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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. FALK PHARMA GMBH,

Petitioner

v.

ELLODI PHARMACEUTICALS, L.P.,
Patent Owner

Case No. IPR2024-01197
Patent No. 8,771,729

PETITIONER'S REPLY BRIEF

Dr. Falk Pharma v. Ellodi Pharmaceuticals
IPR2025-00054
Dr. Falk Pharma Ex. 1117

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1001	U.S. Patent No. 8,771,729 to Perrett et al.
1002	U.S. Publication No. 20070111978 to Dohil et al.
1003	EP2482822B1 that was revoked by the European Patent Office
1004	The Opposition Division of the European Patent Office decision revoking EP2484822B1 with auxiliary requested claims
1005	"Guidance for Industry: Orally Disintegrating Tablets," U.S. Food & Drug Administration, Center for Drug Evaluation and Research (CDER), 2008.
1006	Notice of Publication of FDA Guidance for Industry on Orally Disintegrating Tablets, Federal Register, Vol. 73, No. 242 at 76366, December 16, 2008.
1007	"DRAFT Guidance for Industry: Orally Disintegrating Tablets," U.S. Food & Drug Administration, Center for Drug Evaluation and Research (CDER), 2007.
1008	International Publication No. WO2000044351 to Grother et al.
1009	Svoboda et al., "Oral formulations of budesonide: a novel treatment for inflammatory bowel disease," Drugs of Today, 44:857-863 (2008) at 857.
1010	Tan et al., "Eosinophilic gastroenteritis treated with non-enteric-coated budesonide tablets," European Journal of Gastroenterology & Hepatology, 13:425-427 (2001)
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1015	Aceves et al., "Oral Viscous Budesonide: A potential new therapy for eosinophilic esophagitis in children," American Journal of Gastroenterology, 102:1-9 (2007)
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1017	Danckwerts, "Intraoral Drug Delivery: A Comparative Review," American Journal of Drug Delivery, 1:171-186 (2003).
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1025	Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 11th edition, eds. Brunton, Lazo, Parker, 2005
1026	Budenofalk® Brochure (2005)
1027	Budenofalk® Advertisement (2007)
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1030	Declaration of Alan F. Parr, Pharm.D., Ph.D.
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1032	Prosecution history excerpts from U.S. Application No. 15/816,154, which issued as U.S. 10,632,069
1033	Teitlebaum et al., Eosinophilic esophagitis in children: Immunopathological analysis and response to fluticasone propionate," Gastroenterology 122:1216-1225 (2002)
1034	Noel et al., "Clinical and immunopathologic effects of swallowed fluticasone for eosinophilic esophagitis," Clinical Gastroenterology and Hepatology 2:568-575 (2004)
1035	U.S. Patent No. 7,122,198 to Singh et al.
1036	U.S. Patent No. 7,229,641 Cherukuri et al.
1037	RESERVED
1038	Ellodi Response to the Grounds of Opposition filed by Dr. Falk Pharma GmbH in opposition proceedings in EP2484822B1
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1071	U.S. Publication No. US20110189299 to Okubo and Davies et al.
1072	2025-07-02 Deposition transcript of Dr. Martyn Davies
1073	Schoepfer et al., "Variation in Endoscopic Activity Assessment and Endoscopy Score Validation in Adults With Eosinophilic Esophagitis," Clinical Gastroenterology and Hepatology, 17:1477-1488 (2019).

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1074	2021-04-19 Assignment of U.S. Patent No. 8,771,729 from Adare Pharmaceuticals US, L.P. to Ellodi Pharmaceuticals, L.P. recorded at Reel 055966, Frame 0658.
1075	International Publication No. WO2003074029 to McEntee et al.
1076	International Publication No. WO2009078872 to Martin et al.
1077	U.S. Patent Publication No. 20030124184 to Mezaache et al.
1078	U.S. Patent Publication No. 20050019393 to Augsburger et al.
1079	U.S. Patent No. 7,384,921 to Tang et al.
1080	U.S. Patent Publication No. 20080132535 to Singh et al.
1081	U.S. Patent Publication No. 20090022799 to Barman
1082	Than, "Individualized Drugs for Individual Needs," Review of Optometry, 146:38-43 (2009)
1083	Iorgulescu, "Saliva between normal and pathological. Important factors in determining systemic and oral health," Journal of Medicine and Life 2:3003-307 (2009)
1084	2015-09-18 Assignment of U.S. Patent Application No. 10/827,106 (which published as Venkatesh, EX1020) to Adare Pharmaceuticals, Inc. recorded at Reel 036554, Frame 0829
1085	U.S. Patent No. 6,139,865 to Friend et al.
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1087	Narmada et al., "Formulation, evaluation and optimization of fast dissolving tablets containing amlodipine besylate by sublimation method," ARS Pharmaceutica, 50:129-144 (2009)

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1088	Khan et al., "Taste masking of ondansetron hydrochloride by polymer carrier system and formulation of rapid-disintegrating tablets," AAPS PharmSciTech 8:E1-E7 (2007)
1089	CLARITIN® (loratadine) FDA-approved package insert
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1093	Declaration of Alan F. Parr, Pharm.D., Ph.D. supporting Petitioner Reply for U.S. 8,771,729

I. INTRODUCTION

The '729 patent claims are obvious over the cited prior art. Dohil discloses solid budesonide compositions in the form of a lozenge or tablet that dissolves rapidly in a patient's mouth. A defining characteristic of an orally dissolving tablet (ODT) is that it disintegrates rapidly in a patient's mouth. Dohil therefore teaches and suggests formulating rapidly dissolving solid compositions, including ODTs, that render the challenged claims obvious. Patent Owner's Response (POR) criticizes Dohil for additionally disclosing liquid formulations and argues that Dohil's lozenge must dissolve slowly. The EPO soundly rejected these same arguments from Patent Owner (PO), and they should be rejected again here. EX1004 ¶¶26.2-26.8.

Grother contains the same disclosures as the '729 patent—both teach ODTs containing corticosteroids such as budesonide and fluticasone. PO accuses Petitioner of arbitrarily picking budesonide and fluticasone to use in Grother's ODT. Not so. Grother itself instructs the POSA to use budesonide and fluticasone in Grother's ODT.

Turning to Venkatesh, PO asserts this reference requires taste-masking with a water-insoluble polymer coating, which it argues would prevent a drug from being topically deposited in the upper gastrointestinal tract. This argument is not credible. PO previously told the USPTO (and the POSA) in its own prior art patent that such a coating releases a drug immediately after it passes through the mouth such that the drug is deposited in the upper gastrointestinal tract.

PO's purported expert, Dr. Davies, is not credible either. He has no experience working with ODTs. EX1072 10:16-11:3. He didn't perform any literature searches to educate himself on the features of ODTs that he mistakenly believed were missing from the prior art. *Id.* 42:15-43:14, 56:16-57:9, 134:8-135:7, 183:17-21. Still further, PO's counsel shielded him from highly relevant evidence that directly contradicts his opinions by withholding the EPO's decision, wherein the EPO determined that Dohil describes an ODT. *Id.* 77:22-78:9.

PO makes unsubstantiated accusations that Petitioner used impermissible hindsight. The cited prior art, however, contains strong teachings to motivate a POSA to arrive at the claimed subject matter. The Board should cancel the challenged claims.

II. THE CLAIMS OF THE '729 PATENT ARE OBVIOUS

A. A POSA Would Have Been Motivated Based On Dohil

The Petition provides compelling evidence of obviousness based on Dohil in view of the knowledge of a POSA (Ground 1), and further in view of Venkatesh (Ground 3). Petition 18-34, 52-57. PO raises unconvincing arguments, many of which are repeated several times. Petitioner succinctly Replies as follows.

1. Dohil Teaches, Suggests, And Motivates Formulating Orally Disintegrating Compositions/Tablets

Dohil discloses solid budesonide compositions in the form of a lozenge or tablet that "dissolve[s] rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus." EX1002 ¶[0032]. It was desirable for a rapidly dissolving tablet

to dissolve within "several seconds to about a minute." EX1018 434. Indeed, the FDA Guidance recommends that orally dissolving tablets (ODTs) should "disintegrate[] rapidly, usually within a matter of seconds." EX1005 2. Such rapid disintegration is a defining characteristic of an ODT, as confirmed by PO's expert. *Id.*; EX1072 15:10-16:14. Dohil therefore teaches, suggests, and motivates formulating rapidly dissolving solid compositions, including ODTs. Petition 23-25; EX1030 ¶¶117-120.

The EPO previously determined that Dohil's instruction to formulate budesonide in a rapidly dissolving lozenge or similar tablet renders obvious ODTs containing budesonide. EX1004 ¶¶26.3-4, 36.8. PO had a full and fair opportunity to litigate this issue at the EPO.[1] PO now asks the Board to reach the opposite conclusion by (i) obfuscating Dohil's teachings of ***solid*** ODT formulations of budesonide and selectively emphasizing Dohil's ***liquid*** formulations, (ii) incorrectly asserting that all lozenges must dissolve slowly, (iii) mischaracterizing the amount of saliva available to dissolve ODTs, and (iv) misinterpreting Dohil's other embodiments. Each of PO's arguments should be rejected.

[1] PO argues that the EPO decision is "irrelevant." POR 21-22. However, "notwithstanding any differences in the law," an EPO decision is "relevant" and "probative" in an IPR. *Ericsson, Inc. v. Intellectual Ventures II LLC*, IPR2014-00915, Paper 37 at 7 (PTAB 2015).

a) Dohil Teaches And Motivates Solid ODT Formulations

PO attempts to distract from Dohil's rapidly dissolving lozenges and tablets (which are solid compositions) by focusing on Dohil's allegedly preferred liquid compositions. POR 2-3, 11-12, 19, 24-25, 28-29. Dohil, however, is "considered for everything that it teaches, not simply [its] preferred embodiment." *In re Applied Materials, Inc*., 692 F.3d 1289, 1298 (Fed. Cir. 2012).

Dohil instructs the POSA to formulate budesonide as a rapidly dissolving lozenge or tablet to treat inflammation of the esophagus. EX1002 ¶[0032]. The Board recognized that Dohil teaches "corticosteroid compositions in the form of 'a dissolving tablet, a dissolving wafer, a capsule, or a gel capsule,' including embodiments wherein such 'tablets, wafers, and capsules are formulated with at least one excipient to deliver a viscous form of the corticosteroid to the esophagus.'" Institution Decision 9 (quoting EX1002 ¶[0013]).

Dohil's instruction to formulate budesonide as a rapidly dissolving lozenge/tablet was intuitive and compelling to a POSA in view of Dohil's express desire to treat EOE. EX1002 ¶¶[0010], [0011], [0015]. A primary symptom of EOE is difficulty swallowing, EX1033 1218 (Table 1), as admitted by PO. EX1001 1:24-28; EX1073 1478 (admitting

"dysphagia is the most frequent complaint of adult EOE patients");[2] EX1072 22:16-23:5; EX1093 ¶¶16-18. Rapidly dissolving tablets were especially desirable for treating patients that experience difficulty swallowing. EX1005 1; EX1018 434; Petition 7-12.

PO asserts there was no motivation to follow Dohl's instruction to prepare a solid rapidly dissolving lozenge/tablet because Dohil did not recognize any problems with the liquid formulation used in Dohil's working examples. POR 29, 31. PO ignores that rapidly dissolving solid formulations were known to have several advantages, such as "[c]onvenience of administration and accurate dosing as compared to liquid formulations," EX1019 311, and "good stability, accurate dosing, easy manufacturing, small packaging size, and easy handling by patients." EX1018 434; EX1030 ¶71; EX1093 ¶19; Institution Decision 41.

Dohil's liquid formulations were rudimentary and merely provided a proof-of-concept that oral formulations of budesonide successfully treat EOE. EX2011 71:16-72:2. Dohil calls for "larger placebo-controlled clinical trials [to] provide more information about dosing, efficacy and long-term safety." EX1002 ¶[0067]. PO's expert admitted that conducting such clinical trials with Dohil's rudimentary liquid

[2] EX1073 was co-authored and funded (*id.* 1477, 1488) by Adare Pharmaceuticals, which was the previous assignee of the '729 patent that changed its name to Ellodi Pharmaceuticals in 2020. EX1074.

formulation would require a medical team to mix Pulmicort with 10 packages of Splenda twice daily for three months (i.e., 180 times) ***per patient***, EX1072 93:7-95:7, 96:17-24, which would need to be repeated for hundreds to thousands of patients across several different countries, *id.* 87:14-88:19, 89:13-90:18. It was a natural next step for the POSA to follow Dohil's instruction to formulate budesonide as a solid rapidly dissolving lozenge/tablet because the known benefits of solid compositions such as convenient administration and good stability would facilitate Dohil's larger clinical trial. EX2011 72:11-24; EX1093 ¶20. Any of these benefits "provide a reason for combining the elements in the manner claimed." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 420 (2007).

b) <u>Rapidly disintegrating lozenges</u>

PO argues that Dohil ¶[0032] cannot teach or suggest a rapidly dissolving solid formulation because it uses the word "lozenge," which PO asserts requires a slowly dissolving formulation. POR 13-14, 25-27. PO unsuccessfully raised this argument at the EPO. EX1004 ¶26.2. The EPO rejected PO's argument and determined that Dohil ¶[0032] "clearly describes a lozenge or similar tablet, which rapidly dissolves in the mouth" and "at least overlap[s]" with orally dissolving tablets. *Id.* ¶26.4; *id.* ¶¶26.1-26.8.

The EPO is correct. Dohil ¶[0032] clearly discloses a "rapidly" dissolving lozenge. Dohil ¶[0032] also discloses similar "tablets" that dissolve "rapidly" in the

mouth. Dohil's tablet that rapidly dissolves in the mouth fairly teaches and suggests an ODT, especially in view of the industry accepted ODT definition as "a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." Institution Decision 37; EX1005 2; *supra* Section II.A.1.

PO incorrectly interprets Dohil's lozenge as only providing "an initial rapid release of drug and then dissolv[ing] slowly." POR 13-14, 25. The plain reading of Dohil ¶[0032] is that "[t]he lozenge" (i.e., the entire lozenge) would dissolve rapidly in the mouth. EX1093 ¶¶21-22. Dohil ¶[0032] contrasts its "rapidly" dissolving lozenge with other formulations "designed for slow release." *Id.* ¶22. PO's interpretation incorrectly combines these two distinct formulations into one slow release formulation. PO implies that this interpretation is required because rapidly dissolving lozenges were unknown in the prior art. POR 13. PO is wrong. Dohil's rapidly dissolving lozenge disclosure is reinforced by numerous other examples in the prior art:

- McEntee teaches "[f]ast melt formulations are typically in the form of tablets or lozenges that dissolve or disperse in a patient's mouth within a minute without the need of water or chewing" and "improve patient compliance." EX1075 3:20-28.
- Martin teaches "orally disintegrating tablets, wafers, pellets, or lozenges of the

present invention release their analgesic content" including within "about 20 seconds to about 60 seconds, when placed into human saliva," EX1076 ¶[0067], and "[g]enerally, a sublingual tablet, wafer, pellet, or lozenge should dissolve or disintegrate quickly, allowing the analgesic to be rapidly absorbed," *id.* ¶[0060].

- Mezaache teaches quick dissolving compositions "such as tablets and lozenges, which, when ingested, quickly dissolve in the mouth," EX1077 ¶¶[0002], [0003], "generally in less than 30 seconds," *id.* ¶[0040].
- Augsburger teaches "rapidly-disintegrating dosage forms" that are "capable of being compressed into tablets or lozenges which have rapid disintegration rates," EX1078 ¶[0043], including "a rapidly disintegrating lozenge," *id.* ¶[0143].
- Tang teaches "a tablet or lozenge" that dissolves in a patient's mouth within a minute. EX1079 14:9-14.
- Singh teaches a "quick-dissolving lozenge or tablet." EX1080 Claim 11, ¶[0057].
- Barman teaches a "fast dissolving lozenge or troche dissolved in the mouth." EX1081 Claims 31, 33, ¶[0044].
- Than teaches a "quick-dissolving lozenge." EX1082 2; EX1093 ¶¶23-35.

Dohil's use of the word "lozenge" to describe a rapidly dissolving solid composition of budesonide is appropriate because lozenges are typically used to formulate topical drugs that "have very few systemic adverse effects" and "treat[] local mouth diseases and sore throats." EX1017 181; EX1093 ¶36. A primary

symptom of EOE is difficulty swallowing due to inflammation of the throat/esophagus. *Supra* Section II.A.1.a. Budesonide was known to topically treat inflammation of the esophagus. Petition 5-6. Dohil's description of a rapidly dissolving "lozenge" appropriately signals to the POSA that the formulation will rapidly dissolve to release budesonide to topically treat a patient's inflamed throat/esophagus.

PO rehashes its unsuccessful argument from the EPO that Dohil's rapidly dissolving lozenge/tablet cannot include a disintegrant. POR 13-14, 25-27; EX1004 ¶26.2. In rejecting this argument, the EPO explained that Dohil's ¶[0032] rapidly dissolving tablets "necessarily require an excipient which facilitates their dispersion and dissolution." EX1004 ¶26.4. Dohil discloses disintegrants for use in its formulations. EX1002 ¶[0037]. It was known that the rapid disintegration of a lozenge or tablet is desirably aided by at least one disintegrating agent. EX1018 446-47; EX1030 ¶¶109-111; EX1076 ¶[0064]; EX1077 ¶[0010]; EX1078 ¶¶[0083]-[0084], [0079], [0085]; EX1080 ¶¶[0061], [0083]; EX1093 ¶37.

c) <u>Patients produce sufficient saliva to coat the esophagus</u>

PO asserts that Dohil requires a large volume (8-12 mL) of a viscous liquid to coat the esophagus. PO argues that a patient's saliva is of insufficient volume (1-2 mL)

and viscosity to coat the esophagus with a rapidly dissolving lozenge or tablet. POR 12, 25-26, 31-32, 35-36. There are multiple problems with PO's argument.

First, PO's argument goes against Dohil's express disclosure. Dohil teaches that its rapidly dissolving lozenge/tablet does "dissolve rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus." EX1002 ¶[0032]. Dohil explains that its tablets "are formulated with at least one excipient to deliver a viscous form of the corticosteroid to the esophagus." *Id.* ¶[0013]. Such an excipient "increase[s] the resulting liquid viscosity of the dissolved tablet, enabling it to reach the esophagus, for example, to coat the esophagus." *Id.* ¶[0037]; *id.* ¶[0043]. Based on Dohil's teachings, a POSA reasonably expected that the patient's saliva would successfully mix with the rapidly dissolving lozenge/tablet to produce a solution of sufficient volume and viscosity to coat the esophagus. EX1093 ¶¶38-40.

Second, PO mischaracterizes Dr. Parr's deposition testimony to infer that a patient would "only produce 1-2 mL of liquid" with Dohil's lozenge/tablet. POR 31. Dr. Parr actually testified that a patient tends to ***swallow*** 1-2 mL of liquid at a time. EX2011 50:17-24. It was known that 1-2 mL of saliva triggers a swallowing reflex. EX1083 304. PO failed to ask Dr. Parr how much saliva a patient produces ***when a lozenge or tablet is placed in the mouth***. It was known that placing a substance in the oral cavity (such as a lozenge/tablet) causes a patient's saliva production to increase to about 4-5 mL/min or more. *Id.* 303-304. This 4-5 mL/min of saliva trickles

slowly down the esophagus as it is swallowed approximately 1-2 mL at a time. *Id.* 304; EX2011 50:17-51:3, 52:6-8. This volume of saliva is sufficient to dissolve Dohil's lozenge/tablet and produce the viscous solution disclosed by Dohil that coats the esophagus. EX1002 ¶¶[0032], [0013], [0037], [0043]; EX1093 ¶¶41-43. Also, PO's expert admitted that 1-2 mL of saliva is, in fact, sufficient to deposit a corticosteroid topically in the upper gastrointestinal tract. EX1072 25:15-27:5.

PO incorrectly argues that a POSA would not have followed Dohil's instruction to prepare a solid rapidly dissolving lozenge/tablet because it would "change the principle of operation of Dohil's liquid formulation" and render the lozenge/tablet "unsatisfactory for its intended purpose." POR 19, 28-30. Dohil explains that its rapidly dissolving lozenge/tablet operates by dissolving "rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus." EX1002 ¶[0032]; *id.* ¶¶[0013], [0037], [0043]. Dohil's rapidly dissolving lozenge/tablet therefore has the same principle of operation as its liquid formulations, which is to provide a solution of budesonide that coats the esophagus. Dohil's prior art embodiments operate on the same principles and support a finding of obviousness. *See In re Umbarger*, 407 F.2d 425, 430-31 (CCPA 1969); EX1093 ¶44.

Dohil's solid lozenge/tablet was expected to operate for Dohil's intended purpose of coating the esophagus. The excipients in Dohil's rapidly dissolving

lozenge/tablet mix with the patient's saliva to produce a viscous solution containing budesonide that coats the esophagus. EX1002 ¶¶[0032], [0013], [0037], [0043]; EX1072 17:19-22; EX1093 ¶45. The EPO explained that Dohil's rapidly dissolving lozenges/tablets provide an "indirect way of forming a budesonide-containing liquid in situ in the mouth, which is able to coat the esophagus," EX1004 ¶36.3, because these formulations contain excipients "which are meant to increase the viscosity of the liquid resulting from the dissolution of the tablet," *id.* ¶26.7.

It was obvious for a POSA to follow Dohil's instruction to prepare rapidly dissolving solid lozenges/tablets to improve budesonide formulations for patients suffering from inflammation of the esophagus. *See KSR*, 550 U.S. at 417 ("if a technique has been used to improve one [composition], and a [POSA] would recognize that it would improve similar [compositions] in the same way, using the technique is obvious").

d) <u>PO misinterprets Dohil's alternative embodiments</u>

Dohil discloses a rapidly dissolving lozenge/tablet that is dissolved ***in a patient's mouth***, and it also discloses a second (alternative) embodiment where the lozenge is "ground or otherwise dissolved" ***in a liquid prior to administration*** for the minority of patients that "may have difficulty with a dissolving lozenge" as follows:

> The lozenge or other similar tablet, capsule, or other solid, wo[u]ld dissolve rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus. ***Or***, for children or other patients that may have difficulty with a dissolving lozenge, the lozenge may be ground or otherwise dissolved in a small volume of water or other pharmaceutically suitable liquid….

EX1002 ¶[0032]. These are clearly two alternative embodiments of administration because they are separated by the word "***Or***." *Id.*

PO argues that Dohil's second embodiment of administering Dohil's rapidly dissolving lozenge/tablet cannot suggest an ODT because an ODT is not permitted to be ground/dissolved before administration. POR 13-14, 26. This is nonsense. Dohil's second embodiment of administering a lozenge by grinding/dissolving prior to administration is appropriate for the subpopulation of patients that experience difficulty with a dissolving lozenge (likely due to dexterity, reflex, or other symptomatic issues). EX1002 ¶[0032]; EX1093 ¶¶46-48. A POSA would have also recognized that many other patients would benefit from following the first embodiment of administering a rapidly dissolving lozenge/tablet to a patient's mouth because the prior art recognizes that rapidly dissolving lozenges/tablets desirably provide convenient oral administration to improve compliance for many patients. Petition 7-10. This teaches and suggests an ODT, *supra* Section II.A.1.a, and is

more than sufficient for obviousness because any need or problem can "provide a reason for combining the elements in the manner claimed." *KSR*, 550 U.S. at 420.

2. Dohil In Combination With Venkatesh Motivates Formulating Orally Disintegrating Solids/Tablets

Venkatesh (EX1020) and the '729 patent share co-inventor Gopi M. Venkatesh. EX1020 was assigned to Adare Pharmaceuticals, EX1084, which changed its name to Ellodi Pharmaceuticals in 2020, EX1074. In Venkatesh, PO previously disclosed the same limitations it later claimed in claims 8 and 16-18 of the '729 patent.

Here, PO asserts that Venkatesh requires taste-masking by coating microparticles with a water-insoluble polymer and it argues the coating "would prevent [Dohil's] corticosteroid from being topically deposited in the upper gastrointestinal tract." POR 23, 33-34, 36-37, 39-40.

PO's argument has no merit. The '729 patent and Venkatesh incorporate-by-reference another of PO's patents, U.S. 6,139,865 ("the '865 patent," EX1085).[3] *See* EX1001 2:32-34, 14:44-46; EX1020 ¶¶[0012], [0027]. In the '865 patent, PO repeatedly explained that taste-masking with a water-insoluble polymer does ***not***

[3] The '865 patent was assigned to Adare Pharmaceuticals, EX1086, which changed its name to Ellodi Pharmaceuticals, EX1074.

prevent topical disposition of drug in the upper gastrointestinal tract. Rather, the taste-masking allows the drug to be released "virtually immediate[ly]" and "shortly" after passage through the mouth such that the drug is deposited in the upper GI tract:

- "Although the use of polymeric materials, particularly cellulosic polymers, to taste mask bittertasting drugs is known… the present invention provides for far more effective taste masking than previously possible, using high coating levels ***while nevertheless achieving virtually immediate release of drug***." EX1085 2:65-3:3.[4]
- "The composition comprises microcapsules of drug ***and a substantially water-insoluble polymeric material, typically a cellulosic polymer***.… These high coating levels give rise to effective taste masking, while nevertheless allowing targeted release of drug, ***so that the drug is released shortly after passage through the mouth***." *Id.* Abstract.
- "[T]he invention provides for extremely effective taste masking ***while also providing for release of drug shortly after the drug passes through the mouth***." *Id.* 1:67-2:2.

PO's '865 patent explains that the water-insoluble coating has pores that facilitate rapid release of the drug from the microparticles:

> [I]t is believed that the polymeric walls of the microcapsules, particularly those formed by coacervation, typically have pores. It is

[4] All emphases supplied unless otherwise noted.

> further believed that drug dissolution from the microcapsules occurs through these pores. ***Thus, it is believed that water enters the pores and forms a highly concentrated solution of drug and water inside the microcapsule, and that the resulting concentration gradient from the highly concentrated solution to the surrounding aqueous fluid drives diffusion of the drug out through the pores to the surrounding aqueous fluid***. Another mechanism of release which is believed to occur is breakage of the coating on the microcapsule, possibly caused or promoted by swelling of the core material due absorption of water.

Id. 9:31-45; *id.* 7:52-56, 9:54-55, 15:60-63. PO's expert conceded that such coatings contain pores, EX1072 127:16-128:3, and PO's exhibit confirms that the polymers used for such coatings were "hygroscopic," which means they absorb water. EX2015 192, 477; EX1072 136:20-137:7.

PO's expert failed to consider the '865 patent. EX1072 120:4-122:2, 134:8-135:7. PO's '865 patent, which is incorporated-by-reference into Venkatesh and the '729 patent, is highly relevant and must be considered. *See Ultradent Prods., Inc. v. Life-Like Cosmetics, Inc*., 127 F.3d 1065, 1068-69 (Fed. Cir. 1997); EX1093 ¶¶74-78.

The '729 patent teaches that taste-masking via coating with water-insoluble polymers is compatible with rapidly dissolving tablets to treat inflammation of the esophagus. EX1001 13:59-67, 14:19-67, 16:44-17:9. Thus, PO's position that taste-masking prevents a drug from contacting the esophagus is contradicted by its own

'729 specification and '865 patent. In reality, a POSA expected Venkatesh's taste-mask coating to beneficially prevent the drug from contacting the tastebuds within the patient's mouth, and then release the drug "virtually immediate[ly]" after it passes through the mouth thereby allowing the drug to contact the esophagus. EX1085 Abstract, 1:67-2:2, 2:65-3:3; EX1093 ¶¶79-80.

A POSA was motivated to turn to Venkatesh in formulating Dohil's rapidly dissolving lozenge/tablet with a reasonable expectation of success based on the detailed disclosures within Venkatesh regarding the manufacture of such rapidly dissolving formulations having "a pleasant taste and smooth creamy mouthfeel" that "leads to better compliance with dosing regimen and as a consequence, to enhanced therapy." Institution Decision 11; EX1020 ¶[0002]; Petition 54-57; EX2011 89:14-18, 91:9-14.

3. <u>There was a reasonable expectation of success</u>

PO wrongly asserts that Petitioner and its expert were unable to identify any prior art ODT containing a topically active drug deposited in the upper gastrointestinal tract. POR 35, 9-11. Petitioner and its expert identified Dohil, Grother, Singh, and Cherukuri. Petition 5-6, 10-11. These references disclose ODTs containing budesonide. *Id.*

Budesonide was known to be topically active. *Id.* 5. ODTs rapidly dissolve in the mouth (which is part of the upper gastrointestinal tract), thereby depositing

the drug in the upper gastrointestinal tract. *Id.* 6-7. Petitioner also provided a review article that teaches ODTs were designed to "release the drug to the oral mucosa," EX1017 178, and that many prior art studies had shown topical therapy with corticosteroids to treat inflammatory mucosal diseases, *id.* 176. Other prior art teaches that ODTs are beneficial "when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething." EX1087 129; EX1088 E1; EX1093 ¶¶7-8.

PO asserts that Petitioner only addresses the reasonable expectation of success for Ground 1 limitation 1[iv] and claim 2, and "makes conclusory statements" for Ground 3. POR 37. The expectation of success provided by Petitioner applies to all challenged claims. The claims are merely directed to orally disintegrating compositions. Formulating such compositions was within the level of ordinary skill in the art. For example, Dohil teaches the POSA how to formulate orally disintegrating compositions of budesonide. Petition 24-25. So do Grother, Singh, and Cherukuri. *Id.* 10-11, 40-41. There were at least 30 commercial orally disintegrating products guiding the POSA to successfully arrive at the claimed formulations. *Id.* 8-10. The FDA Guidance confirms that "relatively rapid disintegration is readily achievable across a variety of products." Institution Decision 10; EX1005 2.

The '729 specification admits that orally disintegrating compositions are prepared via a "conventional granulator," a "conventional oven," and a "conventional rotary tablet press." EX1001 16:31-43; EX1093 ¶66. The specification does not provide any special contribution to the field regarding the formulation of orally disintegrating compositions, which is consistent with the maxim that "a patent need not teach and preferably omits, what is well known in the art." *Hybritech Inc v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986). There was a reasonable expectation of success.

4. Dohil Teaches And Suggests The Dosages Recited In Claims 1[i] And 27[i] With An Expectation Of Success

PO asserts that a POSA cannot extrapolate dosage amounts from Dohil's successful treatment of EOE using ***liquid*** formulations from Examples 1-3 because there are supposedly different considerations in formulating ***solid*** compositions. POR 38.

First, PO and its expert fail to articulate how any supposedly different consideration for a solid versus liquid formulation would be material to Dohil's budesonide dosages. The unexplained and unsupported assertion by PO's expert is entitled to no weight. EX2007 ¶¶109-110; 37 C.F.R. §42.62 ("Expert testimony that does not disclose the underlying facts or data… is entitled to little or no weight.").

Second, PO ignores that Dohil teaches appropriate dosages for budesonide that apply to its solid formulations, which provides a reasonable expectation of success. EX1002 ¶¶[0015], [0031]; Petition 20-25.

Third, the POSA's expectation of success is bolstered by numerous FDA-approved examples of solid ODT formulations that have the same drug dosage amount as the corresponding liquid formulation, including:

- CLARITIN® (loratadine) ODT and liquid syrup are dosed at 10 mg, EX1089 2;
- ZOFRAN® (ondansetron) ODT and oral solution are both dosed at either 4 or 8 mg, EX1090 5:125-128;
- CLARINEX® (desloratadine) ODT and liquid syrup are dosed at 5 mg, EX1091 19; and
- PEPCID® (famotidine) ODT and oral suspension are dosed at 40 mg, EX1092 1-2; EX1093 ¶¶49-52.

5. Dohil Teaches And Suggests The Claimed Methods Of Treatment (Claims 29-34)

For claims 29-34, PO repeats its previous assertion that Dohil does not teach or suggest the claimed orally disintegrating composition. POR 38-39. PO is incorrect. *Supra* Section II.A.1.

PO also repeats its previous assertion that Dohil does not provide an expectation of success in achieving the volume/viscosity required to cover the esophagus. POR 39. PO is, again, incorrect. *Supra* Section II.A.1.c; EX1093 ¶¶53-54.

6. Dohil And Venkatesh Render Obvious Claims 16-18

For claims 16-18, PO repeats its argument that Venkatesh's taste-masking prevents the drug from being deposited in the upper gastrointestinal tract. POR 39-40. PO is wrong. *Supra* Section II.A.2; EX1093 ¶81.

B. A POSA Would Have Been Motivated Based On Grother In View Of The FDA Guidance

The Petition provides compelling evidence of obviousness based on Grother in view of the FDA Guidance (Ground 2), and further in view of Venkatesh (Ground 4). Petition 34-51, 58-68. PO's counter-arguments on these grounds are worse than those for Grounds 1 and 3. Petitioner provides the following succinct Reply.

1. Grother And The FDA Guidance Teach, Suggest, And Motivate Formulating Orally Disintegrating Compositions/Tablets

Grother teaches an ODT formulation, EX1008 12:10-19, in which any drug may be used, including budesonide and fluticasone. *Id.* 15:19-20, 18:15-18; Petition 34-37. Grother's instruction to use budesonide and fluticasone in its ODT formulation teaches, suggests, and motivates their use in Grother's ODT.

PO accuses Petitioner of "arbitrarily pick[ing] budesonide and fluticasone" from "disparate embodiments" and "misstat[ing] the law." POR 43-45, 16-17. It is PO, however, that misapplies the law. Petitioner has not arbitrarily picked budesonide and fluticasone from disparate embodiments within Grother. Grother itself undeniably instructs that budesonide and fluticasone should be predictably used in its ODT formulation. EX1008 15:19-20, 18:15-18. The Board found that Grother "teaches that examples of suitable drugs include corticosteroids including, e.g., budesonide." Institution Decision 9-10. PO makes no allegation that Grother teaches away from its instruction to use these drugs. The motivation to use these compounds comes directly from Grother, which is appropriate because "[t]he motivation to combine [can come] from the prior art reference itself." *Acoustic Tech., Inc. v. Itron Networked Sols.*, 949 F.3d 1366, 1375 (Fed. Cir. 2020).

PO's expert seeks to diminish Grother's instruction to use budesonide and fluticasone because they are included in a "long list" of other drugs that may also be used with Grother's "platform" ODT formulation. EX2007 ¶¶115-118; POR 41-44. Yet, when confronted with his own "platform" formulation, he inconsistently testified that ***all*** classes of drugs included in his long lists are suitable for his formulation. EX1072 178:7-179:1, 180:18-181:3; EX1071 Abstract, ¶¶[0043]-[0044]. Regardless of his inconsistent positions, Grother is "relevant for all [it] contain[s]" and must be considered for "its power to suggest solutions" to the POSA.

In re Young, 927 F.2d 588, 591 (Fed. Cir. 1991). Grother's instruction to use budesonide and fluticasone is more than sufficient for obviousness. *See In re Fulton*, 391 F.3d 1195, 1200 (Fed. Cir. 2004) ("the combination claimed [need not be] the preferred or most desirable combination" suggested by the prior art).

Grother's instruction to use budesonide in its ODT formulation is reinforced by at least three other prior art references that also teach the use of budesonide and/or fluticasone in ODTs—Dohil, Cherukuri, and Singh. Petition 10-11 (citing EX1002, EX1035, EX1036); EX1093 ¶¶56-58.

PO asserts that Grother does not suggest using a "topical/non-systemic drug" in its ODT formulation because Grother did not expressly state that budesonide is a topically acting drug. POR 40; *id.* 3, 41-46, 49. A POSA knew that budesonide was a potent topically acting drug that successfully treats inflammation of the gastrointestinal tract, including EOE. Petition 5-6. This background knowledge must be considered in reading the prior art. *See Randall Mfg. v. Rea*, 733 F.3d 1355, 1362 (Fed. Cir. 2013). Grother appropriately refrained from providing such "information readily understood by practitioners, lest every patent be required to be written as a comprehensive tutorial and treatise for the generalist, instead of a concise statement for persons in the field." *Verve, LLC v. Crane Cams, Inc.*, 311 F.3d 1116, 1119 (Fed. Cir. 2002); EX1093 ¶59.

PO asserts non-obviousness because Grother doesn't state that its ODT topically deposits a drug in the upper gastrointestinal tract. POR 42. Such an express statement is not required because Grother teaches that its ODT rapidly releases the drug in a patient's oral cavity, which was known to deposit the drug in the upper gastrointestinal tract. Petition 41; EX1008 3:18-22, 1:10-11, 32:10; *supra* Section II.A.3. The FDA Guidance confirms that ODTs are designed and expected to deposit drugs in the upper gastrointestinal tract. EX1005 1; EX1093 ¶¶60-61.

2. Grother, FDA Guidance, and Venkatesh Motivate Formulating Orally Disintegrating Solids/Tablets

PO repeats its argument that Venkatesh's taste-masking would prevent the drug from being deposited in the upper gastrointestinal tract. POR 47-50. PO is incorrect. *Supra* Section II.A.2.

PO asserts there is no motivation for a POSA to look to Venkatesh. POR 48. A POSA was motivated to turn to Venkatesh in formulating Grother's ODT with a reasonable expectation of success based on the detailed disclosures within Venkatesh regarding the manufacture of such rapidly dissolving formulations having "a pleasant taste and smooth creamy mouthfeel" that "leads to better compliance with dosing regimen and as a consequence, to enhanced therapy." Institution Decision 11; EX1020 ¶[0002]; Petition 59-68; EX1093 ¶¶82-83; EX2011 89:14-18, 91:9-14.

PO repeats its assertion that Petitioner and its expert were unable to identify prior art ODTs containing a topically active drug deposited in the upper gastrointestinal tract. POR 49. PO is incorrect. *Supra* Section II.A.3.

PO asserts that there are supposedly different considerations in formulating systemic drugs in ODTs than topical drugs. POR 48-49. First, PO and its expert fail to articulate how any supposedly different consideration is material to Grother's express instruction that "[a]ny drug may be used" in its ODT, including "budesonide" and "fluticasone." EX1008 15:19-20, 18:15-18; Petition 34-37. PO's expert provides no explanation or support for his assertion, and it is therefore entitled to no weight. EX2007 ¶121; 37 C.F.R. §42.62. Second, the expectation of success from Grother is reinforced by other prior art references that likewise provide an express instruction to use budesonide and/or fluticasone in ODTs—Dohil, Cherukuri, and Singh. Petition 10-11 (citing EX1002, EX1035, EX1036); EX1093 ¶¶62-65.

The '729 specification admits that orally disintegrating compositions are prepared via a "conventional granulator," a "conventional oven," and a "conventional rotary tablet press." EX1001 16:31-43; EX1093 ¶66. The claims are obvious because "the claimed invention adds nothing beyond the teachings of [the prior art]." *Merck & Co. Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1374 (Fed. Cir. 2005).

3. Grother And The FDA Guidance Teach And Suggest The Dosages Recited In Claims 1[i], 27[i], 28, And 38-40 With An Expectation Of Success

PO asserts that a POSA would not have been motivated to arrive at the claimed dosage amounts with a reasonable expectation of success because there are supposedly different considerations in formulating solid ODTs to deposit a topical drug in the upper gastrointestinal tract than formulating liquid compositions, enterically coated tablets, and rectal foam. POR 51. This assertion is unavailing for several reasons.

First, PO's expert admits that "there is no dispute that budesonide, fluticasone, or other topical corticosteroids could be used to treat inflammation of the upper gastrointestinal tract." EX2007 ¶65; *id.* ¶76. Second, PO and its expert fail to articulate how any supposedly different consideration in formulating solid ODTs to deposit a topical drug in the upper gastrointestinal tract versus other types of formulations would be material to the dosage amount of drug used in Grother's ODT. Third (and contrary to PO's assertions otherwise, POR 51-52), the Petition and Dr. Parr explain that a POSA was motivated to formulate Grother's ODTs with budesonide at, e.g., 3 mg, with a reasonable expectation of success based on Grother's instruction that its compositions should normally have 1-20% by weight active ingredient and the general knowledge in the art that topically administrable formulations of budesonide typically contain, e.g., 3 mg of budesonide. Petition 36-

37; EX1030 ¶176; EX1093 ¶¶67-70. Fourth, the POSA's expectation of success is bolstered by numerous FDA-approved examples of solid ODT formulations having the same drug dosage as the corresponding liquid formulation. *Supra* Section II.A.4. Fifth, the '729 patent fails to distinguish between different dosage amounts across different formulations. EX1001 7:18-60; EX1093 ¶¶71-72. Sixth, PO's expert admits that Grother's ODT formulation "works with any class of drugs." EX2007 ¶118.

4. Grother, the FDA Guidance, and Venkatesh render obvious claims 16-19

For claims 16-19, PO repeats its argument that Venkatesh's taste-masking prevents the drug from being deposited in the upper gastrointestinal tract. POR 52. PO is incorrect. *Supra* Section II.A.2; EX1093 ¶84.

III. CONCLUSION

The challenged claims should be cancelled.

Dated: July 14, 2025

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that this PETITIONER'S REPLY BRIEF contains 5,587 words according to the word-processing program used to prepare this paper. The foregoing word count complies with the 5,600-word type-volume limit specified by 37 C.F.R. § 42.24(c)(1).

Dated: July 14, 2025

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CERTIFICATE OF SERVICE

The undersigned hereby certifies that on the date below a copy of this **PETITIONER'S REPLY BRIEF** was served by email on the Patent Owner at the following email addresses:

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