

**UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY**

BAUSCH HEALTH IRELAND
LIMITED, *et al.*,

Plaintiffs/Counterclaim Defendants,

v.

PADAGIS ISRAEL
PHARMACEUTICALS LIMITED, *et al.*,

Defendants/Counterclaimants.

Civil Action No. 20-5426 (SRC) (CLW)
(CONSOLIDATED)

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**PLAINTIFFS' PROPOSED FINDINGS OF
FACT AND CONCLUSIONS OF LAW**

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I. FINDINGS OF FACT¹

A. Introduction and Procedural Background

1. This is a consolidated action for patent infringement of U.S. Patent Nos. 8,809,307 (“the ’307 patent”), 10,478,502 (“the ’502 patent”), 10,251,895 (“the ’895 patent”), and 10,426,787 (“the ’787 patent”), arising under the Drug Price Competition and Patent Term Restoration Act of 1984 (commonly referred to as the “Hatch-Waxman Act”), Pub. L. No. 98-417, 98 Stat. 1585, between Bausch Health Ireland Limited, Bausch Health Americas Inc., and Bausch Health US, LLC (collectively, “Bausch”), and Padagis Israel Pharmaceuticals Ltd. and Padagis US LLC (collectively, “Padagis”). ECF No. 1; ECF No. 1, Civ. Act. No. 20-11807.

2. This action concerns Defendants’ proposed generic versions of Plaintiffs’ Bryhali® (halobetasol propionate .01%) and Duobrii® (halobetasol propionate 0.01%, tazarotene 0.045%) lotion products, indicated for the treatment of psoriasis. Final Pretrial Order, Stipulation of Facts, ECF No. 166, § 3 (“Stip. F.”) ¶¶ 8, 18.

¹ Plaintiffs submit the following proposed Findings of Fact (“FF”) and Conclusions of Law (“CL”) concerning infringement of the Bryhali and Duobrii Patents and Padagis’s assertions of invalidity. Should the Court determine that any Finding of Fact identified in this list is more properly considered to be a Conclusion of Law, it should be so considered. Should the Court determine that any Conclusion of Law identified herein is more properly considered a Finding of Fact, it should be so considered. Plaintiffs reserve the right to revise and/or supplement these findings and conclusions consistent with existing or future orders of the Court.

3. Padagis has submitted two Abbreviated New Drug Applications (“ANDAs”) requesting FDA approval for the commercial marketing of its own generic versions of Bryhali® and Duobrii® lotions before the expiration of the ’307, ’502, ’895, and ’787 patents. Stip. F. ¶¶ 14, 27.

4. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202. ECF No. 1 at ¶ 8. No party contests personal jurisdiction or venue. ECF No. 28 ¶¶ 10, 16.

5. Civil Action Nos. 20-5426 and 20-11807 were consolidated on September 3, 2020. ECF No. 19.

6. On October 6, 2021, Defendants filed an amended answer by leave of the Court to add claims that the asserted patents were unenforceable due to inequitable conduct. ECF No. 77. After discovery, on May 20, 2022, the Court granted Plaintiffs’ motion for summary judgment against Defendants’ inequitable conduct claims. ECF No. 144.

7. A bench trial in the consolidated actions was conducted on October 4, 6, and 7, 2022. ECF Nos. 209, 210, 211.

8. At trial, Plaintiffs asserted claims 13, 16, and 20 of the ’307 patent, claims 4 and 16 of the ’502 patent, claims 3 and 6 of the ’895 patent, and claims 4, 5, and 7 of the ’787 patent (collectively, the “Asserted Claims”). ECF No. 91 at 2.

9. Padagis has stipulated that it infringes all of the Asserted Claims. ECF No. 91 at 2-3; ECF No. 199 at 1-2.

10. Padagis argues that the Asserted Claims of the '307 patent, '502 patent, '895 patent, and '787 patent are invalid for alleged obviousness under 35 U.S.C. § 103.

11. Padagis argues that the Asserted Claims of the '307 patent and '502 patent are invalid as indefinite under 35 U.S.C. § 112.

12. Padagis further argues that claim 16 of the '502 patent is invalid for lack of written description and enablement under 35 U.S.C. § 112.

1. Plaintiffs

13. Plaintiff Bausch Ireland is a company incorporated in Ireland located at 3013 Lake Drive, Citywest Business Campus, Dublin 24, Ireland. Stip. F. ¶ 1.

14. Plaintiff Bausch Americas is a company incorporated under Delaware law located at 400 Somerset Corporate Blvd., Bridgewater, New Jersey 08807. Stip. F. ¶ 2.

15. Plaintiff Bausch US is a company organized under Delaware law located at 400 Somerset Corporate Blvd., Bridgewater, New Jersey 08807. Stip. F. ¶ 3.

16. Valeant Pharmaceuticals North America LLC and Dow Pharmaceutical Sciences, Inc. are predecessor entities to some of the Bausch entities named as Plaintiffs. Stip. F. ¶ 4.

2. Defendants

17. Defendant Padagis US is a limited liability company with a place of business at 1251 Lincoln Road, Allegan, Michigan. Stip. F. ¶ 5.

18. Defendant Padagis Israel is an Israeli corporation with a place of business at 1 Rakefet St., Shoham 608500, Israel. Stip. F. ¶ 6.

19. Defendants Padagis Israel and Padagis US are both wholly owned subsidiaries of Padagis LLC. Stip. F. ¶ 7.

3. Bausch's New Drug Application No. 209355 (Bryhali®)

20. Bryhali® is a topical lotion containing the active ingredient halobetasol propionate ("HP"), 0.01% w/w, indicated for the treatment of plaque psoriasis. Stip. F. ¶ 8.

21. Padagis has stipulated that Bryhali® embodies the Asserted Claims of the '307 and '502 patents. ECF No. 208.

22. Bausch Americas holds New Drug Application ("NDA") No. 209355 for Bryhali® (HP 0.01%). Stip. F. ¶ 9.

23. The '307 and '502 patents are listed in the Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") for Bryhali®. Stip. F. ¶ 10.

4. Padagis's Abbreviated New Drug Application No. 214285

24. Padagis has submitted ANDA No. 214285 (Padagis's HP ANDA") to the United States Food & Drug Administration ("FDA") seeking approval to market

Padagis's generic halobetasol propionate (HP 0.01%) lotion ("Padagis's HP ANDA Product"). Stip. F. ¶ 14.

25. In connection with Padagis's HP ANDA, Padagis sent Bausch a letter dated March 19, 2020 concerning, *inter alia*, the '307 and '502 patents. ECF No. 1 at 6; ECF 25 at 7.

5. Bausch's New Drug Application No. 209354 (Duobrii®)

26. Duobrii® is a topical lotion containing the active ingredients HP, 0.01% and tazarotene ("Taz"), 0.045%, indicated for the treatment of plaque psoriasis. Stip. F. ¶ 18.

27. Padagis has stipulated that Duobrii® embodies the Asserted Claims of the '307, '502, '895, and '787 patents. ECF No. 208; ECF No. 199 at 2.

28. Bausch Americas holds the approved NDA No. 209354 for Duobrii® (HP 0.01%; Taz 0.045%). Stip. F. ¶ 19.

29. The '307, '502, '895, and '787 patents are listed in the Orange Book for Duobrii®. Stip. F. ¶ 20.

6. Padagis's Abbreviated New Drug Application No. 214646

30. Padagis has submitted ANDA No. 214626 ("Padagis's HP/Taz ANDA") to the FDA seeking approval to market Padagis's generic halobetasol propionate and tazarotene (HP 0.01%; Taz 0.045%) lotion ("Padagis's HP/Taz ANDA Product"). Stip. F. ¶ 27.

31. In connection with Padagis's HP/Taz ANDA, Padagis sent Bausch a letter dated July 15, 2020 concerning, *inter alia*, the '307, '502, '895, and '787 patents. ECF No. 1, Civil Action No. 20-11807, at 6; ECF 28, Civil Action No. 20-5426, at 9.

7. The Asserted Patents

a. The '307 and '502 Patents (the "Bryhali Patents")

i. The '307 patent

32. The '307 patent, entitled "Pharmaceutical Formulations Containing Corticosteroids for Topical Administration," issued on August 19, 2014. Stip. F.

¶ 38. The '307 patent names Arturo Angel and Gordon Dow as inventors. Stip. F.

¶ 39. Bausch Ireland is the assignee of the '307 patent. Stip. F. ¶ 40.

33. The '307 patent claims priority to U.S. Provisional Application No. 61/458,339, filed on November 22, 2010. Stip. F. ¶ 36. Padagis has not challenged the entitlement of the '307 patent to this priority date. The '307 patent is, therefore, accorded the benefit of the November 22, 2010 filing date. The Orange Book lists November 2, 2031 as the expiration date for the '307 patent. Stip. F. ¶ 41.

34. The '307 patent states that "[t]he potency of a topical corticosteroid in a pharmaceutical formulation is maintained even when the concentration of the corticosteroid is substantially reduced by providing the corticosteroid in a formulation containing a liquid oil component that includes a dicarboxylic acid ester and/or a monocarboxylic acid ester." JTX-001 ('307 Patent) at Abstract.

35. Table 1 of the '307 patent lists 7 classes of corticosteroids. All of the listed superpotent corticosteroids, the most potent class (Class 1), contain a concentration of .05% or higher. JTX-001 ('307 Patent) at Table 1.

36. The specification of the '307 patent states that the high potency of Class 1 (superpotent) corticosteroids “correlates with a high incidence of severity of systemic side effects, including hypothalamic-pituitary-adrenal (HPA) axis suppression” which limits their duration of use to 2 weeks. JTX-001 ('307 Patent) at 2:36-41.

37. Claim 13 of the '307 patent is directed to a pharmaceutical composition for topical application to the skin of an individual comprising halobetasol propionate at a concentration of 0.025% or less and a liquid oil component comprising diethyl sebacate, and wherein at least 50% of the halobetasol propionate is solubilized in the liquid oil component at 22 °C. JTX-001 ('307 Patent).

38. Claim 16 of the '307 patent is directed to a method for treating a disorder of the skin that is amenable to treatment with a topical corticosteroid, the method comprising providing a pharmaceutical composition comprising (i) halobetasol propionate at a concentration of 0.04% or less and (ii) a liquid oil component comprising one or more dicarboxylic acid esters selected from the group of diethyl sebacate, diisopropyl adipate, and dibutyl sebacate and (iii) wherein at least 25% of the halobetasol propionate is solubilized in the liquid oil component at 22 °C,

wherein (iv) the concentration of the liquid oil component is sufficient to dissolve the amount of halobetasol propionate in the composition at a temperature of 22 °C $\pm$ 2 °C, and applying an amount to the skin that is effective in ameliorating the signs or symptoms of the disorder. JTX-001 ('307 Patent).

39. Claim 20 of the '307 patent is directed to a pharmaceutical composition for topical application to the skin of an individual comprising halobetasol propionate at a concentration of 0.04% or less and a liquid oil component comprising diethyl sebacate and light mineral oil, and wherein at least 25% of the halobetasol propionate is solubilized in the liquid oil component at 22 °C. JTX-001 ('307 Patent).

40. During prosecution, Dr. Gordon Dow (an inventor on the '307 patent) submitted a declaration to the U.S. Patent & Trademark Office explaining that a person of ordinary skill in the art ("POSA") would have expected that reducing the concentration of halobetasol to a concentration of 0.04% or less would have "resulted in too great a reduction in efficacy of the halobetasol composition to provide a pharmaceutically useful product." JTX-005 (Certified Copy of Pros. Hist. for '307 Patent) at BAU00000204.

ii. The '502 patent

41. The '502 patent, titled "Pharmaceutical Formulations Containing Corticosteroids for Topical Administration," issued on November 19, 2019. Stip. F.

¶ 44. The '502 patent names Arturo Angel and Gordon Dow as inventors. Stip. F.

¶ 45. Bausch Ireland is the assignee of the '502 patent. Stip. F. ¶ 46.

42. The '502 patent claims priority to U.S. Provisional Application No. 61/458,339 filed on November 22, 2010. Stip. F. ¶ 42. Padagis has not challenged the entitlement of the '502 patent to this priority date. The '502 patent is, therefore, accorded the benefit of the November 22, 2010 filing date. The Orange Book lists November 2, 2031 as the expiration date for the '502 patent. Stip. F. ¶ 47.

43. The specification of the '502 patent is substantially identical to that of the '502 patent. JTX-004 ('502 Patent).

44. Claim 4 of the '502 patent is directed to a pharmaceutical composition for topical application to the skin of an individual comprising: a liquid oil component comprising diethyl sebacate and halobetasol propionate at a concentration less than 0.01%, and an aqueous component comprising water, wherein the composition is free of white petrolatum. JTX-004 ('502 Patent).

45. Claim 16 of the '502 patent is directed to a method of treating a disorder of the skin that is amenable to treatment with a topical corticosteroid, the method comprising applying a pharmaceutical composition comprising (i) a liquid oil component comprising diethyl sebacate (ii) a corticosteroid selected from the group consisting of halobetasol propionate, clobetasol propionate, betamethasone dipropionate, diflorasone diacetate, and fluocinonide at a concentration less than

0.05%; (iii) an aqueous component comprising water, (iv) wherein the composition is free of white petrolatum, to the skin of an individual having the disorder in an amount that is effective in ameliorating the signs or symptoms of the disorder. JTX-004 ('502 Patent).

b. The '895 and '787 patents (the “Duobrii Patents”)

i. The '895 patent

46. The '895 patent, entitled “Topical Compositions and Methods for treating Psoriasis,” issued on April 9, 2019. Stip. F. ¶ 50. The '895 patent names Gordon Dow, Radhakrishnan Pillai, and Varsha Bhatt as inventors. Stip. F. ¶ 51. Bausch Health Ireland is the assignee of the '895 patent. Stip. F. ¶ 52.

47. The '895 patent claims priority to U.S. Provisional Application Serial No. 62/181,481 filed on June 18, 2015. Stip. F. ¶ 48. Padagis has not challenged the entitlement of the '895 patent to this priority date. The '895 patent is, therefore, accorded the benefit of the June 18, 2015 filing date. The Orange Book lists June 6, 2036 as the expiration date for the '895 patent. Stip. F. ¶ 53.

48. The '895 patent describes “[t]opical pharmaceutical compositions [comprising] a combination of a corticosteroid [and] a retinoid; and methods for treating psoriasis with the same.” JTX-002 ('895 Patent) at Abstract.

49. The '895 patent describes the results of a Phase II clinical study of IDP-118 (Duobrii®). JTX-002 ('895 Patent) at 10:44-50. The results from the clinical

demonstrate that IDP-118 demonstrated a synergistic efficacy and a synergistic reduction in adverse events; that is, it outperformed the expectation in both of these areas from the combination of halobetasol alone in the vehicle with tazarotene alone in the vehicle. JTX-002 ('895 Patent) at Tables 8, 9, 13.

50. Claim 3 of the '895 patent is directed to a topical pharmaceutical composition for treating psoriasis the composition comprising: (a) active ingredients consisting of: (i) halobetasol propionate, at a concentration of 0.01 percent by weight of the composition; and (ii) tazarotene at a concentration of 0.045 percent by weight of the composition; and (b) a dermatologically acceptable carrier; wherein the composition is an oil-in-water emulsion; wherein an oil phase in the oil-in-water emulsion comprises a liquid oil component; wherein the liquid oil component is liquid at 22°C and consists of diethyl [] sebacate and light mineral oil; and wherein the composition comprising the halobetasol propionate and the tazarotene at said concentrations is capable of providing synergistic efficacy and synergistic reduction of at least an adverse event selected from the group consisting of itching, burning, and stinging, for said treating, and wherein the topical pharmaceutical composition is also a lotion. JTX-002 ('895 Patent) at Claim 3.

51. Claim 6 of the '895 patent is directed to a topical pharmaceutical composition for treating psoriasis the composition comprising: (a) active ingredients consisting of: (i) halobetasol propionate, at a concentration of 0.01 percent by weight of the

composition; and (ii) tazarotene at a concentration of 0.045 percent by weight of the composition; and (b) a dermatologically acceptable carrier; wherein the composition is an oil-in-water emulsion; wherein an oil phase in the oil-in-water emulsion comprises a liquid oil component; wherein the liquid oil component is liquid at 22°C and consists of diethyl [] sebacate at a concentration of 2.5-3.5 percent and light mineral oil at a concentration of 7.5-8.5 percent by weight; and wherein the composition comprising the halobetasol propionate and the tazarotene at said concentrations is capable of providing synergistic efficacy and synergistic reduction of at least an adverse event selected from the group consisting of itching, burning, and stinging, for said treating, and wherein the aqueous phase of the emulsion comprises a carbomer copolymer type B at a concentration of 0.3-0.5 percent by weight of the composition, and a carbomer homopolymer type A at a concentration of 0.5-0.7 percent by weight. JTX-002 ('895 Patent) at Claim 6.

52. During prosecution, Dr. Jeffrey Sugarman submitted a declaration to the U.S. Patent & Trademark Office explaining that he was surprised by the clinical results of IDP-118, which unexpectedly achieved synergistic efficacy over the combination of the individual monotherapies. JTX-006-4 (Declaration Under 37 C.F.R. § 1.132) at 2.

ii. The '787 patent

53. The '787 patent, entitled "Topical Compositions and Methods for Treating Psoriasis," issued on October 1, 2019. Stip. F. ¶ 56. The '787 patent names Gordon Dow, Radhakrishnan Pillai, and Varsha Bhatt as inventors. Stip. F. ¶ 57. Bausch Health Ireland is the assignee of the '787 patent. Stip. F. ¶ 58.

54. The '787 patent claims priority to U.S. Provisional Application Serial No. 62/181,481, which was filed on June 18, 2015. Stip. F. ¶ 54. Padagis has not challenged the entitlement of the '787 patent to this priority date. The '787 patent is, therefore, accorded the benefit of the June 18, 2015 filing date. The Orange Book lists June 6, 2036 as the expiration date for the '787 patent. Stip. F. ¶ 59.

55. The specification of the '787 patent is substantially identical to that of the '895 patent. JTX-003 ('787 Patent).

56. Claim 4 of the '787 patent is directed to a method of treating psoriasis, the method comprising topically applying a pharmaceutical composition to an affected area of a body of a subject suffering from psoriasis; wherein the composition is an oil-in-water emulsion comprising: (a) halobetasol propionate at a concentration of 0.01 percent by weight of the composition; (b) tazarotene at a concentration of 0.045 percent by weight of the composition; and (c) an aqueous dermatologically acceptable carrier comprising carbomer copolymer type B, carbomer homopolymer type A, and a liquid oil comprising diethyl sebacate and light mineral oil; wherein

said applying is carried out one or more times per day for a period of time sufficient to treat such psoriasis and wherein the composition comprising the halobetasol propionate and the tazarotene at said concentrations is capable of providing synergistic efficacy and synergistic reduction of at least an adverse event selected from the group consisting of itching, burning, and stinging in said treating, wherein said halobetasol propionate and said tazarotene are dissolved in a component of said liquid oil of the oil-in-water emulsion. JTX-003 ('787 Patent) at Claim 4.

57. Claim 5 of the '787 patent is directed to a method of treating psoriasis, the method comprising topically applying a pharmaceutical composition to an affected area of a body of a subject suffering from psoriasis; wherein the composition is an oil-in-water emulsion and a lotion comprising: (a) halobetasol propionate at a concentration of 0.01 percent by weight of the composition; (b) tazarotene at a concentration of 0.045 percent by weight of the composition; and (c) an aqueous dermatologically acceptable carrier comprising carbomer copolymer type B, carbomer homopolymer type A, and a liquid oil comprising diethyl sebacate and light mineral oil; wherein said applying is carried out one or more times per day for a period of time sufficient to treat such psoriasis and wherein the composition comprising the halobetasol propionate and the tazarotene at said concentrations is capable of providing synergistic efficacy and synergistic reduction of at least an

adverse event selected from the group consisting of itching, burning, and stinging in said treating. JTX-003 ('787 Patent) at Claim 5.

58. Claim 7 of the '787 patent is directed to a method of treating psoriasis, the method comprising topically applying a pharmaceutical composition to an affected area of a body of a subject suffering from psoriasis wherein said applying is carried out once per day for eight weeks, wherein the composition comprises: (a) halobetasol propionate at a concentration of 0.01 percent by weight of the composition; (b) tazarotene at a concentration of 0.045 percent by weight of the composition; and (c) an aqueous dermatologically acceptable carrier comprising carbomer copolymer type B, carbomer homopolymer type A, and a liquid oil comprising diethyl sebacate and light mineral oil; wherein said applying is carried out one or more times per day for a period of time sufficient to treat such psoriasis and wherein the composition comprising the halobetasol propionate and the tazarotene at said concentrations is capable of providing synergistic efficacy and synergistic reduction of at least an adverse event selected from the group consisting of itching, burning, and stinging in said treating, wherein the method continues to provide relief to said psoriasis for a period of four weeks after said eight weeks of application of said composition. JTX-003 ('787 Patent) at Claim 7.

B. Summary of Findings

1. The Bryhali Patents

59. The Court finds that, as discussed in § I.F.1 below, Padagis has failed to meet its burden of proving obviousness with respect to claims 13, 16, and 20 of the '307 patent and claims 4 and 16 of the '502 patent by clear and convincing evidence.

60. The gravamen of Padagis's argument is that a person of ordinary skill in the art would have been motivated to develop topical halobetasol formulations with a concentration less than the 0.05% concentration of Ultravate®, the existing commercial halobetasol product at the time, in order to avoid the two-week limitation imposed by the FDA due to the risk of systemic absorption.

61. Padagis also contends the skilled artisan would turn to old prior art references from the 1980's and 1990's (the '295 patent, DX-003, the '566 patent, DX-004, and JP '228, DX-005) to pick out a particular solvent, diethyl sebacate, as well as other ingredients such as light mineral oil, to arrive at the lower-concentration halobetasol formulations claimed in the Bryhali Patents.

62. But the problem of systemic absorption with halobetasol and the other superpotent corticosteroids had been well known since at least the 1970's, long before Ultravate® came out in 1990. Tr. 206:19-207:6. (Stern cross examination). And Ultravate®, which had been developed by the global pharmaceutical company Bristol-Myers Squibb, came out with a 0.05% halobetasol concentration, not a lower

concentration. Tr. 212:25-213:18 (Stern cross examination); Tr. 398:6-18 (Michniak-Kohn cross examination).

63. In the 20 years between the time Ultravate® came out in 1990 and the November 22, 2010 priority date of the Bryhali Patents, no one even experimented with a halobetasol concentration of less than 0.05%, much less came out with a commercial halobetasol product of less than 0.05%. It cannot seriously be argued that a person of ordinary skill in the art would have been motivated to lower the concentration of halobetasol when nobody did it for 20 years. Tr. 302:22-303:18 (Stern).

64. There is also no basis for contending that a person of ordinary skill in the art would have been motivated to turn to the old prior art references Padagis asserts to pick and choose ingredients for a lower-concentration formulation, even if there had been a motivation to reduce the concentration. These old prior art references taught the use of penetration enhancers to push the drug all the way through the skin, which was a common approach in those years but which would have exacerbated the problem of systemic absorption. This is the opposite of the approach taken by the Bausch inventors in the Bryhali Patents. *E.g.*, Tr. 494:14-495:1; 501:5-502:3 (Lane).

65. In short, Padagis's obviousness case is belied by what actually happened in the real world and bears all the hallmarks of a hindsight-driven analysis. The invention of the Bryhali Patents was contrary to the common wisdom that lowering

the concentration of a superpotent corticosteroid would reduce its potency and efficacy, at a time when practitioners wanted the most powerful drugs possible to treat psoriasis, a stubborn and debilitating disease. Tr. 486:4-9 (Lane); Tr. 625:17-19, 626:20:627:2 (Stein Gold). Indeed, one of the prior art references Padagis cites, Blum, actually taught away from using a lower concentration. *Infra* at § I.F.1.q.

66. Based on the entire record in this case, it is clear that the invention of the Bryhali Patents was innovative and would not have been obvious to a person of ordinary skill in the art as of the priority date of the Bryhali Patents.

67. The Court further finds that, as discussed in § I.F.2 below, Padagis has failed to meet its burden of proving indefiniteness with respect to claims 13, 16, and 20 of the '307 patent and claims 4 and 16 of the '502 patent by clear and convincing evidence.

68. Both Plaintiffs' and Defendants' formulation experts agreed that a person of ordinary skill in the art could readily understand what is meant by "liquid oil component" as that term has been construed by the Court. Tr. 421:12-422:2; 575:23-576:13.

69. Padagis's only argument that the claims are indefinite is the fact that Table 2 of the Bryhali Patents does not include an emulsifying agent (specifically, sorbitan monooleate), which is a "liquid oil component" as the term is defined by the Court, in its calculation of the liquid oil component. Tr. 576:14-579:8; 582:15-25.

70. However, Bausch's formulation expert, Dr. Lane, explained that a person of ordinary skill would understand that Table 2 only includes the solvent ingredients under the header "Concentration of Liquid Oil Component" because the table is calculating the solubility of halobetasol. Tr. 577:11-578:8; JTX-001 ('307 patent) at Table 2.

71. Thus, the term "liquid oil component" as construed by the Court is clear and understandable by a person of ordinary skill in the art and is not rendered unclear or ambiguous by the specification of the Bryhali Patents.

2. The Duobrii Patents

72. While Padagis's experts did not present their obviousness case for the Duobrii Patents this way in their direct testimony, on cross examination it became clear that Padagis's argument is that the specific IDP-118 formulation would have been obvious, that it inherently has the synergies claimed in the Duobrii Patents, and that a person of ordinary skill in the art would reasonably have expected that IDP-118 would have the claimed synergies.

73. Nothing but hindsight would lead a person of ordinary skill in the art to have picked the specific formulation for IDP-118 (minus the tazarotene) from the broad disclosures and examples of the '824 Publication which Padagis relies upon as the primary reference for its obviousness case.

74. Padagis's clinical expert, Dr. Stern, expressly admitted that he was relying on the Duobrii Patents themselves to identify the particular example (Formula 4A) in the '824 Publication which discloses the IDP-118 formulation minus the tazarotene. Tr. 221:12-223:7 (Stern cross examination).

75. Padagis's formulation expert, Dr. Michniak-Kohn, also admitted there was no particular reason for a person of ordinary skill in the art to have selected Formula 4A, and that a different example with a 0.025% halobetasol concentration was identified as a preferred embodiment. Tr. 376:15-22 (Michniak-Kohn); Tr. 429:18-430:13 (Michniak-Kohn cross examination).

76. Even if a person of ordinary skill in the art would have selected Formula 4A, Padagis did not prove that the skilled artisan would have been motivated to add tazarotene to the formulation, and to add it at the specific 0.045% concentration of tazarotene in IDP-118 and as claimed in the Duobrii Patents. *Infra* at § I.G.1.f.

77. The only disclosure of tazarotene and halobetasol together at the precise concentrations in IDP-118 is the IDP-118 Study, a report on the ClinicalTrials.gov website of the experimental IDP-118 product being used in a Phase II clinical trial. But the IDP-118 Study is not prior art under the experimental use doctrine and, even if it is, Padagis's expert Dr. Stern admitted that people in the field would not have been motivated to pursue a product that someone else already has that far along in development. Tr. 287:13-17 (Stern cross examination); *infra* at § I.G.1.n- I.G.1.o.

Thus, there would have been no motivation to combine the IDP-118 Study with the ‘824 Publication.

78. Finally, even if the IDP-118 formulation would have been obvious, Padagis has not shown that a person of ordinary skill would have had a reasonable expectation that IDP-118 would have the synergies claimed in the Duobrii Patents. Dr. Stern relies on statements made in two prior art references, Gollnick and Gandhi, that combinations of tazarotene and halobetasol (or a corticosteroid) would have “synergy” or “synergistic” effects. But the record is clear that “synergy” and “synergistic” is used in more than one way in the literature, and Dr. Stern admitted that he had no way of knowing that Gollnick or Gandhi were using “synergy” in the same way it is used in the Duobrii Patents. Tr. 291:18-294:3 (Stern cross examination).

79. Accordingly, even if the IDP-118 formulation would have been obvious, Padagis did not prove that a person of ordinary skill in the art would reasonably have expected it would have the claimed synergies. And the unrebutted testimony was that the inventors were clearly surprised by the extraordinary results demonstrated by IDP-118 in its Phase II clinical trial.

C. Witnesses Presented at Trial

1. Plaintiffs' Expert Witnesses

a. Dr. Linda Stein Gold

80. The Court accepted Dr. Stein Gold as a qualified expert in the field of dermatology, including dermatological clinical studies, psoriasis and the topical treatment of skin disease including psoriasis. Tr. 38:9-17.

81. Dr. Stein Gold received her B.S. in 1985 from the University of Pennsylvania. Dr. Stein Gold received her M.D. in 1989 from the University of Pennsylvania and completed her residency in dermatology at Henry Ford Hospital in 1993. Tr. 35:9-14; PTX-341 (Stein Gold *Curriculum Vitae*) at 1.

82. Dr. Stein Gold is a board-certified dermatologist by the American Board of Dermatology. Tr. 34:24-35:8. She currently serves as the elected Vice President of the American Academy of Dermatology, the premier association for board-certified dermatologists in the United States. Tr. 35:2-8.

83. Dr. Stein Gold has served as the Director of Dermatology Clinical Research at Henry Ford Health System for the last two decades. Tr. 34:24-35:8; PTX-341 (Stein Gold *Curriculum Vitae*) at 1.

84. Dr. Stein Gold is a practicing medical dermatologist who sees medical patients three days per week. Tr. 35:20-23.

85. Dr. Stein Gold works with pharmaceutical companies and has served as principal investigator on dozens of clinical trials relating to psoriasis. Tr. 36:2-14;

37:11-21. In addition to her medical patients, she treats clinical research patients at least one day per week. Tr. 35:20-23.

86. Dr. Stein Gold also regularly speaks nationally and internationally on topical treatments for psoriasis. Tr. 36:22-25; PTX-341 (Stein Gold *Curriculum Vitae*) at 2-3.

87. Dr. Stein Gold previously served on the Academy's Board of Directors from 2016 to 2020 and has served on various executive, priorities, corporate relations, and budget committees of the American Academy of Dermatology since 2015. PTX-341 (Stein Gold *Curriculum Vitae*) at 2.

88. Dr. Stein Gold has served as a member of several academic and professional boards and foundations, including the National Psoriasis Foundation Medical Board, and the Skin Disease Education Foundation. Dr. Stein Gold has authored more than 200 publications in journals such as the New England Journal of Medicine and the Journal of the American Academy of Dermatology, many of which relate to the treatment of psoriasis. Tr. 36:15-21.

89. By November 2010 (as well as June 2015), Dr. Stein Gold met and exceeded the qualifications of a person of skill in the art for the Bryhali Patents and the Duobrii Patents, under either Plaintiffs' or Defendants' definition. Tr. 34:20-38:8; PTX-341 (Stein Gold *Curriculum Vitae*).

90. Dr. Stein Gold offered credible testimony on the causes and treatment of psoriasis with topical medications (specifically, superpotent corticosteroids and retinoids), the use of combination products to treat psoriasis, the expectations and needs of clinicians relating to low-dose concentrations of halobetasol propionate and tazarotene, the unpredictability of clinical trials, the use of the term “synergy” in the field of clinical dermatology, and the rarity of synergy in fixed-dose combination products particularly for psoriasis.

91. Dr. Stein Gold also offered credible testimony on the subject of the non-obviousness of the Asserted Claims of the '307, '502, '895, and '787 patents, Padagis's asserted prior art references, and certain objective indicia of non-obviousness, including the long-felt need for a safe, efficacious, longer-term topical therapy for psoriasis met by Bryhali® and Duobrii®, unexpected results of the synergistic efficacy and synergistic reduction in adverse events shown in the Duobrii Patents, unexpected results in achieving a treatment with a superpotent corticosteroid for a period of 8 weeks, the failure of others to combine halobetasol propionate and tazarotene in a single commercial product prior to Duobrii®, skepticism of those skilled in the art regarding combining 0.01% halobetasol propionate with tazarotene, and the industry praise received by Duobrii®.

b. Dr. Majella Lane

92. The Court accepted Dr. Lane as a qualified expert in the field of topical pharmaceutical formulations, including development and testing of topical pharmaceutical formulations. Tr. 468:23-469:8.

93. Dr. Lane received her B.Sc. in Pharmaceutical Science from Trinity College, University of Dublin, Ireland. Dr. Lane received her Ph.D. in Pharmaceutical Science in 1997 from Trinity College, University of Dublin, Ireland. Tr. 468:6-10; PTX-085 (Lane *Curriculum Vitae*) at 1.

94. Dr. Lane is currently an Associate Professor and Director of the Skin Research Group at University College in London, England (“UCL”). Tr. 467:6-10. Dr. Lane has held this position since October 2008. PTX-085 (Lane *Curriculum Vitae*) at 1.

95. In her role at UCL, Dr. Lane instructs students on topics such as topical preparations and conducts research that focuses on topical formulations specifically with reference to the skin, nails, and other mucous membranes. A primary goal of Dr. Lane’s research is to develop safe and effective medicines for the treatment of skin diseases. PTX-085 (Lane *Curriculum Vitae*) at 4; Tr. 467:25-468:5.

96. Dr. Lane consults with a wide range of pharmaceutical companies in industry on developing topical formulations. Tr. 468:18-19.

97. In addition to her activities at UCL, Dr. Lane also serves as a member of the European Medicines Agency Working Group on topical medicines, as well as a member of the Chemistry, Pharmacy and Standards Expert Advisory Group of the Medicines and Healthcare Regulatory Agency of the United Kingdom. PTX-085 (Lane *Curriculum Vitae*) at 5.

98. Dr. Lane has authored numerous book chapters and peer-reviewed journal articles on the subject of topical pharmaceutical formulations. PTX-085 (Lane *Curriculum Vitae*) at 6-12.

99. By November 2010 (as well as June 2015), Dr. Lane met and exceeded the qualifications of a person of skill in the art for the Bryhali Patents and the Duobrii Patents, under either Plaintiffs' or Defendants' definition. Tr. 467:6-468:17; PTX-085 (Lane *Curriculum Vitae*).

100. Dr. Lane offered credible testimony on issues related to validity including the non-obviousness of the Asserted Claims (or certain elements of the asserted claims) of the '307, '502, '895, and '787 patents, Padagis's asserted prior art references, certain objective indicia of non-obviousness, including unexpected results, and the definiteness of certain terms of the Bryhali Patents.

c. Dr. Sean Sheridan

101. The Court accepted Dr. Sheridan as a qualified expert in the field of economics. Tr. 732:4-14.

102. Dr. Sheridan is a Principal in the Life Sciences practice at Charles River Associates (“CRA”) in its Chicago office. His consulting work has been primarily related to the valuation and strategic management of intellectual property assets. PTX-333 (Sheridan *Curriculum Vitae*) at 1.

103. Dr. Sheridan received a B.S. in biology from Appalachian State University. He then received his M.B.A. in Finance and Economics from the University of Chicago Booth School of Business and received a Ph.D. in genetics from the University of Chicago. PTX-333 (Sheridan *Curriculum Vitae*) at 1.

104. Dr. Sheridan has valued intellectual property rights in connection with litigation, licensing, divestitures and acquisitions, and in a variety of other contexts. PTX-333 (Sheridan *Curriculum Vitae*) at 1.

105. Dr. Sheridan has been named to the IAM Patent 1000 – *The World’s Leading Patent Professionals* (as a recommended economic expert) every year since 2019, based on nominations from industry participants. PTX-333 (Sheridan *Curriculum Vitae*) at 1.

106. Dr. Sheridan has authored numerous publications focused on life science intellectual property issues and intellectual property valuation. PTX-333 (Sheridan *Curriculum Vitae*) at 8-9.

107. Dr. Sheridan offered credible testimony on the commercial success of the Duobrii® product as an objective indicia of non-obviousness with regards to the

Asserted Claims of the '895 and '787 patents, including but not limited to the market for plaque psoriasis treatments, the demand and relevant market for Duobrii®, financial performance trends for recently launched pharmaceuticals, and the financial performance of the Duobrii® product (including but not limited to sales in the relevant market, profits, market share, insurance and commercial coverage), and the commercial performance of the drug.

2. Defendants' Expert Witnesses

a. Dr. Robert Stern

108. Padagis offered expert testimony from Dr. Robert Stern, a professor of dermatology at Harvard Medical School. Tr. 150:5-8. Dr. Stern was proffered as an expert in the treatment of psoriasis. Tr. 149:8-14.

109. Dr. Stern stated that he is an attending dermatologist at the Beth Israel Deaconess Medical Center, but also stated that he curtailed his medical practice in early 2020 and has not treated dermatology patients since that time. Tr. 150:6-21.

110. Dr. Stern's research does not focus on topical treatments for psoriasis. Tr. 151:13-19.

111. To the extent Dr. Stern's medical practice and research included treatment of psoriasis patients, his focus was not on topical treatments, but on treatment with ultraviolet ("UV") light therapy. DX-208 (Stern *Curriculum Vitae*) at e.g., 9, 13-14, 18-19.

112. Dr. Stern has never served as a principal investigator on a clinical trial for a topical fixed-dose combination product, or a topical superpotent corticosteroid product. Tr. 195:7-18.

113. Because Dr. Stern was not offered as an expert in dermatological clinical studies, Dr. Stern's opinions are entitled to less weight than the testimony of more qualified experts (such as Plaintiffs' clinician expert, Dr. Stein Gold) on the subject of development and clinical testing of topical therapies for the treatment of psoriasis.

114. At trial, Dr. Stern also indicated that he would rely on a formulator to render certain of his opinions relating to the interpretation of certain references (specifically, the '824 publication) that he purported to be offering opinions on in his testimony. Tr. 229:10-230:1.

115. Thus, Dr. Stern's opinions are entitled to less weight than the testimony of more qualified experts (such as Plaintiffs' formulation expert, as Dr. Lane) on the subject of interpretation of the '824 publication.

116. At trial, the opinions of Dr. Stern were often conclusory, unsupported by any documentary evidence or data, and driven by hindsight, which detracted from the weight accorded to his testimony.

b. Dr. Bozena Michniak-Kohn

117. Padagis offered expert testimony from Dr. Bozena Michniak-Kohn, a Pharmaceutics professor at Rutgers University, in the field of pharmaceutical

science, particularly in the area of the development and evaluation of dermatological formulations. Tr. 318:13-16; DX-184 (Michniak-Kohn *Curriculum Vitae*) at 1.

118. At trial, the opinions of Dr. Michniak-Kohn were often conclusory, unsupported by any documentary evidence or data, and driven by hindsight, which detracted from the weight accorded to her testimony.

c. Dr. Mickey Ferri

119. Padagis offered expert testimony from Dr. Mickey Ferri, an economist at Insight Economics, in the field of economics. Tr. 762:20-21; DX-245 (Ferri *Curriculum Vitae*) at 1-2.

120. At trial, the opinions of Dr. Ferri were often conclusory and unsupported by any documentary evidence or data, which detracted from the weight accorded to his testimony.

3. Witnesses Called by Deposition Testimony

121. At trial, Padagis played the videotaped deposition testimony of three Bausch fact witnesses: Arturo Angel, Dr. Binu Alexander, and Sean Humphrey. Tr. 793:18-797:8 (Angel); 437:14-453:22 (Alexander); 454:7-462:3 (Humphrey).

a. Arturo Angel

122. At the time of his deposition, Arturo Angel was an executive director at Bausch. Tr. 794:3-11.

123. Mr. Angel is also a named inventor on the Bryhali Patents. JTX-001 ('307 Patent) at Cover Page.

124. In portions of his videotaped deposition played by Padagis at trial, Mr. Angel discussed certain aspects of the development work performed at Bausch in connection with the IDP-118 project, such as, for example, the selection of solvents as part of the pre-formulation work. *E.g.*, Tr. 794:12-19; 795:13-796:2.

b. Dr. Binu Alexander

125. At the time of his deposition, Dr. Binu Alexander was an executive director of pharmacovigilance at Bausch & Lomb. Tr. 437:21-438:2. He provided testimony on certain subject matter as a corporate representative for Bausch. Tr. 438:10-24.

126. In portions of his videotaped deposition testimony, Dr. Alexander described his role regarding the submission of information to Clinicaltrials.Gov in connection with the clinical studies of IDP-118. *E.g.*, Tr. 441:3-13; 443:7-14. Dr. Alexander also testified regarding updates that were made to IDP-118's posted information on the Clinicaltrials.Gov website. *E.g.*, Tr. 449:21-450:7; 452:5-20.

c. Sean Humphrey

127. At the time of his deposition, Sean Humphrey was the Director of Regulatory Affairs at Bausch. Tr. 454:14-24.

128. In portions of his videotaped deposition testimony, Mr. Humphrey testified about the submission of regulatory documents to FDA in connection with Bausch's Bryhali® and Duobrii® products. *E.g.*, Tr. 456:8- 457:1; Tr. 458:8-459:2.

4. Inventor Evidence

a. Dr. Radhakrishnan Pillai

129. Dr. Radhakrishnan Pillai is the Vice President for Research and Development at Bausch. Tr. 57:6-8.

130. Dr. Pillai is a named inventor on the '895 and '787 patents. JTX-002 ('895 Patent) at Cover Page; JTX-003 ('787 Patent) at Cover Page; Tr. 57:19-21.

131. Dr. Pillai was responsible for the overall management of the Bryhali® and Duobrii® projects, including formulation development, analytical development, clinical, non-clinical, and clinical pharmacology. Tr. 59:18-60:4.

132. The development project began in 2008 with the idea for the combination product that would combine a retinoid and corticosteroid, preferably a superpotent corticosteroid. Tr. 60:5-20; 61:19-62:4. The development (from conception to development of the final vehicle) took about three to four years. Tr. 89:1-4.

133. At the beginning of the project in 2008, the Bausch development team was considering and experimenting with concentrations that were different (either higher or lower) from the marketed concentrations as well as different types of formulations (*e.g.*, gels, lotions, creams, liposomal formulations). Tr. 69:19-70:1; 70:24-71:1.

134. The first step in development was the pre-formulation phase, during which the solubility of halobetasol propionate and tazarotene were individually evaluated in different solvents or in different ratios of those solvents. Tr. 68:16-69:5; 71:23-

72:5; PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.2.1-1, Table 5.2.1-2. Once the solubility of the active ingredients had been studied individually, they were then evaluated together in the same solvent. Tr. 73:13-74:13; PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.2.1-3.

135. After the solubility studies, the compatibility of the two active ingredients with the solvents was conducted. Tr. 74:16-75:1; PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.2.2. During this part of the development, one particular solvent (dibutyl sebacate) was eliminated from consideration because it was surprisingly incompatible with tazarotene. Tr. 75:14-76:14.

136. Once the compatibility studies were conducted, the development team began to prototype development. Tr. 76:19-23. Many prototypes were developed and studied, and selection from those varied prototypes was based on multiple considerations including stability. Tr. 76:24-77:13; 78:19-23; *e.g.*, PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.3.1-1. The prototypes contained different concentrations of halobetasol, including .01%, .025%, and .035%. Tr. 78:24-79:3.

137. The prototypes were tested in Vasoconstrictor Assay (“VCA”) studies, which evaluate skin blanching (or whitening) which correlates with steroid potency.

Tr. 77:24-78.18. Dr. Pillai did not have any expectation of which prototypes would perform better than the others in the VCA studies. Tr. 79:4-11. The results of the VCA studies showed the prototypes with the lower concentrations of halobetasol propionate, including 0.01%, were able to demonstrate the same level of skin blanching as Ultravate®. Tr. 79:12-; 80:21; PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.3.1-1. Dr. Pillai stated that these results were “very surprising.”

138. A second round of VCA testing was subsequently performed. Tr. 80:22-81:6. This study evaluated two different concentrations of halobetasol propionate, 0.01% and 0.025%, and included different formulations with the 0.01% concentration, with the goal of confirming the surprising results of the first VCA panel. Tr. 81:9-82:5. The second VCA study also included continued testing based on solvent evaluated during the solubility studies and other ingredients based on the needs of the formulation. Tr. 82:6-21. The second study confirmed that the .01% halobetasol prototypes could maintain potency compared to a higher concentration superpotent corticosteroid. Tr. 83:10-18. PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.3.2-1. Dr. Pillai stated that the second VCA study confirmed and validated the first set of results and was very exciting. Tr. 83:19-84:7.

139. After the second round of VCA studies, an *in vitro* skin penetration study was performed on some of the 0.01% and 0.025% concentration halobetasol prototypes in combination with .09% concentration tazarotene. Tr. 84:8-14; 84:21-85:6. The results of the *in vitro* skin penetration showed the drugs were being pushed into the receptor phase and into systemic circulation. Tr. 85:7-86:16; PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.3.3-2. After considering the results of the *in vitro* skin penetration study, one ingredient in the prototype formulations (propylene glycol) was replaced with a different ingredient (sorbitol). Tr. 86:17-87:9.

140. In addition, after considering the results of the *in vitro* skin penetration study, the development team made the decision to decrease the amount of tazarotene from 0.09% to 0.045%. Tr. 87:10-87:17. The 0.045% concentration of tazarotene was not studied, modified, or tested any further. Tr. 87:10-87:23. Testing would be required to determine whether a different concentration of tazarotene (for example, 0.035% or 0.025%) might work better than 0.045%. Tr. 87:21-88:3.

141. Ultimately, two lead compositions were identified—one containing 0.01% halobetasol propionate and 0.025% halobetasol propionate. Tr. 88:2-13; PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at Table 5.3.4-1. Ultimately, Bausch selected the 0.01% halobetasol propionate formulation and subsequently conducted further studies, including animal, non-clinical, and

clinical testing on this formulation (both with and without 0.045% tazarotene). Tr. 88:15-89:2; 89:5-23.

142. These further studies included both VCA and clinical studies comparing Bryhali® and Ultravate® which further confirmed that the lower concentration could maintain potency and efficacy compared to the higher-concentration Ultravate®. Tr. 89:23-93:19; JTX-012-10 (Study V01-122A-203) at 9.1. These studies also included testing of the Duobrii® product, including the pivotal Phase 2 study in which the product unexpectedly demonstrated unprecedented clinical results, including over 50 percent treatment success as well as the claimed synergies. Tr. 93:23-96:19; 98:8-19; 101:13-103:12; JTX012-9 (Study V01-118A-201) at Table 1; PTX-243 (Email re Topline Tables).

D. A Person of Ordinary Skill in the Art

143. Plaintiffs' experts Dr. Lane and Dr. Stein Gold testified that a person of ordinary skill in the art pertaining to the '307 patent and '502 patent in 2010, and the '895 patent and '787 patent in 2015, would have several years of experience working in the design and evaluation of formulations for the topical treatment of diseases of the skin, having either a Ph.D. (or equivalent degree) or an M.D. (or equivalent degree) and at least two to three years of post-graduate experience studying and/or treating skin diseases in the field of dermatology or a related field or a degree in chemistry, pharmaceutical chemistry, pharmacy, medicine, clinical pharmacology,

pharmacokinetics, or another pharmaceutical science related field, and at least five years of experience in designing, developing, evaluating, and/or testing pharmaceutical formulations for topical treatment of skin diseases. Tr. 474:1-15; Tr. 621:25-622:5 (discussing the definition shown on PDX4-5).

144. Defendants' experts testified that a person of ordinary skill in the art would have worked as part of a multi-disciplinary team of scientists and medical professionals, which included at least a person with an advanced degree in chemistry, pharmacy, or a related discipline, and several years of experience developing topical pharmaceutical formulations or, alternatively, a person with a Bachelor's degree in chemistry, pharmacy, or a related discipline, and a greater degree of experience developing topical pharmaceutical formulations and (a clinician with several years of experience using topical pharmaceutical formulations to treat patients with skin disorders (including psoriasis), and an understanding of the considerations relevant to evaluating the clinical effects, for example safety and efficacy, of topical pharmaceutical formulations. Tr. 156:16-157:7; Tr. 313:6-314:2.

145. Dr. Lane and Dr. Stein Gold explained they understood Defendants' definition of a person of skill in the art to differ slightly from Plaintiffs' definition. Tr. 474:16-23; Tr. 622:6-8. However, Dr. Lane and Dr. Stein Gold both testified that their opinions would not change if Defendants' definition of a POSA were applied. Tr. 474:24-475:3; Tr. 622:6-8.

146. Defendants' experts similarly agreed their opinions would not change under Plaintiffs' definition. Tr. 157:11-17; Tr. 314:10-15

147. The Court adopts Plaintiffs' definition of a person of skill in the art.

E. Background And General Findings of Fact

1. Treatment of psoriasis

148. Psoriasis is an inflammatory skin disease caused by a defect in the immune system. Tr. 39:8-11 (Stein Gold). It affects seven to eight million people in the United States. It causes red, thick skin which can be painful and itchy. In addition to the serious physical symptoms, it can also mentally impact patients as the appearance of the psoriatic skin can cause embarrassment and anxiety. Tr. 38:19-39:6; 39:15-17 (Stein Gold).

149. In healthy patients, skin cells start in the lower level of skin (called the basal layer) and migrate to the upper layer of the skin (called the epidermis). As the cell passes through various skin layers, the cell learns to perform a different function associated with each layer in a process known as 'differentiation.' Once the skin cells arrive at the epidermal layer, a properly differentiated skin cell is 'sloughed off' or shed. In a healthy patient, it takes about a month for a skin cell to migrate from the basal layer to the epidermis, where it will ultimately slough off. Tr. 39:20-40:4 (Stein Gold).

150. In psoriasis patients, the body instructs the skin cells to replicate very rapidly. The skin cells can move from the basal layer to the epidermis in a matter of, for example, days instead of a month. In this rapid growth process, the skin cells do not learn to perform their different functions and so are not appropriately differentiated. Once they arrive at the epidermis, they do not shed in the way healthy cells do. This causes the build-up of the characteristic thick, scaly, and inflamed red plaques associated with psoriasis. Tr. 40:5-17 (Stein Gold).

151. Psoriasis patients have options for treatment depending on the severity of their psoriasis and the location of their psoriasis. These may include, for example, oral systemic medications or biologic medications. However, for patients with localized disease, a topical agent is the standard of care. Tr. 40:18-25; Tr. 645:10-20.

152. Within topical therapies for psoriasis treatments, there are three main categories: topical corticosteroids, vitamin A analogues (retinoids), and vitamin D analogues. Among topical therapies, corticosteroids are the mainstay of therapy for psoriasis patients. Tr. 41:3-9 (Stein Gold). Using more than one therapy at a time in a combination regimen (*i.e.*, two different drugs, with two different mechanisms of action, applied at different times) was the standard of care for psoriasis patients. Tr. 52:6-15 (Stein Gold).

a. Use of topical superpotent corticosteroids to treat psoriasis

153. Topical corticosteroids refer to the class of anti-inflammatory drugs that are applied directly to the skin. They are used in the treatment of psoriasis. Tr. 41:12-17 (Stein Gold).

154. There are seven different potency classes of steroids: Class 1 (Superpotent), Class 2 (Potent), Class 3 (Upper-Mid-Strength), Class 4 (Mid-strength), Class 5 (Lower Mid-strength), Class 6 (Mild), Class 7 (Least Potent). JTX-001 ('307 patent) at Table 1.

155. For psoriasis patients who are managing painful and inflamed skin, the standard of care is to prescribe the most potent corticosteroids, which are the Class 1 (superpotent) corticosteroids. The clinician's goal is to use the highest potency drug available to get the disease under control as quickly as possible. Tr. 42:1-16 (Stein Gold).

156. Superpotent corticosteroids are associated with serious side effects. In particular, the absorption of superpotent corticosteroids into the bloodstream can cause a side effect in patients known as hypothalamic-pituitary-adrenal ("HPA") axis suppression, a hormonal abnormality. Tr. 41:18-25; Tr. 483:20-484:5. The risk of HPA axis suppression limits the use of superpotent corticosteroids to two weeks. Tr. 483:20-484:5.

157. However, this two-week limitation posed a problem for patients, as two weeks of treatment with a superpotent corticosteroid was typically not long enough to treat psoriasis patients. Tr. 50:15-18; Tr. 638:20-639:5.

i. Halobetasol Propionate

158. Halobetasol propionate is a superpotent corticosteroid used in the treatment of psoriasis. Stip. F. ¶ 31; Tr. 43:11-17. It was first invented in 1978. Tr. 44:2-3.²

159. Halobetasol propionate was first commercialized in 1990 under the brand name Ultravate®. Tr. 43:18-22; PTX-358 (Westwood Squibb Ultravate® (Halobetasol Propionate) Approved, The Pink Letter) at BAU01199696.

160. Ultravate®, which was available as a cream or an ointment, contains halobetasol propionate in a concentration of 0.05%. Tr. 43:23-44:1.

161. The U.S. Food & Drug Administration (“FDA”) limited the use of Ultravate® to two consecutive weeks due to the risk associated with HPA axis suppression. Tr. 50:6-14; Tr. 636:4-9.

162. Ultravate® cream and Ultravate® ointment do not contain diethyl sebacate as an ingredient. Tr. 393:16-18; PTX-396 (Ultravate® Cream Label) at HALOBET0019226.

² Halobetasol propionate is sometimes referred to herein as “halobetasol” or “HP.”

163. Ultravate® cream and Ultravate® ointment do not contain light mineral oil as an ingredient. Tr. 64:9-11; PTX-396 (Ultravate® Cream Label) at HALOBET0019226.

164. Ultravate® ointment contained white petrolatum as an ingredient. Tr. 64:12-20.

ii. Clobetasol Propionate

165. Clobetasol propionate is another superpotent corticosteroid indicated for the treatment of psoriasis. It has been marketed in an emollient form called Temovate E® since 1996. Tr. 399:21-23. The concentration of clobetasol propionate in Temovate E® is 0.05% by weight. PTX-086 at HALOBET0019792.

166. Temovate E® does not include diethyl sebacate as an ingredient. PTX-086 (Temovate E® Label) at HALOBET0019792.

167. Temovate E® does not include light mineral oil as an ingredient. PTX-086 (Temovate E® Label) at HALOBET0019792.

b. Use of Topical Retinoids to Treat Psoriasis

168. Retinoids are another class of medications used to treat psoriasis. At a high level, retinoids aid in the treatment of psoriasis by facilitating the appropriate differentiation of skin cells. Tr. 44:4-17.

i. Tazarotene

169. A topical retinoid used to treat psoriasis is tazarotene, marketed under the brand name Tazorac®. Tr. 44:18-35. Tazorac® is indicated for the treatment of psoriasis in both 0.1% and 0.05% concentrations. Tr. 623:21-624:3.

170. Because tazarotene has the potential to cause skin irritation, it was rare for dermatologists to use tazarotene as a monotherapy for treating psoriasis. Tr. 47:4-10; Tr. 624:15-25.

171. Tazorac® (0.1% and 0.05%) does not contain diethyl sebacate as an ingredient. DX-010 (Tazorac® Label) at HALOBET0019206.

172. Tazorac® (0.1% and 0.05%) does not contain light mineral oil as an ingredient. DX-010 (Tazorac® Label) at HALOBET0019206.

F. The Bryhali Patents

173. Padagis has challenged the validity of the Asserted Claims of the Bryhali Patents on grounds of obviousness, indefiniteness, lack of written description, and lack of enablement. For the reasons discussed below. Padagis has failed to prove that any of the Asserted Claims of the Bryhali Patents are invalid.

1. Padagis Failed to Prove That the Asserted Claims of the Bryhali Patents Are Invalid for Obviousness

a. Formulation Science Generally

174. At trial, the experts for both parties agreed that formulations play an enormous role in the delivery of any drug, including in topical treatments for skin

diseases such as psoriasis. Tr. 475:22-25 (Lane); Tr. 382:11-17 (Michniak-Kohn); Tr. 198:23-199:15 (Stern). Indeed, Padagis's formulation expert, Dr. Michniak-Kohn, admitted on cross examination that "the formulation makes all the difference in the delivery of the drug" (Tr. 382:11-13) and that a person of ordinary skill in the art "would have known how important a formulation is for a topical corticosteroid product" as of the 2010 priority date of the Bryhali Patents. Tr. 382:18-20 (Michniak-Kohn cross examination).

175. Both parties' formulation experts also agreed that there was a vast range of options available to a person of skill in the art for developing topical formulations as of 2010. Tr. 477:18-478:4 (Lane); Tr. 383:1-5 (Michniak-Kohn).

176. At trial, both parties' formulation experts referred to the *Handbook of Pharmaceutical Excipients* (DX-201), which Dr. Michniak-Kohn acknowledged contained thousands of different excipients. Tr. 394:19-395:6 (Michniak-Kohn cross); *see also* Tr. 477:23-478:1 (Lane).

177. As Dr. Michniak-Kohn admitted, there was also an "extensive literature available to a POSA describing ingredients and different formulations that could be used in topical corticosteroids." Tr. 383:1-5 (Michniak-Kohn); *see also* Tr. 478:5-7 (Lane) ("so not just the textbook we saw earlier today in court, there are a huge range of textbooks, reference sources, databases that we can consult").

178. As Dr. Lane testified, having all those options and information available does not mean that a POSA would have a guideline or framework to take one to a particular formulation. Tr. 478:8-10. And as Dr. Lane further testified, formulation development almost always involves working with excipients that have long been in the formulation arts. Tr. 478:10-12 (Lane). Dr. Michniak-Kohn did not disagree.

b. Formulation Science is an Unpredictable Art

179. It is undisputed that formulation science is an unpredictable art. Bausch's formulation expert, Dr. Lane, gave that opinion. Padagis's formulation expert, Dr. Michniak-Kohn, did not disagree.

180. Both experts agreed that there are a series of interactions that must be managed in the development of topical formulations. Tr. 476:4-19 (Lane); Tr. 384:20-385:22 (Michniak-Kohn). As Dr. Lane testified, these include vehicle-drug interactions, vehicle-skin interactions, drug-skin interactions, and vehicle-drug-skin interactions. Tr. 476:4-19.

181. Dr. Lane further testified that the formulation of topical treatments is an unpredictable art. Tr. 476:1-3 ("So formulation science is unpredictable. It's rigorous. It requires trial and error experimentation. There are no predictable outcomes in this field."); Tr. 475:16-476:19; 477:8-17; 478:16-479:20 (Lane).

182. Dr. Lane explained that the selection of a vehicle for a topical pharmaceutical formulation requires consideration of many factors. She presented

Table 2 from Bronaugh (PTX 307), which she uses in teaching undergraduate students, to illustrate why the formulation of topical formulations for application to the skin is an unpredictable art. Tr. 478:19-23.

183. Table 2 provides a series of considerations and sometimes “competing challenges” the formulation scientist can be faced with in formulation development. Tr. 478:24-479:20 (Lane).

184. Dr. Lane further testified that there have been additional factors beyond those enumerated in Table 2 that researchers have learned must be taken into account since Table 2 was published in 2002.

185. The same book chapter in which Table 2 appears, written by Dr. Eric Smith, further corroborates Dr. Lane’s testimony that formulation science is an unpredictable art. Dr. Smith wrote:

As outlined here, many factors influence the development, the choice, the performance and, hence, the clinical effectiveness of the vehicle. These factors are often viewed from different perspectives by patients, chemists, formulators, and clinicians. Due to this complexity, no uniform and comprehensive recommendations and guidelines are available for the development and the use of semi-solid formulations. Dermatological vehicle treatment may therefore remain an “art” gleaned by personal experience, rather than a defined, textbook science.

PTX 307 at BAU01199966. *See also* Tr. 480:18-481:6 (“... [W]hat Dr. Smith is telling us here that it’s not just science. Topical formulation is actually an art that

is gleaned from your own personal experience as a formulator”) (Lane); Tr. 568:9-12 (“It’s unpredictable. We have no way of knowing the outcome of experimentation that we conduct. There can be failures. Formulation programs can take years. Sometimes they never result in a product.”) (Lane).

186. Dr. Lane’s testimony that formulation science is an unpredictable art was unrebutted. Padagis did not cross examine Dr. Lane on this topic and Padagis’s formulation expert, Dr. Michniak-Kohn, did not address the unpredictability of formulation science in her testimony.

187. Accordingly, the Court accepts Dr. Lane’s unrebutted testimony that formulating topical treatments is an unpredictable art, which the Court finds straightforward, supported, and credible.

c. The Problem of Systemic Risk Associated With the Use of Superpotent Corticosteroids Had Been Well Known In the Field Since At Least the 1970s

188. The problem addressed by the invention of the Bryhali Patents arises from the systemic risk associated with the topical use of superpotent corticosteroids to treat skin diseases.

189. As explained in the Background of the Invention section of the Bryhali Patents, the high potency of superpotent corticosteroids “is correlated with a high incidence and severity of systemic side effects, including hypothalamic-pituitary-adrenal (HPA) axis suppression” JTX-004 (‘502 patent) 2:47-50; *see also* Tr.

332:4-12 (Michniak-Kohn) (reading this passage into the record); Tr. 331:10-18 (Michniak-Kohn); Tr. 161:17-22 (Stern).

190. Dr. Lane similarly testified that “superpotent corticosteroids have a side effect that if they are absorbed all the way through the skin and into the blood supply, they can cause this problem of hypothalamic-pituitary-adrenal axis suppression.” Tr. 483:21-24.

191. Padagis’s clinical expert, Dr. Stern, testified “it was well-known that super-high potent corticosteroids pose a risk of systemic side effects.” Tr. 204:12-14 (Stein cross examination).

192. It is undisputed that the problem of systemic risk associated with the topical use of superpotent corticosteroids had been well known for decades as of the 2010 priority date of the Bryhali Patents. Padagis’s clinical expert, Dr. Stern, admitted on cross examination that the problem of systemic risk with corticosteroids, and specifically with halobetasol, was known at least from the 1970s:

Q. And this problem of systemic risk with corticosteroids, and then halobetasol in particular, was long – known for a long time before Ultravate® came out [in 1990]. Isn’t that true?

A. That’s correct.

Q. This problem with halobetasol was known from the 70’s. Isn’t that true, sir?

A. At least from then, yes.

Tr. 206:25-207:6 (Stern) (emphasis added).

193. Similarly, Padagis's formulation expert, Dr. Michniak-Kohn, admitted on cross examination that the risk of adverse events with halobetasol "was known well before Ultravate® came out" in 1990. Tr. 398:9-15. (Michniak-Kohn cross examination).

194. As a result of the systemic risk associated with the use of superpotent corticosteroids, topical treatment with superpotent corticosteroids was generally limited in duration to two weeks. JTX-001 ('307 patent) 2:36-41; Tr. 50:6-11 (Stein Gold); 161:14-162:7 (Stern); 317:3-7, 332:4-11 (Michniak-Kohn); 483:17-484:12 (Lane).

195. Thus, for example, the use of the existing commercial 0.05% halobetasol product, Ultravate®, was limited to two weeks. Tr. 483:17-484:12 (Stein Gold); 317:3-7, 332:4-11 (Michniak-Kohn).

196. Use of the existing commercial 0.05% clobetasol product, Temovate E®, was also limited to two weeks, with an exception for use up to four weeks if applied to 5% to 10% of body surface area. DX-006.

197. Use of the three other available superpotent corticosteroids was also limited to two weeks. Tr. 485:8-24 (Lane); JTX-001 ('307 patent) Table 1, 1:27-35 (listing commercially-available 0.05% superpotent corticosteroids).

198. All of the experts agreed that the two week limitation was a serious drawback because two weeks of treatment is generally not long enough to treat most

patients' psoriasis. Tr. 50:15-18 (Stein Gold); 484:8-24 (Lane); 161:14-162:7, 302:22-303:18 (Stern); 332:12-17 (Michniak-Kohn).

199. Accordingly, given the two week limitation, there was a long-felt and unmet need for an efficacious superpotent steroid that could be administered for more than two weeks. JTX-001 ('307 patent) 2:46-51 ("Chronic skin conditions, such as psoriasis, however often require long periods of treatment, greater than 2 weeks, to manage such conditions. Therefore, it would be desirable to have a superpotent corticosteroid formulation with a reduced incidence and/or severity of systemic side effects so that therapy can be continued for durations longer than 2 weeks."); Tr. 643:5-12 (Stein Gold); 302:22-303:18 (Stern) (agreeing in response to a question from the Court that for 20 years after Ultravate® was approved "it's been known that Ultravate® at the 0.05% concentration can only be used for two weeks at a stretch and that that is a very serious drawback because of the side effects that would occur if you used it beyond two weeks"); 331:10-332:22 (Michniak-Kohn).

d. The Solution Provided by the Bryhali Patents Would Not Have Been Obvious

200. Padagis argued at trial that the invention of the Bryhali Patents would have been obvious because a person of ordinary skill in the art would have been motivated to develop a topical formulation with a halobetasol concentration of less than the 0.05% concentration of the commercial halobetasol product, Ultravate®, in order to

reduce the risk of systemic absorption and to permit treatments of psoriasis patents for longer than two weeks.

201. Padagis further argued it would have been obvious to develop the claimed formulations of the Bryhali Patents based on various combinations of five prior art references: U.S. Patent No. 4,233,295 (the “295 patent”) (DX-003), Blum and Yawalkar, “Multicenter, Double-Blind Comparative Observation of Application of 0.02%, 0.05% CGP 14 458 Ointments and Dermovate Ointment in the treatment of Chronic Psoriasis (“Blum”) (DX-002), U.S. Patent No. 5,326,566 (the “566 patent”) (DX-004), JP S63-255228 (“JP ‘228”) (DX-005), and the Temovate E® Label (DX-006).

202. In addition, Padagis argued that it would have been obvious to use a claimed topical composition comprising halobetasol for a period of longer than two weeks.

203. For reasons discussed below, the Court finds Padagis has not proven that the invention of the Asserted Claims of the Bryhali Patents would have been obvious to a person of ordinary skill in the art as of November 22, 2010.

e. There Was No Motivation to Use a Halobetasol Concentration of Less Than 0.05%

204. Padagis contends that as of November 2010, a person of ordinary skill in the art would have been motivated to use concentrations of halobetasol lower than the 0.05% concentration of Ultravate®, the existing commercial halobetasol product, to

as low as 0.01%, to treat psoriasis. Tr. 162:15-163:9, 164:22-165:19 (Stern); 331:8-332:22 (Michniak-Kohn).

205. Padagis's experts testified that a person of ordinary skill would have been motivated to lower the concentration because psoriasis requires treatment for longer than two weeks and a lower concentration would be expected to lower the risk of systemic side effects and thus allow treatment for longer than two weeks. *Id.*

206. Both Dr. Stern and Dr. Michniak-Kohn relied (*inter alia*) on a 1986 publication by Blum and Yawalkar ("Blum") (DX-002) as providing motivation to lower the concentration of halobetasol. Blum disclosed a clinical test comparing a 0.05% halobetasol ointment, a 0.02% halobetasol ointment, and Dermovate ointment, a 0.05% clobetasol product. According to Drs. Stern and Michniak-Kohn, Blum disclosed that the 0.02% halobetasol ointment had only a modest decrease in efficacy from the 0.05% concentration. Thus, Padagis's experts argued, Blum would have motivated a person of ordinary skill in the art to "further reduce the concentration with an expectation that all or most efficacy would be preserved." Tr. 165:4-10 (Stern); 325:3-15 (Michniak-Kohn) (Blum teaches "lowering the concentration was still effective").

207. Dr. Michniak-Kohn further testified that a person of ordinary skill in the art also would have been motivated to use halobetasol topical formulations with

halobetasol concentrations of less than 0.05% and of 0.04% or less based on the ‘295 patent, the ‘566 patent, and JP ‘228. Tr. 333:24-334:10; 350:5-25.

208. Contrary to Padagis’s contention, however, the Court finds that a person of ordinary skill in the art would not have been motivated to develop a topical halobetasol formulation with a halobetasol concentration of 0.05% or less. There are a number of reasons for this conclusion.

f. There Was No Motivation to Select Halobetasol Rather Than One of the Other Corticosteroids

209. First, as a threshold matter, Padagis did not establish that a person of ordinary skill in the art would have been motivated to pick halobetasol to work with rather than a different superpotent corticosteroid.

210. Dr. Stern testified that a person of ordinary skill would have been motivated to use concentrations of halobetasol as low as 0.01% but he offered no explanation why a person of ordinary skill would have picked halobetasol rather than another corticosteroid. He simply assumed a person of ordinary skill would have selected halobetasol in his analysis.

211. Padagis’s other expert, Dr. Michniak-Kohn, admitted on cross examination that a person of ordinary skill could have picked a different superpotent corticosteroid:

Q. And there is no specific reason for a POSA to have picked halobetasol rather than clobetasol, correct?

A. Well, they would have known that corticosteroids in general have a problem, and one of the marketed products happens to be halobetasol.

Q. Let me try my question again.

There was no specific reason for a POSA to have picked halobetasol rather than clobetasol, correct?

A. It's possible that another POSA would have taken the other drug for the same reason.

THE COURT: Doctor, please answer the question as asked.

THE WITNESS: Okay.

Could you repeat the question?

BY MR. STEINDLER: Sure.

Q. There was no specific reason for a POSA to have picked halobetasol rather than clobetasol, correct?

A. They could have picked either.

Tr. 389:11-390:4 (Dr. Michniak-Kohn cross examination).

212. And while Dr. Michniak-Kohn acknowledged that a person of ordinary skill could have picked clobetasol, a skilled artisan could also have picked any of the three other superpotent corticosteroids on the market. JTX-001 ('307 patent) Table 1, 1:32-42 (superpotent corticosteroids included betamethasone dipropionate ointment 0.05%, fluocinonide 0.1%, and diflorasone diacetate ointment 0.05%). Indeed, given that the asserted claims of the Bryhali Patents are not limited treatment of psoriasis, a skilled artisan could have selected any available corticosteroid for use

in developing a topical formulation. There are dozens of possible corticosteroids disclosed in the Bryhali Patents. *See, e.g.*, JTX-001 ('307 patent) Table 1, 1:26-2:8.

213. Thus, while Padagis's experts testified that a person of ordinary skill in the art would have been motivated to use halobetasol concentrations as low as 0.01%, they provided no explanation or evidence to support their conclusory assertion that a person of ordinary skill in the art would have selected halobetasol rather than a different corticosteroid of which dozens are disclosed to in the Bryhali Patents. At its very outset, therefore, Padagis's selection of halobetasol from among the five available superpotent corticosteroids bears the hallmarks of a hindsight-driven analysis.

g. There Was No Motivation to Lower the Concentration

214. Second, the clear weight of the evidence shows that a person of ordinary skill in the art would not have been motivated in 2010 to use concentrations of halobetasol lower than the 0.05% concentration in the commercial Ultravate® product. Certainly, Padagis did not prove to the contrary, as required to discharge its burden.

215. As Bausch's clinical expert, Dr. Stein Gold, testified, practitioners in the field wanted stronger medicines, not weaker medicines, to treat psoriasis. Tr. 625:3-22 (Stein Gold). Dr. Stein Gold testified that "dermatologists prescribe superpotent steroids far more than any other type of steroids. Even if you add the Class 2 and

Class 3 together, it doesn't really match the superpotents. We've got to get the patient under control. Give us the biggest guns that you have." Tr. 626:20:627:2 (Stein Gold).

216. Dr. Stein Gold further testified that a person of ordinary skill would not have sought "to create a less potent, less efficacious drug, as Dr. Stern suggests." Tr. 628:17-18 (Stein Gold).

217. She testified that if clinicians wanted a less potent drug to treat psoriasis, there were already numerous options available. It is undisputed that as of 2010, there was a wide range of corticosteroids available in the market, from superpotent Class 1 topical corticosteroids down to least potent Class 7 topical corticosteroids. JTX-001 ('307 patent) Table 1, 1:32-2:19. As Dr. Stein Gold stated: "So we have a whole lot of topical corticosteroids. We have corticosteroids that are Class 2, Class 3, Class 4, 5, 6, 7. We have tons of them. That's not an unmet need." Tr. 628:19-22.

218. Dr. Stein Gold further explained:

We already have less potent drugs. If you want a less potent drug, just prescribe one that's on the market. Why do you want to go make a new one? We have those already. It doesn't make sense to make something that's less potent. We want more potent, or something else that gives us another benefit for the patient.

Tr. 628:23-629:3 (Stein Gold).

219. In addition, Dr. Stein Gold testified that that the predominant treatment practice at the time was not to start a patient on a weaker treatment and then scale

up. She explained that “these patients are suffering. They’re suffering physically. The psoriasis, it’s itchy. It’s painful. They’re humiliated by it. They’re suffering from anxiety and depressions. You want to get the patient under control as quickly as possible.” Tr. 629:4-12 (Stein Gold).

220. A person of ordinary skill thus would not have been motivated to create a less potent medication by lowering the concentration.

221. The common wisdom at the time was that decreasing concentration would decrease efficacy. Tr. 486:4-13 (Lane); 628:11-16 (Stein Gold). As Dr. Stein Gold testified, “the art taught that as you decrease the concentration, you tend to get a less potent and less efficacious drug.” Tr. 625:17-19 (Stein Gold).

222. Dr. Lane illustrated the correlation between concentration and efficacy through an example drawn from the specification of the Bryhali Patents. Tr. 486:14-487:14.

223. As discussed above, Table 1 of the ‘307 patent (1:32-2:18) is a potency chart of topical corticosteroids, listing them from superpotent Class 1 to least potent Class 7. One of the corticosteroids listed is called fluocinonide. The chart shows that the potency of fluocinonide ranged from superpotent Class 1 at a 0.1% concentration to mild Class 6 at a 0.01% concentration. Tr. 486:14-487:14 (Lane). Dr. Lane thus explained that “[a] tenfold drop in concentration moved this drug all the way down

from being a superpotent corticosteroid to what is classified as a mild corticosteroid.” *Id.*

224. Moreover, the Blum reference (DX-002) that Padagis’s experts relied upon also shows that lowering the concentration of halobetasol reduces efficacy. Blum states: “In the treatment of severe chronic psoriasis vulgaris, the ointment with the lower concentration (i.e., 0.02% CGP 14 458) was *less effective* than that with concentration of 0.05% and Dermovate ointment. DX-002 at HALOBET0020220 (emphasis added); Tr. 487:15-488:3 (Lane).

225. While Blum states that this difference was not statistically significant, Dr. Stein Gold explained that the study was “not powered appropriately to show a statistically significant difference between the different arms of the study” and thus it is not meaningful “whether there was a statistical difference or not” because this statement is just saying that “the study was not powered to show a statistically significant difference.” Tr. 719:24-721:3 (Stein Gold).

226. In addition to showing that lowering the concentration reduces efficacy, Blum teaches away from using the lower concentration. Blum states that “*the 0.05% CGP 14 458 ointment will provide a favorite treatment weapon* for chronic, localized, severe, or refractory skin diseases that have effect with corticosteroids.” DX-002 at HALOBET0020220 (emphasis added). Blum further states in conclusion that “*0.05% CGP 14 457 ointment would be a welcome addition* to the therapeutic

armamentarium for chronic localized severe or recalcitrant dermatoses.” *Id.* Blum does not make such statements regarding the lower 0.02% concentration, which it says is “less effective” than the 0.05% concentration.

227. Thus, a person of ordinary skill in the art would have understood that Blum evaluated both the 0.02% and 0.05% halobetasol concentrations and recommends the higher 0.05% concentration, concluding that 0.05% halobetasol would be a “favorite treatment weapon.” Tr. 631:3-6 (Stein Gold).

228. Dr. Stein Gold further testified that the data in Blum supports its conclusion. Tr. 631:19-633:6. While the study was not well-designed, it does show lower efficacy with severe psoriasis patients (which Blum identifies as the “most reliable measurement” for comparing efficacy) and lower efficacy with overall psoriasis patients as well. Tr. 631:10-633:6 (Stein Gold). The data further shows that the lower 0.02% concentration had a higher incidence of local side effects than the 0.05% concentration and that the incidence of “atrophy” or thinning of the skin was equivalent in the 0.02% and 0.05% concentrations. Tr. 632:5-20 (Stein Gold). The data from the clinical study thus supports Blum’s recommendation of the higher 0.05% concentration.

229. A person of ordinary skill in the art thus would understand that Blum recommends the 0.05% halobetasol concentration and teaches away from the lower 0.02% concentration. *Id.*

230. The undisputed evidence further shows that when Ultravate® came out in 1990, four years after the 1986 Blum article, it used a 0.05% halobetasol concentration. PTX-087 (Ultravate® label). As Padagis's expert, Dr. Stern admitted on cross examination, what happened in the real world is inconsistent with Padagis's contention that Blum would have motivated a person of ordinary skill in the art to use a halobetasol concentration of less than 0.05%:

Q. Blum is published in 1986, right?

A. Yes.

Q. And Ultravate® came out in 1990, right?

A. Right.

Q. And Ultravate® has that higher 0.05 percent concentration, right?

A. Yes.

Q. So the developers of Ultravate® didn't follow what you contend is the motivation of Blum to lower the concentration below 0.05%. Isn't that correct?

A. They – they were –

THE COURT: We want to know the answer to the question. Answer it.

THE WITNESS: Yes.

BY MR STEINDLER:

Q. And what the Ultravate® developers did was consistent with the express teaching of Blum; that the higher 0.05 percent concentration was preferable. Right?

A. Yes.

Tr. 212:25-213:18 (Stern cross examination).

231. Moreover, as Dr. Stein Gold testified, a person of ordinary skill would have reasonably believed that the Ultravate® 0.05% concentration had been optimized. Tr. 625:25-626:9 (Stein Gold).

232. As Dr. Stein Gold explained, Ultravate® was “put out by a premier drug company, Bristol Myers Squibb,” and a person of ordinary skill would have expected that Bristol Myers Squibb had studied the drug in its development program and picked the formulation that gave “the best safety and efficacy for that particular topical treatment.” Tr. 625:25-626:10; 708:13-16; 727:8-728:14 (Stein Gold).

233. While Dr. Stein Gold acknowledged she was not involved in the halobetasol clinical trial and has not seen any documents that confirm that Ultravate® was optimized (Tr. 729:20-23), based on her experience in running numerous clinical trials she testified that clinical trials for new chemical entities such as halobetasol usually involve looking at different concentrations and possibly different formulations, and that dose finding studies are normally part of drug development. Tr. 727:17-728:14 (Stein Gold redirect). A person of ordinary skill in the art would have reasonably assumed that Bristol Myers Squibb had optimized the concentration of halobetasol in Ultravate®.

234. Padagis bears the burden of proof on this issue, and neither of its experts (Dr. Stern and Dr. Michniak-Kohn) disputed Dr. Stein Gold’s credible testimony

that a person of ordinary skill would have reasonably believed that the 0.05% halobetasol concentration of Ultravate® was optimized.

235. The belief that the halobetasol concentration of Ultravate® had been optimized would have provided a powerful motivation for a person of ordinary skill in the art *not* to use a lower concentration of halobetasol, which as discussed below is precisely what happened in the real world for 20 years after Ultravate® was approved. The record shows that no one even experimented with a halobetasol concentration of less than 0.05% until the Bausch inventors did so in the development program that led to the Bryhali Patents.

236. Further, Dr. Michniak-Kohn admitted on cross examination that the risk of adverse events with halobetasol was known well before Ultravate® came out and that it came out at 0.05%:

Q. In your first bullet, you say there was a motivation to formulate a lower concentration of halobetasol to minimize the risk of known adverse events while still maintaining efficacy, right?

A. Correct.

Q. And that risk of adverse events was known well before Ultravate® came out, right?

A. Correct.

Q. Ultravate® was approved in 1990, as we've said, right?

A. Correct.

Q. And it came out at a 0.05% concentration, not a lower concentration, right?

A. When it came out as 0.05%.

Tr. 398:6-18 (Michniak-Kohn cross examination).

237. This is a clear admission from Padagis's expert that in the real world, the longstanding and well-known risk of systemic effects with halobetasol did *not* motivate the developers at Bristol Myerson Squibb to formulate a concentration of halobetasol at lower than 0.05%, as Padagis contends. What happened in the real world is directly contrary to Padagis's central thesis in this case.

238. Dr. Michniak-Kohn further admitted on cross examination that Blum looked at both the 0.02% and 0.05% concentrations and recommends the 0.05% concentration, but she testified nonetheless that a person of ordinary skill would ignore Blum's recommendation and be motivated by Blum to pick a lower concentration:

Q. You will agree with me that Blum looked at both the 0.02 percent concentration and the 0.05 percent concentration and recommends the 0.05% concentration, right?

A. Correct.

Q. And your contention is that even though Blum looked at both the 0.02 and 0.05 percent concentration and recommends the higher concentration, that a POSA would ignore Blum's recommendation and rely on the Blum article as a motivation to pick a lower concentration. Is that your testimony?

A. Yes, it is.

Tr. 408:2-12 (Michniak-Kohn cross examination).

239. The Court finds Dr. Michniak-Kohn's testimony that a person of ordinary skill in the art would ignore Blum's express recommendation to use the 0.05% concentration and would be motivated to use a concentration lower than 0.05% is not credible. This conclusion is underscored by the real-world evidence that the Ultravate® developers were not motivated to use a lower concentration.

240. Finally, perhaps the most powerful evidence that a person of ordinary skill in the art would not have been motivated to lower the concentration of halobetasol to less than 0.05% is that no one ever did it in the 20 years between the time Ultravate® was approved in 1990 and the 2010 priority date of the Bryhali Patents. Padagis's expert, Dr. Stern, admitted this central fact in response to a question from the Court:

THE COURT: Okay. I have one, Doctor, just so I understand, all right?

A. Ultravate® is approved by the FDA in 1990.

THE WITNESS: Yes.

THE COURT: The invention date of the patents involved here is 2010. Is that correct?

THE WITNESS: For the single product, 2010; for the duo product, 2015.

THE COURT: Okay. So if I understand your testimony, for 20 years it's been known that Ultravate® at the 0.05%

concentration can only be used for two weeks at a stretch and that that is a very serious drawback because of the side effects that would occur if you used it beyond two weeks. Is that correct?

THE WITNESS: Yes.

THE COURT: And are you aware of whether or not in that 20-year period any commercial product was approved for use to treat this disease with a concentration of less than 0.05 percent HP?

THE WITNESS: Not with halobetasol, no.

THE COURT: Thank you.

Tr. 302:22-303:18 (Stern).

241. Moreover, not only was there no *commercial* product approved to treat this disease with a concentration of less than 0.05 percent HP, there is no evidence in the record even of any *experimental* product with a halobetasol concentration of less than 0.05% in the 20-year period between the approval of Ultravate® in 1990 and the 2010 priority date of the Bryhali Patents. Blum is the only reference in the record with a formulation containing less than 0.05% halobetasol, but Blum is from 1986, four years prior to the approval of Ultravate®.

242. Of the other references cited by Padagis's experts against the Bryhali Patents, only the '566 patent discloses example formulations with halobetasol. Tr. 401:20-22 (Michniak-Kohn admission that '295 patent does not disclose halobetasol); Tr. 411:10-12 (Michniak-Kohn admission that halobetasol not mentioned in JP '228). And as Dr. Michniak-Kohn admitted on cross examination,

the halobetasol concentration is 0.05% in each and every one of the example halobetasol formulations in the '566 patent. Tr. 415:20-416:7 (Michniak-Kohn cross examination).

243. Thus, there is no evidence in the record that anyone even experimented with halobetasol concentrations of less than 0.05% after Ultravate® was approved in 1990 until Bausch did so in the development program that led to the invention of the Bryhali Patents.

244. In addition, Dr. Stern further admitted that Ultravate® defined the problem that he contends would have motivated a person of ordinary skill to lower the concentration and that the longer a problem goes unsolved, the less obvious it is:

Q: All right. Well, wouldn't you agree that Ultravate® is central to your obviousness analysis?

A: It is central to – yes.

Q: And it defines the problem you say would have motivated a POSA to lower the concentration, right?

A: That's correct.

Q: And wouldn't you agree that the longer a problem goes unsolved, the less obvious it is?

A: Yes.

Tr. 205:14-22 (Stern cross examination).

245. In this case, it is undisputed that the problem went on unsolved for 20 years.

246. Based on the entirety of the evidence and the credibility of the witnesses, therefore, the Court finds that as of November 22, 2010, a person of ordinary skill in the art would not have been motivated to use a halobetasol concentration of less than 0.05%.

247. The Court also finds that Padagis has not shown that a person of ordinary skill would have been motivated to use a concentration of less than 0.05% of any of the other corticosteroids recited in the Asserted Claims of the Bryhali Patents.³

h. There Was No Motivation to Use a Lower Concentration Formulation for Longer Than Two Weeks.

248. It follows from the conclusion that a person of ordinary skill in the art would not have been motivated to use a corticosteroid concentration of less than 0.05% that a person of ordinary skill also would not have been motivated to use a topical composition comprising a corticosteroid at concentrations of less than 0.05% for a period of longer than two weeks.

³ Each of the Asserted Claims of the ‘307 patent (claims 13, 16 and 19) recites only halobetasol. Claim 4 of the ‘502 patent also is limited to halobetasol. However, claim 16 of the ‘502 patent, which ultimately depends on claim 1, requires “a corticosteroid selected from the group consisting of halobetasol propionate, clobetasol propionate, betamethasone dipropionate, diflorasone diacetate, and fluocinonide at a concentration less than 0.05%.” Padagis adduced no evidence and did not argue at trial that a person of ordinary skill would have been motivated to use any of the recited corticosteroids in claim 1 of the ‘502 patent other than halobetasol at a concentration of less than 0.05%.

249. In other words, if, a threshold matter, a person of ordinary skill would not have been motivated to use a corticosteroid concentration of less than 0.05%, then *a fortiori* a person of ordinary skill would not have been motivated to use a lower concentration for longer than two weeks.

250. Thus, the Court finds that as of November 22, 2010, a person of ordinary skill in the art would not have been motivated to use a corticosteroid concentration of less than 0.05% for longer than two weeks, as required by claim 16 of the ‘502 patent.

i. In Addition to the Concentration Limitations, The Other Limitations Also Would Not Have Been Obvious Based on the Prior Art References Padagis Asserts

251. The Court’s findings that as of November 22, 2010 a person of ordinary skill in the art would not have been motivated to use a concentration of less than 0.05% of halobetasol or of any of the other corticosteroid options recited in the Asserted Claims dispose of Padagis’s contention that the Asserted Claims would have been obvious. A concentration of less than 0.05% is required for each of the Asserted Claims of the Bryhali Patents.⁴

⁴ Claim 13 of the ‘307 patent requires halobetasol at a concentration of 0.025% or less. Claim 16 of the ‘307 patent, which ultimately depends on claim 1, requires halobetasol at a concentration of 0.04% or less. Claim 20 of the ‘307 patent, which also ultimately depends on claim 1, requires halobetasol at a concentration of 0.04% or less. Claim 4 of the ‘502 patent requires halobetasol at a concentration of 0.01% or less. Claim 16 of the ‘502 patent, which ultimately depends on claim 1, requires

252. In addition, however, Padagis has not shown that the other limitations of the Asserted Claims of the Bryhali Patents would have been obvious.

253. At trial, the alleged obviousness of the other limitations of the Asserted Claims was addressed principally by Dr. Michniak-Kohn, although both Dr. Stern and Dr. Michniak-Kohn offered opinions regarding the alleged obviousness of the method of use limitation of claim 16 of the '502 patent. As noted above, both Dr. Stern and Dr. Michniak-Kohn offered opinions regarding the alleged obviousness of the concentration limitations which the Court has rejected.

254. Dr. Michniak-Kohn contended at trial that all of the limitations of the Asserted Claims would have been obvious based on various combinations of the '295 patent, Blum, JP '228, the '566 patent, and the Temovate E® Label.

255. But Dr. Michniak-Kohn admitted on cross examination that all of this prior art is old and that no one made the invention of the Bryhali Patents until Bausch did it in 2010.

Q: So the '295 patent is 1980, Blum is 1986, JP '228 is 1988, the '566 patent is 1994, and the Temovate E Label is 1996, right?

A: Correct.

a corticosteroid selected from the group consisting of halobetasol propionate, clobetasol propionate, betamethasone dipropionate, diflorasone diacetate, and fluocinonide at a concentration less than 0.05%.

Q: And you contend that the Bryhali patents would have been obvious to a POSA in 2010 based on these references, correct?

A: Correct.

Q: But you agree that nobody ever made this invention during all those years until Bausch did it in 2010, right?

A: Well, that's what happened in industry.

Tr. 399:24-400:8 (Michniak-Kohn cross examination).

256. Dr. Michniak-Kohn's admission is more comprehensive than Dr. Stern's admissions in that Dr. Michniak-Kohn's admission pertains to the complete invention of the Bryhali Patents, not just the concentration limitations.

257. And what "happened in industry," in Dr. Michniak-Kohn's words – that is, in the real world – in the 30 years following the issuance of the '295 patent is powerful evidence that the complete invention of the Bryhali Patents would not have been obvious to a person of ordinary skill in the art as of November 22, 2010.

258. Against this background, Dr. Michniak-Kohn's presentation appears to be a hindsight-driven analysis that involves picking and choosing elements from old references using the Bryhali Patents as a starting point. Tr. 494:14-495:1 (Lane).

259. An analysis of each of the asserted references follows.

i. The '295 Patent

260. The '295 patent is the primary reference for each of the combinations Dr. Michniak-Kohn alleges render the Asserted Claims obvious.

261. The ‘295 patent issued in 1980, 30 years before the priority date of the Bryhali Patents. DX-003 (‘295 patent); Tr. 400:19-401:4 (Michniak-Kohn cross examination).

262. The ‘295 patent is one of three old references Dr. Michniak-Kohn asserts that are directed to the use of penetration enhancers for topical corticosteroids to push the active ingredient all the way through the skin. Tr. 489:25-491:21 (Lane). The others are the ‘566 patent (1994) and JP ‘228 (1988).

263. As Dr. Lane testified, “[a]t the very beginning of the ‘295 patent, the authors tell us that they want to achieve percutaneous absorption, so delivery of the drug through the skin.” Tr. 496:25-497:2 (Lane); DX-003 (‘295 patent), col 1:10-16 (“Topical corticosteroid formulations are extensively employed in the treatment of skin disorders, such as dermatitis. To be therapeutically effective, the active ingredient preferably should be in a molecular dispersion to facilitate desired *percutaneous absorption* which is particularly important in achieving a therapeutic response for the management of psoriasis.”) (emphasis added).

264. As Dr. Lane explained, the ‘295 patent is one of the references from the 1980s and 1990s that “reflected the understanding in the field that the way to succeed with your formulation is to push it all the way through the skin.” Tr. 491:8-11.

265. Dr. Lane further explained:

But science moves on, especially the field of topical formulation. So since these 1980s and 1990s references,

we understand that our goal is actually more subtle than that. To treat skin disease, we have to try and localize the drug in the skin. We do not want to push it all the way through the skin. So the inventors of the Bryhali patents have explained they want to achieve localized delivery. So to the skin, not through the skin.

Tr. 491:12-21 (Lane).

266. In other words, the '295 patent is teaching the opposite of the approach taken by the inventors of the Bryhali Patents. As the inventors explained in the specification of the Bryhali Patents, their approach was to "provide[] delivery of the corticosteroid preferentially into the skin rather than providing transdermal delivery through the skin and into the systemic circulation." JTX-001 ('307 patent) 4:40-45. That was the inventors' hypothesis for how their invention works.

267. At trial, the Court asked Dr. Lane whether her testimony was "that the traditional penetration enhancers that existed in the art in the '80s and '90s would, in fact, have been dysfunctional for the use of HP because they would tend to, in fact, increase systemic absorption of HP." Tr. 492:20-25. Dr. Lane responded as follows:

So that's a really good question because, you know, when people use the term "penetration enhancers," right, sometimes they're not penetration enhancers and sometimes they are. So that's one problem. But as I said, back then, the field and scientists in the field thought if we push it all through, then we are making a super effective formulation. But that misses for skin diseases like eczema, psoriasis, rosacea. Your target is in the skin, so you really want the drug to stay in the skin. So you said, were they

dysfunctional. It's very hard to study penetration enhancers. We probably didn't have the analytical techniques available to us. We do now, so that's some of the stuff I do. So I don't think – you know, I wouldn't say they were dysfunctional. They were doing the best they could but, you know, we have better science available now.

THE COURT: Thank you.

Tr. 492:20-493:17 (Lane).

268. Given the risk of systemic absorption with the use of superpotent corticosteroids, the Court finds that a person of ordinary skill in the art would not have been motivated in 2010 to use the penetration enhancers disclosed in the '295 patent in 1980 to develop a topical formulation for halobetasol or any other superpotent corticosteroid.

269. The '295 patent is entitled "Corticosteroid formulations containing sebacates." DX-003, face page. Like the title, the Abstract states that the '295 patent is directed to "[c]orticosteroid formulations" wherein the corticosteroid "is dissolved in a sebacate carrier, such as dibutyl sebacate." *Id.*

270. The '295 patent is directed to formulations for use with any corticosteroid. DX-003 ('295 patent) 1:5-64 (Description of the Invention), Claim 1 (claiming "[a] steroid composition . . ."). Dr. Michniak-Kohn testified that the '295 patent explicitly states that its disclosures are applicable to any topically active anti-inflammatory

steroid, Tr. 329:23-25, and that the utility of the invention is not limited to superpotent corticosteroids. Tr. 401:17-25 (Michniak-Kohn cross examination).

271. The '295 patent focuses on a group of exemplary steroids that include halcinonide. DX-003 ('295 patent) 1:52-56, 6:63-11:5 (examples of steroid formulations with halcinonide, including three unnumbered examples and Examples 2, 3, 5, 10, 11); Tr. 498:7-14 (Lane). Halcinonide is not a superpotent corticosteroid. *Id.*

272. There are many different types of corticosteroids, ranging from superpotent Class 1 to least potent Class 7. *E.g.*, JTX-001 ('307 patent) Table 1, 1:26-2:8.

273. The '295 patent does not specifically disclose halobetasol, at any concentration. Tr. 401:20-25, 402:17-25 (Michniak-Kohn). None of the examples in the '295 patent use halobetasol. DX-003 ('295 patent) 6:27-11:5.

274. The '295 patent thus discloses a series of broad ranges of concentrations for the broad genus of all corticosteroids that can be used in the steroid compositions of the invention. The specification states:

The active ingredient employed in the formulation of the invention will preferably comprise a steroid which will be present in an amount of from about 0.001 to about 3% by weight, and preferably from about 0.025 to about 0.2% based on the total weight of the composition, depending upon the type of steroid employed and its solubility in the sebacate containing vehicle.

DX-003 ('295 patent) at 1:45-51 (emphasis added).

275. This passage expressly states that the applicability of the disclosed ranges will depend “upon the type of steroid employed and its solubility in the sebacate containing vehicle.” As Dr. Lane testified, a person of ordinary skill in the art would know that the ranges would not be applicable to all corticosteroids, Tr. 498:1-6 (Lane), and there is no teaching in the patent as to what ranges would be applicable to any particular corticosteroid or even any particular class or group of corticosteroids.

276. Thus, nothing in the ‘295 patent teaches a range that would be applicable to halobetasol or to any other superpotent corticosteroid. Nor is there any teaching of how to determine the appropriate amount of corticosteroid to include in any formulation suggested by the ‘295 patent. Tr. 402:11-14 (Michniak-Kohn cross examination).

277. The specification further states:

With regard to the lotion formulation of the invention where the steroid is to be all-in-solution, the lotion will contain from about 0.005 to about 0.6% and preferably from about 0.02 to about 0.05% by weight of the active ingredient based on the weight of the entire lotion formulation, and from about 5 to about 75% and preferably from about 10 to about 50% by weight of the sebacate based on the weight of the entire lotion formulation, depending upon the solubility of the particular ingredient in the sebacate.

DX-003 (‘295 patent) 2:61-3:2.

278. Here again, this passage also does not disclose whether or to what extent these ranges would apply to any particular type of steroid from within the broad class of all corticosteroids, and in particular does not specify whether these ranges would be applicable to halobetasol or to any other superpotent corticosteroid.

279. The specification of the ‘295 patent further states: “The present invention relates to pharmaceutical formulations which include a dialkyl sebacate, such as dibutyl sebacate or diisopropyl sebacate as a vehicle for the pharmaceutical.” DX-003 (‘295 patent) 1:5-10.

280. The ‘295 patent discloses a class of compounds called dialkyl sebacates to use in formulations with corticosteroids. Tr. 401:13-16 (Michniak-Kohn cross examination).

281. There are multiple different species of dialkyl sebacates. Tr. 403:7-404:13 (Michniak-Kohn cross examination). The ‘295 patent specifically discloses only two species of sebacates, dibutyl sebacate and diisopropyl sebacate. *Id.* The ‘295 patent does not specifically disclose diethyl sebacate as claimed in the Bryhali Patents. *Id.* All of the sebacates in the examples in the ‘295 patent are limited to dibutyl sebacate or diisopropyl sebacate. *Id.* None of the examples in the ‘295 patent use diethyl sebacate.

282. Padagis contends that a person of ordinary skill in the art would have been motivated to select diethyl sebacate from the general class of sebacates disclosed in

the ‘295 patent. According to Dr. Michniak-Kohn, selection of diethyl sebacate would have been a matter of “routine optimization” based on the solubility of the corticosteroid. Tr. 371:4-19 (Michniak-Kohn).

283. But in the 30 years since the ‘295 patent was published, diethyl sebacate was never used in any formulation for a halobetasol product. Tr. 404:4-17 (Michniak-Kohn cross examination). While Dr. Michniak-Kohn qualified her response when this point was put to her on cross examination by saying “not a marketed one, no,” *id.*, there is no evidence in the record in this case of *any* halobetasol formulation – marketed or otherwise – that includes diethyl sebacate apart from examples in the Bryhali and Duobrii Patents.

284. In addition, Dr. Michniak-Kohn admitted as of 2010, “there were no commercial formulations for corticosteroids for treating psoriasis that contained diethyl sebacate.” Tr. 391:7-10 (Michniak -Kohn cross examination). Her admission covered all commercial corticosteroid products for treating psoriasis, not just halobetasol products. None of them use diethyl sebacate.

285. Dr. Michniak-Kohn specifically admitted that “Ultravate®, the prior art halobetasol product, doesn’t use diethyl sebacate.” Tr. 393:16-18 (Michniak-Kohn cross examination).

286. She further admitted that one would assume that when Bristol-Myers Squibb developed Ultravate®, they went through the process of trying to pick the best

solvent for halobetasol, and they did not pick diethyl sebacate. Tr. 393:19-24 (Michniak-Kohn cross examination). And she confirmed that diethyl sebacate “was already out there in the art as a potential oleaginous solvent at the time BMS was developing Ultravate®.” Tr. 393:25-394:3 (Michniak-Kohn cross examination).

287. Dr. Michniak-Kohn said she “disagreed” that “what actually happened in the real world teaches us that a formulation team working on a halobetasol product would not have selected diethyl sebacate as a solvent,” even though “the development team at BMS that developed Ultravate® did not pick diethyl sebacate as a solvent.” Tr. 394:4-12 (Michniak -Kohn cross examination). But she never explained the basis for her disagreement. The Court finds Dr. Michniak-Kohn’s disagreement to be unsupported by evidence and not credible.

288. More broadly, Dr. Michniak-Kohn contended that a person of ordinary skill would have chosen diethyl sebacate as a solvent because it is oily or oleaginous. Tr. 391:16-18 (Michniak-Kohn cross examination). But she admitted on cross examination there were other oily or oleaginous solvents that were potential candidates for a person of ordinary skill to choose from as of 2010, although she did not know how many. Tr. 391:19-392:8 (Michniak-Kohn cross examination).

289. Dr. Michniak-Kohn also admitted that there is no experimental evidence in the prior art that shows diethyl sebacate is better at dissolving halobetasol than any of the other oleaginous solvents. Tr. 393:2-5 (Michniak-Kohn cross examination).

290. In the end, notwithstanding that no one had ever used diethyl sebacate in a commercial corticosteroid product or, indeed, in any halobetasol formulation (commercial or experimental) in the 30 years after the ‘295 patent issued, it is Dr. Michniak-Kohn’s contention “that a POSA would have relied on the generic disclosure of sebacates in the ‘295 patent to pick out the specific diethyl sebacate that’s claimed in the Bryhali patents.” Tr. 404:8-13 (Michniak-Kohn cross examination). Her response was only, “[i]t’s part of the prior art.” *Id.*

291. The Court finds Dr. Michniak-Kohn’s arguments regarding the ‘295 patent unpersuasive and driven by hindsight. The Court finds Padagis has not proven that a person of ordinary skill in the art would have been motivated to rely on the generic disclosure of sebacates in the ‘295 patent to pick out the specific diethyl sebacate claimed in the Bryhali Patents.

292. Finally, the ‘295 patent also does not disclose the use of light mineral oil or teach the exclusion of white petrolatum, each of which is an element of certain of the Asserted Claims of the Bryhali Patents. Tr. 496:16-24 (Lane).

ii. The ‘566 patent

293. The ‘566 patent is entitled “Use of dibutyl adipate and isopropyl myristate in topical and transdermal products.” DX-004 (‘566 patent). It issued on July 5, 1994, 16 years before the priority date of the Bryhali Patents. *Id.* It is discussed in the Background section of the Bryhali Patents. JTX-001 (‘307 patent) 3:28-44.

294. The ‘566 patent is another of the old references relied upon by Padagis’s expert that is focused on the use of penetration enhancers to drive the drug through the skin. Tr. 501:5-502:3 (Lane). This is the opposite of the approach taken in the Bryhali Patents. *Id.* The specification of the ‘566 patent states: “The present invention relates to the enhancement as well as the control of epidermal, dermal, and transdermal penetration of various topically applied preparations.” DX-004 (‘566 patent) 3:57-60.

295. As Bausch’s formulation expert, Dr. Lane, explained at trial, the face page of the ‘566 patent discloses a figure depicting the results of an experiment measuring the amount of drug that is penetrated all the way through the skin. Tr. 502:19-503:7 (Lane). Dr. Lane explained that “in these experiments, we clamp a piece of skin in a special cell and we measure how much drug the formulation drives through the skin.” Tr. 502:23-25 (Lane).

296. The procedure for these *in vitro* skin penetration experiments is described in Example 1 of the ‘566 patent. DX-004 (‘566 patent) 7:35-8:18. As Dr. Lane had briefly explained (Tr. 502:17-503:7), a piece of skin is mounted on a diffusion cell, a sample of test formulation is placed on top of the skin, and the amount of drug that penetrates all the way through the skin into “receptor fluid” in a “receptor compartment” below the skin is then measured “by HPLC or by scintillation counter for radioactive drug.” *Id.* The results of certain of these *in vitro* skin penetration

experiments are depicted in Figures 1, 2 and 3 of the '566 patent. DX-004 ('566 patent) 4:23-31.

297. There is no evaluation in the '566 patent of the penetration of the drug into the skin, which Dr. Michniak-Kohn testified was the teaching of the '566 patent. Rather, all of the experimental data in the '566 patent regarding skin penetration pertains to the penetration of the drug all the way through the skin.

298. Thus, as Dr. Lane testified, "[t]his patent is all about penetration enhancement. I see no motivation to lower the concentration of corticosteroid. The goal is systemic absorption." Tr. 503:22-24 (Lane). Dr. Lane explained this in a colloquy with the Court:

THE COURT: Do I understand you're saying that this patent, in effect, teaches the use of penetration enhancers, which makes it likelier that the active ingredient will be systemically absorbed?

THE WITNESS: Yes, Your Honor. Because the inventor says this is a very important achievement. He tells us we can achieve systemic delivery in the document. I haven't shown that, but it is in the patent.

THE COURT: Thank you.

Tr. 503:8-16 (Lane).

299. At trial, Dr. Michniak-Kohn disagreed with the proposition that one of the objects of the invention of the '566 patent was to enhance delivery of the active ingredient systemically. Tr. 419:25-420:7 (Michniak-Kohn cross examination). But

her trial testimony was directly contradicted by the sworn testimony she gave at deposition:

QUESTION: You would agree that one object of the invention, though, would be to enhance delivery of the active ingredient systemically, right?

ANSWER: That is mentioned here by the inventors. That's why probably, most likely, they included isopropyl myristate.

Id.

300. The '566 patent is specifically directed to the use of dibutyl adipate or a mixture of dibutyl adipate and isopropyl myristate as penetration enhancers. The specification states:

[D]ermal and transdermal penetration of a pharmaceutically active compound can be substantially improved by incorporating the compound into a composition containing a dermal or transdermal penetration enhancing amount of dibutyl adipate or a mixture of dibutyl adipate and isopropyl myristate.

DX-004 ('566 patent) 4:37-43.

301. As Dr. Michniak-Kohn admitted on cross examination, the '566 patent does not disclose diethyl sebacate. Tr. 418:9-23 (Michniak-Kohn cross examination). And as Dr. Michniak-Kohn further admitted, the two excipients the '566 patent does disclose, dibutyl adipate and isopropyl myristate, are not sebacates. *Id.*

302. The '566 patent discloses example formulations containing halobetasol. But as Dr. Michniak-Kohn admitted, each of the example formulations in the '566 patent

uses the 0.05% concentration of halobetasol. Tr. 415:20-416:7 (Michniak-Kohn cross examination). Dr. Michniak-Kohn further admitted that “[t]he ‘566 patent doesn’t contain any reference to a halobetasol formulation with a concentration of less than 0.05 percent.” *Id.*

303. Dr. Michniak-Kohn had cited the ‘566 patent in her direct testimony for the proposition that a person of ordinary skill in the art would have been motivated to use halobetasol topical formulations with halobetasol at 0.04% or less. Tr. 387:14-17 (Michniak-Kohn). But Dr. Michniak-Kohn admitted on cross examination that “there’s nothing in the ‘566 patent that would motivate a POSA [to] use HP at 0.04 percent or less.” Tr. 416:10-18 (Michniak-Kohn cross examination).

304. In addition, Dr. Michniak-Kohn further admitted that “there’s nothing in the ‘566 patent that directs a POSA to use halobetasol at less than 0.025 percent.” Tr. 416:23-417:4 (Michniak-Kohn cross examination).

305. Further, as of 2010, there was no commercially available superpotent corticosteroid for the treatment of psoriasis that uses the vehicle described in the ‘566 patent. Tr. 417:7-14 (Michniak-Kohn cross examination).

306. Particularly in light of Dr. Michniak-Kohn’s admissions, the Court finds that the ‘566 patent would not have motivated a person of ordinary skill in the art as of November 22, 2010 to use a halobetasol concentration of less than 0.05%.

iii. Blum

307. Dr. Michniak-Kohn contends that Blum would have motivated a person of ordinary skill in the art to use a halobetasol concentration of less than 0.05%, less than 0.04%, less than 0.025%, and 0.01% or less. For the reasons described above, however, the Court disagrees and finds that Blum would not have motivated a person of ordinary skill to use a halobetasol concentration of less than 0.05%, less than 0.04%, less than 0.025%, or 0.01% or less. The Court finds that Blum teaches away from using a lower concentration.

iv. JP ‘228

308. JP ‘228 is an unexamined Japanese patent application entitled “Steroid Cream Preparation.” DX-005 (JP ‘228) at HALOBET0020451. It was published on October 21, 1988, 22 years prior to the priority date of the Bryhali Patents. *Id.*

309. JP ‘228 was before the examiner during prosecution of the Bryhali Patents. ‘502 patent, face page (listed under References Cited – Foreign Patent Documents); Tr. 409:18-20 (Michniak-Kohn cross examination).

310. JP ‘228 is another of the old references relied upon by Padagis’s expert that is focused on the use of certain excipients to solve the problem of inadequate transdermal absorption.

311. The specification states that “[t]he objective of the present invention is to provide a steroid cream preparation that incorporates as its principal agent the

aforesaid highly liposoluble steroid, and consequently has a good drug release behavior and *transdermal absorption* . . .” DX-005 (JP ‘228) at HALOBET0020452 (emphasis added). As discussed above, this is the opposite of the approach taken in the Bryhali Patents. Tr. 501:5-502:3 (Lane).

312. Thus, as Dr. Lane explained, “the inventors tell us we have solved the problem of inadequate transdermal absorption. So just as I said earlier, they taught transdermal absorption is our goal and our invention solves the problem of inadequate transdermal absorption.” Tr. 504:9-13 (Lane).

313. JP ‘228 discloses steroid cream preparations that contain 0.01-0.5% by weight of the steroids represented by a depicted generic structure. DX-005 (JP ‘228) at HALOBET0020451 and HALOBET0020452; *see also id.* at HALOBET0020453 (“For the steroids, any known steroids represented by the aforesaid generic expression (1) may be used.”).

314. But as Dr. Lane testified, the generic structure depicted in JP ‘228 does not include halobetasol. Tr. 504:14-22 (Lane). Padagis’s expert, Dr. Michniak-Kohn, did not dispute this or testify that the generic structure disclosed in JP ‘228 includes halobetasol. Tr. 339:18-342:23 (Michniak-Kohn). Dr. Michniak-Kohn further acknowledged that halobetasol is not mentioned anywhere in JP ‘228. Tr. 411:9-12 (Michniak-Kohn cross examination). As Dr. Lane further testified, the generic

structure depicted in JP ‘228 does not even appear to include superpotent corticosteroids. Tr. 504:25-505:4 (Lane). Dr. Michniak-Kohn did not dispute this.

315. Thus, while JP ‘228 discloses that the cream preparations of the invention contain 0.01-0.5% by weight of the steroids represented by the disclosed generic structure, there is no evidence that the generic structure includes halobetasol or any other superpotent corticosteroid and thus no evidence that JP ‘228 discloses halobetasol or any of the other superpotent corticosteroids of the Asserted Claims of the Bryhali Patents in a range of 0.01-0.5%.

316. Moreover, all of the examples in JP ‘228 use steroid concentrations of 0.05%, and a person of ordinary skill in the art would not take from the disclosed range that any specific corticosteroid with that generic structure could be used at any concentration within that range. Tr. 505:15-23 (Lane).

317. In addition, JP ‘228 discloses steroid cream preparations where the steroid is dissolved in diisopropyl adipate, diethyl sebacate, or triacetin. DX-005 (JP ‘228) at HALOBET0020451; Tr. 339:18-25 (Michniak-Kohn). There are three “embodiment examples” that use each of these excipients, respectively. DX-005 (JP ‘228) at HALOBET0020455-56. Example 1 uses diisopropyl adipate; Example 2 uses triacetin; and Example 3 uses diethyl sebacate. *Id.*

318. Dr. Michniak-Kohn relies upon JP ‘228 (*inter alia*) to pick out diethyl sebacate as a potential solvent. She admitted, however, that there is “no data in JP

‘228 which shows that diethyl sebacate is preferable to the other two solvents.” Tr. 411:16-22 (Michniak-Kohn cross examination).

319. She further admitted that the example with diethyl sebacate was not tested, while other samples that did not include diethyl sebacate were tested:

Q. All five of the cream preparations that were actually tested have diisopropyl adipate as the solvent except for B, which has propylene glycol as the solvent, right?

A. Correct.

Q. None of the samples they tested had diethyl sebacate, right?

A. Correct.

* * *

Q. So again, when the inventors tested their invention and reported these results, they chose cream preparations with diisopropyl adipate or propylene glycol and not diethyl sebacate, right?

A. Correct.

Tr. 413:5-11, 413:25-414:4 (Michniak-Kohn cross examination).

320. Dr. Michniak-Kohn further admitted that in the 22 years between the publication of JP ‘228 and the priority date of the Bryhali Patents, no one ever used any of the solvents disclosed in JP ‘228 in a marketed topical corticosteroid product.

Tr. 414:5-11 (Michniak-Kohn cross examination).

321. Moreover, there is no evidence in this case that diethyl sebacate was used in *any* topical corticosteroid formulation, whether marketed or experimental, in the 22 years between the publication of JP ‘228 and the priority date of the Bryhali Patents.

322. The Court finds that a person of ordinary skill in the art would not have been motivated by JP ‘228 as of November 22, 2010 to select diethyl sebacate for use in a topical formulation containing halobetasol or any of the other corticosteroids of the Asserted Claims of the Bryhali Patents. The Court agrees with Bausch that Dr. Michniak-Kohn’s contention to the contrary involves picking and choosing from an old reference in a manner that appears to be based on hindsight.

323. For this reason as well, the Court further finds that a person of ordinary skill in the art would not have been motivated by JP ‘228 to solubilize at least 25% or at least 50% of halobetasol used in a pharmaceutical composition in a liquid oil component comprising diethyl sebacate at room temperature. (‘307 patent, Claims 13, 20).

324. The Court also finds that a person of ordinary skill in the art would not have been motivated by JP ‘228 to use diethyl sebacate in the liquid oil component of a pharmaceutical composition to completely dissolve the halobetasol propionate in the composition at a temperature of 22° C +/-2° C. JTX-001 (‘307 Patent) at Claim 16.

325. In addition, for the reasons set out above, the Court finds that a person of ordinary skill would not have been motivated by JP ‘228 to use halobetasol at less

than 0.05%, less than 0.04%, less than 0.025%, or 0.01% or less. While Dr. Michniak-Kohn contended that JP ‘228 discloses compositions where the steroid is present in a range of 0.01% to 0.5%, the steroids disclosed in JP ‘228 are not halobetasol or any of the other superpotent corticosteroids recited in the Asserted Claims of the Bryhali Patents.

v. Temovate E® Label

326. Temovate E® is the brand name for a commercial topical emollient cream formulation comprising clobetasol propionate at 0.05%. The Temovate E® Label is the package insert used with the Temovate E® product. DX-006.

327. Temovate E® was approved by the FDA in 1996. Tr. 399:21-23 (Michniak-Kohn cross examination). The Temovate E® Label used as an exhibit in this case is dated July 2000. DX-006 at HALOBET0019793. However, it is reasonable to assume, and the Court does assume, that this label is not substantively different from the original label used when Temovate E® was approved in 1996, 14 years before the priority date of the Bryhali Patents.

328. In the Precautions section, the Temovate E® Label warns, “Clobetasol propionate is a highly potent topical corticosteroid that has been shown to suppress the HPA axis at doses as low as 2 g/day.” DX-006 (Temovate E® Label) at 1, Precautions. It further states: “Systemic absorption of topical corticosteroids can

produce reversible HPA axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal from treatment.” *Id.*

329. In the Indications and Usage section, the Temovate E® Label states that “[t]reatment beyond 2 consecutive weeks is not recommend, and the total dosage should not exceed 50g/week because of the potential for the drug to suppress the hypothalamic-pituitary-adrenal (HPA) axis.” *Id.*, Indications and Usage.

330. The Label further provides:

In the treatment of moderate to severe plaque-type psoriasis, TEMOVATE E Emollient applied to 5% to 10% of body surface area can be used up to 4 consecutive weeks. The total dosage should not exceed 50 g/week. When dosing for more than 2 weeks, any additional benefits of extending treatment should be weighed against the risk of HPA suppression. treatment beyond 4 consecutive weeks is not recommended. Patients should be instructed to use TEMOVATE E Emollient for the minimum amount of time necessary to achieve the desired results (see PRECAUTIONS and INDICATIONS AND USAGE).

Id.

331. The Label further states:

Patients applying a topical steroid to a large surface area or to areas under occlusion should be evaluated periodically for evidence of HPA axis suppression. This may be done by using the ACTH stimulation, A.M. plasma cortisol, and urinary free cortisol tests. Patients receiving super-potent corticosteroids should not be treated for more than 2 weeks at a time, and only small areas should be treated at any one time due to the increased risk of HPA suppression.

In a controlled clinical trial involving patients with moderate to severe plaque-type psoriasis, TEMOVATE E Emollient applied to 5% to 10% of body surface area resulted in additional benefits in the treatment of patients for 4 consecutive weeks.

Id., Precautions.

332. Dr. Michniak-Kohn relies on the Temovate E® Label to support the obviousness of Claim 16 of the ‘502 patent, which as noted above is directed to a “method of treating a disorder of the skin” by applying “the pharmaceutical composition of claim 1” over “a period of treatment of longer than two weeks.” Tr. 352:18-353:12 (Michniak-Kohn).

333. But apart from reading portions of the Temovate E® Label into the record asserting the Temovate E® Label “teaches the use of a corticosteroid for the treatment of psoriasis for four weeks,” Dr. Michniak-Kohn provided no explanation of why or how the Temovate E® Label allegedly renders Claim 16 obvious. *See* Tr. 352:18-354:23 (Michniak-Kohn).

334. Padagis’s clinical expert, Dr. Stern, also relied on the Temovate E® Label for the proposition that a person of ordinary skill in the art “would have reasonably expected success in treating psoriasis for a period longer than two weeks with concentrations of halobetasol propionate as low as 0.01 percent prior to November of 2010.” Tr. 166:25-167:10 (Stern).

335. Unlike Dr. Michniak-Kohn, Dr. Stern did explain what he was contending regarding the Temovate E® Label, testifying that the label “tells me that certainly when applied to body surface area below 10 percent, lowering the concentration to 0.01 percent of halobetasol would mean less topical product applied and should further decrease the risks of HPA axis suppression, making four weeks of therapy – more than two weeks of therapy even safer.” Tr. 167:5-10 (Stern).

336. Dr. Stern admitted on cross examination that he does not contend that “the Temovate E® Label provides a motivation to lower the concentration of a halobetasol product to less than 0.05%.” Tr. 214:14-18 (Stern cross examination). Dr. Stern’s contention regarding the Temovate E® Label was limitation to reasonable expectation of success.

337. In addition, Dr. Stern further admitted that “the Temovate label is teaching a way to use a high potency steroid product for longer than two weeks without lowering the concentration.” Tr. 214:19-22 (Stern cross examination).

338. This was consistent with Dr. Lane’s analysis. Dr. Lane testified that the Temovate E® Label provides an alternative approach to that of the Bryhali Patents to address the two-week limitation, namely limiting the area of the body to which the formulation is applied rather than lowering the concentration. Tr. 506:2-10 (Lane).

339. As Dr. Lane testified, the Temovate E® Label actually teaches away from the Bryhali Patents by providing a different solution to the two-week limitation problem. Tr. 565:21-566:9 (Lane). The Court agrees.

340. Finally, it is undisputed that there was no similar four-week exception for Ultravate®, the commercial halobetasol product. Both Dr. Stern and Dr. Michniak-Kohn admitted this on cross examination. Tr. 214:23-215:3 (Stern cross examination); 420:14-421:4 (Michniak-Kohn cross examination).

341. And Dr. Stern admitted that he didn't offer any data to support his contention that a low concentration halobetasol would be expected to perform in the same way as the 0.05% clobetasol. Tr. 215:11-13 (Stern cross examination).

342. Dr. Stern also was not able to say whether a person of ordinary skill would "expect that a halobetasol concentration composition could be used safely for longer than two weeks if the concentration was lowered to, say, 0.04 percent." Tr. 215:15-216:25 (Stern cross examination). He was only able to say "[o]ne would think it might be possible, but you'd have to test that." *Id.*

343. Dr. Stern further confirmed that he did not do any kind of testing and that he doesn't "actually have any experimental evidence to support [his] contention" on this point. *Id.*

344. As Dr. Stein Gold testified, a person of ordinary skill would understand from the fact that there was a four-week administration indicated for Temovate E® but

not for Ultravate® that “these are different drugs” and that, given that no four-week exception has been applied to Ultravate® “even after 20 years,” a person of ordinary skill would have understood it was not safe to use halobetasol for longer than two weeks. Tr. 638:8-14 (Stein Gold).

345. In sum, Padagis does not contend that the Temovate E® Label would have provided a motivation to lower the concentration of a corticosteroid below 0.05%, and Padagis did not establish that a person of ordinary would have reasonably expected success in treating psoriasis for a period longer than two weeks with concentrations of halobetasol propionate as low as 0.01 percent prior to November of 2010.

j. There Was No Motivation to Combine With a Reasonable Expectation of Success Any of the Asserted Prior Art References

346. Dr. Michniak-Kohn contended at trial that the Asserted Claims of the Bryhali Patents would have been obvious based on four combinations:

- (1) the ‘295 patent in view of Blum;
- (2) the ‘295 patent in view of Blum and the ‘566 patent;
- (3) the ‘295 patent in view of Blum and JP ‘228; and
- (4) the ‘295 patent in view of Blum and the Temovate® Label.

Tr. 322:24-323:14 (Michniak-Kohn).

347. Dr. Michniak-Kohn contended at trial that each of combinations (1), (2) and (3) would have rendered claims 13, 16, and 20 of the ‘307 patent and claim 4 of the

‘502 patent obvious. Tr. 352:2-16 (Michniak-Kohn). Dr. Michniak-Kohn did not contend that combination (4) would have rendered any of these claims obvious. *See id.*

348. Dr. Michniak-Kohn also contended that combinations (1), (2) and (4) would have rendered claim 16 of the ‘502 patent obvious. Tr. 355:14-21 (Michniak-Kohn). Dr. Michniak-Kohn did not contend that combination (3) (‘295 patent, Blum, JP ‘228) would have rendered claim 16 of the ‘502 patent obvious. *See id.*

k. There Was No Motivation to Combine Because There Was No Motivation to Lower the Concentration

349. Dr. Michniak-Kohn’s contention that a person of ordinary skill would have been motivated to combine the prior art references rests on the premise that a person of ordinary skill would have been motivated to prepare a halobetasol formulation at a concentration of less than 0.05%, and thus would have been motivated to turn to the other references to develop a formulation for use with the lower concentrations.

350. For reasons discussed above, Padagis has not proven that a person of ordinary skill in the art would have been motivated to use a concentration of halobetasol or any other superpotent corticosteroid of less than 0.05%. *E.g., supra* at §§ I.F.1.e - I.F.1.g.

351. Padagis cannot reasonably contend that a person of ordinary skill in the art would have been motivated to lower the concentration of halobetasol when nobody did it for 20 years.

352. And because of this, Padagis cannot prove that a person of ordinary skill would have been motivated to combine any of the four sets of references Dr. Michniak-Kohn asserts against the Bryhali Patents.

I. There Was No Motivation to Combine the Old References

353. Moreover, even if a person of ordinary skill had been motivated to use a lower concentration of halobetasol, the record in this case does not support Padagis's contention that a person of ordinary skill in 2010 would have been motivated to rely on the old references Dr. Michniak-Kohn asserts ('295 patent, '566 patent, JP '228) to select a vehicle to use for a lower concentration formulation.

354. Dr. Michniak-Kohn contends a person of ordinary skill would have been motivated to turn to the '295 patent, the '566 patent and JP '228 because they are "all directed to improving release and/or penetration of corticosteroids from topical formulations." Tr. 342:20-23 (Michniak-Kohn).

355. But as Dr. Lane explained, these references teach use of penetration enhancers to push the drug all the way through the skin. *Supra* at §§ I.F.1.i; I.F.1.ii; I.F.1.iv. And while the use of penetration enhancers was a common approach in the 1980s and 1990s, the use of penetration enhancers to push the drug all the way through the skin would have been the opposite of the approach a person of ordinary skill would have been motivated to take in 2010. *E.g.*, Tr. 501:5-502:3 (Lane).

356. Thus, the Court finds that a person of ordinary skill would not have been motivated to turn to the '295 patent, the '566 patent, or JP '228 as of November 22, 2010 to provide elements for a vehicle for a topical formulation using a concentration of halobetasol or another superpotent corticosteroid of less than 0.05%.

m. Because Formulation Science Is Unpredictable, a Person of Ordinary Skill in the Art Would Not Have Had a Reasonable Expectation of Success in Devising the Invention of the Asserted Claims

357. In addition, there is insufficient evidence in the case to establish that a person of ordinary skill in the art would have had a reasonable expectation of success with any of the combinations asserted by Padagis, even if there had been a motivation to combine these old references.

358. As discussed above, the undisputed evidence in this case is that formulation science is an unpredictable art.

359. Given the unpredictability of the art, the Court finds that Padagis has not proven that a person of ordinary skill would have had a reasonable expectation of success, even if there had been a motivation to combine the prior art references in the manner asserted by Padagis.

360. While Dr. Michniak-Kohn contends that Blum would have provided a person of ordinary skill with a reasonable expectation of success with a lower concentration formulation because it disclosed a 0.02% halobetasol formulation, it is undisputed that Blum does not disclose the formulation used with the 0.02%

concentration other than it is an ointment. Tr. 209:18-22 (Stern cross examination); Tr. 406:10-12 (Michniak-Kohn cross examination).

361. Moreover, as Dr. Michniak-Kohn herself admitted, “a formulation makes all the difference in the delivery of the drug,” including with respect to “the topical formulations we’re talking about in this case.” Tr. 382:11-20 (Michniak-Kohn cross examination).

362. In light of importance of the formulation, a skilled artisan’s complete lack of knowledge of the formulation used in Blum and the unpredictability in the art, the Court cannot conclude that a person of ordinary skill would have had a reasonable expectation of success in developing a formulation with a halobetasol concentration of less than 0.05% based on Blum, either alone or in combination with any of the references relied upon by Padagis.

n. Padagis’s Four Asserted Combinations

i. The First Combination: ‘295 Patent and Blum

363. Dr. Michniak-Kohn contends that a person of ordinary skill in 2010 would have been motivated to combine the 30-year old ‘295 patent with the 24-year old Blum reference because “[a] skilled artisan preparing a topical halobetasol formulation at a lower concentration would have been motivated to select a vehicle that would facilitate adequate drug delivery” and “a POSA would have [] had a reasonable expectation that solubilizing halobetasol in a diaklyl sebacate, as taught

in the ‘295 patent, would have improved the release of halobetasol from the formulation and improved the penetration from the skin.” Tr. 329:20-331:3 (Michniak-Kohn).

364. Dr. Michniak-Kohn further testified that Blum “would have provided the POSA a motivation to formulate a lower dose of halobetasol formulation with an expectation of success.” *Id.*

365. As noted above, the Court finds that a person of ordinary skill in the art would not have been motivated “to prepare a topical formulation at a lower concentration,” which is the starting point of Dr. Michniak-Kohn’s analysis.

366. Neither the ‘295 patent, Blum, nor a person of ordinary skill’s knowledge of the two-week limitation problem with 0.05% halobetasol provide such motivation. The two-week limitation with Ultravate® was known for 20 years, and the problem of systemic risk with superpotent corticosteroids had been known well before Ultravate® was approved. *E.g., supra* at § I.F.1.c.

367. There is no evidence in the record that anyone even experimented with a concentration of halobetasol or any other superpotent corticosteroid of less than 0.05% after Blum was published in 1986, 24 years before the priority date of the Bryhali Patents.

368. All of the experimental halobetasol formulations in the record, such as all of the halobetasol examples of the '566 patent, used halobetasol at 0.05%. Tr. 415:25-416:7 (Michniak-Kohn cross examination).

369. And Blum actually taught away from the lower concentrations of halobetasol claimed in the Bryhali Patents. Tr. 560:21-561:12 (Lane).

370. Moreover, as previously discussed, Dr. Stein Gold credibly testified that a person of ordinary skill in the art would have assumed that the concentration for Ultravate® had been optimized when it came out at 0.05% in 1990. Tr. 625:25-626:10. There is no evidence in the record to the contrary. Indeed, all of the commercial superpotent corticosteroid products as of 2010 had a 0.05% concentration '307 patent, Table 1. It is not surprising, therefore, that people in the field were not motivated to develop a topical treatment with a lower concentration.

371. For reasons also discussed above, even if a person of ordinary skill had been motivated to prepare a topical formulation at a lower concentration, such person of ordinary skill would not have been motivated to look to a 30-year-old reference (the '295 patent) for a class of solvents (sebacates) to select from for use in a corticosteroid formulation, from among the whole universe of other solvents disclosed in the art. Tr. 560:21-561:12 (Lane).

372. Moreover, even if one had turned to the '295 patent, there is nothing in the '295 patent that would have directed a person of ordinary skill to select the specific

diethyl sebacate solvent from within the broader class of sebacates disclosed in the ‘295 patent. Tr. 403:15-404:13 (Michniak-Kohn cross examination). There is no evidentiary support for Dr. Michniak-Kohn’s conclusory assertion that a person of ordinary skill would have arrived at diethyl sebacate by routine experimentation. Tr.392:10-394:11.

ii. The Second Combination: ‘295 patent, Blum and ‘566 patent

373. Dr. Michniak-Kohn contends that a person of ordinary skill would have been motivated to combine the teachings of the ‘566 and ‘295 patents in combination with Blum because the ‘566 and ‘295 patents are “directed to improving release and/or penetration of corticosteroids from topical formulations.” Tr. 342:10-343:10 (Michniak-Kohn).

374. She further testified these references “achieve this goal by completely dissolving the steroid in a liquid oil phase containing a dicarboxylic acid ester. And, of course, the POSA knows that you have to dissolve the steroid. In fact, any drug needs to be dissolved to pass through a membrane like skin. So that’s the basic fundamental knowledge that they would also know. And one of skill would have further understood that these teachings were applicable to halobetasol given the knowledge in the art and examples that we have in the ‘566 patent.” *Id.*

375. The Court finds that a person of ordinary skill would not have been motivated to make the second combination of ‘295 patent plus Blum plus the ‘566

patent for the same reasons the skilled person would not have been motivated to make the first combination.

376. A person of ordinary skill would not have been motivated to make a formulation with a lower concentration and thus would not have been motivated to turn to the '295 or '566 patents in the first place, given Dr. Michniak-Kohn's contention that these references are directed to improving release or enhancing penetration which would be required of a lower concentration formulation.

377. Moreover, even if a person of ordinary skill had been motivated to turn to the '295 and '566 patents, a person would not have been motivated to select the elements of the Asserted Claims from these references.

378. Thus, for example, as discussed above, a person of ordinary skill would not have selected diethyl sebacate from the broad class of sebacates disclosed in the '295 patent. And the '566 patent does not even disclose sebacates, much less the specific diethyl sebacate claimed in the Bryhali Patents.

iii. The Third Combination: '295 Patent, Blum, and JP '228

379. The only difference between Dr. Michniak-Kohn's third combination and her second combination is that her third combination adds JP '228 to the '295 patent and Blum in lieu of the '566 patent. Dr. Michniak-Kohn's analysis of motivation to combine remains the same. Tr. 342:15-23 (Michniak-Kohn). And for the same reasons a person of ordinary skill would not have been motivated to make the second

combination, the Court finds that a person of ordinary skill in the art would not have been motivated to make the third combination.

iv. The Fourth Combination: The ‘295 Patent, Blum, and Temovate E® Label

380. Dr. Michniak-Kohn did not provide any explanation for why a skilled artisan would have been motivated to make her fourth combination, *i.e.*, the ‘295 patent, Blum and the Temovate E® Label. Tr. 352:18-353:17 (Michniak-Kohn). Here again, there is a failure of proof.

381. Nor would there have been any such motivation. A person of ordinary skill would not have been motivated to use a concentration of halobetasol of less than 0.05% for the reasons set out above, and thus would not have been motivated to combine the ‘295 patent and Blum for the reasons set out with respect to Dr. Michniak-Kohn’s first combination.

382. And even if there had been a motivation to combine the ‘295 patent and Blum, there would have been no motivation to add the Temovate E® Label to these references.

383. As discussed above, the Temovate E® Label teaches an entirely different approach to addressing the two-week limitation problem of the 0.05% halobetasol concentration. As the Court previously concluded, the Temovate E® Label actually teaches away from the invention of the Bryhali Patents.

384. As Dr. Stein Gold testified, the four-week exception for Temovate E® had been known in the field, but Ultravate®, the commercial halobetasol product, had not obtained a comparable exception even after 20 years. As noted above, Temovate E is a clobetasol product, not halobetasol.

385. Thus, a person of ordinary skill would not have been motivated to develop a lower concentration halobetasol product based on the Temovate E® Label.

386. Indeed, as noted above, Padagis's clinical expert, Dr. Stern, admitted he was not relying on the Temovate E® Label as motivation to lower the concentration of a halobetasol product to less than 0.05%. Tr. 214:23-215:10 (Stern cross examination).

387. Moreover, given the fact that the commercial halobetasol product Ultravate® never obtained approval for a four-week exception, a person of ordinary skill would not have had a reasonable expectation of success that a lower concentration halobetasol product could be used for longer than two weeks based on the Temovate E® Label.

o. Dr. Michniak-Kohn Failed to Present a Particularized Analysis of How the Asserted Claims of the Bryhali Patents Allegedly Would Have Been Obvious Based on the Four Asserted Combinations

388. Even if Padagis had established there was a motivation to combine each of the four sets of prior art references, Padagis failed to meet its burden of proving the Asserted Claims would have been obvious at least for the reason that Dr. Michniak-

Kohn never presented a specific analysis of how each combination allegedly would have met all of the limitations of the Asserted Claims.⁵

389. While Dr. Michniak-Kohn stated that the Asserted Claims would have been obvious based on the four combinations, she did not apply these four combinations where she presented her obviousness analysis of the individual claims but rather jumbled all of the references together. *E.g.*, Tr. 343:18-345:17 (Michniak-Kohn) (analysis of claim 13 of the '307 patent).

390. Thus, for example, while Dr. Michniak-Kohn contended that claim 16 of the '502 patent would have been obvious based on combinations (1) ('295 patent, Blum), (2) ('295 patent, Blum, '566 patent) and (4) ('295 patent, Blum, Temovate E® Label), she never presented an analysis of the individual limitations of claim 16 based on these three specific combinations.

391. To the contrary, when she presented her analysis of claim 16, she specifically relied for a portion of her analysis on the analysis of claim 4 of the '502 patent. This is apparent from the transcript at Tr. 353:5 (Michniak-Kohn) ("We can see '502 patent claim 4 analysis above"), as well as on her demonstrative slide DDX3.38 ("See '502 patent claim 4 analysis above").

⁵ This was the basis for Bausch's motion at the close of Padagis's case-in-chief under Federal Rule of Civil Procedure 52(c) for judgment on partial findings that Padagis had failed to prove that the Asserted Claims of the Bryhali Patents are invalid. The Court took Bausch's Rule 52(c) motion under advisement. Tr. 462:18-463:25.

392. It is unclear why Dr. Michniak-Kohn made reference to ‘502 patent claim 4 in her analysis of claim 16, given that claim 16 does not depend on claim 4 but rather depends on claim 13, which in turn depends on claim 1 (not claim 4).

393. But nonetheless, if one tracks down her analysis of ‘502 patent claim 4, which is in the transcript at Tr. 350:2-351:25 (Michniak-Kohn) and in her demonstrative slide DDX3.36, one sees that Dr. Michniak-Kohn includes JP ‘228 among the references she cites for the alleged obviousness of claim 4, and thus by reference for claim 16.

394. But JP ‘228 is not one of the references included in the three combinations (1), (2) and (4) that Dr. Michniak-Kohn says she is asserting against claim 16. JP ‘228 is only included in combination (3). Dr. Michniak-Kohn did not assert combination (3) against claim 16.

395. Moreover, the analysis of the individual claim elements of claim 16 would be different depending on which combination is applied – an analysis Dr. Michniak-Kohn never presented but rather leaves to others to do.

396. Thus, for example, one of the elements of claim 1 of the ‘502 patent, and thus by dependency of claim 16, is that the pharmaceutical composition must comprise diethyl sebacate.

397. As can perhaps most readily be seen from Dr. Michniak-Kohn’s demonstrative slide DDX3.36, Dr. Michniak-Kohn did not contend in her analysis

that the cited references would have motivated a POSA specifically to select diethyl sebacate, but rather that the ‘295 patent, ‘566 patent, and JP ‘228 all disclose “dicarboxylic acid esters to dissolve and deliver corticosteroids.” Tr. 350:20-22 (Michniak-Kohn) (“the POSA would have been motivated to use liquid oil component comprising one or more dicarboxylic acid esters. Again, that’s in the ‘295, ‘566, and JP ‘228. And the ‘295, ‘566 and JP ‘228 all disclose dicarboxylic acid esters to dissolve and deliver the corticosteroid.”).

398. Of course, Claim 1 (and thus Claim 16) does not recite “one or more dicarboxylic acid esters,” as Dr. Michniak-Kohn testified. The claim recites, in pertinent part, a pharmaceutical composition comprising “a liquid oil component comprising diethyl sebacate” JTX-004 (‘502 patent), Claim 1.

399. But as noted, Dr. Michniak-Kohn included JP ‘228 among the references she relies upon to contend this limitation would have been met. JP ‘228 is not included in any of the three combinations Dr. Michniak-Kohn has asserted against claim 16 of the ‘502 patent.

400. One is therefore forced to make a choice. On the one hand, perhaps Dr. Michniak-Kohn intended to assert a combination that includes JP ‘228. That would present one analysis.

401. If, on the other hand and contrary to Dr. Michniak-Kohn’s testimony at trial, one were to simply exclude JP ‘228 from consideration, the analysis changes.

402. Setting aside for the moment that there would have been no motivation to combine any of these references, of these three old references only JP ‘228 specifically discloses diethyl sebacate. The ‘295 patent only discloses the class of sebacates, while the ‘566 patent discloses an entirely different group of excipients. So while there would have been no reason for a person of ordinary skill to have selected diethyl sebacate from among the other excipients disclosed in JP ‘228, the analysis of the obviousness of selecting diethyl sebacate is even further attenuated when JP ‘228 is excluded and is based on the combinations Dr. Michniak-Kohn actually said she was asserting.

403. In the end, Dr. Michniak-Kohn’s failure to present an analysis of the individual limitations of claims based on the specific combinations she testified she was asserting leaves the Court with the burden of picking through her trial testimony to determine what, exactly, Padagis contends would have rendered the Asserted Claims obvious. But that burden properly rests with Padagis. By failing to present an analysis of the individual claims based on the asserted combinations, Padagis has failed to prove its case by clear and convincing evidence.

p. Independent Evidence of Non-Obviousness: Long-Felt Need

404. As discussed above, it was undisputed at trial that topical superpotent corticosteroids posed a significant risk of systemic side effects which limited their use to two weeks. *E.g.*, Tr. 50:6-11, 483:17-484:12 (Stein Gold); Tr. 161:14-162:7,

Tr.204:12-14 (Stern); Tr. 317:3-7, Tr. 331:10-18, 332:4-11 (Michniak-Kohn); Tr. 483:17-484:12, 485:8-24 (Lane).

405. Both sides' clinician experts agreed that this two-week limitation was insufficient to treat most psoriasis patients. Tr. 45:12-17; Tr. 50:15-18 (Stein Gold); Tr. 162:20-22 (Stern).

406. Dr. Stein Gold explained,

So, again, these [psoriasis] patients are suffering. We want to use the most potent medication possible, and our hands have been tied because we can use a potent drug, but we're then advised you have to stop after two weeks. But the patient -- it takes longer than two weeks -- as Dr. Stern agrees, it takes longer than two weeks to get that psoriasis under control. You're kind of just starting to get improvement and then you've got to pull back.

Tr. 638:23-639:5.

407. Dr. Stein Gold also explained the need for a superpotent corticosteroid that can be used for longer than two weeks existed "for decades," essentially "since we've had topical therapy and superpotent steroids." Tr. 639:6-9.

408. Padagis's experts also agreed that the problem with superpotent corticosteroids was known long before Ultravate® was approved in 1990, and in fact dated back until at least the 1970s. Tr. 398:9-15 (Michniak-Kohn); Tr. 206:19-207:6 (Stern).

409. The Court also questioned Dr. Stern at trial on the length of time the need for longer treatments existed in the field:

THE COURT: Okay. So if I understand your testimony, for 20 years it's been known that Ultravate® at the 0.05 concentration can only be used for two weeks at a stretch and that that is a very serious drawback because of the side effects that would occur if you used it beyond two weeks.

Is that correct?

THE WITNESS: Yes.

THE COURT: And are you aware of whether or not in that 20-year period any commercial product was approved for use to treat this disease with a concentration of less than 0.05 percent HP?

THE WITNESS: Not with halobetasol, no.

Tr. 303:6-17. Dr. Stern further admitted that “the longer a problem goes unsolved, the less obvious it is.” Tr. 205:20-22 (Stern cross examination).

410. Dr. Stein Gold explained in her testimony that the Bryhali Patents met the long-felt need with the invention of “a very sophisticated vehicle [which allows for the] use a lower concentration of active drug, understanding if we can lower that concentration of drug, the impact to the systemic circulation should go down and we should now have a safer drug that therefore should be able to be used for longer.” Tr. 639:13-19.

q. Independent Evidence of Non-Obviousness: Teaching Away

411. Several of Padagis’s asserted prior art references actually teach away from the limitations of the Asserted Claims of the Bryhali Patents.

412. As discussed above, the Blum reference, which Padagis relies upon as providing the motivation to decrease the concentration to less than 0.05%, recommends use of the higher concentration and therefore teaches away from lowering the concentration of halobetasol to less than 0.05%.

413. Blum disclosed a clinical test comparing a 0.05% halobetasol ointment, a 0.02% halobetasol ointment, and Dermovate ointment, a 0.05% clobetasol product. DX-002 (Blum) at HALOBET0020218.

414. Dr. Stern conceded that Blum unequivocally recommends the higher dose (0.05%)—not the lower dose (0.02%)—as the “favorite treatment weapon” and a “welcome addition to the therapeutic armamentarium.” Tr. 211:8-11; 19-22; Tr. 210:8-19; Tr. 212:22-24; DX-002 (Blum) at HALOBET0020220.

415. In addition to Blum’s express statements, the clinical data in Blum support the article’s recommendation of the higher dose ointment. Specifically, as Dr. Stein Gold explained, the lower concentration demonstrates a lower efficacy in the patients with severe psoriasis (which Blum identifies as the “most reliable measurement” for comparing efficacy), and a lower efficacy overall. Tr. 631:10-632:1.

416. In addition, as Dr. Stein Gold also explained, the adverse event data in Blum shows that the reduction in concentration from 0.05% to 0.02% halobetasol actually resulted in a *higher* incidence of irritation. Tr. 632:2-12. Further, the incidence of

skin atrophy (thinning), a problem associated with superpotent corticosteroids, was the same between the higher and lower concentrations used in Blum. Tr. 632:3-17; Tr. 632:23-633:6.

417. Thus the lower concentration (0.02%) halobetasol ointment in Blum was disclosed to be “a less effective drug that was maybe equivalent or maybe a little bit worse in terms of side effects.” Tr. 632:18-20.

418. The Temovate E® Label also teaches away from the Asserted Claims of the Bryhali Patents. As discussed in more detail *infra*, the Temovate E® Label refers to the package insert of a clobetasol propionate (0.05%) product indicated for psoriasis, which permits application for up to four weeks if the patient restricts the application of the product to a specific body surface area. Tr. 420:22-23 (Michniak-Kohn); DX-006 (Temovate E® Label) at HALOBET0019792.

419. As Dr. Lane explained, the Temovate E® Label teaches away from the Asserted Claims of the Bryhali Patents because it provides a different solution (as opposed to reducing the concentration of superpotent corticosteroid) the two-week limitation problem. Tr. 566:7-9. Padagis’s expert, Dr. Stern agreed that the Temovate E® Label “is teaching a way to use a high potency steroid product for longer than two weeks *without lowering the concentration.*” Tr. 214:19-22 (emphasis added).

420. Moreover, the Temovate E® Label explicitly warns about the downsides of usage beyond two weeks, including the risk of HPA axis suppression. Tr. 638:15-19 (Stein Gold).

r. Independent Evidence of Non-Obviousness: Unexpected Results

421. The parties have stipulated that Bausch's Bryhali® product is a commercial embodiment of the Asserted Claims of the Bryhali Patents. ECF No. 206-1 at ¶ 1.

422. A person of ordinary skill in the art would not have expected that lowering the concentration of halobetasol below 0.05% would achieve comparable efficacy to a 0.05% concentration. Tr. 83:23; JTX-005-2 (Declaration of Dr. Gordon Dow) at BAU00000204, ¶¶ 8, 11; Tr. 486:4-9; 488:24-489:5 (discussing DX-196 (Gao) at HALOBET0019237-238) (Lane); Tr. 633:22-634: 9; 636:21-24; 649:18-24 (Stein Gold).

423. The common wisdom at the time of the invention of the Bryhali Patents was that decreasing the concentration of a drug in formulation would compromise the efficacy. Tr. 486:4-9 (Lane); Tr. 625:17-19 (Stein Gold).

424. As Dr. Lane explained, this principle is illustrated in the Background section of the Bryhali Patents, which shows, by way of example, fluocinonide at 0.1% concentration (Class 1-Superpotent), 0.05% (Class 2-Potent, Class 3- Upper Mid-Strength, depending on formulation), and 0.01% (Class 6-Mild). Tr. 486:14-487:14.

425. That a decrease in concentration would have been expected to yield an attendant drop in efficacy is demonstrated through the development history of the Bryhali® product. The results of the initial VCA study performed during the development project, which ultimately led to the Bryhali Patents, demonstrated that the low concentration (0.01%, 0.025%, 0.035%) halobetasol formulations had comparable efficacy to Ultravate®. These results were “exciting” and “extremely surprising” to the development team. Tr. 77:24-78:6; Tr. 76:6-7; Tr. 80:7-81:2; Tr. 81:23-82:2; PTX-067 (IDP-118 Lotion QbD Pharmaceutical Development Report: FPD-182) at BAU01194364, Table 5.31-1.

426. Prior to conducting the first VCA study, Dr. Pillai did not have an expectation as to what the outcome would be. Tr.79:4-11.

427. The results of the first VCA panel were so unexpected and surprising that Dr. Pillai recalled the development team performing a second “confirmatory” VCA panel to make sure that the results from the first panel could be replicated. Tr. 80:22-6; Tr. 81:13-82:5.

428. A head-to-head study comparing Bryhali® and Ultravate® confirmed in patients that the lower concentration Bryhali® product maintains potency and efficacy compared to the higher-concentration Ultravate®. Tr. 89:23-93:19; JTX-012-10 (Study V01-122A-203) at 9.

**s. The Asserted Claims Would Not Have Been Obvious:
Claim-By-Claim Analysis**

i. The Asserted Claims of the '307 Patent

429. The asserted claims of the '307 patent are claims 13, 16, and 20.

(a) Claim 13 Would Not Have Been Obvious

430. Claim 13 of the '307 patent depends from claim 1. The full text of both claims is set out below.

431. Claim 1 of the '307 patent states:

1. A pharmaceutical composition for topical application to the skin of an individual comprising halobetasol propionate at a concentration of 0.04% or less and a liquid oil component comprising one or more dicarboxylic acid esters, wherein the dicarboxylic acid esters are selected from diethyl sebacate, diisopropyl adipate, and dibutyl sebacate and wherein at least 25% of the halobetasol propionate is solubilized in the liquid oil component at 22° C.

JTX-001 ('307 patent) at Claim 1.

432. Claim 13 of the '307 patent further recites:

13. The pharmaceutical formulation of claim 1 wherein the halobetasol propionate is at a concentration of 0.025% or less, the liquid oil component comprises diethyl sebacate, and wherein at least 50% of the halobetasol propionate is solubilized in the liquid oil component at room temperature.

JTX-001 ('307 patent) at Claim 13.

433. Padagis has failed to prove that Claim 13 of the '307 patent would have been obvious for at least the following reasons.

434. First, as discussed above, Padagis has failed to prove that a person of ordinary skill in the art would have been motivated to develop a pharmaceutical formulation for topical application with a reasonable expectation of success wherein the halobetasol propionate is lower than 0.05%, much less at a concentration of 0.25% or less as required by Claim 13.

435. Second, as further discussed above, Padagis has failed to prove that a person of ordinary skill in the art would have been motivated to combine the asserted prior art references in any of the combinations asserted by its experts to achieve a lower concentration halobetasol formulation through the use of penetration enhancers disclosed in these old references.

436. Third, even if there was a motivation to combine these old references, nothing but hindsight guides a person of ordinary skill in the art to select diethyl sebacate (as required by Claim 13) from the '295 patent, the '566 patent, or JP '228.

437. As of 2010, there were no commercial formulations of any corticosteroid product for treating psoriasis that contained diethyl sebacate. Tr. 391:7-11 (Michniak-Kohn cross examination). The commercial halobetasol product, Ultravate®, approved 10 years after the '295 patent issued, did not use diethyl sebacate. Tr. 393:16-394:3 (Michniak-Kohn cross examination). Dr. Michniak-Kohn admitted there is no experimental evidence in the prior art that shows diethyl

sebacate is better at dissolving halobetasol than any of the other oleaginous solvents.

Tr. 393:2-5 (Michniak-Kohn cross examination).

438. The ‘295 patent discloses the class of sebacates but there is nothing in the ‘295 patent to point a person of ordinary skill specifically to diethyl sebacate and no evidence that a person of ordinary skill experimenting with sebacates would select diethyl sebacate through “routine optimization” as Dr. Michniak-Kohn alleges. The ‘566 patent discloses an entirely different set of solvents. JP ‘228 discloses diethyl sebacate along with other solvents; but while there are test results reported in JP ‘228, none are for formulations with diethyl sebacate. There is nothing but hindsight that would guide a person of ordinary skill to select diethyl sebacate from among the other solvents disclosed in JP ‘228.

(b) Claim 16 Would Not Have Been Obvious

439. Claim 16 of the ’307 patent incorporates the composition of claim 4, which depends on claim 1. The text of claim 1 is set out above. The full text of claims 4 and 16 is set out below.

440. Claim 4 of the ’307 patent recites:

4. The pharmaceutical composition of claim 1 wherein the concentration of the liquid oil component is sufficient to dissolve the amount of halobetasol propionate in the composition at a temperature of $22^{\circ}\text{C} \pm 2^{\circ}\text{C}$.

JTX-001 (’307 patent) at Claim 4.

441. Claim 16 of the ’307 patent further recites:

16. A method for treating a disorder of the skin that is amenable to treatment with a topical corticosteroid comprising providing a pharmaceutical composition of claim 4 and applying an amount to the skin that is effective in ameliorating the signs or symptoms of the disorder.

JTX-001 ('307 patent) at Claim 16.

442. Padagis has failed to prove that Claim 16 of the '307 patent would have been obvious for essentially the same reasons it has failed to prove Claim 13 would have been obvious.

443. Padagis has failed to prove that a person of ordinary skill would have been motivated to develop a pharmaceutical composition for topical application with a reasonable expectation of success comprising halobetasol propionate at a concentration of 0.04% or less; that a person of ordinary skill would have been motivated to combine the asserted prior art references; or that, even if there had been a motivation to combine, a skilled artisan would have selected diethyl sebacate as a solvent. And because the claimed pharmaceutical composition would not have been obvious, it would not have been obvious to apply the claimed composition to treat a disorder of the skin.

(c) Claim 20 Would Not Have Been Obvious

444. Claim 20 of the '307 patent depends from claim 19, which depends from claim 1. The text of claim 1 is set out above. The full text claims 19 and 20 is set out below.

445. Claim 19 of the '307 patent recites:

19. The pharmaceutical composition of claim 1, wherein the liquid, oil component further comprises light mineral oil.

JTX-001 ('307 patent) at Claim 19.

446. Claim 20 of the '307 patent further recites:

20. The pharmaceutical composition of claim 19, wherein the liquid oil component comprises diethyl sebacate and light mineral oil.

JTX0991 at Claim 20.

447. Padagis has failed to prove that Claim 20 of the '307 patent would have been obvious for the same reasons it has failed to prove Claim 16 would have been obvious, but also for the additional reason that even if a skilled artisan had been motivated to lower the concentration and to combine the references, nothing but hindsight would have motivated the skilled artisan to include light mineral oil.

448. At trial, Dr. Michniak-Kohn relied on the *Handbook of Pharmaceutical Excipients* as a basis for concluding that a person of ordinary skill in the art would have selected light mineral oil to include in a lower-concentration formulation. Tr. 394:16-396:22 (Michniak-Kohn cross examination). But Dr. Michniak-Kohn admitted there are thousands of excipients disclosed in the *Handbook of Pharmaceutical Excipients*. *Id.* Setting aside that the *Handbook* is not one of the references Dr. Michniak-Kohn relied upon in any of her four combinations, there is

nothing in the *Handbook* that would have guided a person of ordinary skill to use light mineral oil.

449. Dr. Michniak-Kohn also relied on the ‘295 patent, the ‘566 patent, and JP ‘228 for the alleged obviousness of including light mineral oil. *Id.* But there is nothing but hindsight that would have guided a person of ordinary skill to use light mineral oil based on these references.

450. As Dr. Michniak-Kohn admitted on cross examination, the Ultravate® product does not have light mineral oil and thus the development team at BMS was not motivated to include light mineral oil in their halobetasol formulation. Tr. 395:17-24 (Michniak-Kohn cross examination).

451. Moreover, as Dr. Michniak-Kohn further admitted, Temovate E®, the commercial clobetasol product, does not use light mineral oil. Tr. 396:6-10 (Michniak-Kohn cross examination).

452. And as Dr. Michniak-Kohn further admitted, “light mineral oil was not in any of the other commercially available topical products for treatment of psoriasis as of 2010.” Tr. 395:25-396:4 (Michniak-Kohn cross examination).

453. Thus, the Court concludes there is nothing but hindsight that would have led a person of ordinary skill in the art in 2010 to include light mineral oil in a topical halobetasol formulation. Padagis has not proved that it would have been obvious to include light mineral oil in the claimed formulation.

ii. The Asserted Claims of the '502 Patent

454. The asserted claims of the '502 patent are claims 4 and 16.

(a) Claim 4 Would Not Have Been Obvious

455. Claim 4 of the '502 patent depends from claim 1. The full text of both claims is set out below.

456. Claim 1 of the '502 patent states:

1. A pharmaceutical composition for topical application to the skin of an individual comprising: a liquid oil component comprising diethyl sebacate and a corticosteroid selected from the group consisting of halobetasol propionate, clobetasol propionate, betamethasone dipropionate, diflorasone diacetate, and fluocinonide at a concentration less than 0.05%; and an aqueous component comprising water; wherein the composition is free of white petrolatum.

Ex. 2 ('502 patent) at Claim 1.

457. Claim 4 of the '502 patent recites:

4. The pharmaceutical composition of claim 1, wherein the corticosteroid is halobetasol propionate and the concentration of the halobetasol propionate is 0.01% (w/w) or less.

Ex. 2 ('502 patent) at Claim 4.

458. Padagis has failed to prove that Claim 4 of the '502 patent would have been obvious for essentially the same reasons it has failed to prove that Claim 13 of the '307 patent would have been obvious, but also for the additional reason that even if a skilled artisan had been motivated with a reasonable expectation of success to

lower the halobetasol concentration to 0.01% and to make the three combinations Dr. Michniak-Kohn asserts against this claim, nothing but hindsight would have motivated the skilled artisan to exclude white petrolatum.

459. Dr. Michniak-Kohn contended it would have been obvious to exclude white petrolatum because “it’s greasy and undesirable.” Tr. 397:1-17 (Michniak-Kohn cross examination). But she also admitted there is white petrolatum in Ultravate® ointment, a commercial halobetasol product. *Id.* Again, real-world evidence contradicts Dr. Michniak-Kohn’s testimony.

460. Dr. Michniak-Kohn also contended the skilled artisan would have been motivated to exclude white petrolatum based on the ‘295 patent, the ‘566 patent, and JP ‘228. *Id.*

461. But as Dr. Michniak-Kohn testified, the ‘295 patent simply discloses examples free of white petrolatum. Tr. 404:14-20 (Michniak-Kohn cross examination). The fact that it discloses examples that do not include white petrolatum would not have affirmatively motivated a skilled artisan to exclude white petrolatum in a halobetasol formulation.

462. Dr. Michniak-Kohn further testified that JP ‘228 “does not teach the use of white petrolatum.” *Id.* But again, the fact that JP ‘228 does not teach use of white petrolatum would not have motivated a skilled artisan to exclude its use.

463. Dr. Michniak-Kohn alleged that the ‘566 patent teaches advantages of excluding white petrolatum. *Id.* But Dr. Michniak-Kohn only included the ‘566 patent in her Combination (2) with Blum and the ‘295 patent. While Dr. Michniak-Kohn did not present a particularized analysis based on this asserted combination, even if there would have been a motivation to combine these references (which there was not), neither the ‘566 patent nor the ‘295 patent specifically disclose diethyl sebacate. The ‘566 patent discloses a different set of solvents, and there is nothing in the ‘295 patent to guide a person of ordinary skill to diethyl sebacate from the disclosure of the broad class of sebacates in the ‘295 patent.

464. Thus, even assuming (contrary to fact) that there would have been a motivation to lower the halobetasol concentration 0.01% or less and to combine the references as Padagis asserts, Padagis has not established that all of the limitations of Claim 4 of the ‘502 patent would have been obvious even if it is assumed that the ‘566 patent would have motivated a skilled artisan to exclude white petrolatum.

(b) Claim 16 Would Not Have Been Obvious

465. Claim 16 of the ‘502 patent incorporates claim 13, which depends from claim 1. The text of claim 1 is set out above. The full text of claims 13 and 16 is set out below:

466. Claim 13 of the ‘502 patent recites:

13. A method of treating a disorder of the skin that is amenable to treatment with a topical corticosteroid, the

method comprising applying the pharmaceutical composition of claim 1 to the skin of an individual having the disorder in an amount that is effective in ameliorating the signs or symptoms of the disorder.

Ex. 2 ('502 patent) at Claim 13.

467. Claim 16 of the '502 patent further recites:

16. The method of claim 13, wherein the method comprises applying the pharmaceutical composition over a period of treatment longer than two weeks.

Ex. 2 ('502 patent) at Claim 16.

Padagis has failed to prove that Claim 16 of the '502 patent would have been obvious for essentially the same reasons it has failed to prove that Claim 4 of the '502 patent would have been obvious, with the proviso that Claim 16 requires a halobetasol concentration of less than 0.05% (not 0.01% or less) and for the additional reason that the Temovate E® Label does not establish a reasonable expectation of success in using the claimed formulation for a period of longer than two weeks.

2. Padagis Failed to Prove That the Term “Liquid Oil Component” Is Indefinite

468. All claims of the '307 and '502 patents include a “liquid oil component.” JTX-001 ('307 Patent) at 12:51-14:49; JTX-004 ('502 Patent) at 12:64-14:29.

469. The Court construed the term “liquid oil component” as follows: “the ‘liquid oil component’ includes all ingredients of the formulation that are practically

insoluble or insoluble in water and which are liquid at room temperature of 22°C.”

ECF No. 83 at 24.

470. Dr. Lane (Plaintiffs’ expert) and Dr. Michniak-Kohn (Defendants’ expert) both agreed at trial that a POSA in 2010 would have understood whether any particular ingredient is a “liquid oil component” as that term has been construed by the Court because a POSA would know whether any ingredient is “practically insoluble or insoluble in water” and “liquid at room temperature of 22°C.” Tr. 576:5-13 (Dr. Lane); Tr. 421:7-422:2 (Dr. Michniak-Kohn). As Dr. Michniak-Kohn admitted on cross examination:

Q. Now, the Court has construed the term “liquid oil component,” correct?

A. Correct.

Q. And the construction is, “The liquid oil component includes all ingredients of the formulation that are practically insoluble or insoluble in water and which are liquid at room temperature of 22° degrees C,” correct?

A. Correct.

Q. Now, a person of ordinary skill would reasonably understand what it means for an ingredient to be practically insoluble or insoluble in water, correct?

A. Correct.

Q. * * * A person of ordinary skill would reasonably understand what it means for an ingredient to be liquid at room temperature of 22° degrees C, correct?

A. Correct.

Tr. 421:9-422:2 (Michniak-Kohn cross examination).

471. Dr. Lane and Dr. Michniak-Kohn also agreed at trial that a POSA in 2010 would have understood that sorbitan monooleate, an emulsifying agent, would fall within the Court's definition of part of the "liquid oil component" because sorbitan monooleate is both "practically insoluble or insoluble in water" and "liquid at room temperature of 22°C." Tr. 576:21-577:4 (Dr. Lane); Tr. 358:6-15 (Dr. Michniak-Kohn).

472. Dr. Michniak-Kohn contended at trial that nonetheless, the term "liquid oil component" is indefinite because sorbitan monooleate is excluded from the calculations set out in Table 2 of the '307 and '502 patents under the header "Components of Liquid Oil Component (% w/w)." JTX-001 ('307 patent) 10:12-22; Tr. 356:10-362:8 (Michniak-Kohn). According to Dr. Michniak-Kohn, because of this "inconsistency" in excluding sorbitan monooleate from the liquid oil component section in Table 2, "the person of ordinary skill in the art cannot tell you with reasonable certainty what the scope of the term "liquid oil component" would be, making that term indefinite." Tr. 362:4-8 (Michniak-Kohn).

473. The Court disagrees with Dr. Michniak-Kohn's analysis and finds that a person of ordinary skill could reasonably determine by studying the specification that Table 2 reflects only the *solvent* ingredients of the liquid oil component and not *all* of the ingredients of the liquid oil component. The person of ordinary skill would

further understand that sorbitan monooleate is not a solvent and was excluded from Table 2 for that reason.

474. As Dr. Lane explained at trial, Table 2 of the '307 and '502 patents calculates the solubility of halobetasol propionate in the solvents of test formulations A-D shown in Table 1. Thus, the calculations shown in Table 2 include only the solvent ingredients of the liquid oil component; for example, in test formulation A of Table 1, the calculation in Table 2 includes diethyl sebacate and light mineral oil. Tr. 577:11-578:9; JTX-001 ('307 Patent) at Tables 1, 2.

475. A person of ordinary skill would reasonably understand that the calculations shown in Table 2 do not include sorbitan monooleate because sorbitan monooleate is an emulsifying agent, and is not a solvent for halobetasol propionate. Tr. 578:9-17; Tr. 578:18-579:8.

476. Therefore, a POSA would understand and be able to apply the meaning of the term "liquid oil component" with reasonable certainty, without perceiving a conflict with Table 2 of the specification. Tr. 580:16-21; 582:9-25 (Lane).

3. Padagis Failed to Prove That the Asserted Claims of the Bryhali Patents Lack Written Description

477. At trial, Padagis appeared to assert during cross examination of Bausch's experts that Claim 16 of the '502 patent, which is directed to a method of using a pharmaceutical composition of the claimed invention for a period of longer than two weeks, lacks written description because the specification does not expressly state

that the claimed compositions can be used for longer than two weeks. *E.g.*, Tr. 677:1-17 (Stein Gold cross examination).

478. The Court finds there is written descriptive support in the specification for the limitation in claim 16 that the claimed compositions can be used for longer than two weeks.

479. Column 2, lines 42-62 of the specification of the '502 patent provides:

The superpotent corticosteroids are utilized for skin conditions that are not satisfactorily responsive to lower potency corticosteroids. Such conditions include psoriasis and certain severe types of eczema. Unfortunately, because of the high potency of the Class 1 corticosteroids, which correlates with a high incidence and severity of systemic side effects, including hypothalamic-pituitary-adrenal (HPA) axis suppression, topical treatment with superpotent corticosteroids is generally limited in duration to 2 weeks. Such side effects may also occur with treatment with Class 2 potent corticosteroids. Additionally, the occurrence of local adverse reactions limits the duration of use of superpotent and potent corticosteroids with respect to treatment of chronic or recurrent skin diseases.

Chronic skin conditions, such as psoriasis, however often require long periods of treatment, greater than 2 weeks, to manage such conditions. Therefore, it would be desirable to have a superpotent corticosteroid formulation with a reduced incidence and/or severity of systemic side effects so that therapy can be continued for durations longer than 2 weeks.

JTX-004 ('502 patent) at BAU00000017.

480. As Dr. Stein Gold explained at trial, column 2, lines 42-62 of the '502 patent “explains to us is that there is an unmet need because we have this limitation of two

weeks for superpotent steroids, and we have an unmet need to use them for a longer period of time to get the psoriasis patients basically under control.” Tr. 642:24-643:12.

481. Column 3, lines 6-14 of the specification of the ’502 patent provides:

Because of the tendency of all superpotent corticosteroids to cause serious systemic effects, the FDA (Food and Drug Administration) requires that the prescribing information for currently marketed topical compositions of superpotent corticosteroids, such as clobetasol and halobetasol, except for a particular spray formulation of clobetasol, carry the warning that treatment beyond 2 consecutive weeks is not recommended, and the total dosage should not exceed 50 g of the composition per week.

JTX-004 (’502 patent) at BAU00000018.

482. As Dr. Stein Gold explained at trial, column 3, lines 13-22 of the ’502 patent “makes reference to . . . the fact that any and all of the superpotent corticosteroids have the problem of potentially getting into the systemic circulation and causing the HPA axis suppression.” Tr. 643:13-22.

483. Column 9, lines 6-23 of the specification of the ’502 patent provides:

Additionally, because of the reduced concentration of corticosteroid in the formulation compared to that in the prior art compositions and the concomitant reduction in amount of corticosteroid that is available to enter the systemic circulation upon topical administration of the formulation, it is conceived that the formulation may have similar efficacy but improved safety compared to prior art formulations that contain higher concentrations of corticosteroid. Thus the formulations of this application

have particular utility in infants and children in treating skin diseases such as atopic dermatitis and in both adults and children for treating recalcitrant or chronic skin diseases such as psoriasis. It is conceived that the present invention provides an equivalent or better efficacy in treating steroid responsive skin diseases compared to that produced by presently available topical formulations, and with potentially reduced local and systemic side effects.

JTX-004 ('502 patent) at BAU00000021.

484. As Dr. Stein Gold explained at trial, column 9, lines 6-23 of the '502 patent explains that “there is an enhanced vehicle. And because we can potentially reduce the concentration of the corticosteroid, we should then be able to administer the lower concentration which should then be safer and decrease the potential risk for HPA axis suppression.” Tr. 643:23-644:8.

485. Column 4, lines 2-12 of the specification of the '502 patent provides:

Due to the much reduced concentration of the corticosteroid in the formulation, reduced amounts of corticosteroid are available to enter the systemic circulation and, therefore, the tendency of such formulations to cause undesirable systemic side effects should likewise be reduced. Thus, the formulations and methods of this application are especially useful for the treatment of chronic or recalcitrant skin diseases, such as psoriasis, due to the concerns regarding safety when topical corticosteroids are used in multiple course treatments over time.

JTX-004 ('502 patent) at BAU00000018.

486. As Dr. Stein Gold explained at trial, column 4, lines 2-12 of the '502 patent “talks about when you have a much reduced concentration of topical corticosteroid,

the chance of getting – or it's much more likely then you have a significantly reduced exposure to the systemic circulation, therefore, you decrease the likelihood of having any type of systemic side effect so you should be able to use it potentially for a longer period of time.” Tr. 644:12-25.

487. Moreover, Dr. Stern expressly admitted that the ‘824 Publication – a document with substantially the same disclosure as the ‘502 patent – tells a person of ordinary skill “about 0.01 percent halobetasol in a lotion that can be used for more than two weeks.” Tr. 183:5-8.

488. Padagis also appeared to assert during cross examination of Bausch’s experts that Claim 16 of the ‘502 patent, which recites a pharmaceutical composition comprising “a corticosteroid selected form the group consisting of halobetasol propionate, clobetasol propionate, betamethasone dipropionate, diflorasone diacetate, and fluocinonide at a concentration less than 0.05%” lacks written description. *E.g.*, Tr.588:13-591:24. But the specification expressly provides that “[t]he corticosteroid that is included in the formulation of the invention is preferably a superpotent corticosteroid according to [VCA], such as clobetasol, halobetasol, betamethasone dipropionate . . . diflorasone diacetate . . and fluocinonide at 0.1%[.]” JTX-004 (‘502 Patent) 4:63-5:1.

489. The Court finds there is written descriptive support in the specification for the limitation in claim 16 that the claimed compositions comprise a corticosteroid

selected from the group consisting of halobetasol propionate, clobetasol propionate, betamethasone dipropionate, diflorasone diacetate, and fluocinonide at a concentration less than 0.05%.

4. Padagis Failed to Prove That the Asserted Claims of the Bryhali Patents Are Not Enabled

490. To the extent Padagis contends that the Bryhali Patents are not enabling, Padagis provided no evidence at trial that a person of ordinary skill in the art would not have been able to make and use the invention of the Asserted Claims of the Bryhali Patents without undue experimentation. Thus, the Court finds Padagis failed to prove the Bryhali Patents are not enabling.

G. The Duobrii Patents

1. Padagis Failed to Prove That the Asserted Claims of the Duobrii Patents Are Invalid For Obviousness

491. Bausch has asserted Claims 3 and 6 of the '895 patent and Claims 4, 5, and 6 of the '787 patent.

492. Claim 1 of the '895 patent is representative. It states:

1. A topical pharmaceutical composition for treating psoriasis the composition comprising:

(a) active ingredients consisting of: (i) halobetasol propionate, at a concentration of 0.01 percent by weight of the composition; and (ii) tazarotene at a concentration of 0.045 percent by weight of the composition; and

(b) a dermatologically acceptable carrier, wherein the composition is an oil-in-water emulsion; wherein an oil phase in the oil-in-water emulsion comprises a liquid

oil component; wherein the liquid oil component is liquid at 22° C. and consists of diethyl [] sebacate and light mineral oil; and wherein the composition comprising the halobetasol propionate and the tazarotene at said concentrations is capable of providing synergistic efficacy and synergistic reduction of at least an adverse event selected from the group consisting of itching, burning, and stinging, for said treating.

JTX-002 ('895 Patent) at Claim 1.

493. Padagis's experts contended at trial that all of the Asserted Claims of the Duobrii Patents would have been obvious based on five references: (1) United States Patent Application Publication U.S. 2012/0129824, published May 24, 2012 (DX-142) (the "'824 Publication"); (2) Gollnick and Menter, "Combination therapy with tazarotene plus a topical corticosteroid for the treatment of plaque psoriasis," British Journal of Dermatology 1999, 140 (Suppl. 54; 18-23 (DX-140) ("Gollnick"); (3) an Indian patent application published March 30, 2012 (DX-141) ("Gandhi"); and (4) a study record from ClinicalTrials.Gov for IDP-118, first posted January 24, 2014 (DX-064) (the "IDP-118 Study"); and (5) the label for Tazaroc, the commercial tazarotene product available in 0.05% and 0.1% concentrations (DX-010) (the "Tazorac® Label").

494. Padagis's clinical expert, Dr. Stern, specifically testified that the Asserted Claims would have been obvious based on three combinations of these references:

(1) the '824 Publication + Gollnick + the Tazorac® Label;

(2) the ‘824 Publication + Gollnick + the IDP-118 Study;
and

(3) the ‘824 Publication + Gollnick + Gandhi.

Tr. 167:16-168:3 (Stern); *see also* DDX 2.15.

495. Padagis’s formulation expert, Dr. Michniak-Kohn, testified that the only prior art she was relying on for her analysis was the ‘824 Publication. Tr. 422:3-8, 422:24-423:3 (confirming that “the ‘824 Publication is the sole reference you rely on to conclude that the formulation limitations of the Duobrii Patents would have been obvious”) (Michniak-Kohn cross examination). However, Dr. Michniak-Kohn also referred to U.S. Patent No. 8,808,716 (the “’716 patent”) and certain passages from Bausch’s IND in her direct testimony.

496. In his direct testimony, Dr. Stern contended that the ‘824 Publication discloses “every limitation” of the Asserted Claims except the 0.045% tazarotene and synergy limitations. Tr. 170:10-17 (Stern).

497. He contended that a person of ordinary skill in the art would have been motivated to add tazarotene at a concentration of 0.045% to the ‘824 Publication’s 0.01% halobetasol propionate lotion and would have reasonably expected the combination to be capable of providing synergistic efficacy and synergistic reduction of an adverse event. Tr. 170:10-17 (Stern).

498. Dr. Stern also testified that that the claimed synergies are an inherent property of the IDP-118 formulation. *Id.*; Tr. 185:17-186:2 (Stern).

499. Dr. Stern further testified that Gollnick, Gandhi and the IDP-118 Study provided motivation to combine halobetasol and tazarotene, that the ‘824 Publication provided motivation to use 0.01% halobetasol, and that the Tazorac® label provided motivation to use 0.045% tazarotene. Tr. 182:19-184:17 (Stern).

500. Dr. Stern further also testified that the claimed synergies would have been expected based on statements made in Gollnick and Gandhi suggesting that combining halobetasol and tazarotene would likely have “synergistic effects.” Tr. 184:20-185:16 (Stern).

501. In her direct testimony, Dr. Michniak-Kohn contended that all of the formulation limitations of the Asserted Claims would have been obvious, based “for example” on Formula 4A of the ‘824 Publication. Tr. 374:17-378:23 (Michniak-Kohn). Formula 4A is the formula for IDP-118, minus the 0.045 % tazarotene.

502. Dr. Michniak-Kohn further asserted that a person of ordinary skill would have been motivated to combine tazarotene with the “teachings” of the ‘824 Publication, although she provided no explanation whatsoever as to why this would have been the case. Tr. 379:8-19 (Michniak-Kohn).

503. In addition, Dr. Michniak-Kohn testified that “incorporating tazarotene into, for example, the formulation we discussed, 4A, would have been routine optimization.” Tr. 371:15-19 (Michniak-Kohn). She also testified that a person of

ordinary skill would have arrived at the specific 0.045% concentration of tazarotene by “routine experimentation.” Tr. 377:1-9 (Michniak-Kohn).

a. Padagis Limited Its Obviousness Case to the Contention that the Asserted Claims Would Have Been Obvious Based on the Specific IDP-118 Formulation

504. Despite having made general statements in their direct testimony that the Asserted Claims of the Duobrii Patents would have been obvious, both Dr. Stern and Dr. Michniak-Kohn clarified on cross examination that their contentions were based on the narrow argument that a person of ordinary skill in the art would have been motivated to arrive at the specific IDP-118 formulation, not all of the compositions of the Asserted Claims, and that the IDP-118 formulation inherently has the synergies claimed in the Duobrii Patents.

505. Thus, Dr. Stern testified:

Q. You’re only contending that a POSA would have been motivated to arrive specifically at the IDP-118 formulation and that the synergies are inherent properties of IDP-118, correct?

A. Yes.

* * *

A. And just for clarity, in this second bullet [of DDX 2.31], this is exactly what you’re arguing. You’re only arguing that if synergy is present, it is an inherent property of IDP-118 formulation and not any other formulations that might fall within the claims of the Duobrii patent, right?

A. I – I think so. I don't mean to be difficult, but what I'm talking about is IDP-118 and synergy limitations being an inherent property, yes.

Tr. 217:20-218:10 (Stern cross examination).

Q. What you mean to be saying here [in DDX2.16] is that the '824 Publication discloses every limitation of IDP-118. Is that your testimony, sir?

A. Except for the addition of tazarotene, yes.

Q. Understood. Understood.

A. And the synergy limitations.

Tr. 218:17-22 (Stern cross examination).

506. Dr. Michniak-Kohn similarly testified as follows:

Q. Now, I want to know exactly what you're contending based on the '824 Publication. Are you contending that a POSA would have been motivated to arrive specifically at the IDP-118 composition based on the '824 Publication?

A. Correct.

Q. You're not contending that a POSA would have been motivated to arrive at all of the compositions of the asserted claims of the Duobrii patents, correct?

A. Correct.

Tr. 423:4-13 (Michniak-Kohn cross examination).

507. Thus, Padagis's argument is limited to the contention that the specific formulation of IDP-118 would have been obvious to a person of ordinary skill in the art and that IDP-118 inherently has the claimed synergies.

508. The limitation on Padagis's argument can be discerned even from the direct testimony of Padagis's experts, even though much of the testimony of Padagis's experts was broader.

509. The only evidence Padagis adduced from its experts regarding the claimed synergies was Dr. Stern's testimony that the claimed synergies are an inherent property of IDP-118.

510. Dr. Stern did not argue that the claimed synergies are an inherent property of any other species of the genus of compositions claimed in the Duobrii Patents. Dr. Michniak-Kohn did not address the synergy limitations.

511. Accordingly, the only evidence Padagis adduced at trial with respect to the inherency of the synergy limitations pertains to the specific IDP-118 formulation. Thus, Padagis's obviousness argument is necessarily limited to the contention that a person of ordinary skill would have been motivated to arrive at the specific IDP-118 formulation and that this renders all of the Asserted Claims obvious. Padagis adduced no evidence that any other species of the Asserted Claims (or the compositions of the Asserted Claims generally) inherently has the claimed synergies.

512. This is not, however, how Padagis put on its case through its experts in their direct presentations. Neither Dr. Stern nor Dr. Michniak-Kohn testified in the direct

examinations that a person of ordinary skill would have been motivated to arrive at the specific IDP-118 formulation.

b. Nothing But Hindsight Guides a Person of Ordinary Skill in the Art to the Specific IDP-118 Formulation

513. Based on the record as a whole, the Court finds that a person of ordinary skill in the art would not have arrived at the specific IDP-118 formulation without the benefit of hindsight.

514. Dr. Stern expressly admitted on cross examination that he was relying on the Duobrii Patents themselves to identify the relevant formulation for IDP-118 in the ‘824 Publication.

515. By way of background to this point, Example 3 in the ‘824 Publication describes vasoconstriction assay (VCA) testing done on different halobetasol compositions at three different concentrations (0.035%, 0.025%, 0.01%). ‘824 Publication (DX-142) at [0039-40]. The ‘824 Publication discloses in Table 3 and ¶ 40 that each of these three concentrations provided a VCA score similar to the prior art formulation of Ultravate®. *Id.* at Table 3, [0040].

516. Dr. Stern confirmed on cross examination that “[t]he ‘824 Publication does not state that any one of these concentrations is a preferred or a particularly preferred embodiment of the invention.” Tr. 222:9-12 (Stern cross examination).

517. But when asked whether Dr. Stern was contending that formula C in Table 3 with the 0.01% halobetasol concentration formulation is the formulation a person

of ordinary skill in the art would have picked, he testified it was not and that he considered Formula 4A (the formulation of IDP-118 minus the 0.045% tazarotene) to be the preferred one *based on the Duobrii Patents*:

Q. Is it your contention that a person of ordinary skill in the art reading the '824 Publication would have picked formula C to experiment with?

A. I believe if we go on further in the patent, it shows the 0.01 percent in the final formulation, which I believe is – I took to be the preferred one. So if you continue on the patent, I think it's table 4A.

Q. So you say it shows the final formulation, which you took to be the preferred one. Why did you – what was the basis for that, sir?

A. I – if we could turn to – to the – further on, where I believe it demonstrates the exact formulation that is used in the combination patents and, by its use, seemed to me to be the selection of the preferred one.

Tr. 222:19-223:7 (Stern cross examination) (emphasis added).

518. Perhaps recognizing the box he was in, later in his cross examination Dr. Stern refused to answer whether a person of ordinary skill in the art would have selected Formula 4A from the '824 Publication, saying he would rather leave that to a formulation expert. Tr. 223:23-226:12 (Stern). He testified:

Q. In your bottom bullet, you say a POSA would have been motivated to use the 0.01 percent HP lotion from the '824 Publication.

A. Yes.

Q. You say "the 0.01 percent HP location." Do you mean the lotion of formula C?

A. I'd have to ask the formulation person.

Q. All right. So you don't know what you're talking about. Strike that. Strike that. You don't actually know what you've said here when you say "motivated to use the 0.01 percent HP lotion." You don't have a basis for knowing what that is, right?

A. In terms of which was the final and specific constituents, no.").

Tr. 229:12-230:1 (Stern cross examination).

519. Dr. Stern made this admission even though he had testified in his direct examination that "the '824 Publication discloses every limitation except the simple addition of tazarotene and the synergy limitations of the combination patents." Tr. 170:4-9 (Stern).

520. Dr. Stern's admissions on cross examination cast doubt on the credibility of much of the testimony he gave on direct. And his candid admission that he was relying on the Duobrii Patents themselves to identify the example in the '824 Publication that discloses the formulation for IDP-118 (other than the 0.045% tazarotene) is revealing and supports the conclusion that Padagis's obviousness case is driven by hindsight.

521. Padagis's formulation expert, Dr. Michniak-Kohn, did not testify on direct that a person of ordinary skill in the art would have selected Formula 4A from the other examples and the broad disclosures of the '824 Publication. Rather, her testimony was based "for example" on Formula 4A, without any explanation as to

why a person of ordinary skill would have selected Formula 4A from the disclosures in the '824 Publication.

522. Thus, for Claim 6 of the '895 patent, Dr. Michniak-Kohn presented a chart in her slide DDX2.64 which compared the elements of Claim 6 to Formulation 4A, without explanation as to why a person of ordinary skill would have selected Formulation 4A in the absence of hindsight rather than one of the other examples from the '824 Publication or indeed an entirely different composition based on the broad disclosures in the '824 Publication. She testified:

And what I did with all of this information is I put it in tabular form, which we see below. You see Claim 6, percentage by weight of composition. We have those values and the ranges put in for each of the drug and the tazarotene and the other excipients. And then what I did in the far end portion of this, I put formulation 4A from the '824 Publication and compared the values there to those of Claim 6.

Tr. 376:15-22 (Michniak-Kohn).

523. As can be seen from the above, Dr. Michniak-Kohn's analysis simply assumed, without explanation, that a person of ordinary skill would have selected Formula 4A.

524. As noted, Formula 4A does not include 0.045% tazarotene. Dr. Michniak-Kohn did not explain why a person of ordinary skill would have been motivated to add tazarotene to Formula 4A or indeed to any of the formulations disclosed in the '824 patent, but asserted that a person of ordinary skill would have been motivated

to include 0.045% tazarotene to Formula 4A through “routine optimization.” 377:1-9 (Michniak-Kohn) (“Tazarotene, of course, in Claim 6 is 0.045, and that’s very close, by the way, as we established, to the already existing and marketed formulation which is at 0.05%. It’s slightly less – when we would have added, as a person of ordinary skill in the art or the team that’s there, would have added the tazarotene, we would have probably looked at various concentrations of tazarotene, and routine optimization would have included something as similar to the original tazarotene concentration as 0.045.”); *see also* DDX3.64.

525. For reasons discussed below, the Court finds that it would not have been obvious to make the IDP-118 formulation, including the 0.045% tazarotene.

c. The IDP-118 Formulation Would Not Have Been Obvious Based on the ‘824 Publication

526. Dr. Stern defers to Dr Michniak-Kohn on the question of whether it would have been obvious to make the specific IDP-118 formulation. Dr. Michniak-Kohn agreed that “the ‘824 Publication is the sole reference you rely on to conclude that the formulation limitations of the Duobrii patents would have been obvious.” Tr. 422:25-423:3 (Michniak-Kohn cross examination).

527. However, Dr. Michniak-Kohn did not establish that the IDP-118 formula would have been obvious based on the ‘824 publication.

d. No Motivation to Add Tazarotene to the Halobetasol Compositions of the ‘824 Publication

528. Padagis did not show that a person of ordinary skill in the art would have been motivated to add tazarotene to the halobetasol compositions of the ‘824 Publication.

529. Dr. Michniak-Kohn asserted that “one of skill in the art would have been motivated to combine tazarotene with the teachings of the ‘824 Publication” Tr. 379:13-14 (Michniak-Kohn). But she did not provide any explanation as to how or why that would have been the case.

530. Such a conclusory statement from an expert is insufficient to establish that a person of ordinary skill would have been motivated to combine tazarotene with the teachings of the ‘824 Publication.

531. Moreover, the weight of the evidence clearly shows that a person of ordinary skill would not have been motivated to combine tazarotene with the halobetasol compositions disclosed in the ‘824 Publication as of the June 18, 2015 priority date of the Duobrii Patents.

532. The evidence shows that fixed-dose combination products are rare, particularly for the treatment of psoriasis. Tr. 646:20-647:8 (Stein Gold). The FDA has set a high bar for approval of combination products. Tr. 646:24-647:5 (Stein Gold). The FDA mandates that efficacy of the combination must be superior to the efficacy of each of the individual active ingredients in the combination. Tr. 665:18-

23 (Stein Gold cross examination); *see also* 291:18-21 (Stern cross examination) (agreeing that “when the FDA is evaluating combination products, it’s looking to see whether the combination is better than the individual monads”).

533. The rarity of combination products in psoriasis treatment is illustrated by the fact that there are only two other fixed dose combination products in addition to Duobrii®. Tr. 646:20-647:17 (Stein Gold). The other products, Enstilar® and Taclonex®, are a combination of a topical corticosteroid and a vitamin D analogue in different vehicles. Tr. 688:9-23 (Stein Gold cross examination).

534. Although Dr. Stern, Padagis’s dermatology expert, testified that there is a “long history of dermatologic products being combined successfully[,]” he did not identify in his testimony any combination products for treating psoriasis (other than Enstilar® and Taclonex®). Tr. 179:9-14 (Stern). Dr. Stein Gold clarified that there is a history of combination products in acne, but that acne is a “very different disease” from psoriasis. Tr. 647:9-16 (Stein Gold).

535. Padagis’s own prior art references would have taught away combining a steroid and tazarotene in a fixed-dose combination product. Gollnick – which is included in all three of Dr. Stern’s combinations which he asserts against the Duobrii Patents – describes studies which applied steroids and tazarotene on alternating days or on the morning/night of the same day. Dr. Stein Gold testified this would have informed a person of ordinary skill that steroids and tazarotene should be used “as

far apart as possible.” Tr. 647:17-648:9 (Stein Gold); DX-140 (Gollnick) at HALOBET0019241.

536. Moreover, Gollnick would have taught a person of ordinary skill not to use a superpotent corticosteroid such as halobetasol with tazarotene. Tr. 651:22-652:11 (Stein Gold). The clinical data from Gollnick’s additive study would have taught a person of ordinary skill to use a mid-potency corticosteroid, while the alternating study described in Gollnick included only low-or mid-potency steroids. *Id.* Thus, Gollnick would have guided a person of ordinary skill to a low- or mid-potency corticosteroid, not a superpotent corticosteroid. *Id.*

537. In addition, a person of ordinary skill in the art would not have been motivated to combine tazarotene with a 0.01% halobetasol concentration from the ‘824 Publication because the low 0.01% halobetasol concentration would not have been expected to be able to ameliorate the irritation of the tazarotene in a fixed dose combination product. Tr. 649:25-650:3 (Stein Gold).

538. Dr. Stein Gold explained that a person of ordinary skill would have expected to need more potent steroid action to combat the irritating effects of tazarotene in a fixed dose combination product. Tr. 650:17-651:2 (Stein Gold).

539. Dr. Jeffrey Sugarman (a dermatologist) similarly explained in his declaration submitted during prosecution of the Duobrii Patents that a POSA would not have expected such a low concentration would be enough to significantly reduce

the side effects of tazarotene monotherapy. JTX-006-4 (Declaration Under 37 C.F.R. §1.132) at BAU00001402-1403, ¶12.

540. In addition, IDP-118 is a lotion. A person of ordinary skill in the art would not have been motivated to combine a steroid and tazarotene into a lotion product because lotions tend to be less efficacious among the various other types of topical formulations (ointments, creams, etc.). Tr. 648:10-15 (Stein Gold); PTX-122 (FERENCE) at HALOBET0020587. As Dr. Stein Gold testified, the goal was to have more potent and more efficacious psoriasis treatments, not less potent or less efficacious treatments. *Id.*

541. Further, a person of ordinary skill in the art would not have had a reasonable expectation of success that they could dissolve tazarotene in diethyl sebacate. Testing would be required. Tr. 571:20-25 (Lane).

542. In fact, as Dr. Lane pointed out in her testimony, evidence at trial showed that dibutyl sebacate – which has a similar chemical structure to diethyl sebacate – was not compatible with tazarotene. Tr. 572:20-573:18 (Lane).

543. Dr. Michniak-Kohn relies on U.S. Patent No. 8,808,716 as “prior art” that purportedly demonstrated tazarotene could be dissolved in diisopropyl adipate, a dicarboxylic acid ester. Tr. 373:2-21 (Michniak-Kohn); DX-203 (‘716 patent). However, the ‘716 patent is not one of Dr. Michniak-Kohn’s asserted prior art references. Dr. Michniak-Kohn testified she was only relying on the ‘824

Publication with regard to the Duobrii Patents. Moreover, the '716 patent does not provide any information on the specific dicarboxylic acid ester in IDP-118, namely diethyl sebacate, and it does not address the unpredictability in similar solvents as Dr. Lane identified in her testimony.

544. Thus, the Court concludes that Padagis has not established that a person of ordinary skill in the art would have been motivated to add tazarotene to the halobetasol compositions of the '824 Publication based on the '824 publication, as Dr. Michniak-Kohn contends.

e. Nothing But Hindsight Would Lead to the Specific IDP-118 Formulation (Minus the Tazarotene) in the '824 Publication

545. Moreover, Padagis did not establish that a person of ordinary skill in the art would have selected the specific IDP-118 formulation from among the broad disclosures and examples of the '824 Publication.

546. As noted, given that Dr. Michniak-Kohn (and Dr. Stern) are only contending that the IDP-118 formulation would have been obvious, and Dr. Stern ultimately did not provide an opinion that the IDP-118 formulation would have been obvious, it was left to Dr. Michniak-Kohn to establish that a person of ordinary skill would have been motivated to combine 0.045% tazarotene specifically with Formula 4A of the '824 Publication in order to arrive of IDP-118. And Dr. Michniak-Kohn did not even purport do so.

547. Dr. Michniak-Kohn agreed that “the ‘824 Publication does not stand out from the overall literature available to a person of ordinary skill in the art as of 2015.” Tr. 423:25-424:3 (Michniak-Kohn cross examination). Dr. Stern also agreed this was the case. Tr. 423:25-424:3 (Stern cross examination).

548. Bausch’s formulation expert, Dr. Lane, also agreed that the ‘824 Publication would not have stood out among the multitude of references available to a person of ordinary skill in the art in 2015. Tr. 570:20-571:7 (Lane). Dr. Lane testified that a person of ordinary skill would have had no reason to select the ‘824 Publication from all of the other references in this crowded field without the Duobrii Patents in hand. *Id.*

549. Dr. Michniak-Kohn also agreed that the ‘824 Publication contains a broad disclosure of ingredients and concentrations that can be used, and that most of the ingredients and concentrations do not fall within the scope of the claims of the Duobrii Patents. Tr. 424:5-11 (Michniak-Kohn cross examination).

550. Thus, Dr. Michniak-Kohn agreed that the ‘824 Publication broadly discloses a large number of solvents, including monocarboxylic acid esters and dicarboxylic acid esters. Tr. 425:9-15. IDP-118 contains only a single dicarboxylic acid ester: diethyl sebacate. Tr. 425:16-18; Tr. 574:13-19; DX-142 (‘824 Publication) at HALOBET0018651, [0020].

551. Dr. Michniak-Kohn also agreed that the '824 Publication broadly discloses compositions with a wide range of concentrations of active ingredient, including 0.035%, 0.025%, and 0.01%. Tr. 426:25-427:16 (Michniak-Kohn cross examination). By contrast, IDP-118 contains only 0.01% halobetasol. Tr. 427:7-8; DX-142 ('824 Publication) at HALOBET0018653, Table 1.

552. Dr. Michniak-Kohn also agreed that there is no claim in the '824 Publication that specifies a 0.01% concentration of halobetasol propionate. Tr. 432:10-12 (Michniak-Kohn cross examination).

553. Dr. Michniak-Kohn further agreed that the '824 Publication broadly discloses a large number of other lipophilic liquids. Tr. 426:6-14 (Michniak-Kohn cross examination). By contrast, IDP-118 contains only a single lipophilic liquid: light mineral oil. Tr. 574:20-575:2; DX-142 ('824 Publication) at HALOBET0018652, [0026].

554. In addition, Dr. Michniak-Kohn agreed that the '824 Publication broadly discloses many corticosteroids for use with the invention. Tr. 424:16-425:3 (Michniak-Kohn cross examination). By contrast, IDP-118 contains a single superpotent corticosteroid: halobetasol. Tr. 425:4-6; Tr. 575:3-8; DX-142 ('824 Publication) at HALOBET0018650-18651, [0017].

555. Dr. Michniak-Kohn also agreed the '824 Publication broadly discloses different types of formulation vehicles, including lotions, gels, creams, and

ointments. Tr. 425:21-426:2. By contrast, IDP-118 is a lotion formulation. Tr. 575:9-14; DX-142 ('824 Publication) at HALOBET0018651, [0023].

556. Dr. Michniak-Kohn further acknowledged that the '824 Publication discloses a series of example formulations in Example 1, Table 1, which are listed as Formulations A, B, C, D, and E, and that Formulations A, B, and C each have different concentrations of halobetasol. Tr. 426:15-428:4 (Michniak-Kohn cross examination). She agreed that Formulation A has 0.035% halobetasol, Formulation B has 0.025% halobetasol, and Formulation C has 0.01% halobetasol. *Id.*

557. She further acknowledged that paragraph 40 states that each of these three formulations provided a VCA score similar to that of the prior art Ultravate® formulation. *Id.* She agreed that the '824 Publication does not state that any one of these concentrations is a preferred or particularly preferred embodiment of the invention. *Id.*

558. Dr. Michniak-Kohn also confirmed that in Example 5, the inventors actually made an example lotion and tested it to see whether it met FDA stability requirements. Tr. 428:5-429:8 (Michniak-Kohn cross examination).

559. Dr. Michniak-Kohn agreed that the '824 Publication shows a “particular preference” for this formulation:

Q. This is the formulation the inventors chose to test to see whether it would meet the FDA requirements for a commercial product, right?

A. For that purpose, yes.

Q. And it shows the inventors had a particular preference for this formulation, correct?

A. Correct, the stability studies.

Q. And it was the only formulation the inventors chose to test to see if it met FDA standards, right?

A. As reported in the patent -- or the application, yes.

Tr. 429:5-14 (Michniak-Kohn cross examination).

560. Dr. Michniak-Kohn confirmed that the preferred formulation the inventors chose to test to see if it met FDA requirements for a commercial product had a 0.025% halobetasol concentration as shown in Table 5, not the 0.01% halobetasol concentration of IDP-118. Tr. 429:18-430:2 (Michniak-Kohn cross examination).

561. Dr. Michniak-Kohn also admitted that there is no test data of any kind disclosed in the '824 Publication for Formula 4A or 4B. Tr. 430:10-12 (Michniak-Kohn cross examination).

562. Dr. Michniak-Kohn further admitted there is test data disclosed in the '824 Publication for five different formulas. Tr. 431:13-15 (Michniak-Kohn cross examination).

563. Dr. Michniak-Kohn also admitted that while there were claims submitted as part of the '824 Publication, there is no claim in the '824 Publication that specifies a 0.01% halobetasol formulation. Tr. 432:10-12 (Michniak-Kohn cross examination)

564. Shortly after having agreed that the stability testing showed the inventors had a “particular preference” for the 0.025% halobetasol formulation of Table 5, Dr. Michniak-Kohn said she “disagreed” that “by testing the formulation in Table 5 to determine whether it met FDA requirements, the inventors were expressing a preference for that 0.025% halobetasol formulation in the ‘824 Publication.

Q. Isn't it true that by testing the formulation in Table 5 to determine whether it met FDA requirements, the inventors were expressing a preference for that 0.025 percent halobetasol formulation in the ‘824 Publication?

A. I disagree.

Q. So it's your view that when the ‘824 Publication only tests one formulation to see whether it met FDA requirements for a commercial product, that is not a preference for that concentration?

A. I believe not.

Tr. 432:13-22 (Michniak-Kohn cross examination).

565. Dr. Michniak-Kohn's disagreement with a proposition she had agreed with only moments earlier illustrates a lack of credibility of her testimony.

566. Ultimately, Dr. Michniak-Kohn admitted that there is no reason for a person of ordinary skill in the art to have picked Formula 4A:

Q. There's no reason for a POSA to have picked Formula 4A, which you use in your explanation, which has no test data reported in the patent over the five formulas disclosed in the ‘824 Publication that do have test data. Isn't that correct?

A. The POSA would have considered all of them, I agree.

Tr. 431:21-432:1 (Michniak-Kohn cross examination).

567. Based on a careful review of the '824 Publication as a whole and the other evidence in this case, including the credibility of the witnesses, the Court finds that a person of ordinary skill in the art would not have been motivated to select Formula 4A from the '824 Publication.

568. The '824 Publication is clearly expressing a preference for the other formulations that were tested, including particularly the 0.025% halobetasol concentration of Table 5 that was tested to determine whether it met FDA requirements for a commercial product. There is no test data in the '824 Publication for Formula 4A.

569. Selecting Formula 4A from among the examples and broad disclosures of the '824 Publication would be the result of hindsight, as Dr. Stern candidly admitted on adverse examination.

f. Nothing But Hindsight Would Have Led to the Specific 0.045% Tazarotene Concentration

570. Dr. Michniak-Kohn testified it would have been a matter of routine experimentation to arrive at 0.045% tazarotene. She contended this is so because 0.045% is “close” to the 0.05% concentration of Tazorac®. Tr. 435:16-17 (Michniak-Kohn).

571. But the fact that 0.045% is “close” to the 0.05% concentration of Tazorac® is an insufficient basis to conclude that a person of ordinary skill would have arrived

at the precise 0.045% tazarotene concentration of IDP-118 by “routine experimentation.”

572. Dr. Michniak-Kohn also admitted that she did not have any experimental evidence to support her position that a person of ordinary skill would have arrived at 0.045% by routine optimization:

Q. You don't have any experimental evidence to establish that the optimal concentration of tazarotene in the formulation of the '824 patent [sic] would have been 0.045 rather than 0.040 percent or 0.035 percent or even 0.01 percent, right?

A. Correct.

Q. You've got no way of knowing whether what you call routine experimentation would have arrived at the 0.045 percent concentration, correct?

A. I absolutely disagree.

Q. But you didn't do any optimization testing yourself, correct?

A. Correct.

Q. And as far as you know, Padagis didn't do any optimization testing to try to establish that 0.045 percent concentration is the optimal concentration in this formulation, right?

A. Correct.

Tr. 435:22-436:14 (Michniak-Kohn cross examination).

573. The Court finds that Dr. Michniak-Kohn did not establish that combining the 0.045% tazarotene concentration with the compositions disclosed in the '824

Publication would have been obvious based on the ‘824 Publication and “routine optimization.”

574. While Dr. Michniak-Kohn said she “absolutely disagree[d]” that she had no way of knowing whether routine optimization would have arrived at 0.045% concentration rather than a different concentration, she never provided an explanation of the basis for her disagreement.

575. There is nothing in the record that supports Dr. Michniak-Kohn’s claim that a person of ordinary skill would have arrived at the specific 0.045% tazarotene concentration by routine optimization. It was undisputed that Bausch did not optimize the 0.045% tazarotene concentration in IDP-118. Tr. 87:10-23 (Pillai).

576. Unlike Dr. Michniak-Kohn, Padagis’s other expert, Dr. Stern candidly admitted there was no evidence that a person of ordinary skill would have arrived at 0.045% by “routine optimization.”

577. Dr. Stern contended in his direct testimony that the Tazorac® label would have motivated a person of ordinary skill to use a 0.045% concentration of tazarotene. As noted, Dr. Stern acknowledged he was not relying on the Tazorac® label as motivation to combine tazarotene and halobetasol, but rather only as a motivation to arrive at the specific 0.045% concentration. Tr. 282:16-22 (Stern cross examination).

578. But on cross examination, Dr. Stern testified that he was only saying the Tazorac® label would lead a person of ordinary skill to “consider” lowering the concentration:

Q. Now, in your third bullet, you say a POSA would have been motivated by the Tazorac label to use 0.045 percent tazarotene to reduce irritation, correct?

A. Yes.

Q. But there’s nothing in the Tazorac label that would teach a POSA to use the specific 0.045 percent concentration that’s in IDP-118, correct?

A. That – by the label itself, that’s correct.

Q. Tazorac already came in both a higher and a lower concentration, right?

A. Yes.

Q. The lower concentration was 0.05 percent, correct.

A. Yes.

Q. If a POSA wanted to reduce irritation, they would use the lower 0.05% concentration Tazorac, correct?

A. A POSA would use that as a starting point.

Q. So Tazorac was approved in 1997, correct?

A. Yes.

Q. That was 18 years before the invention date of the Duorbii patents, right?

A. Yes.

Q. And in those 18 years, no one ever made a tazarotene product with less than this lower 0.05 percent

concentration of tazarotene in order to reduce irritation, right?

A. Not to my knowledge.

Q. So, again, you say a POSA would have been motivated to lower the concentration. But nobody ever did it in 18 years, right?

A. I said to consider lowering it, yes.

Tr. 283:22-284:25 (Michniak-Kohn cross examination) (emphasis added).

579. Dr. Stern's admission that a person of ordinary skill would only "consider" lowering the 0.05% concentration disposes of his argument that the 0.045% tazarotene concentration would have been obvious based on the Tazorac® label. A motivation to "consider" lowering the concentration falls short of the required motivation to actually lower the concentration.

580. And indeed, Dr. Stern ultimately conceded that there is nothing in the Tazaroc label that would have led a person of ordinary skill to the specific 0.045% concentration:

Q. Now, even if a POSA had been motivated to consider lowering the concentration of tazarotene, there is nothing in the Tazorac label that would have led a POSA to the specific 0.045 percent concentration, correct?

A. That is correct.

Tr. Tr. 285:1-5 (Stern cross examination).

581. Moreover, unlike Dr. Michniak-Kohn, Dr. Stern admitted on cross examination he had no evidence that a person of ordinary skill would have arrived at the specific 0.045% concentration, rather than a different concentration.

Q. You don't have any evidence that 0.045% is the optimal concentration for tazarotene in this combination, correct?

A. That's correct.

Q. And you don't have any evidence that the optimal concentration isn't some other concentration, like 0.040 percent or 0.035 percent, right?

A. That's correct.

Q. You didn't do any optimization testing yourself, correct?

A. That's correct.

Q. And as far as you know, no one at Padagis did any optimization testing, correct?

A. Correct.

Q. You don't have any actual evidence that a POSA would have arrived at the specific 0.045 percent concentration, correct?

A. That's correct.

Tr. 285:9-286:1 (Stern cross examination) (emphasis added).

582. Dr. Stern's admissions effectively dispose of Padagis's argument that a person of ordinary skill would have arrived at the specific 0.045% tazarotene

concentration of IDP-118 by routine optimization or that the Tazorac® label would have guided a skilled artisan to the 0.045% concentration.

583. But in addition, as Dr. Stein Gold explained, in going from the high dose (0.1%) to the low dose (0.05%) of Tazorac® – which reduces the concentration of tazarotene by 50% – the side effect profile is essentially unchanged. Tr. 663:15-19. A person of ordinary skill thus would not have been expected that a reduction in concentration of tazarotene to 0.045%—another 10% decrease in concentration—would favorably impact the drug’s tolerability profile. Tr. 648:16-649:3 (Stein Gold). A person of ordinary skill therefore would not have been motivated to reduce the concentration of tazarotene below the 0.05% in the Tazorac® Label. Tr. 649:15-17 (Stein Gold).

584. Thus, the Court finds that Padagis has failed to prove that it is a person of ordinary skill in the art would have been motivated to select Formula 4A of the ‘824 Publication and would have added to it the specific 0.045% concentration of tazarotene.

g. No Obviousness Based on Dr. Stern’s Three Asserted Combinations

585. As discussed above, the Court concludes that Dr. Michniak-Kohn did not establish that the IDP-118 formulation would have been obvious.

586. But in addition, Dr. Stern also did not establish that the Asserted Claims of the Duobrii Patents would have been obvious based on the IDP-118 formulation.

587. As noted, Dr. Stern relies on three sets of combinations to allege that the Asserted Claims of the Duobrii Patents would have been obvious:

- (1) ‘824 Publication + Gollnick + Tazorac® label;
- (2) ‘824 Publication + Gollnick + IDP-118 Study; and
- (3) ‘824 Publication + Gollnick + Gandhi

588. Dr. Stern did not establish that the Asserted Claims would have been obvious based on any of these three combinations.

589. With respect to the first combination (‘824 Publication + Gollnick + Tazorac® label), as discussed above the Tazorac® label would not have directed a person of ordinary skill in the art to the specific 0.045% concentration of tazarotene in IDP-118.

590. Dr. Stern also admitted he does not contend that the other two references in the first combination (the ‘824 Publication and Gollnick) would have “motivated a person of ordinary skill to use the specific 0.045 percent tazarotene.” Tr. 289:2-5 (Stern cross examination).

591. Thus, even if a person of ordinary skill would have selected Formula 4A from the ‘824 Publication, Dr. Stern’s first combination would not guide a skilled artisan to the 0.045% tazarotene concentration of IDP-118. Therefore, Dr. Stern’s first combination does not render the Asserted Claims obvious.

592. Dr. Stern's admission that he does not contend the '824 Publication or Gollnick would have motivated a person of ordinary skill to use the specific 0.045% concentration of tazarotene (Tr. 289:2-5) also applies to Dr. Stern's third combination ('824 Publication + Gollnick + Gandhi). The only additional reference in the third combination is Gandhi.

593. But Dr. Stern also admitted he does not contend "that Gandhi would have motivated a POSA to use the specific 0.045 percent concentration of tazarotene." Tr. 289:9-12 (Stern cross examination).

594. Accordingly, even if a person of ordinary skill would have selected Formula 4A from the '824 Publication, the third combination would not have guided a skilled artisan to the 0.045% tazarotene concentration of IDP-118. Dr. Stern's third combination does not render the Asserted Claims obvious.

595. Dr. Stern's second combination is the '824 Publication + Gollnick + the IDP-118 Study. Dr. Stern's admission that neither the '824 Publication nor Gollnick would not have motivated a skilled artisan to use the 0.045% tazarotene concentration applies to the first two references in the third combination.

596. Dr. Stern does not say the same of the IDP-118 Study, which discloses the 0.045% tazarotene concentration in combination with 0.01% halobetasol. Tr. 180:9-16 (Stern); Tr. 286:16-18 (Stern cross examination).

597. But the IDP-118 Study disclosed a Phase II clinical trial, and Dr. Stern candidly admitted on cross examination that there is no motivation in the pharmaceutical industry to make a drug that someone else already has that far along in development:

Q. Wouldn't you agree that there's no motivation in the pharmaceutical industry for someone to make a drug that somebody else already has that far along in the development process?

A. That's probably correct.

Tr. 287:13-17 (Stern cross examination).

598. Dr. Stern's admission means that a person of ordinary skill in the art would not have been motivated to pursue the combination disclosed in the IDP-118 Study and thus would not have been motivated to combine the IDP-118 Study with the '824 Publication and Gollnick, the other two references in Dr. Stern's third combination.

599. Therefore, even if a person of ordinary skill in the art would have been motivated to select Formula 4A from the '824 Publication, Dr. Stern's third combination does not render the Asserted Claims obvious because there would have been no motivation to combine the IDP-118 Study with the other references.

600. Moreover, the third combination does not render the Asserted Claims obvious for the additional reason that the IDP-118 Study is not available as prior art because it is connected to an experimental use (as discussed *infra*).

601. Accordingly, the Court finds that none of the three combinations Dr. Stern asserts against the Duobrii Patents would have rendered the IDP-118 formulation or the Asserted Claims obvious.

602. In addition, as discussed above, the IDP-118 formulation, and thus the Asserted Claims, would not have been obvious based on the '824 Publication alone, as Dr. Michniak-Kohn contends.

603. These are all the bases upon which Padagis contends the Asserted Claims would have been obvious. None establish that the Asserted Claims would have been obvious.

h. Even If The IDP-118 Formulation Would Have Been Obvious, Padagis Has Not Established That the Claimed Synergies Would Have Been Reasonably Expected

604. While Padagis did not prove that the IDP-118 formulation would have been obvious, even if Padagis had done so it did not prove that a person of ordinary skill would have reasonably expected the IDP-118 formulation would have the claimed synergies.

605. The only evidence that a person of ordinary skill in the art would have expected the claimed synergies comes from Padagis's clinical expert, Dr. Stern.

606. Dr. Stern contended that a person of ordinary skill would have expected the claimed synergies based on statements made regarding synergy in Gollnick and Gandhi. Tr. 184:20-185:16 (Stern).

607. Padagis also identified statements made by Bausch to the FDA regarding synergy during the cross examination of Dr. Pillai. Tr. 111:20-114:21, 125:2-17 (Pillai cross examination).

608. Dr. Stern relied on the statement in Gollnick that “[c]ombination therapy with tazarotene and a topical corticosteroid appears logical because these agents have some different (as well as some common) mechanisms of action, and thus are likely to have additive or synergistic effects.” Gandhi (DX-140) at 2; Tr. 185:5-10 (Stern). Dr. Stern also testified that Gollnick discloses that the combinations reduced skin irritation. Tr. 178:10-179:2 (Stern).

609. In addition, Dr. Stern relied on the statement in Gandhi that “when combined in a single formulation, [halobetasol and tazarotene] have synergistic effects which lead to more rapid clearing and are notably effective for types of psoriasis which have not responded to either corticosteroids or retinoids alone.” Gandhi (DX-141) at 7; Tr. 179:21-180:4 (Stern).

610. Based on these two references, Dr. Stern testified that “a person of skill in the art would have reasonably expected the combination to provide synergistic efficacy and synergistic reduction of an adverse event.” Tr. 185:13-16 (Stern).

611. Notably, Dr. Stern did not testify that a skilled artisan would have had a reasonable expectation that the specific IDP-118 formulation would have the claimed synergies.

612. He made only a general assertion that a person of skill in the art would have reasonably expected that the combination of halobetasol and tazarotene would provide the claimed synergies, without any limitation as to the concentrations of either halobetasol or tazarotene or the identities or concentrations of the other components of the formulation. Dr. Stern also failed to provide any explanation as to why this purported expectation would have specifically extended to the claimed synergistic reduction in adverse events.

613. It bears noting here (as discussed above) that Padagis's formulation expert, Dr. Michniak-Kohn, testified that the formulation makes "all the difference" in the delivery of the drug. Tr. 382:11-17 (Michniak-Kohn cross examination).

614. There is no evidence in the record that the expectation described by Dr. Stern might apply to the specific IDP-118 formulation.

615. But even if it could be inferred that Dr. Stern's assertion applies to the specific IDP-118 formulation, Dr. Stern admitted on cross examination that he had no basis for concluding that Gollnick and Gandhi actually used the term "synergy" in the same way it is used in the Duobrii Patents.

Q. Now, you're aware that when the FDA is evaluating combination products, it's looking to see whether the combination is better than the individual monads, right?

A. Yes.

Q * * * So with halobetasol and tazarotene, the FDA is looking to see whether the combination is better than halobetasol alone and better than tazarotene alone, right?

A. Yes.

* * *

Q. But you would agree that [the FDA] is looking to see whether the combination is better than either of the monads alone, correct?

A. Yes.

Q. * * * But in the patents, as the Court has construed them, “synergy” means something different. Isn’t that true?

A. Yes.

* * *

Q. The word “synergy” as it’s sometimes used in the literature doesn’t necessarily have the same meaning as it’s used in the patents, correct?

A. It has been used incorrectly in the literature, that’s correct.

Q. Now, you rely on statements made by Gollnick and Gandhi about the likelihood of additive or synergistic effects, right?

A. Yes.

Q. You don’t have any way to know what these authors mean by synergy or synergistic when they use those terms in the articles, right?

A. That’s correct.

Q. There's no data in either of these publications that would show what they mean by synergistic effects, right?

A. That's correct.

Q. So in the absence of data, you can't know what Gollnick or Gandhi mean when they say the combination is likely to have synergistic effects, right?

A. Correct.

Tr. 291:18-294:3 (Stern cross examination) (emphasis added).

616. Thus, even if Dr. Stern's testimony about "reasonable expectation" can be extended to the specific IDP-118 formulation, his admission that he does not know what Gollick or Gandhi meant by "synergy" or "synergistic" effectively disposes of his contention that a person of ordinary skill would have reasonably expected the IDP-118 formulation would provide the *claimed* synergies.

i. There Are At Least Two Meanings of "Synergy" Used In the Literature

617. As Bausch's clinical expert, Dr. Stein Gold, explained, the terms "synergy" or "synergistic" are used in at least two different ways in the literature:

Q. What do you understand synergy to mean in the dermatological literature?

A. So this can be a little bit confusing because synergy is used in two different ways.

When we look at the literature – and I'm going to try to explain this as simply as possible. But sometimes we use synergy, the word "synergy," to be complimentary or meaning that the two drugs work in harmony together. They make sense to be used together. They would be

synergistic. And that just means that they work maybe by different mechanisms of action. And that's kind of what we would refer to as more of the complimentary effect.

So that's in direct contrast to the second definition of what we're talking about today.

Here we're talking about for a fixed combination you have two active ingredients. So you have the efficacy of the first active, you have the efficacy of the second active and when you add these together the efficacy of the fixed combination is greater than the added amount of the two when you take the vehicle out of each arm.

THE COURT: In short, you're saying, one plus one does not equal two; one plus one equals three.

THE WITNESS: Exactly.

Tr. 655:16-656:13 (Stein Gold) (emphasis added).

618. It is undisputed that this latter meaning “synergy” – one plus one equals three – is how the terms “synergy” or synergistic” are used in the Duobrii patent claims as construed by the Court. *See* ECF No. 83; ECF No. 105.

619. These two meanings of “synergy” were also explained by Dr. Pillai, who testified that “the word [synergy] is used in the literature in multiple different ways.” Tr. 126:18-23 (Pillai cross examination). Dr. Pillai also testified that “when [synergy] is used in the literature, to me it means . . . you have one and the second one, and both of them are mutually beneficial for each other. That's the general interpretation . . . from the literature.” Tr. 144:19-145:4. He further explained that

the claimed synergy, or ‘1+1=3’ synergy, is “where . . . one plus one would be greater than two.” Tr. 145:7-12. (Pillai)

620. Dr. Pillai noted that another section of the IND which referred to “[s]ynergy-selected APIs” similarly referred to the ‘complementary’ type of synergy. Tr. 123:16-126:6; JTX-011-3 (IND 111218 Section 2.3.P - Drug Product) at BAU00054957.

j. No Reasonable Expectation of the Claimed Synergies

621. As discussed, Padagis’s only evidence that a person of ordinary skill would have expected the claimed synergies came from Dr. Stern. Dr. Stern admitted on cross examination that he does not know what Gollnick and Gandhi, the only two references he relies on for this opinion, mean by “synergy” or “synergistic.”

622. Dr. Stein Gold credibly testified that neither Gollnick nor Gandhi show the claimed synergies. Tr. 657:23-658:14 (Stein Gold).

623. The statements Bausch made to the FDA do not show that the inventors expected IDP-118 would have the type of synergies (“1+1=3”) claimed in the Duobrii Patents. As Dr. Pillai explained, all of those statements referred to the additive or complementary meaning of “synergy,” as distinct from the claimed synergies of the Duobrii Patents. And in any event these confidential statements to the FDA are not prior art that Padagis can rely upon for its obviousness case.

624. Padagis has not proved that any of the statements Bausch made to the FDA pertained to “synergy” as that term is used in the Duobrii Patents.

625. Therefore, the Court thus finds that even if the IDP-118 formulation would have been obvious, Padagis did not prove that a person of ordinary skill in the art would have had a reasonable expectation that the IDP-118 formulation would achieve the claimed synergies.

k. Independent Evidence of Patentability: Unexpected Results

i. The Inventors Were Surprised by The Phase II Clinical Study Results

626. It was undisputed at trial that the inventors were surprised by the results obtained in the Phase II clinical study regarding IDP-118.

627. Dr. Pillai testified that he recalled receiving an email containing the results from the Phase II clinical study—the “TopLine Data” —on the day before Thanksgiving in 2015. Tr. 101:9-21; PTX-243 (Email re TopLine Tables). “TopLine Data” refers to the standard practice of organizing clinical data after the completion of a clinical study, and typically includes key efficacy, safety, and demographic tables for the assessment of whether the study was successful. Tr. 101:22-102:8 (Pillai).

628. On review of the TopLine Data, Dr. Pillai referred to the Duobrii® Phase II clinical study results as “one of the best I’ve ever seen,” “beyond any expectations

for us,” and “better than anything that had come prior to that in terms of its efficacy... for any topical psoriatic clinical study.” Tr. 102:11-23 (Pillai).

629. These results were so surprising because, as Dr. Pillai explained “we were hoping...that it would be better [than other existing treatments]...but we just didn’t expect it to be this good.” Tr. 102:24-103:5 (Pillai).

630. In the time period following Dr. Pillai’s receipt of the TopLine Data, it was subsequently confirmed that the data demonstrated synergistic behavior. Tr. 103:4-7 (Pillai).

ii. The Unexpected Results Are Confirmed in The Prosecution History of The Duobrii Patents

631. That IDP-118’s synergistic benefits were unexpected is confirmed in the prosecution history. During prosecution of the Duobrii Patents, Dr. Sugarman submitted a declaration in which he explained that he was “very surprised when the applicants showed the results of the clinical trials of the Invention to [him]. As summarized in Tables 7 and 8 of the specification, the Invention unexpectedly achieved the synergistic efficacy over the combination of halobetasol propionate and tazarotene monotherapies.” JTX-006-4 (Declaration Under 37 C.F.R. §1.132) at BAU00001402, ¶11.

iii. Duobrii® Demonstrated Other Unexpected Benefits

632. Duobrii® demonstrated an additional unexpected benefit in the clinical setting related to post-treatment maintenance of effect.

633. While superpotent corticosteroids can help control psoriasis quickly, the disease can actually return more aggressively once the use of the steroid is stopped. This is known as the rebound effect. Tr. 659:18-24.

634. Tazarotene monotherapy does not have the rapid effect that corticosteroids have, but due to its mechanism of action—which includes “reprogram[ming]” of the skin cells—it has a more prolonged effect which can last beyond use of the drug. Tr. 659:25-660:6.

635. Dr. Stern opined that Gollnick would have provided a POSA with a reasonable expectation of success that a combination of 0.01% halobetasol and 0.045% tazarotene would continue to provide relief for 4 weeks after stopping treatment. Tr. 192:9-193:2. However, Dr. Stein Gold explained a POSA would not have understood Gollnick to apply to a fixed dose combination product. In fact, it was unclear for a combination product containing halobetasol propionate and tazarotene, which drug’s effect would “win” out—the corticosteroid “that wants to rebound” or the tazarotene “that wants to keep effect.” Tr. 660:7-11.

636. Clinical data for Duobrii® showed that in the fixed-dose combination of tazarotene, the post-treatment effects of tazarotene win out and show sustained effect after the cessation of treatment with the drug at 8 weeks. Tr. 660:7-13.

637. This maintenance effect allows patients to potentially stop using Duobrii® and maintain their effect or even possibly improve when assessed at 12 weeks (*i.e.*, 4 weeks after stopping treatment). In other words, “you can stay where you are or you might even get a little bit better even without any drug.” Tr. 660:14-25; PTX-383 (Lebwohl) at BAU01199824, Fig. 4.

I. Independent Evidence of Patentability: Industry Skepticism

638. Before the clinical studies of Duobrii®, advisory boards which included dermatologists were skeptical of IDP-118. Bausch was told that the fixed-dose combination project was “a waste of money” and “[didn’t] make any sense.” Tr. 652:15-24.

639. Dr. Pillai, an inventor of the Duobrii Patents, explained that dermatologists were consulted on the design of the IDP-118 clinical studies, and that the dermatologists offered unsolicited advice on the IDP-118 product. Tr. 94:6-13. Those dermatologists were surprised that Bausch was developing a product with a low concentration of halobetasol propionate, even characterizing Bausch as being “crazy” for moving forward with it. Tr. 94:6-20 (Pillai).

640. Dr. Stein Gold stated her own opinion at the time was that using such a low dose of halobetasol in combination with tazarotene “didn’t make any sense.” Tr. 654:22-25 (Stein Gold).

m. Independent Evidence of Patentability: Commercial Success

641. The parties have stipulated that Bausch’s Duobrii® product is a commercial embodiment of the Asserted Claims of the Duobrii Patents. ECF No. 199 at ¶ 5.

i. Duobrii® Has Achieved Significant Sales in the Relevant Market

642. The evidence in this case shows that Duobrii has managed to achieve significant sales in the relatively short time it has been on the market despite having been launched shortly before onset of the Covid-19 pandemic.

643. From its time of launch in May 2019 through December 2021, [REDACTED] Tr. 734:19-735:3; PTX-219 (P&L Spreadsheet); PTX-224 (Financial Spreadsheet-US Derm—2021 Actual).

644. Defendants’ economics expert, Dr. Ferri, [REDACTED] Tr. 789:3-11.

645. As Dr. Sheridan explained, these are significant sales in the relevant market for three reasons.

646. First, Duobrii® has been on the market for less than three years, while industry study has shown that most pharmaceutical products do not achieve peak sales within the first five years, sometimes taking as long as 12 years to reach peak sales. Tr. 735:4-15; Tr. 742:17-23.

647. Second, the psoriasis market is very competitive. In particular, it is crowded and heavily genericized, with 95% of topical treatments being generic. Thus, the achievement of sales in this marketplace indicates that the product has distinguished itself. Tr. 735:4-23.

648. Third, Duobrii® launched less than a year before the global Covid-19 pandemic, which impacted dermatology practice as well as dermatology sales overall. However, the pandemic particularly impacted recently launched dermatology products. Tr. 735:4-736:7. [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] Tr. 737:1-21; PTX-073 (Bausch Health Q3 2020 In Review) at BAU00562904.

649. While Dr. Ferri disagreed that Duobrii® was disproportionately affected by the Covid-19 pandemic, his basis for this opinion was an article about the global psoriasis market. He did not identify in his testimony any evidence about the psoriasis market in the United States to reach his conclusions about the impact of the

pandemic about Duobrii®'s launch in the United States. Tr. 784:5-21. Dr. Ferri also agreed that independent third-party analyses from 2020 identified that Duobrii® was disproportionately impacted by Covid-19. Tr. 784:22-786:18; PTX-075 (Schmidt).

650. Dr. Ferri, stated that there is no specific threshold of sales required for a product to be commercially successful. Tr. 778:12-779:2. He also testified that a product need not even be profitable to be commercially successful. Tr. 779:15-25.

ii. [REDACTED]
[REDACTED]

651. In addition to sales data, Dr. Sheridan also explained that Duobrii® has established market share in its short time on the market. In evaluating Duobrii®'s market share, Dr. Sheridan considered Duobrii®'s performance [REDACTED]
[REDACTED]

652. Dr. Sheridan explained that he considered this market [REDACTED]
[REDACTED]

[REDACTED] Tr. 738:10-23. Defendants' economics expert, Dr. Ferri, agreed that Bausch has more direct experience with evaluating Duobrii®, including the markets Bausch engages in to market Duobrii®, than anyone else. Tr. 780:19-781:3.

653. [REDACTED]
[REDACTED]

[REDACTED]

[REDACTED]

654. [REDACTED]

[REDACTED]

[REDACTED]

655. [REDACTED]

[REDACTED]

[REDACTED]

656. In evaluating Duobrii®'s market share, Dr. Sheridan also considered Duobrii®'s performance against Enstilar®, Taclonex®, and a third product—an oral medication called Otezla® (the “Branded Combinations + Otezla” market). [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] Tr. 740:4-8; Tr. 751:13-16.

657. [REDACTED]

[REDACTED]

[REDACTED]

658. [REDACTED]

[REDACTED]

[REDACTED]

659. Defendants' economics expert, Dr. Ferri, stated that there is no specific threshold of market share required for a product to be commercially successful. Tr. 779:3-5. He also testified that even a product with the lowest market share in a market could be a commercially successful product. Tr. 779:6-11.

iii. Pricing And Marketing Do Not Drive Sales Of Duobrii®

660. Pricing and marketing do not drive sales of Duobrii®, as Dr. Sheridan explained. In particular, [REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED] Tr. 741:23-742:23.

iv. Duobrii® Is A Commercially Successful Product

661. As Dr. Sheridan testified, in light of its significant sales and profits, market share, and the fact that its performance in the marketplace is not driven by pricing and marketing, Duobrii® is a commercially successful product. Tr. 733:9-13.

662. The Court agrees with Dr. Sheridan that the evidence shows that Duobrii is a commercially successful product.

n. The Phase II Clinical Study of Duobrii® Was Performed for the Purpose of Experimentation

663. The pivotal Phase II Study of IDP-118 is described in the specification of the Duobrii Patents. JTX-002 ('895 Patent) at 10:44-12:37; Tr. 95:18-96:11. The Phase II Study is also referred to as the "V01-118A-201" Study, or simply the "201 Study." Tr. 95:10-18; JTX-012-9 (Study V01-118A-201 Clinical Study Report) at BAU00249125.

664. The 201 Study measured the safety and efficacy of IDP-118 against halobetasol propionate by itself in the same vehicle, tazarotene propionate by itself in the same vehicle, and the vehicle itself (with no active ingredient). Tr. 95:23-96:11.

665. The 201 Study took place between February and October of 2014. JTX-012-9 (Study V01-118A-201 Clinical Study Report) at BAU00249125.

666. Two hundred and twelve patients participated in the 201 Study. JTX-002 ('895 Patent) at 11:35-41; JTX-012-9 (Study V01-118A-201 Clinical Study Report) at BAU00249178.

667. The results of the 201 Study, as set out in the Duobrii Patents, provide the basis in the Duobrii Patents for concluding that IDP-118 is capable of providing a synergistic efficacy and a synergistic reduction in at least one adverse event. JTX-002 ('895 Patent) at Tables 7-9, 13.

668. Bausch was required by the FDA to conduct the 201 Study as part of the development of IDP-118. Tr. 98:8-11.

669. The 201 Study was a standard way of evaluating the efficacy and safety of IDP-118 in humans. As Bausch explained in its regulatory documents, “[t]he design of this study is a standard design for evaluating the safety and efficacy following topical administration of a combination product for the treatment of moderate to severe plaque psoriasis. The efficacy and safety parameters are consistent with what is generally expected for a psoriasis product containing a corticosteroid and retinoid component.” JTX-012-9 (Study V01-118A-201 Clinical Study Report) at BAU00249141.

670. IDP-118 was not sold during the 201 Study. Tr. 98:20-21.

671. Duobrii® was not sold commercially until 2019. Tr. 749:4-7. Thus, Bausch did not market IDP-118 during the 201 Study, which took place in 2014.

672. The 201 Study lasted 12 weeks, which included eight weeks of treatment with IDP-118, followed by a four-week follow-up period. Twelve weeks is not an unusually long period for a clinical study. Tr. 98:24-99:3.

673. The 201 Study was a “double-blind” study, meaning that patients and investigators/evaluators, as well as all individuals closely associated with the study, did not know what treatment was being administered. JTX-012-9 (Study V01-118A-201 Clinical Study Report) at BAU00249148.

674. Bausch controlled the conduct of the 201 Study, and employed and directed third party contract research organizations (CROs) in connection with the study. These CROs included a biostatistics group, database management group, medical monitors, dermatologist investigators, and others. Tr. 99:4-13.

675. The CROs who participated in the 201 Study all submitted to a confidentiality agreement. Tr. 99:4-13.

676. Testing was performed according to pre-specified protocols under the supervision of investigators trained on the methods and protocols for evaluation. JTX-012-9 (Study V01-118A-201 Clinical Study Report) at BAU00249151; BAU00249169.

677. Detailed records were maintained during the 201 Study. Tr. 99:14-16. For example, the 201 Study was performed according to a protocol, which required systematic patient assessment and data collection at predetermined and regular time

periods. The data was collected in a central database. Tr. 99:17-100:7; JTX-012-9 (Study V01-118A-201 Clinical Study Report) at BAU00249140-143.

678. Bausch's clinical operations team monitored the conduct of the 201 Study. Tr. 100:8-11.

o. The Posting Of IDP-118 Was A Mandatory Requirement Associated With The Phase II Clinical Trial

679. The FDA required information about the 201 Study to be posted on a public website, Clinicaltrials.Gov, prior to the start of the 201 Study. Tr. 100:12-16.

680. The 201 Study is associated with the identifier "NCT 02045277" on Clinicaltrials.Gov. Tr. 460:11-19.

681. The information that Bausch posted on Clinicaltrials.Gov in January 2014 included the concentrations of halobetasol propionate and of tazarotene. Tr. 445:11-21; DX-064 (IDP-118 Study) at HALOBET0019360.

682. In videotaped deposition testimony, Dr. Binu Alexander explained that subsequent versions of the posting about the 201 Study on Clinicaltrials.Gov removed the information containing the concentrations of the active ingredients. Tr. 452:5-15. As Dr. Alexander explained, the information about the concentrations was not required for disclosure, so it was removed so as not to remain "public front-facing information." Tr. 452:21-453:3. Tr. 453:13-21.

683. Dr. Alexander also explained that information is never removed from Clinicaltrials.Gov, so the information from the prior posting (specifically, the

information about the concentration of the active ingredients) remains available in the website's audit history. Tr. 443:20-444:1; Tr. 452:5-20.

II. CONCLUSIONS OF LAW

684. To the extent that the findings of fact contain issues and conclusions of law, such findings of fact shall be considered as issues and conclusions of law.

A. General Legal Principles

1. Legal Standards for Declaratory Judgment

685. A declaratory judgment action that arises from a patent law action for infringement is “properly characterized as an action arising under an Act of Congress relating to patents.” *Medtronic, Inc. v. Mirowski Fam. Ventures, LLC*, 571 U.S. 191, 197 (2014) (internal quotations omitted).

686. “The operation of the Declaratory Judgment Act” is “only procedural” and leaves “substantive rights unchanged.” *Id.* at 199 (internal citations and quotations omitted).

687. The burden of proving patent infringement in a declaratory judgment action rests on the patent holder. *See id.* at 199-201.

2. Infringement

a. Infringement Under 35 U.S.C. § 271(a)

688. Under 35 U.S.C. § 271(a), “whoever without authority makes, uses, offers to sell, or sells any patented invention, within the United States or imports into the United States any patented invention during the term of the patent therefor, infringes the patent.”

689. “Literal infringement occurs when each element of at least one claim of the patent is found in the alleged infringer’s product.” *ALZA Corp. v. Andrx Pharms., LLC*, 607 F. Supp. 2d 614, 623 (Fed. Cir. 2006); *see also DeMarini Sports, Inc. v. Worth, Inc.*, 239 F.3d 1314, 1331 (Fed. Cir. 2001).

690. For patent infringement under 35 U.S.C. § 271(a), “[t]he patentee bears the burden of proving infringement by a preponderance of the evidence.” *SRI Int’l v. Matsushita Elec. Corp.*, 775 F.2d 1107, 1123 (Fed. Cir. 1985).

b. Infringement Under 35 U.S.C. § 271(b)

691. A party may be liable for inducing infringement even though it does not directly infringe a method patent. 35 U.S.C. § 271(b).

692. A party that makes, uses, sells, offers to sell within, or imports into the United States a product (and/or by a process) that does not literally meet all of the elements of a claim and thus does not literally infringe that claim, can still directly infringe if that product (and/or that process) satisfies the claim elements “under the doctrine of equivalents.” 35 U.S.C. § 271(b) provides that “[w]hoever actively induces infringement of a patent may still be liable as an infringer.”

693. Direct infringement is a necessary predicate for a finding of induced infringement in ordinary patent infringement cases. *Limelight Networks, Inc. v. Akamai Techs., Inc.*, 134 S. Ct. 2111, 2117 (2014).

694. Inducement liability requires that “the defendant possessed specific intent to encourage another’s infringement and not merely that the defendant had knowledge of the acts alleged to constitute infringement.” *DSU Med. Corp. v. JMS Co.*, 471 F.3d 1293, 1306 (Fed. Cir. 2006).

695. Circumstantial evidence can support a finding of specific intent to induce infringement. *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010) (citing *Water Techs. Corp. v. Calco, Ltd.*, 850 F.2d 660, 668 (Fed. Cir. 1988)).

696. “Inducement can be found where there is ‘[e]vidence of active steps taken to encourage direct infringement,’ which can in turn be found in ‘advertising an infringing use or instructing how to engage in an infringing use.’” *Takeda Pharm. U.S.A., Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625, 630–31 (Fed. Cir. 2015) (alteration in original) (quoting *Metro-Goldwyn-Mayer Studios Inc. v. Grokster, Ltd.*, 545 U.S. 913, 936 (2005)).

697. When proof of specific intent depends on the label accompanying the marketing of a drug inducing infringement by physicians and patients taking the drug, “[t]he label must encourage, recommend, or promote infringement.” *Takeda*, 785 F.3d at 631.

698. The contents of the label itself may permit the inference of specific intent to encourage, recommend, or promote infringement. *Vanda Pharms. Inc. v. W.-Ward*

Pharms. Int'l Ltd., 887 F.3d 1117, 1129 (Fed. Cir. 2018) (citing *Sanofi v. Watson Labs. Inc.*, 875 F.3d 636, 646 (Fed. Cir. 2017)).

699. Induced infringement can be proven where the instructions in a proposed label would inevitably lead at least some consumers (e.g., patients and/or their instructing physicians) to practice a claimed method of a patent. *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010).

700. A patentee in a Hatch-Waxman litigation asserting method patents does not have to prove that prior use of the ANDA-approved drug satisfies the limitations of the asserted claims. *See, e.g., Sanofi*, 875 F.3d at 643 (affirming inducement finding where the district court found that “the inducing act will be the marketing by [ANDA applicants] of their generic dronedarone drugs with the label described” and “the induced act will be the administration of dronedarone by medical providers to patients meeting the criteria set forth in the [claims at issue]”); *Eli Lilly & Co. v. Teva Parenteral Meds., Inc.*, 845 F.3d 1357, 1368 (Fed. Cir. 2017) (“not requir[ing] evidence regarding the general prevalence of the induced activity”); *AstraZeneca*, 633 F.3d at 1057 (affirming district court’s grant of a preliminary injunction based on claims of induced infringement where the district court found that “the proposed label would cause some users to infringe the asserted method claims”); *see also Warner-Lambert*, 316 F.3d at 1364 (“The infringement case is therefore limited to

an analysis of whether what the generic drug maker is requesting authorization for in the ANDA would be an act of infringement if performed.”).

701. Accordingly, Plaintiff “can satisfy its burden to prove the predicate direct infringement by showing that if the proposed ANDA product were marketed, it would infringe the [asserted patents].” *Vanda*, 887 F.3d at 1130; *see, e.g., Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1401, 1408 (Fed. Cir. 2014) (“The infringement determination is thus based on consideration of all relevant evidence, and because drug manufacturers are bound by strict statutory provisions to sell only those products that comport with the ANDA’s description of the drug, the ANDA itself dominates the analysis.” (alterations and internal quotation marks omitted)); *AstraZeneca*, 633 F.3d at 1060 (explaining that the district court “correctly determined” that language in the ANDA label “would inevitably lead some consumers to practice the claimed method”).

702. Even if the proposed generic ANDA product has “substantial noninfringing uses,” the generic ANDA applicant may still be liable for inducing infringement. *Vanda*, 887 F.3d at 1133 (“Section 271(b), on inducement, does not contain the ‘substantial noninfringing use’ restriction of section 271(c), on contributory infringement.” (quoting *Sanofi*, 875 F.3d at 646)).

703. Thus, “a person can be liable for inducing an infringing use of a product even if the product has substantial noninfringing uses[.]” *Id.* (citing *Grokster*, 545 U.S. at 934–37).

c. Infringement Under 35 U.S.C. § 271(c)

704. Under 35 U.S.C. § 271(c), an accused infringer is liable for contributory infringement if it “offers to sell or sells within the United States or imports into the United States a component of a patented machine, manufacture, combination or composition, or a material or apparatus for use in practicing a patented process, constituting a material part of the invention, knowing the same to be especially made or especially adapted for use for an infringement of such patent, and not a particular staple article or commodity of commerce suitable for substantial noninfringing use.”

705. A patentee can prove contributory infringement by showing “1) that there is direct infringement, 2) that the accused infringer has knowledge of the patent, 3) that the component has no substantial noninfringing uses, and 4) that the component is a material part of the invention.” *Fujitsu Ltd. v. Netgear Inc.*, 620 F.3d 1321, 1325 (Fed. Cir. 2010).

d. Infringement Under 35 U.S.C. § 271(e)

706. A § 271(e)(2)(A) infringement suit differs from typical infringement suits (e.g., a § 271(a) infringement suit) in that infringement inquiries “are hypothetical

because the allegedly infringing product has not yet been marketed.” *Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1365 (Fed. Cir. 2003) (emphasis added); see *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1570 (Fed. Cir. 1997) (“The relevant inquiry is whether the patentee has proven by a preponderance of the evidence that the alleged infringer will likely market an infringing product.”).

707. In a Hatch-Waxman Act suit, the §271(e) infringement inquiry is a hypothetical inquiry because it is conducted and determined prior to any actual marketing, sale, or use of one or more generic proposed drug products based upon an analysis of the proposed generic product and administration instructions that the accused infringer is likely to sell and provide following FDA approval. *Abbott Labs. v. Torpharm, Inc.*, 300 F.3d 1367, 1373 (Fed. Cir. 2002).

708. “A patentee may prove infringement by any method of analysis that is probative of the fact of infringement, and circumstantial evidence may be sufficient[.]” *Martek BioSciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1372 (Fed. Cir. 2009) (citation and internal quotation marks omitted); *Liquidia Dynamics Corp. v. Vaughan Co.*, 449 F.3d 1209, 1219 (Fed. Cir. 2006).

709. To prove infringement under §271(e), the patentee need only show that it is more likely than not that the proposed ANDA product would, if commercially marketed, satisfy the claim limitations of at least one of the claims of the patents-in-

suit. *Adams Respiratory Therapeutics, Inc. v. Perrigo Co.*, 616 F.3d 1283, 1287 (Fed. Cir. 2010); *Abbott Labs.*, 300 F.3d at 1373.

710. In determining whether a proposed ANDA product would more likely than not infringe at least one claim of at least one of the patents-in-suit, a court must consider all relevant evidence, including the ANDA filing itself and other evidence provided by the parties. *Id.*

3. Invalidity

711. The claims of an issued patent are presumed to be valid, and the burden of proving invalidity of each claim rests with the patent challenger. 35 U.S.C. § 282.

712. The presumption that an issued patent claim is valid requires that an invalidity defense or counterclaim be proven by clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship*, 131 S. Ct. 2238, 2242 (2011).

713. Clear and convincing evidence is evidence that gives rise to an “abiding conviction that the truth of [the] factual contentions are ‘highly probable.’” *Colorado v. New Mexico*, 467 U.S. 310, 316 (1984).

714. The presumption of validity and corresponding burden of proof in overcoming that presumption applies to each patent claim independently. *See Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1050 (Fed. Cir. 1988); *Carroll Touch, Inc. v. Electro Mechanical Sys., Inc.*, 15 F.3d 1573, 1581 (Fed. Cir. 1993).

4. Patent Claim Interpretation

715. Patentability is assessed from the perspective of the hypothetical person of ordinary skill in the art (“POSA”). *See, e.g., Life Techs., Inc. v. Clontech Labs., Inc.*, 224 F.3d 1320, 1325 (Fed. Cir. 2000). A person of ordinary skill in the art “may be a composite of different types of individuals.” *AstraZeneca Pharm. LP v. Anchen Pharm., Inc.*, 2012 WL 1065458, at *19-22 (D.N.J. Mar. 29, 2012) (explaining that, even in patents claiming formulations, the hypothetical person of ordinary skill in the art may include persons beyond a formulator, such as a clinician).

716. When interpreting claims, the correct interpretation is to “inquire into how a person of ordinary skill in the art would have understood claim terms at the time of the invention.” *Pfizer, Inc. v. Teva Pharms., USA, Inc.*, 429 F.3d 1364, 1372 (Fed. Cir. 2005). “Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification.” *Id.*

717. The level of ordinary skill in the art is that of a hypothetical person presumed to have known the relevant art at the time of the invention (a person of skill in the art, or “POSA”). Factors that may be considered in evaluating the level of skill in the art are (1) “types of problems encountered in the art,” (2) “prior art solutions to those problems,” (3) rapidity with which innovations are made,” (4) “sophistication

of the technology,” and (5) “educational level of active workers in the field.” *In re GPAC*, 57 F.3d 1573, 1579 (Fed. Cir. 1995).

718. A POSA may rely on other experts. *McCoy v. Heal Sys., LLC*, 850 F. App’x 785, 788 (Fed. Cir. 2021).

5. Obviousness

a. General Principles

719. “The determination of obviousness is a legal conclusion based on underlying facts.” *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1290–91 (Fed. Cir. 2013). A patent claim is invalid for obviousness if “the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains.” 35 U.S.C. § 103.

720. The “underlying factual considerations in an obviousness analysis include the scope and content of the prior art, the differences between the prior art and the claimed invention, the level of ordinary skill in the art, and any relevant secondary considerations[,]” which include “commercial success, long-felt but unresolved needs, failure of others, and unexpected results.” *Allergan*, 726 F.3d at 1290–91 (citations omitted); see *Graham v. John Deere Co.*, 383 U.S. 1, 7–18 (1966); see also

KSR Int'l v. Teleflex Inc., 550 U.S. 398, 415 (2007) (re-affirming the Graham factor analysis as the appropriate test for determining obviousness).

721. Padagis has the burden of proof with respect to all of the factors, including any alleged absence of objective indicia of nonobviousness. *Am. Hosp. Supply Corp. v. Travenol Labs., Inc.*, 745 F.2d 1, 8 (Fed. Cir. 1984).

722. It is imperative to consider how a person of ordinary skill in the art would have viewed the relevant art to ascertain whether the subject matter as a whole “would have been obvious at the time the invention was made”; that is, to avoid the insidious effect of a hindsight syndrome. 35 U.S.C. § 103(a) (2004); *KSR*, 550 U.S. at 41; *Star Scientific, Inc. v. R.J. Reynolds Tobacco Co.*, 655 F.3d 1364, 1375 (Fed. Cir. 2011) (“Importantly, the great challenge of the obviousness judgment is proceeding without any hint of hindsight.”); *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1088 (Fed. Cir. 2008); see *In re Rouffet*, 149 F.3d 1350, 1358 (Fed.Cir.1998); see also *MedPointe Healthcare Inc. v. Hi-Tech Pharmacal Co.*, 2006 WL 3780783, at *4 (D.N.J. Dec. 21, 2006).

723. “The genius of invention is often a combination of known elements which in hindsight seems preordained.” *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351 (Fed. Cir. 2001). For centuries, the Supreme Court has protected such inventions. *Parks v. Booth*, 102 U.S. 96, 102 (1880) (“Modern inventions very often consist merely of a new combination of old elements.”); *KSR Int'l Co. v. Teleflex*

Inc., 550 U.S. 398, 418–19 (2007) (“[I]nventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.”); *accord Pentec, Inc. v. Graphic Controls Corp.*, 776 F.2d 309, 317 (Fed. Cir. 1985) (“[V]irtually every claimed invention is a combination of old elements”).

724. A patent challenger must not “import hindsight into the obviousness determination by using the invention as a roadmap to find its prior art components.” *Princeton Biochemicals, Inc. v. Beckman Coulter, Inc.*, 411 F.3d 1332, 1337 (Fed. Cir. 2005). “The inventor’s own path itself never leads to a conclusion of obviousness; that is hindsight.” *Otsuka Pharm. Co. v. Sandoz, Inc.*, 678 F.3d 1280, 1296 (Fed. Cir. 2012). The patentability of an invention “shall not be negated by the manner in which the invention was made.” 35 U.S.C. § 103; *Honeywell Int’l Inc. v. Mexichem Amanco Holding S.A.*, 865 F.3d 1348, 1356 (Fed. Cir. 2017) (explaining that this provision “was enacted to ensure that routine experimentation does not necessarily preclude patentability”).

725. Where “a defendant urges an obviousness finding by ‘merely throw[ing] metaphorical darts at a board’ in hopes of arriving at a successful result, but ‘the prior art gave ... no direction as to which of many possible choices is likely to be successful,’ courts should reject ‘hindsight claims of obviousness.’” *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d

1063, 1070-071 (Fed. Cir. 2012) (quoting *In re Kubin*, 561 F.3d 1351, 1359 (Fed. Cir. 2009)).

726. “[O]bvious to try’ is not to be equated with obviousness under 35 U.S.C. § 103.” *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 724 (Fed. Cir. 1990) (citing cases). A challenger cannot establish that the POSA would have had a reason to make the claimed invention on the basis that it was “obvious to try” unless (1) there “there are a finite number of identified, predictable solutions” and (2) those predictable solutions “lead[] to the anticipated success.” *KSR*, 550 U.S. at 421. Thus, the challenger must show that “the possible options skilled artisans would have encountered were ‘finite,’ ‘small,’ or ‘easily traversed,’ and that skilled artisans would have had a reason to select the route that produced the claimed invention.” *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d at 1072.

727. Ultimately, Padagis’s obviousness analysis “pick[s] and choos[es] among individual parts of assorted prior art references as a mosaic to recreate a facsimile of the claimed invention.” *Akzo N.V. v. U.S. Int’l Trade Comm’n*, 808 F.2d 1471, 1481 (Fed. Cir. 1986).

b. The Prior Art

i. Content of the Prior Art

728. Obviousness must be assessed on the basis of the prior art as a whole. *In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986); *Sanofi-Aventis Deutschland GmbH v. Glenmark Pharm. Inc.*, 821 F. Supp. 2d 681, 689 (D.N.J. 2011); Failure to consider the prior art as a whole compels rejection of an obviousness contention. *Ortho-McNeil Pharm., Inc. v. Mylan Labs., Inc.*, 520 F.3d 1358, 1364 (Fed. Cir. 2008) (rejecting obviousness challenge on the basis that challenger’s expert “discounted the number and complexity of the alternatives”); *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1383 (Fed. Cir. 1986) (“Focusing on the obviousness of substitutions and differences instead of on an invention as a whole ... was a legally improper way to simplify the difficult determination of obviousness.”).

729. All of the relevant teachings of the prior art must be considered, as it is improper to “pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art.” *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 448 (Fed. Cir. 1986) (quoting *In re Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965)).

730. Even where “all claim limitations are found in a number of prior art references, the burden falls on the challenger of the patent to show by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success in doing so.” *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, 1361 (Fed. Cir. 2007); see also *Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 471 F.3d 1369, 1379–80 (Fed. Cir. 2006) (“[T]o establish a *prima facie* case of obviousness based on a combination of elements in the prior art, the law requires a motivation to select the references and to combine them in the particular claimed manner to reach the claimed invention.”).

ii. Motivation to Select/Combine

731. A showing of obviousness requires proof by clear and convincing evidence that a person of ordinary skill in the art, at the time of the priority date, would have had a reason or motivation to combine references in the prior art to solve the problems in the relevant field by making the claimed invention. *InTouch Techs., Inc. v. VGo Commc’ns, Inc.*, 751 F.3d 1327, 1347 (Fed. Cir. 2014). “Thus, the claimed invention is not obvious if a person of ordinary skill would not select and combine the prior art references to reach the claimed composition or formulation.” *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1361 (Fed. Cir. 2011).

732. “A reason for combining disparate prior art references is a critical component of an obviousness analysis; ‘this analysis should be made explicit.’” *InTouch Techs.*, 751 F.3d at 1351 (quoting *KSR*, 550 U.S. at 418).

733. “[A] patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art.” *KSR*, 550 U.S. at 418; *see In re Kotzab*, 217 F.3d 1365, 1369–70 (Fed. Cir. 2000). “Obviousness requires more than a mere showing that the prior art includes separate references covering each separate limitation in a claim under examination. Rather, obviousness requires the additional showing that a [POSA] would have selected and combined those prior art elements.” *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011).

734. Reason or motivation must be assessed with respect to the actual goals and motivations in the field. *Institut Pasteur & Universite Pierre Et Marie Curie v. Focarino*, 738 F.3d 1337, 1345–46 (Fed. Cir. 2013).

735. Mere compatibility of teachings is insufficient to demonstrate a motivation to combine. *See DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1326 (Fed. Cir. 2009) (obviousness requires not only an “expectation that prior art elements are capable of being physically combined, but also that the combination would have worked for its intended purpose.”).

736. “[K]nowledge of a problem and motivation to solve it are entirely different from motivation to combine particular references to reach the particular claimed method.” *Innogenetics, N.V. v. Abbott Labs.*, 512 F.3d 1363, 1373–74 (Fed. Cir. 2008); *see also Cardiac Pacemakers, Inc. v. St. Jude Med., Inc.*, 381 F.3d 1371, 1377 (Fed. Cir. 2004) (“Recognition of a need does not render obvious the achievement that meets that need . . . Recognition of an unsolved problem does not render the solution obvious.”); *Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1353–54 (Fed. Cir. 2013) (holding that because the prior art did not disclose the discovered problem, there was no motivation to combine prior art references to solve the problem”); *Novartis Pharm. Corp. v. Watson Labs., Inc.*, 611 F. App’x 988, 995 (Fed. Cir. 2015) (“Even an obvious solution, however, does not render an invention obvious if the problem solved was previously unknown.”); *id.* at 996 (“Although the addition of an antioxidant would have been an obvious solution for a formulation with known oxidation problems, here Watson failed to prove that a rivastigmine formulation was known to be susceptible to oxidative degradation.”).

737. A POSA would not be motivated to implement a modification designed to address one problem if it would likely create an equal or greater problem in another area. *See Institut Pasteur*, 738 F.3d at 1346 (allegedly obvious changes would be avoided because of prior art teaching that such changes would lead to toxicity); *Janssen Pharmaceutica N.V. v. Mylan Pharm., Inc.*, 456 F. Supp. 2d 644, 666–67

(D.N.J. 2006) (finding the POSA would have avoided modifying chemical structure because such modifications are risky and uncertain and other safer, and more conventional, routes to obtaining the desired result existed).

738. “Evidence suggesting reasons to combine cannot be viewed in a vacuum apart from evidence suggesting reasons not to combine.” *Arctic Cat Inc. v. Bombardier Recreational Prods. Inc.*, 876 F.3d 1350, 1363 (Fed. Cir. 2017).

739. It is “important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [claimed] elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.” *KSR*, 550 U.S. at 418–19.

iii. Teaching Away

740. “[A] reference ‘must [be] considered for all it taught, disclosures that diverged and taught away from the invention at hand as well as disclosures that pointed towards and taught the invention at hand.’” *Polaris Indus., Inc. v. Arctic Cat, Inc.*, 882 F.3d 1056, 1069 (Fed. Cir. 2018) (quoting *Ashland Oil, Inc. v. Delta Resins & Refractories, Inc.*, 776 F.2d 281, 296 (Fed. Cir. 1985)).

741. In particular, “statements regarding preferences are relevant to a finding regarding whether a skilled artisan would be motivated to combine that reference with another reference.” *Polaris Indus.*, 882 F.3d at 1069.

742. A reference teaches away from the invention “when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant . . . [or] if it suggests that the line of development flowing from the reference’s disclosure is unlikely to be productive of the result sought by the applicant.” *Tec Air, Inc. v. Denso Mfg. Michigan, Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999) (internal quotation marks omitted); *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1327 (Fed. Cir. 2009); *Unigene Labs., Inc. v. Apotex Inc.*, 655 F.3d 1352, 1361 (Fed. Cir. 2011); *Crocs, Inc. v. Int’l Trade Comm’n*, 598 F.3d 1294, 1308–09 (Fed. Cir. 2010) (explaining that criticisms of patent challenger’s proposed modification taught away from claimed invention.”).

743. The reference need not address an aspect of the invention recited specifically in the claim to teach away. *Institut Pasteur & Universite Pierre Et Marie Curie v. Focarino*, 738 F.3d 1337, 1345–46 (Fed. Cir. 2013) (prior art suggestion that reference would cause toxicity to cells precluded obviousness irrespective of whether claims recited lack of toxicity).

744. If the prior art “teaches away” from the invention rather than motivating the POSA to do what the patentee has done, the invention is nonobvious. *DePuy*, 567 F.3d at 1326. “An inference of nonobviousness is especially strong where the prior art’s teachings undermine the very reason being proffered as to why a person of ordinary skill would have combined the known elements.” *Id.*

745. Prior art references cannot be combined if one of the references teaches away from its combination with another. *See Tec Air, Inc.*, 192 F.3d at 1360 (“There is no suggestion to combine [references] . . . if a reference teaches away from its combination with another source”). A prior art reference that teaches away “alone can defeat [an] obviousness claim.” *Winner Int’l Royalty Corp. v. Wang*, 202 F.3d 1340, 1349–50 (Fed. Cir. 2000).

746. Prior art teachings that do not rise to the level of “teaching away,” including preferences, also can demonstrate the absence of a motivation to combine references or otherwise pursue a particular path. *See Polaris Indus.*, 882 F.3d at 1069; *Apple Inc. v. Samsung Elecs. Co.*, 839 F.3d 1034, 1052 n.15 (Fed. Cir. 2016) (en banc) (“[E]ven if [the reference] does not teach away, its statements regarding users preferring other forms of switches are relevant to a finding regarding whether a skilled artisan would be motivated to combine [the references].”). And whether or not a reference teaches away, the burden remains on the challenger to identify a motivation to combine that reference with other references. *See Rembrandt Wireless Techs., LP v. Samsung*

Elecs. Co., 853 F.3d 1370, 1379–80 (Fed. Cir. 2017) (“[T]he absence of a formal teaching away in one reference does not automatically establish a motivation to combine it with another reference in the same field.”).

iv. Reasonable Expectation of Success

747. As the Federal Circuit has explained post-*KSR*, retracing the path of the inventor with hindsight, and discounting the number and complexity of the alternatives, is always inappropriate for an obviousness test based on the language of 35 U.S.C. § 103 that requires the analysis to examine “the subject matter as a whole” to ascertain if it “would have been obvious at the time the invention was made.” *Ortho-McNeil*, 520 F.3d at 1363–64. The Federal Circuit explained that “at the time of invention, the inventor’s insights, willingness to confront and overcome obstacles, and yes, even serendipity, cannot be discounted.” *Id.*

748. A solution is not obvious because it was obvious to conduct experiments to try to solve a problem. *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988) (“[S]elective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings.”). “[E]ven if it was obvious to experiment with [certain] options,” an invention is not obvious when “there is nothing to indicate that a skilled artisan would have had a reasonable expectation that such an experiment would succeed.” *Leo Pharm.*, 726 F.3d at 1357 (quoted in *Janssen Pharms., Inc. v. Teva Pharms. USA, Inc.*, 571 F. Supp. 3d 281, 310 (D.N.J. 2021)).

749. “[T]o have a reasonable expectation of success, one must be motivated to do more than merely to ... try each of numerous possible choices until one possibly arrived at a successful result.” *In re Stepan Co.*, 868 F.3d 1342, 1347 (Fed. Cir. 2017).

750. “Evidence showing unpredictability in the art” suggests “that one of ordinary skill would not have been motivated to combine the references with a reasonable expectation of success.” *Honeywell Int’l Inc. v. Mexichem Amanco Holding S.A. DE C.V.*, 865 F.3d 1348, 1354 (Fed. Cir. 2017) (quoted in *Janssen Pharms., Inc. v. Teva Pharms. USA, Inc.*, 571 F. Supp. 3d 281, 310 (D.N.J. 2021)).

751. In an unpredictable field like drug development, a lack of relevant data in the prior art can weigh heavily in favor of nonobviousness. *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1384–85 (Fed. Cir. 2019) (“These references provide no more than hope—and hope that a potentially promising drug will treat a particular [disease] is not enough to create a reasonable expectation of success in a highly unpredictable art such as this.”).

752. “[T]o the extent an art is unpredictable, as the chemical arts often are, *KSR*’s focus on . . . ‘identified, predictable solutions’ may present a difficult hurdle [for a patent challenger] because potential solutions are less likely to be genuinely predictable.” *Eisai Co. v. Dr. Reddy’s Labs., Ltd.*, 533 F.3d 1353, 1359 (Fed. Cir. 2008); *Sanofi-Synthelabo v. Apotex, Inc.*, 550 F.3d 1075, 1090 (Fed. Cir. 2008). This

holds true even where the technique used in the claimed invention is known in the art, but the experimental process and its results are complex or unpredictable and there is no reasonable expectation of success. *See, e.g., Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 136, 1378–80 (Fed. Cir. 2006). As part of the obviousness analysis, the burden is on the challenging party to establish that a person of ordinary skill in the art would have a reasonable expectation of success. *Yamanouchi*, 231 F.3d at 1345.

c. Inherent Obviousness

753. “The use of inherency in the context of obviousness must be carefully circumscribed because that which may be inherent is not necessarily known[,] and that which is unknown cannot be obvious.” *Honeywell*, 865 F.3d at 1354.

754. Even if an unknown property is inherent, it can nonetheless be critically important to whether an invention is obvious. “What is important regarding properties that may be inherent, but unknown, is whether they are unexpected. All properties of a composition are inherent in that composition, but unexpected properties may cause what may appear to be an obvious composition to be nonobvious.” *Id.* at 1354–55 (reversing Board for failing to consider unpredictability and unexpectedness of purportedly inherent properties). For that reason, the Court has rejected that “unexpected results do not support nonobviousness [where] they are merely the inherent properties of an otherwise obvious formulation” because

“previously *unknown* and *unexpected* properties of a new and nonobvious formulation constitute additional, objective evidence of nonobviousness.” *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1307 (Fed. Cir. 2015).

d. Definition Of Prior Art/ Experimental Use

i. What Constitutes Prior Art

755. 35 U.S.C. § 102 (pre-AIA) provides that: “A person shall be entitled to a patent unless (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent, or (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States[.]”

756. 35 USC § 102(a) (post-AIA) provides that: “A person shall be entitled to a patent unless— (1) the claimed invention was patented, described in a printed publication, or in public use, on sale, or otherwise available to the public before the effective filing date of the claimed invention; or (2) the claimed invention was described in a patent issued under section 151, or in an application for patent published or deemed published under section 122(b), in which the patent or application, as the case may be, names another inventor and was effectively filed before the effective filing date of the claimed invention.”

757. An invention is “‘on sale’” under section 102(a) when it is “‘the subject of a commercial offer for sale’ and ‘ready for patenting.’” *Helsinn Healthcare S.A. v. Teva Pharm. USA, Inc.*, 139 S. Ct. 628, 630 (2019) (quoting *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 67 (1998)). “[A] commercial sale is one that bears the general hallmarks of a sale pursuant to Section 2-106 of the Uniform Commercial Code.” *Medicines Co. v. Hospira, Inc.*, 827 F.3d 1363, 1365 (Fed. Cir. 2016) (en banc). “[T]he mere sale of manufacturing services by a contract manufacturer . . . does not constitute a ‘commercial sale’” *Id.* at 1373. “A section 102(b) bar is avoided if the primary purpose of the sale was experimental.” *U.S. Envt’l Prods. Inc. v. Westall*, 911 F.2d 713, 716 (Fed. Cir. 1990); *Manville Sales Corp. v. Paramount Sys., Inc.*, 917 F.2d 544, 550 (Fed. Cir. 1990) (“Prior to its testing . . . , there really was no basis for confidence by the inventor that the invention would perform as intended, and hence no proven invention to disclose.”).

758. The party challenging the validity of a patent bears the burden “by clear and convincing evidence on all issues relating to the status of [a publication] as prior art.” *Mahurkar v. C.R. Bard, Inc.*, 79 F.3d 1572, 1576 (Fed. Cir. 1996); *Plexxikon Inc. v. Novartis Pharms. Corp.*, 525 F. Supp. 3d 1104, 1112 (N.D. Cal. Mar. 15, 2021) (“A party challenging patent validity has the burden to prove by clear and convincing evidence that an invalidating reference is prior art.”). The party asserting invalidity bears “the burden of establishing, by clear and convincing evidence, facts

which support the ultimate legal conclusion of invalidity under § 102(g).” *Checkpoint Sys., Inc. v. U.S. Int’l Trade Comm’n*, 54 F.3d 756, 761 (Fed. Cir. 1995).

759. In order to qualify as prior art under § 102(a), a reference must be “by others.” Without a showing that an alleged prior art publication is “the work of another,” the reference cannot stand as prior art under § 102(a). See, e.g., *In re Katz*, 687 F.2d 450, 454 (C.C.P.A. 1982). “Authorship of an article by itself does not raise a presumption of inventorship with respect to the subject matter disclosed in the article.” *Id.* at 455. “What is significant is not merely the differences in the listed inventors, but whether the portions of the reference relied on as prior art... represent the work of a common inventive entity.” *Riverwood Int’l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1356 (Fed. Cir. 2003); *Trebro Mfg. Inc. v. Firefly Equipment LLC*, 748 F.3d 1159, 1169 (Fed. Cir. 2014) (“the same inventive entity . . . cannot qualify as prior art under (previous) 35 U.S.C. § 102(a)”). A common inventive entity may exist even where a co-inventor is not listed as an author on the purported prior art reference. See, e.g., *Trans Ova Genetics, LC v. XY, LLC*, IPR2018-00250, Paper 35, at 7-8, n. 8 (PTAB June 26, 2019), *aff’d*, 819 F. App’x 937 (Fed. Cir. 2020).

760. “[O]ne’s own work is not prior art under § 102(a)” unless “the disclosure occurred more than one year prior to the date of the application.” *In re Katz*, 687 F.2d 450, 454 (C.C.P.A. 1982).

761. When the prior art was considered by the examiner, the challenger bears the additional burden of establishing that PTO was “wrong in its decision to grant the patent.” *PowerOasis, Inc. v. T-Mobile USA, Inc.* 522 F.3d 1299, 1304 (Fed. Cir. 2008) (citing *Am. Hoist & Derrick Co. v. Sowa & Sons*, 725 F.2d 1350, 1360 (Fed. Cir. 1984). “Where, as here, ‘the examiner considered the asserted prior art and basis for the validity challenge during patent prosecution, [the clear and convincing evidence] burden becomes particularly heavy.’” *Mitsubishi Tanabe Pharma Corp. v. Sandoz, Inc.*, 533 F. Supp. 3d 170, 190 (D.N.J. 2021) (quoting *Impax Labs., Inc. v. Aventis Pharms., Inc.*, 545 F.3d 1312, 1314 (Fed. Cir. 2008)).

762. “[A] reference that lacks [an] enabling disclosure is not anticipating, but [the reference] ‘itself may qualify as a prior art reference under § 103, but only for what is disclosed in it.’” *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569, 1578 (1991) (quoting *Reading & Bates Constr. Co. v. Baker Energy Resources Corp.*, 748 F.2d 645, 652 (Fed. Cir. 1984)).

ii. Experimental Use

763. “[A]n inventor who seeks to perfect his discovery may conduct extensive testing without losing his right to obtain a patent for his invention – even if such testing occurs in the public eye.” *Pfaff v. Wells Elecs.*, 525 U.S. 55, 64 (1998). *EZ Dock v. Schafer Sys., Inc.*, 276 F.3d 1347, 1353 (Fed. Cir. 2002) (Linn, J concurring (“The experimental use doctrine permits an inventor to conduct testing to refine his

invention without losing the right to obtain a patent, even if such testing occurs in the public eye.”)).

764. The experimental use doctrine is an exception to the public use bar under pre-AIA § 102(b), *EZ Dock*, 276 F.3d at 1353. Whether a public use qualifies as an experimental use is a question of law and is determined by totality of the circumstances. *See, e.g., Petrolite Corp. v. Baker Hughes Inc.*, 96 F.3d 1423, 1426 (Fed. Cir. 1996). If public use is established by clear and convincing evidence, the burden shifts to the inventor to prove “with convincing evidence that the public use activities fall within the experimental use exception.” *In re Smith*, 714 F.2d 1127, 1135 (Fed. Cir. 1983). “[T]he inquiry is not: (1) was there a public use, and, if so, (2) was the public use for a bona fide experimental purpose and thus excused. Rather, there is only one inquiry—was there a public use within the meaning of section 102(b).” *Tone Bros. v. Sysco Corp.*, 28 F.3d 1192, 1198 (Fed. Cir. 1994).

765. An invention is in “public use” under § 102(a) ““where, before the critical date, the invention is in public use and ready for patenting.”” *Polara Eng’g Inc. v. Campbell Co.*, 894 F.3d 1339, 1348 (Fed. Cir. 2018) (quoting *Invitrogen Corp. v. Biocrest Mfg., L.P.*, 424 F.3d 1374, 1379 (Fed. Cir. 2005)). “The proper test for the public use prong . . . is whether the purported use: (1) was accessible to the public; or (2) was commercially exploited.” *Invitrogen*, 424 F.3d at 1380. “However, ‘an inventor who seeks to perfect his discovery may conduct extensive testing without

losing his right to obtain a patent for his invention— even if such testing occurs in the public eye.” *Polara Eng’g*, 894 F.3d at 1348 (quoting *Pfaff*, 525 U.S. at 64). “A use may be experimental if its purpose is: ‘(1) [to] test claimed features of the invention or (2) to determine whether an invention will work for its intended purpose—itself a requirement of patentability.’” *Id.* (quoting *Clock Spring, L.P. v. Wrapmaster, Inc.*, 560 F.3d 1317, 1327 (Fed. Cir. 2009)) (alteration in original). “[E]vidence of experimental use may negate either the ‘ready for patenting’ or ‘public use’ prong.” *Invitrogen*, 424 F.3d at 1380–81.

766. A public use may occur when “a completed invention is used in public, without restriction.” *Allied Colloids Inc. v. Am. Cyanamid Co.*, 64 F.3d 1570, 1574 (Fed. Cir. 1995); see *W.L. Gore & Assocs., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1549 (Fed. Cir. 1983) (“The nonsecret use of a claimed process in the usual course of producing articles for commercial purposes is a public use.”). “[A] disclosure of some aspects of an invention, but not all, will likely preclude a finding of public use.” *Pronovo Biopharma Norge AS v. Teva Pharm. USA, Inc.*, 549 F. App’x 934, 939 (Fed. Cir. 2013); see *W.L. Gore*, 721 F.2d at 1549 (reversing district court because “looking at the machine in operation does not reveal whether it is stretching, and, if so, at what speed. Nor . . . whether the crystallinity and temperature elements of the invention set forth in the claims are involved”).

767. The experimental use doctrine negates the public use bar under post-AIA § 102, as it did under pre-AIA law. *See Dzinesquare, Inc. v. Armano Luxury Alloys, Inc.*, 2014 WL 12597154, at *4 n.5 (C.D. Cal. 2014) (citing *Pfaff v. Wells Electronics, Inc.*, 525 U.S. 55, 67–68 (1998)) (finding that the on-sale bar, public use, and printed publication bars should be interpreted the same under post-AIA § 102 as it was under pre-AIA § 102).

768. In general, “[a] use may be experimental if its purpose is ‘(1) [to] test claimed features of the invention or (2) to determine whether an invention will work for its intended purpose....’” *Barry v. Medtronic, Inc.*, 914 F.3d 1310, 1328 (Fed. Cir. 2019), *cert. denied*, 140 S. Ct. 869 (2020) (citation omitted).

769. “The experimental-use inquiry asks whether the inventor’s conduct would lead the ‘public’ to reasonably believe the invention was in the public domain, and in particular whether there has been any use of that invention by a person *other than the inventor* who is under no limitation, restriction or obligation of secrecy to the inventor.” *Id.* at 1330 (internal citations omitted) (emphasis added); *see also In re Hamilton*, 882 F.2d 1576, 1581 (Fed. Cir. 1989) (“The experimental use doctrine operates in the inventor's favor to allow *the inventor* to refine his invention or to assess its value relative to the time and expense of prosecuting a patent application. If it is not the inventor or someone under his control or ‘surveillance’ who does these

things, there appears to us no reason why he should be entitled to rely upon them to avoid the statute.”) (emphasis in original).

770. Under the experimental use doctrine, “[p]roof of experimental use serves as ‘a negation of the statutory bars’ of § 102(b). *Polara*, 894 F.3d 1339, 1347, quoting *EZ Dock*, 276 F.3d 1347, 1352 (Fed. Cir. 2002). *See also, e.g., Eli Lilly v. Zenith*, 471 F.3d 1369, 1380 (Fed. Cir. 2006) (“The trial court concluded that Lilly’s clinical trials of olanzapine were not a public, but an experimental use that negated any section 102 bar.”) Thus, proof of experimental use means that use of an invention and associated disclosures are not prior art to a patent on that invention. *See, e.g. In re Cecarelli*, 401 Fed. App’x. 553, 554 (Fed. Cir. 2010), (citing *Dippin’ Dots, Inc. v. Mosey*, 476 F.3d 1337, 1344 (Fed. Cir. 2007)) (“Because the sale was for experimental use, the product sold is not prior art. Therefore, this court reverses the Board’s decision affirming the Examiner’s rejection of claims 3, 4, and 16 under 35 USC 103(a) as obvious in light of the product sold and the Ryder patent.”).

771. Courts have considered 13 factors for determining whether a use is experimental, which are set out in *Polara Eng’g*, 894 F.3d 1339, 1348-49 (Fed. Cir. 2018); *see also Clock Spring, L.P. v. Wrapmaster, Inc.*, 560 F.3d 1317, 1327 (Fed. Cir. 2009) (quoting *Allen Eng’g Corp. v. Bartell Indus., Inc.*, 299 F.3d 1336, 1353 (Fed. Cir. 2002)).

772. Experimentation with a non-claimed utility of the claimed invention may constitute experimental use, even not *explicitly* recited in the claims. See *TP Lab 'ys., Inc. v. Pro. Positioners, Inc.*, 724 F.2d 965, 972 (Fed. Cir. 1984); *Manville Sales Corp. v. Paramount Sys., Inc.*, 917 F.2d 544, 551 (Fed. Cir. 1990) (“[w]hen durability in an outdoor environment is inherent to the purpose of an invention, then further testing to determine the invention’s ability to serve that purpose will not subject the invention to a section 102(b) bar.”); *EZ Dock*, 276 F.3d at 1353–54 (finding experimental use when an invention claiming “a floating dock” was tested in choppy water because “floating docks, by their nature, must endure all kinds of water conditions”).

773. “Several indicia may show the negating experimental character of a use, including (1) the length of the test period, (2) any confidentiality agreement, (3) any records of testing, (4) any monitoring and control of the test results, (5) the number of tests, and (6) the length of the test period in relation to tests of similar inventions.” *Eli Lilly & Co.*, 471 F.3d at 1381 (finding no public use because Lilly “tailored its tests to their experimental drug safety and efficacy purpose, adequately monitored for results, and maintained confidentiality throughout the duration of the study. “).

774. The experimental use doctrine does not apply once an invention has been reduced to practice. See *In re Omeprazole Pat. Litig.*, 536 F.3d 1361, 1372 (Fed. Cir. 2008); see also *Allen Eng’g Corp.*, 299 F.3d at 1354. A pharmaceutical composition

undergoing clinical trials to determine whether the invention will work for its intended purpose has not been reduced to practice. The fact that a clinical trial is required may support that a drug has not yet been reduced to practice. *See Sanofi*, 204 F.Supp.3d at 698 (“[t]he fact that dronedarone’s clinical benefit was uncertain before the critical date is further highlighted by the fact that the FDA and EMEA essentially required that Sanofi hold the ATHENA trial to show that dronedarone could provide a clinical benefit to patients with AF and associated risk factors in a safe and effective manner.”); *see also In re Omeprazole Pat. Litig.*, 536 F.3d at 1373–74 (patentee’s clinical trials demonstrated a need to confirm effectiveness and therefore had not been reduced to practice before the clinical studies were completed).

775. This Court and others have held that clinical trials to determine the efficacy of a drug constitute experimental use within the meaning of the experimental use doctrine. *See, e.g., Gilead Sciences v Sigmapharm Labs*, 2014 US Dist. LEXIS 43240 (D.N.J. Mar. 31, 2014) (stating that “Clinical trials conducted to determine the efficacy of a drug candidate have been found to be an example of experimental use negation of the statutory bar.” (Citing *Pharma AG v. Barr Labs., Inc.*, No. 05–cv–2308, 2008 WL 628592 (D.N.J. Mar. 3, 2008)); *Eli Lilly & Co. v. Zenith Goldline Pharms., Inc.*, 471 F.3d 1369, 1380–81 (Fed. Cir. 2006) (finding that the “experimental character” of the clinical trials negated the public use bar); *Sanofi v.*

Glenmark Pharms. Inc., USA, 204 F. Supp. 3d 665, 698 (D. Del. 2016), *aff'd sub nom. Sanofi v. Watson Lab'ys Inc.*, 875 F.3d 636 (Fed. Cir. 2017) (“a clinical trial seeking to test a particular treatment hypothesis seems to be the quintessential experimental use.”); *Gilead Scis., Inc.*, US Dist LEXIS 43240, at *17 (“[c]linical trials conducted to determine the efficacy of a drug candidate have been found to be an example of experimental use negation of the statutory bar.”); *In re Omeprazole Patent Litig.*, 490 F. Supp. 2d 381, 507 (S.D.N.Y. 2007)); *Boston Sci. Corp., v. Cordis Corp.*, 2008 WL 11387141 at *7 (N.D. Cal. 2008) (finding clinical trials were experimental because the purpose “was to establish...that the GDC system was safe and effective when ‘used to occlude aneurysm and arteriovenous malformations,’” and an element of the claimed invention was “occluding a cavity in humans.”).

776. Experimentation undertaken to satisfy a regulatory requirement is not *per se* experimental but can be experimental for the purpose of negating the statutory bar “if it represents a bona fide effort to perfect the invention or to ascertain whether it will answer its intended purpose.” *Pennwalt Corp. v. Akzona, Inc.*, 740 F.2d 1573, 1580 (Fed. Cir. 1984).

iii. Priority Date

777. Claims are entitled to an earlier filing date if the provisional application on which they claimed priority provided adequate written description under 35 U.S.C. § 112. *Trading Techs. Int’l, Inc. v. eSpeed, Inc.*, 595 F.3d 1340, 1359 (Fed. Cir.

2010). “The ‘prior application itself must describe an invention . . . in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention as of the filing date sought.’” *Id.* (citing *Lockwood v. Am. Airlines*, 107 F.3d 1565, 1572 (Fed. Cir. 1997)).

778. Padagis bears the burden of “convinc[ing] the court that [Bausch] is not entitled to the benefit of the earlier filing date.” *See Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1328 (Fed. Cir. 2008).

779. “Determination of the priority date (e.g., the effective filing date) is purely a question of law if the facts underlying that determination are undisputed.” *E.I. du Pont de Nemours & Co. v. MacDermid Printing Sols., LLC*, 525 F.3d 1353, 1359 (Fed. Cir. 2008).

e. Objective Indicia of Nonobviousness

780. Throughout the consideration of objective indicia of nonobviousness, the burden of proving invalidity by clear and convincing evidence always remains on the party challenging the validity of the patent. *In re Cyclobenzaprine Hydrochloride Extended–Release Capsule Patent Litig.*, 676 F.3d 1063, 1075-79 (Fed. Cir. 2012).

781. Objective evidence is often the most probative and cogent evidence of nonobviousness in the record. *Ortho-McNeil*, 520 F.3d at 1365. It “is not just a cumulative or confirmatory part of the obviousness calculus, but constitutes independent evidence of nonobviousness.” *Id.* Objective evidence such as

unexpected results, failure of others, long-felt but unmet need, commercial success, and industry praise must be considered before a conclusion on obviousness is reached. *Id.* (“[T]his evidence is not just a cumulative or confirmatory part of the obviousness calculus but constitutes independent evidence of nonobviousness.”); *Hybritech*, 802 F.2d at 1380 (“Objective evidence . . . is not merely ‘icing on the cake.’”); *In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Litig.*, 676 F.3d 1063, 1075 (Fed. Cir. 2012) (holding that the district court erred by determining that the patents were obvious before considering the objective evidence of nonobviousness).

782. Objective evidence of nonobviousness must be commensurate in scope with the claims, but “absolute identity” is not required. *Genetics Inst., LLC v. Novartis Vaccines & Diagnostics, Inc.*, 655 F.3d 1291, 1308–09 (Fed. Cir. 2011).

783. Objective evidence relating to a single claimed embodiment should be considered even if the claim covers multiple embodiments. *See In re Glatt Air Techs., Inc.*, 630 F.3d 1026, 1030 (Fed. Cir. 2011); *see also Genetics Inst.*, 655 F.3d at 1309 (applying *Glatt* in the context of unexpected results).

i. Nexus

784. “A nexus between commercial success and the claimed features is required.” *Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1130 (Fed. Cir. 2000)

785. A nexus is present where “the marketed product embodies the claimed features, and is coextensive with them.” *Id.*

786. A presumption of nexus exists when the product relied on to show the objective indicia of nonobviousness is coextensive with the claims. *WBIP, LLC v. Kohler Co.*, 829 F.3d 1317, 1329 (Fed. Cir. 2016) (“[T]here is a presumption of nexus for objective considerations when the patentee shows that the asserted objective evidence is tied to a specific product and that product is the invention disclosed and claimed in the patent.” (citations and internal quotation marks omitted)); *see also Brown & Williamson Tobacco Corp. v. Philip Morris Inc.*, 229 F.3d 1120, 1130 (Fed. Cir. 2000) (stating that the patented invention is to be presumed to have a nexus between commercial success and the claimed features “if the marketed product embodies the claimed features, and is coextensive with them.”). It is not necessary that the patented invention be solely responsible for the objective indicia in order for this factor to be given weight. *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1273 (Fed. Cir. 1991).

ii. Unexpected Results

787. The relevant time period for the “unexpected results” inquiry is whether the results would have been unexpected by one of ordinary skill in the art at the time of the patentee’s application and based on knowledge available at that time. *See, e.g., In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997).

788. Evidence that the claimed invention produces results that are unexpected in view of the closest prior art supports a finding of nonobviousness. *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1306–07 (Fed. Cir. 2015).

789. Unexpected results that inherently flow from the claimed invention are evidence of nonobviousness and need not be described or proven in the patent specification. *See Knoll Pharm. Co. v. Teva Pharms. USA, Inc.*, 367 F.3d 1381, 1385 (Fed. Cir. 2004) (holding that later-developed evidence of unexpected results is relevant to nonobviousness).

790. The patent challenger has the burden of proving that none of the properties of the claimed invention were unexpected. *See Am. Hosp. Supply Corp. v. Travenol Labs., Inc.*, 745 F.2d 1, 8 (Fed. Cir. 1984) (“[Patent holder] is under no compulsion either to prove a new and surprising result Rather, the burden was on [challenger] to establish the lack of new and surprising results or the lack of criticality.”).

791. “Unexpected results must be established by factual evidence. Mere argument or conclusory statements in the specification does not suffice.” *In re De Blauwe*, 736 F.2d 699, 705, (Fed. Cir. 1984).

iii. Long-Felt But Unmet Need

792. Evidence of a long-felt but unmet need for the claimed invention supports a finding of nonobviousness. *Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 998 (Fed. Cir. 2009). Whether a long-felt need is unmet must be evaluated

as to the patent filing's date and not as of the date the patented product first enters the market if the date of market entry is later than the filing date. *Id.*

793. Long-felt need is analyzed based on the date when the problem to be solved was identified. It is not based on the date of the “most pertinent” prior-art references. *Texas Instruments Inc. v. U.S. Intern. Trade Com'n*, 988 F.2d 1165, 1178 (Fed. Cir. 1993).

794. There is no absolute requirement the differences between the patented invention and the prior art be significant for a “long-felt” need to be a secondary consideration. *See Apple Inc. v. Samsung Electronics Co., Ltd.*, 839 F.3d 1034, 1056-57 (Fed. Cir. 2016) (*en banc*).

795. A long-felt need is created by a need in technical knowledge. *See Friskit, Inc. v. Real Networks, Inc.*, 2009 WL 59182, *6 (Fed. Cir. 2009).

iv. Teaching Away

796. Teaching away not only negates a motivation to combine as described above; it also constitutes objective indicia of nonobviousness. *See KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 406 (2007).

v. Commercial Success

797. Commercial success of the invention can provide evidence supporting the inference that an invention is not obvious. *See Al-Site Corp. v. VSI Intern., Inc.*, 174 F.3d 1308, 1325–26 (Fed. Cir. 1999).

798. Commercial success can be “shown by significant sales in a relevant market.” *J.T. Eaton & Co. v. Atlantic Paste & Glue Co.*, 106 F.3d 1563, 1571 (Fed.Cir.1997). If a patentee is able to show commercial success, and “the successful product is the invention disclosed and claimed in the patent, it is presumed that the commercial success is due to the invention.” *Id.*

vi. Skepticism

799. General skepticism of those in the art is persuasive evidence of non-obviousness. *See Amstar Corp. v. Envirotech Corp.*, 730 F.2d 1476, 1478–79 n.3 (Fed. Cir. 1984). If industry participants or skilled artisans are skeptical about whether or how a problem could be solved or the workability of the claimed solution, it favors non-obviousness. *WBIP*, 829 F.3d at 1335.

800. “The Federal Circuit has recognized a range of third-party opinion that can constitute skepticism, including testimony that third parties were worried or surprised as sufficient to establish skepticism.” *Janssen*, 571 F. Supp. 3d at 316 (quoting *Neptune Generics, LLC v. Eli Lilly & Co.*, 921 F.3d 1372, 1378 (Fed. Cir. 2019)) (internal quotation marks omitted).

801. Expressions of disbelief or skepticism from the time of the invention by experts in the field, including the independent technical experts hired by each party during the litigation, “constitute strong evidence of nonobviousness.” *Env’t Designs*,

Ltd. v. Union Oil Co. of Cal., 713 F.2d 693, 697–98 (Fed. Cir. 1983) (citing *United States v. Adams*, 383 U.S. 39, 52 (1966)).

802. Skepticism need not be premised on an idea that the claimed invention would be “impossible,” “unworkable,” or “technically infeasible” to be evidence of non-obviousness. *Neptune Generics, LLC v. Eli Lilly & Co.*, 921 F.3d 1372, 1378 (Fed. Cir. 2019). Indeed, a range of opinions by third parties can be probative, including mere “worry” or “surprise.” *Id.* (citing *Circuit Check Inc. v. QXQ Inc.*, 795 F.3d 1331, 1337 (Fed. Cir. 2015)).

803. Proceeding against accepted wisdom is evidence of nonobviousness. *See Arkie Lures, Inc. v. Gene Larew Tackle, Inc.*, 119 F.3d 953, 958 (Fed. Cir. 1997) (citing *In re Hedges*, 783 F.2d 1038, 1041 (Fed. Cir. 1986)).

6. Indefiniteness

804. A determination of claim definiteness is a question of law. *Personalized Media Commc’ns, LLC v. Int’l Trade Comm’n*, 161 F.3d 696, 705 (Fed. Cir. 1998).

805. A party seeking to prove indefiniteness must do so by clear and convincing evidence. *See Microsoft*, 131 S. Ct. at 2242.

806. Indefiniteness of a claim is evaluated from the perspective of a person skilled in the relevant art. *See Nautilus, Inc.*, 134 S. Ct. at 2128. Moreover, the claim is evaluated in light of the patent's specification and prosecution history, and measured as of the time of the patent application. *Id.*

807. Reference to publications or patents in the specification are part of that disclosure, and are included in the inquiry of whether a claim, read in light of the specification and prosecution history, informs “with reasonable certainty” those skilled in the art about the scope of the invention, even if such references are not incorporated by reference. *Atmel Corp.*, 198 F.3d at 1383 (stating that “the district court erred by failing to consider the knowledge of one skilled in the art that indicated, based on unrefuted testimony, that the specification disclosed sufficient structure corresponding to the high-voltage means limitation” by citing, but not describing, a technical article); *see also Eli Lilly & Co. v. Teva Parenteral Medicines Inc.*, 845 F.3d 1357, 1370-72 (Fed. Cir. 2017) (holding the claim term “vitamin B12” as not indefinite when a person of ordinary skill in the art would understand the claim term in the context of the claim language, specification, and prosecution history).

808. A patent claim is not indefinite if “viewed in light of the specification and prosecution history,” the claim “inform[s] those skilled in the art about the scope of the invention with reasonable certainty.” *Nautilus*, 572 U.S. at 910.

809. “[T]he dispositive question in an indefiniteness inquiry is whether the ‘claims,’ not particular claim limitations, ‘... fail to inform, with reasonable certainty, those skilled in the art about the scope of the invention.’” *Cox Commc’ns, Inc. v. Sprint Commc’n Co. LP*, 838 F.3d 1224, 1231 (Fed. Cir. 2016) (quoting *Nautilus*, 572 U.S. at 908).

810. “The claims as granted are accompanied by a presumption of validity based on compliance with, inter alia, § 112 ¶ 2.” *S3 Inc. v. Nvidia Corp.*, 259 F.3d 1364, 1367 (Fed. Cir. 2001).

811. The definiteness requirement is analyzed “not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art.” *Energizer Holdings v. ITC*, 435 F.3d 1366, 1370 (Fed. Cir. 2006). It “ensure[s] that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe.” *All Dental Prodx, LLC v. Advantage Dental Prod., Inc.*, 309 F.3d 774, 779–80 (Fed. Cir. 2002).

812. “Section 112(b), as construed in *Nautilus*, does not demand the perfection or ‘absolute precision’ inherent in defendants’ position.” *Nite Glow Indus., Inc. v. Cent. Garden & Pet Co.*, 2020 WL 2847857, at *12 (D.N.J. June 1, 2020), *aff’d in part, vacated in part, rev’d in part*, 2021 WL 2945556 (Fed. Cir. 2021).

7. Written Description

813. The written description requirement is met if the specification and the existing knowledge in the art reasonably convey “to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date.” *Ariad*

Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1355 (Fed. Cir. 2010). For a patent claim to be held invalid for lack of written description, it must be proven by clear and convincing evidence that the patent fails to provide a POSA a basis “to recognize that the inventor invented what is claimed.” *Id.* at 1351. The test for reasonably conveying possession of an invention is a flexible one, “requir[ing] an objective inquiry into the four corners of the specification from the perspective of a [POSA].” *Id.*

814. A failure to “specifically mention a limitation that later appears in the claims is not a fatal one when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented.” *All Dental Prodx, LLC v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779 (Fed. Cir. 2002).

815. “Written description is a question of fact, judged from the perspective of one of ordinary skill in the art as of the relevant filing date.” *Immunex Corp. v. Sandoz Inc.*, 964 F.3d 1049, 1063 (Fed. Cir. 2020). “The [written description] requirement is applied in the context of the state of knowledge at the time of the invention.” *Zoltek Corp. v. U.S.*, 815 F.3d 1302, 1308 (Fed. Cir. 2016). The specification therefore “need not include information that is already known and available to the experienced public.” *Id.* (quoting *Space Sys./Loral, Inc. v. Lockheed Martin Corp.*, 405 F.3d 985, 987 (Fed. Cir. 2005)).

816. A specification implicitly satisfies the written description requirement if a POSA would find it “reasonably clear what the invention is and that the patent specification conveys that meaning.” *All Dental Prodx.*, 309 F.3d at 779. That is, the “reasonably conveys” standard does not require the disclosure and claims to match exactly. *Ariad Pharms.*, 598 F.3d at 1352 (“[T]he [written] description requirement does not demand any particular form of disclosure or that the specification recite the claimed invention in haec verba”).

817. Nor will a claim be invalidated simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. *See Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575-76 (Fed. Cir. 1985) (holding that specification’s disclosure preferring a lower operating range, yet indicating no upper limit, combined with the industry knowledge at the time, was sufficient for a POSA to discern that higher ranges could be used).

818. A patent applicant need only convey, “with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the ‘written description’ inquiry, whatever is now claimed.” *Vas-Cath v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991).

819. The word “comprising” in a patent claim “suggests that there may be additional, unclaimed elements,” but such additional elements are not required. *See*

Technical Consumer Prods., Inc. v. Lighting Sci. Grp. Corp., 955 F.3d 16, 22 (Fed. Cir. 2020) (citing *Crystal Semiconductor Corp. v. TriTech Microelecs. Int’l, Inc.*, 246 F.3d 1336, 1348 (Fed. Cir. 2001)).

820. Neither the written description nor enablement requirements of 35 U.S.C. § 112 require support for unclaimed elements. *See Lochner Techs., LLC v. Vizio, Inc.*, 567 F. App’x 931, 938-39 (Fed. Cir. 2014) (vacating summary judgment of invalidity for lack of written description and agreeing with patentee that “there is no precedent requiring a patentee to disclose or enable unclaimed elements”). “[A] patent claim is not necessarily invalid for lack of written description just because it is broader than the specific examples disclosed.” *Martek Biosci. Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1371 (Fed. Cir. 2009). Further, “[a]n applicant is not required to describe in the specification every conceivable and possible future embodiment of his invention.” *Cordis Corp. v. Medtronic AVE, Inc.*, 339 F.3d 1352, 1365 (Fed. Cir. 2003) (quoting *Rexnord Corp. v. Laitram Corp.*, 274 F.3d 1336, 1344 (Fed. Cir. 2001)); *see also Lampi Corp. v. Am. Power Prods., Inc.*, 228 F.3d 1365, 1378 (Fed. Cir. 2000) (holding written description sufficient to support claims covering non-identical half-shells where patent drawings, the only cited written description support, only disclosed identical half-shells).

8. Enablement

821. A patent is enabled if a person of ordinary skill in the field could make and use the invention without having to perform undue experimentation. 35 U.S.C. § 112 ¶ 1; *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986).

822. Factors considered in determining whether experimentation is undue or excessive include: (1) the scope of the claimed invention; (2) the amount of guidance presented in the patent; (3) the amount of experimentation necessary; (4) the time and cost of any necessary experimentation; (5) how routine any necessary experimentation is in the applicable field; (6) whether the patent discloses specific working examples of the claimed invention; (7) the nature and predictability of the field; and (8) the level of ordinary skill in the field. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

823. Even a considerable amount of routine experimentation required to practice a claimed invention does not violate the enablement requirement. *Cephalon, Inc. v. Watson Pharms., Inc.*, 707 F.3d 1330, 1336 (Fed. Cir. 2013); *PPG Indus. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1565 (Fed. Cir. 1996).

824. “[T]he enablement requirement is met if the description enables any mode of making and using the invention.” *Invitrogen Corp. v. Clontech Labs. Inc.*, 429

F.3d 1052, 1070–71 (Fed. Cir. 2005) (quoting *Johns Hopkins Univ. v. Cellpro, Inc.*, 152 F.3d 1342, 1361 (Fed. Cir. 1998)).

825. The specification preferably omits information that would already be known to a POSA. *Streck v. Res. & Diagnostic Sys., Inc.*, 665 F.3d 1269, 1288 (Fed. Cir. 2012).

826. Patent claims do not necessarily lack enablement because they embrace inoperative embodiments, assuming that a POSA in the related field would not be required to perform undue experimentation to determine which embodiments would work. *Atlas Powder Co. v. E.I. du Pont De Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984). Further, “[i]t is not a function of the claims to specifically exclude . . . possible inoperative substances . . .” *Id.* at 1576 (quoting *In re Dinh-Nguyen*, 492 F.2d 856, 858–59, 181 USPQ 46, 48 (C.C.P.A. 1974)).

B. The Person of Ordinary Skill in the Art

827. A person of ordinary skill in the art of the Bryhali Patents is a person with several years of experience working in the design and evaluation of formulations for the topical treatment of diseases of the skin, having either (i) a Ph.D. (or equivalent degree) or an M.D. (or equivalent degree) and at least two to three years of post-graduate experience studying and/or treating skin diseases in the field of dermatology or a related field: or (ii) a degree in chemistry, pharmaceutical chemistry, pharmacy, medicine, clinical pharmacology, pharmacokinetics, or

another pharmaceutical science-related field, and at least five years of experience in designing, developing, evaluating, and/or testing pharmaceutical formulations for topical treatment of skin diseases.

828. A person of ordinary skill in the art of the Duobrii Patents is a person with several years of experience working in the design and evaluation of formulations for the topical treatment of diseases of the skin, having either (i) a Ph.D. (or equivalent degree) or an M.D. (or equivalent degree) and at least two to three years of post-graduate experience studying and/or treating skin diseases in the field of dermatology or a related field: or (ii) a degree in chemistry, pharmaceutical chemistry, pharmacy, medicine, clinical pharmacology, pharmacokinetics, or another pharmaceutical science-related field, and at least five years of experience in designing, developing, evaluating, and/or testing pharmaceutical formulations for topical treatment of skin diseases.

C. Applicable Claim Constructions

829. The following claim constructions apply to this case:

“wherein the liquid oil component . . . consists of diethyl sebacate and light mineral oil” ’895 patent, claim 1	The parties agree that “consists of” renders “liquid oil component” a closed claim element that excludes additional, unrecited components, such that “consists of diethyl sebacate and light mineral oil” means “includes only diethyl sebacate and light mineral oil.”
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“is capable of” ’895 patent, claim 1; ’787 patent, claim 1	The parties agree that “is capable of” should be interpreted according to its plain and ordinary meaning, i.e., “is able to”
“synergistic efficacy” ’895 patent, claim 1; ’787 patent, claim 1	“more efficacious than the combined efficacies of compositions, each comprising only one of the active ingredients”
“liquid oil component” E.g., ’307 patent, claim 1; ’502 patent, claim 1	The “liquid oil component” includes all ingredients of the formulation that are practically insoluble or insoluble in water and which are liquid at room temperature of 22°C
“is capable of providing synergistic efficacy and synergistic reduction of at least an adverse event selected from the group consisting of itching, burning, and stinging ” ’895 patent, claim 1; ’787 patent, claim 1	“a vehicle-adjusted frequency of at least an adverse event (selected from the group of itching, burning, and stinging) that is less than the vehicle-adjusted frequency of patients reporting said adverse event for halobetasol propionate monotherapy plus the vehicle-adjusted frequency of patients reporting said adverse event for tazarotene monotherapy”

D. Padagis’s ANDA Products Infringe All Asserted Claims.

1. Padagis Has Infringed the Asserted Claims of the ’307 Patent

830. As Padagis has stipulated, the submission of its ANDA No. 214285 (“HP ANDA”) to the FDA infringed claims 13, 16, and 20 of the ’307 patent. *See* ECF No. 91 at ¶ 6.

831. As Padagis has stipulated, the manufacture, use, offer to sell, sale, and/or importation of Padagis's generic halobetasol topical lotion, 0.01% ("HP ANDA Product") would infringe claims 13, 16, and 20 of the '307 patent. ECF No. 91 at ¶ 7.

832. As Padagis has stipulated, the submission of its ANDA 214626 ("HP/Taz ANDA") to the FDA infringed claims 13, 16, and 20 of the '307 patent. *See* ECF No. 91 at ¶ 8.

833. As Padagis has stipulated, the manufacture, use, offer to sell, sale, and/or importation of Padagis's generic halobetasol and tazarotene topical lotion, 0.01%/0.045% ("HP/Taz ANDA Product") would infringe claims 13, 16, and 20 of the '307 patent. ECF No. 91 at ¶ 9.

2. Padagis Has Infringed the Asserted Claims of the '502 Patent

834. As Padagis has stipulated, the submission of its HP ANDA to the FDA infringed claims 4 and 16 of the '502 patent. *See* ECF No. 91 at ¶ 6.

835. As Padagis has stipulated, the manufacture, use, offer to sell, sale, and/or importation of Padagis's HP ANDA Product would infringe claims 4 and 16 of the '502 patent.

836. As Padagis has stipulated, the submission of its HP/Taz ANDA to the FDA infringed claims 4 and 16 of the '502 patent. *See* ECF No. 91 at ¶ 8.

837. As Padagis has stipulated, the manufacture, use, offer to sell, sale, and/or importation of Padagis's HP/Taz ANDA Product would infringe claims 4 and 16 of the '502 patent. ECF No. 91 at ¶ 9.

3. Padagis Has Infringed the Asserted Claims of the '895 Patent

838. As Padagis has stipulated, the submission of its HP/Taz ANDA to the FDA infringed claims 3 and 6 of the '895 patent. *See* ECF No. 199 at ¶ 3.

839. As Padagis has stipulated, the manufacture, use, offer to sell, sale, and/or importation of Padagis's HP/Taz ANDA Product would infringe claims 3 and 6 of the '895 patent. *See* ECF No. 199 at ¶ 4.

4. Padagis Has Infringed the Asserted Claims of the '787 Patent

840. As Padagis has stipulated, the submission of its HP/Taz ANDA to the FDA infringed claims 4, 5, and 7 of the '787 patent. *See* ECF No. 199 at ¶ 3.

841. As Padagis has stipulated, the manufacture, use, offer to sell, sale, and/or importation of Padagis's HP/Taz ANDA Product would infringe claims 4, 5, and 7 of the '787 patent. *See* ECF No. 199 at ¶ 4.

E. Padagis Has Failed to Demonstrate that the Asserted Claims of the Bryhali Patents Are Invalid.

1. Padagis Has Failed to Demonstrate a Prima Facie Case of Obviousness.

842. Padagis's *prima facie* case of obviousness relies on the disclosure of broad concentration ranges in its asserted prior art references, specifically, the '295 Patent and JP '228.

843. The Federal Circuit has held that a broad disclosure in the prior art is insufficient to establish a *prima facie* case of obviousness where “the disclosed range is so broad as to encompass a very large number of possible distinct compositions.” *In re Peterson*, 315 F.3d 1325, 1330 n.1 (Fed. Cir. 2003); *In re Baird*, 16 F.3d 380, 382 (Fed. Cir. 1994); *In re Jones*, 958 F.2d 347 (Fed. Cir. 1992); *In re Jones*, 958 F.2d 347, 351 (Fed. Cir. 1992).

844. The concentration ranges in Padagis’s asserted art purport to apply to a wide variety of corticosteroids, with a concentration range where the top end is 3,000 times larger than the bottom end. *See* Tr. 402:5-10 (Michniak-Kohn cross examination). This is a broad range that encompasses an impossibly large number of distinct compositions.

845. Therefore, Padagis has failed to establish a *prima facie* case of obviousness.

2. A POSA Would Not Have Been Motivated Nor Had a Reasonable Expectation of Success in Reaching the Asserted Claims of the Bryhali Patents

846. Padagis has failed to establish that a POSA would have been motivated to use concentrations of halobetasol lower than the 0.05% concentration of halobetasol of Ultravate®.

847. Padagis has failed to establish that a POSA would have been motivated to select halobetasol, as opposed to a different superpotent corticosteroid.

848. Padagis has failed to establish that a POSA would have been motivated to use a topical composition comprising a corticosteroid at concentrations of less than 0.05% for a period of longer than two weeks.

849. Padagis has failed to establish that the other limitations of the claims of the Bryhali Patents would not have been obvious, presenting a hindsight-driven analysis that involves picking and choosing elements from old references with the Bryhali Patents as a starting point.

850. Padagis has failed to establish that there was a motivation to combine any of its asserted prior art references with a reasonable expectation of success.

851. Padagis's contention that a POSA would have been motivated to combine the prior art references rests on the premise that a POSA would have been motivated to prepare a halobetasol formulation at a concentration of less than 0.05%. Because Padagis has failed to show that a POSA would have been motivated to prepare a halobetasol formulation at a concentration of less than 0.05%, Padagis has failed to establish any motivation to combine the asserted prior art references.

852. Padagis has failed to establish that a POSA would have had any motivation to look to old prior art, which focused on the use of penetration enhancers to push more drug through the skin.

853. Because formulation science is unpredictable, a POSA would not have had a reasonable expectation of success in devising the invention of the asserted claims of the Bryhali Patents.

854. Finally, even if Padagis had demonstrated there was a motivation to combine its asserted prior art references, Padagis failed to establish that the Asserted Claims of the Bryhali Patents would have been obvious because it failed to present a specific analysis of how each combination allegedly would have met all of the limitations of the Asserted Claims.

3. The Asserted Claims of the Bryhali Patents Are Not Obvious Based On the Combinations of References Asserted by Padagis.

a. The '307 Patent

855. The '307 patent has a priority date of November 22, 2010, the date of the filing of United States Provisional Patent Application No. 61/458,339.

856. Padagis has failed to prove by clear and convincing evidence that claim 13 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; and (2) Blum.

857. Padagis has failed to prove by clear and convincing evidence that claim 13 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) the '566 Patent.

858. Padagis has failed to prove by clear and convincing evidence that claim 13 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) JP '228.

859. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) '295 Patent; and (2) Blum.

860. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) '295 Patent; (2) Blum; and (3) the '566 Patent.

861. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) '295 Patent; (2) Blum; and (3) JP '228.

862. Padagis has failed to prove by clear and convincing evidence that claim 20 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; and (2) Blum.

863. Padagis has failed to prove by clear and convincing evidence that claim 20 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) the '566 Patent.

864. Padagis has failed to prove by clear and convincing evidence that claim 20 of the '307 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) JP '228.

b. The '502 Patent

865. The '502 patent has a priority date of November 22, 2010, the date of the filing of United States Provisional Patent Application No. 61/458,339.

866. Padagis has failed to prove by clear and convincing evidence that claim 4 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; and (2) Blum.

867. Padagis has failed to prove by clear and convincing evidence that claim 4 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) the '566 Patent.

868. Padagis has failed to prove by clear and convincing evidence that claim 4 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) JP '228.

869. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; and (2) Blum.

870. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) the '566 Patent.

871. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '295 Patent; (2) Blum; and (3) the Temovate E® Label.

c. Objective Indicia Of Nonobviousness Support The Conclusion That The Asserted Claims Of The Bryhali Patents Are Not Obvious.

872. Objective indicia of nonobviousness support the conclusion that claims 13, 16, and 20 of the '307 patent are not obvious.

873. Objective indicia of nonobviousness support the conclusion that claims 4 and 16 of the '502 patent are not obvious.

i. Nexus

874. As Padagis has stipulated, Bausch's Bryhali® product is an embodiment of the asserted claims of the '307 and '502 patents. ECF No. 208 at ¶ 1.

875. As Padagis has stipulated, Bausch's Duobrii® product is an embodiment of the asserted claims of the '307 and '502 patents. ECF No. 208 at ¶ 2.

ii. Teaching Away

876. The Blum reference actually supports and recommends the selection of a higher concentration of steroid, and therefore teaches away from lowering the concentration of halobetasol.

877. The Temovate E® Label provides a different solution (as opposed to reducing the concentration of superpotent corticosteroid) the two-week limitation problem, and therefore teaches away from lowering the concentration of halobetasol.

878. The '295 patent, '566 patent, and JP '228 fail to exclude white petrolatum, and therefore teach away from the asserted claims of the '502 patent which expressly exclude white petrolatum.

iii. Unexpected Results

879. Because a POSA would not have expected significant reduction in the amount of halobetasol propionate formulation to achieve comparable efficacy to the higher concentration Ultravate® product, the results described in the Bryhali Patents (as embodied in the commercial Bryhali® product) are unexpected.

iv. Long-Felt But Unmet Need

880. Because the need for a superpotent corticosteroid that could be administered for more than two weeks existed since at least the 1970's, there was a long-felt but unmet need for the compositions described in the Bryhali Patents (as embodied in the commercial Bryhali® product).

4. The Claims of the Bryhali Patents Are Not Invalid Under 35 U.S.C. § 112

a. The Claims Of The Bryhali Patents Are Not Invalid As Indefinite

881. The term “liquid oil component” would inform a POSA as to the scope of the claim with reasonable certainty. Therefore, Padagis has failed to prove by clear

and convincing evidence that claims 13, 16, and 20 of the '307 patent are invalid under pre-AIA 35 U.S.C. § 112, second paragraph as indefinite.

882. The term “liquid oil component” would inform a POSA as to the scope of the claim with reasonable certainty. Therefore, Padagis has failed to prove by clear and convincing evidence that claims 4 and 16 of the '502 patent are invalid under pre-AIA 35 U.S.C. § 112, second paragraph as indefinite.

883. Even if the phrase “liquid oil component” were deemed to be somewhat unclear, Padagis has not demonstrated by clear and convincing evidence that a POSA would not understand the scope of the claims with reasonable certainty.

b. Claim 16 Of '502 Patent Is Not Invalid For Lack Of Written Description

884. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 112, second paragraph for lack of written description.

c. Claim 16 Of '502 Patent Is Not Invalid For Lack Of Enablement

885. Padagis has failed to prove by clear and convincing evidence that claim 16 of the '502 patent is invalid under pre-AIA 35 U.S.C. § 112, second paragraph for lack of enablement.

F. Padagis Has Failed to Demonstrate that the Asserted Claims of the Duobrii Patents Are Obvious.

886. IDP-118 Study is not prior art because it falls within the experimental use doctrine.

1. A POSA Would Not Have Been Motivated Nor Had a Reasonable Expectation Of Success in Reaching the Asserted Claims of the Duobrii Patents.

887. Padagis has failed to establish that a POSA would select the ingredients and concentrations of IDP-118 with a reasonable expectation of success.

888. Padagis has failed to establish that a POSA would have been motivated to combine halobetasol and tazarotene into a fixed-dose combination lotion product.

889. Padagis has failed to establish that a POSA would have been motivated to select the 0.045% concentration of tazarotene with a reasonable expectation of success.

890. Padagis has failed to establish that a POSA would have been motivated to select IDP-118's 0.01% concentration of halobetasol, particularly in combination with tazarotene.

891. Padagis has failed to establish that a POSA would have a reasonable expectation of success that IDP-118 would achieve the claimed synergistic efficacy.

892. Padagis has failed to establish that a POSA would have a reasonable expectation of success that IDP-118 would achieve the claimed synergistic reduction of adverse events.

2. The '895 Patent

893. The '895 patent has an effective filing date of June 18, 2015, the date of the filing of United States Provisional Patent Application No. 62/181,481.

894. Padagis has failed to prove by clear and convincing evidence that claim 3 of the '895 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Tazorac® Label.

895. Padagis has failed to prove by clear and convincing evidence that claim 3 of the '895 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) IDP-118 Study.

896. Padagis has failed to prove by clear and convincing evidence that claim 3 of the '895 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Gandhi.

897. Padagis has failed to prove by clear and convincing evidence that claim 6 of the '895 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Tazorac® Label.

898. Padagis has failed to prove by clear and convincing evidence that claim 6 of the '895 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) IDP-118 Study.

899. Padagis has failed to prove by clear and convincing evidence that claim 6 of the '895 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Gandhi.

3. The '787 Patent

900. The '787 patent has an effective filing date of June 18, 2015, the date of the filing of United States Provisional Patent Application No. 62/181,481.

901. Padagis has failed to prove by clear and convincing evidence that claim 4 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Tazorac® Label.

902. Padagis has failed to prove by clear and convincing evidence that claim 4 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) IDP-118 Study.

903. Padagis has failed to prove by clear and convincing evidence that claim 4 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Gandhi.

904. Padagis has failed to prove by clear and convincing evidence that claim 5 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Tazorac® Label.

905. Padagis has failed to prove by clear and convincing evidence that claim 5 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) IDP-118 Study.

906. Padagis has failed to prove by clear and convincing evidence that claim 5 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Gandhi.

907. Padagis has failed to prove by clear and convincing evidence that claim 7 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Tazorac® Label.

908. Padagis has failed to prove by clear and convincing evidence that claim 7 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) IDP-118 Study.

909. Padagis has failed to prove by clear and convincing evidence that claim 7 of the '787 patent is invalid under AIA 35 U.S.C. § 103 as obvious over the combination of (1) the '824 Publication, (2) Gollnick, and (3) Gandhi.

4. Objective Indicia of Nonobviousness Support the Conclusion that the Duobrii Patents Are Not Invalid.

a. Nexus

910. As Padagis has stipulated, Duobrii (the commercial name for IDP-118) is an embodiment of the Asserted Claims of the Duobrii Patents. ECF No. 199 ¶ 5.

b. Teaching Away

911. Gollnick teaches away from the invention because it motivates a POSA not to put tazarotene and a corticosteroid together in a single formulation.

912. Gollnick teaches away from the invention because it motivates a POSA to prefer a lower potency of corticosteroid, *i.e.*, a potency other than a Class 1 superpotent corticosteroid.

c. Unexpected Results

913. IDP-118 demonstrates the unexpected property of the claimed synergistic efficacy, *i.e.*, efficacy that is superior to the expected combination of the tazarotene and halobetasol propionate.

914. IDP-118 demonstrates the unexpected property of the claimed synergistic reduction in adverse events, *i.e.*, an adverse event profile lower than what would be expected from the combination of tazarotene and halobetasol propionate.

915. IDP-118 demonstrates the unexpected property of achieving both the claimed synergistic efficacy and the synergistic reduction of adverse events in a single lotion formulation.

d. Skepticism

916. Dermatologists were skeptical that such a low concentration of halobetasol propionate combined with such a low concentration of tazarotene would produce an efficacious psoriasis treatment.

917. Dermatologists were skeptical that such a low concentration of halobetasol propionate would suffice to reduce the irritation of a treatment containing tazarotene.

e. Commercial Success

918. Duobrii has achieved significant sales in the relevant market, and therefore constitutes a commercial success.

919. Duobrii's market share in the Total Psoriasis Market further supports the conclusion that it constitutes a commercial success.

920. Duobrii's market share in the Branded Combos + Otezla Market further supports the conclusion that it constitutes a commercial success.

921. Duobrii's market share in the Branded Combos Market further supports the conclusion that it constitutes a commercial success.

G. Bausch Is Entitled to an Order Barring FDA Approval of Padagis's HP ANDA and Its HP/Taz ANDA.⁶

922. If the product that the ANDA applicant is likely to market would infringe a valid patent claim, then the "patent owner is entitled to an order that FDA approval of the ANDA containing the paragraph IV certification not be effective until the patent expires." *Bristol-Myers Squibb Co. v. Royce Labs., Inc.*, 69 F.3d 1130, 1135 (Fed. Cir. 1995); 21 U.S.C. § 355(j)(5)(B)(iii)(III); 35 U.S.C. § 271(e)(4)(A).

⁶ Should Bausch prevail in this action, it reserves the right to seek additional remedies at an appropriate time, including but not limited to attorney's fees and costs. *See, e.g.*, 35 U.S.C. § 285; Fed. R. Civ. P. 54(d)(1).

923. Padagis's HP ANDA infringes a valid claim of the Bryhali Patents.

924. Padagis's HP/Taz ANDA infringes a valid claim of the Bryhali Patents.

925. Padagis's HP/Taz ANDA infringes a valid claim of the Duobrii Patents.

926. The Court shall issue an order that FDA not finally approve the HP ANDA until after the expiration of the Bryhali Patents.

927. The Court shall issue an order that FDA not finally approve the HP/Taz ANDA until after the expiration of the Bryhali Patents and the Duobrii Patents.

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Respectfully submitted,

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