Felt, Unmet Need Is Detrimental To Patients And To The Future Of Pharmaceutical Innovation

The approach taken by PTAB is contrary to law and has negative policy implications: it threatens to upend the well-established obviousness analysis—solely with respect to patents on technology that requires premarket regulatory approval

such as pharmaceutical patents—and it threatens to impede the development of innovative pharmaceutical treatments necessary to care for patients, particularly patients suffering from conditions for which no treatment otherwise exists.[2] To uphold PTAB's decision that FDA approval is required to show that an innovative treatment satisfies a long-felt, unmet need frustrates the needs of patients to receive treatment and the pharmaceutical industry to protect innovation.

In exchange for the extensive research and development required to invent a new pharmaceutical treatment, innovative pharmaceutical companies receive the reward of patent protection for their inventions. *See, e.g.*, Kristina M.L. Acrinée Lybecker, *Economic Growth and Prosperity Stem from Effective Intellectual Property Rights*, 24 Geo. Mason L. Rev. 865, 868 (2017) ("Without patent protection, and other forms of intellectual property rights to protect an innovator's investment, pharmaceutical drug development will not take place."); Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 Tex. L. Rev. 503, 508 (2009) ("Without some way to delay generic competition . . . pharmaceutical companies would usually find it impossible to recoup their R&D investments and

[2] Olumiant® (baricitinib), which was discovered by Incyte, licensed to Eli Lilly & Co., and received FDA approval less than a month ago on June 13, 2022, is the first-ever treatment for AA to receive FDA approval. *See* Press Release, Eli Lilly & Co., *FDA Approves Lilly and Incyte's OLUMIANT® (baricitinib) As First and Only Systemic Medicine for Adults with Severe Alopecia Areata* (June 13, 2022) (https://investor.lilly.com/node/47401/pdf).

would likely invest their money elsewhere. With strong patent protection, however, firms can expect to enjoy a lengthy monopoly over their drugs, providing them an opportunity to profit from their investment in R&D."). Yet, by insisting on one narrow and inflexible standard applicable only to innovative pharmaceutical patents, PTAB has divorced the legal inquiry from the true nature of pharmaceutical innovation.

The grant of FDA approval to market an innovative treatment to patients almost always comes years after filing the patent application claiming the innovative treatment. This is so because patent laws incentivize innovators to file patent applications on their innovative treatments as early as possible (*see, e.g.*, 35 U.S.C. §102) and empirical research shows that in practice patents claiming innovative treatments are filed well before clinical testing begins (*see, e.g.*, Roin, *Unpatentable Drugs and the Standards of Patentability*, *supra*, at 539 ("Pharmaceutical patents are typically filed when drugs are in early preclinical research."); Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 Mich. Telecomm. & Tech. L. Rev. 345, 348 (2007) (noting that applications for "composition of matter" patents are filed before clinical testing of a molecule begins)).

The practical result of filing a patent application before clinical testing is that generally the patent issues before clinical testing is complete (and therefore also before FDA approval). *See, e.g.*, Erika Lietzan & Kristina M.L. Acri née Lybecker,

Distorted Drug Patents, 95 Wash. L. Rev. 1317, 1332-33 (2020); *see also generally* Erika Lietzan, *The Drug Innovation Paradox*, 83 Mo. L. Rev. 39 (2018) (examining 570 new drug applications approved between August 1984 and August 2016 and finding an average gap of 5.61 years between (1) the date of filing of the earliest-filed patent covering the drug or a method of using the drug and (2) the date FDA permitted clinical trials to begin).

During the ensuing period of time between patent issuance and FDA approval, the patent term, and the corresponding time of market exclusivity, shorten. *See* Michael K. Dunn, *Timing of Patent Filing and Market Exclusivity*, 10 Nat'l Rev. Drug Discov. 487, 488 (2011) (examining the relationship between initial filing date of the earliest patent application and final effective patent life, which the author refers to as "market exclusivity," and illustrating that the initial patent filing date is consistently before the start of clinical trials).

In light of this practical reality, and in order to restore the benefit of market exclusivity to the innovator, the Patent Office allows innovative pharmaceutical companies to restore patent term lost while the claimed innovative treatment product was under premarket regulatory review. *See* 35 U.S.C. §156(a). This patent term extension is needed to correct for the distortion that would otherwise occur due to the reality of drug development: the patent system encourages prompt filing, but the testing required by FDA to bring an innovative treatment to market takes years to

conduct. *See generally Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990); Dunn, *Timing of Patent Filing and Market Exclusivity*, *supra*, at 488 ("[T]he average clinical development time for a drug development project—from the first human dose to regulatory approval—is ~7.3 years."). Demanding simultaneous market availability at the time of patent filing is not only impractical, but illogical.

PTAB's approach, if affirmed, will saddle innovator pharmaceutical companies with a virtually impossible task of simultaneously bringing a clinical treatment to market while at the same time trying to obtain patent protection for the innovative treatment. Nonobviousness is determined at the time the patent application is filed. But in the real world of pharmaceutical development, FDA approval almost always comes years later. These conflicting timelines would compel an absurd result: they would either eviscerate the application of long-felt, unmet need as an objective indicia of nonobviousness in virtually every proceeding involving pharmaceutical treatment patents (because the drug is not approved as of the patent filing date) or, worse yet, all but ensure nonpatentability of virtually every pharmaceutical treatment (if the innovator waits until FDA approval before filing for patent protection). The practical reality of drug development is that clinical trials take years, and inevitably, during the normal course of conducting the clinical trials necessary to receive FDA approval and to market a commercial drug, the validity of patent claims covering the treatment would be compromised if the innovator delays

filing the patent application. Once filed, the application would likely be subject to insurmountable novelty and obviousness rejections.

CONCLUSION

For the foregoing reasons, the final decision of PTAB, concluding that objective indicia of long-felt, unmet need does not support a finding of nonobviousness of the invention claimed in the '149 Patent, should be reversed and a finding that objective indicia of long-felt, unmet need weighs in favor of nonobviousness should be entered in Appellant's favor.

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CERTIFICATE OF COMPLIANCE

This brief complies with the word limitation of Federal Rule of Appellate Procedure 29(a)(5) and Federal Circuit Rule 32(a). The brief contains 6,134 words, excluding the portions exempted by Federal Rule of Appellate Procedure 32(f) and Federal Circuit Rule 32(b).

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