

Case No. PGR2025-00086

Patent No. 12,290,598

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. PGR2025-00086
Patent No. 12,290,598

PATENT OWNER'S PRELIMINARY RESPONSE

37 C.F.R. § 42.107

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Exhibit No.	Description of Document
2001	Request for Certificate of Correction for U.S. Patent No. 12,290,598
2002	Dellon, E.S. et al., Fluticasone Propionate Orally Disintegrating Tablet (APT-1011) for Eosinophilic Esophagitis: Randomized Controlled Trial, <i>Clinical Gastroenterology and Hepatology</i> 20:2485–2494 (2022)
2003	Excerpt from the file history of U.S. Patent No. 10,632,069
2004	<i>Reserved</i>
2005	Iorgulescu, G., Saliva between normal and pathological. Important factors in determining systemic and oral health, <i>Journal of Medicine and Life</i> Vol. 2, No.3, July-September 2009, pp.303-307
2006	Miehkle, S. et al., A randomised, double-blind trial comparing budesonide formulations and dosages for short-term treatment of eosinophilic oesophagitis, <i>Gut</i> 0:1-10 (2015)
2007	Declaration of Martyn Christopher Davies in Support of Patent Owner's Preliminary Response
2008	<i>Curriculum Vitae</i> of Martyn Christopher Davies
2009	<i>Reserved</i>
2010	Clinical Trials Study, "Efficacy, Safety, and Pharmacokinetics of APT-1011 in Subjects With Eosinophilic Esophagitis (EoE)(FLUTE)," last updated Apr. 26, 2023, https://clinicaltrials.gov/study/NCT03191864?tab=results&a=11#outcome-measures
2011	Transcript of the April 9, 2025 Deposition of Alan F. Parr, Pharm.D., Ph.D. from No. IPR2024-01197
2012	"Antrum" Definition, <i>American Medical Dictionary: A Concise and Up-to-Date Guide to Medical Terms</i> (1998)

Exhibit No.	Description of Document
2013	M.E. Aulton (Ed.), <i>Pharmaceutics: The Science of Dosage Form Design</i> (2d. 2002)
2014	“Lozenge” Definition, Dennis B. Worthen (ed.), <i>Dictionary of Pharmacy</i> (2004)
2015	Paul J. Sheskey et al., <i>Handbook of Pharmaceutical Excipients</i> (8d. 2017)
2016	Hahm, H.A., Augsburger, L.L., Ch. 9 Orally Disintegrating Tablets and Related Tablet Formulations
2017	Ghosh, T.K. et al, Drug Delivery to the Oral Cavity Molecules to Market, Ch. 14 Quick dissolving oral dosage forms: Scientific and regulatory considerations from a clinical pharmacology and Biopharmaceutics Perspective (2005)
2018	Transcript of the August 25, 2025 deposition of Alan Parr, Pharm.D. from No. IPR2024-01197
2019	<i>Reserved</i>
2020	Cordova-Fraga T, Sosa M, Wiechers C, et al., Effects of anatomical position on esophageal transit time: a biomagnetic diagnostic technique. <i>World J Gastroenterol</i> 14:5707–11 (2008)
2021	U.S. Patent No. 8,324,192
2022	Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, Patent and Exclusivity for: N213976, Product 001 Budesonide (Eohilia) Suspension 2mg/10ml, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=213976&Appl_type=N
2023	<i>Reserved</i>
2024	<i>Reserved</i>

Exhibit No.	Description of Document
2025	<i>Reserved</i>
2026	<i>Dr. Falk Pharma GMBH v. Ellodi Pharms., L.P.</i> , IPR2024-01197, EX1093 (P.T.A.B. July 10, 2024)
2027	<i>Reserved</i>
2028	<i>Reserved</i>
2029	<i>Reserved</i>
2030	<i>Reserved</i>
2031	Highlights of Prescribing Information for EOHILIA™
2032	Sonnegaard, J.M. et al., Comparative Investigations of Tablet Crushing Force Testers, Pharm. Ind. 67, Nr. 1, 109–115 (2005)
2033	Dr. Schleuniger® Pharmatron Tablet Hardness Measuring Technology, Key Factors Influencing measured tablet hardness (2011)
2034	USP <1151>, Pharmaceutical Dosage Forms, https://www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/pharmaceuticalDosageForms.pdf

I. INTRODUCTION

Eosinophilic esophagitis (“EoE”) is a painful disease, characterized by inflammation of the esophagus and difficulty swallowing. EX1001, 1:31-40. U.S. Patent No. 12,290,598 (the “’598 patent”) claims an orally disintegrating tablet (“ODT”), comprising a topical corticosteroid, which disintegrates within 60 seconds, that deposits a therapeutically effective amount of the corticosteroid in the esophagus to treat EoE. Before the patent family that led to the ’598 patent, no one in the field of pharmaceutical formulation development recognized how an ODT, as claimed in the ’598 patent, could be formulated to deposit a topical corticosteroid in the esophagus and treat EoE.

Petitioner Dr. Falk Pharma GMBH (“Petitioner”) challenges the claims of the ’598 patent based on twelve Grounds, half of which are mooted by correcting a typographical error in claim 1 of the ’598 patent. Pet., 24-51. In the remaining Grounds, Petitioner relies on impermissible hindsight and uses the ’598 patent claims as the blueprint rather than the teachings of the prior art to establish obviousness. Pet., 51-87.

Specifically, in Grounds 1-4, Petitioner argues that because claim 1 recites a range of “4-48 N,” but the ’598 patent’s specification only discloses a hardness value between 8-48 N, the claims are invalid under § 112 for lack of written description, lack of enablement, and indefiniteness. Pet., 24-40. Claim 1 includes an inadvertent

typographical error that was introduced during prosecution and should instead recite a hardness range of “8-48 N.” Patent Owner has submitted a Request for Certificate of Correction to fix this typographical error and would moot Petitioner’s arguments for written description and enablement. EX2001. The Board has stayed Patent Owner’s Request, prior to issuing an institution decision. Paper 7. Patent Owner respectfully requests the stay be lifted so the typographical error can be corrected prior to an institution decision. Doing so would allow the Director to address the merits of Patent Owner’s Request for Certificate of Correction, which is properly the Director’s authority pre-institution, not the Board’s. And once the claims are corrected, the Board can address the merits of the Petition based on the corrected claims. *See Honeywell Int’l Inc. v. Arkema, Inc.*, 939 F.3d 1345, 1349 (Fed. Cir. 2019).

Petitioner also asserts that the claims are not enabled and indefinite because a person of ordinary skill in the art (“POSA”) would not know how to test for hardness. Pet., 34-40. Petitioner ignores its own cited references that illustrate that hardness testing is routine and provide guidance and recommendations for determining the hardness value that is accepted and followed. Petitioner also ignores well-settled precedent establishing that routine or standard industry practice does not need to be described in the specification. *See Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987); *Koito Mfg. Co. v. Turn-Key-Tech, LLC*, 381 F.3d 1142,

1156 (Fed. Cir. 2004). Thus, based on the knowledge of a POSA, Petitioner has not shown how the claims lack enablement or definiteness.

In Grounds 5-6, Petitioner relies on Perrett for anticipation and obviousness, but Perrett is not prior art to the '598 patent. Pet., 41-51. Petitioner relies on the typographical error reciting a hardness value of “4-48 N” made during prosecution to assert that the priority date for the '598 patent cannot be earlier than January 5, 2022, but this is incorrect. Pet., 41. Rather, the '598 patent is entitled to a priority date of October 1, 2009, and should be evaluated as such once the stay on Patent Owner's Request for Certificate of Correction is lifted and the claims are corrected to reciting a hardness value of “8-48 N.”

Finally, in Grounds 7-12, Petitioner relies on two primary references to assert obviousness: Dohil, and Grother. Pet., 51-86. All six Grounds further rely on secondary references Kararli, the FDA Guidance, and USP <701>, <1216>, and <1217>. Pet., 51-66, 68-85. Four of the six grounds further rely on Venkatesh988 or Venkatesh516. Pet., 61-68, 81-86. In each of these Grounds, Petitioner begins with the claims of the '598 patent and works backwards, relying on conclusory expert testimony, to suggest formulating an ODT comprising a topical corticosteroid to treat EoE. In particular, Petitioner begins with the incorrect presumption that a POSA would be motivated to formulate an ODT, rather than the correct presumption that the POSA's motivation would be to treat EoE.

Petitioner's Dohil reference discloses an efficacious aqueous solution comprising budesonide to treat EoE. The only solid formulation Petitioner identifies in Dohil is a passing reference to a lozenge, which is a significantly different formulation from an ODT, and is not exemplified or shown to be effective in the prior art. Petitioner's arguments regarding motivation to combine and reasonable expectation of success are similarly conclusory and do not address why anyone would modify Dohil's efficacious aqueous solution into a solid formulation or how they could successfully do so without first looking at the '598 patent.

Petitioner's Grother reference fares even worse. Petitioner cherry picks two topical corticosteroids out of the hundreds of drugs listed in Grother, which is not directed to any disease and does not teach ODTs designed to topically deposit a topical drug in the esophagus for treatment of EoE. Rather, Grother is directed to eliminating mammalian gelatin from its fast dispersing oral dosage forms. Petitioner again fails to explain why, based on the disclosure in Grother, a POSA would be motivated to formulate an ODT to treat EoE, or had any success in doing so.

Nor do Petitioner's secondary references cure the deficiencies in Dohil or Grother. Kararli is directed to a different type of tablet containing a different type of drug that is not topically deposited in the esophagus. The FDA Guidance and USP chapters provide general guidance and definitions to a POSA that do not direct anyone to formulate an ODT for any specific disease. Venkatesh988 and

Venkatesh516 do not disclose formulating an ODT comprising a topical corticosteroid, but rather teach taste-masking drug particles which would, in fact, *prevent* any drug from contacting the esophagus, defeating the purpose of treating the esophagus. Neither Petitioner, nor its expert, provide any rationale as to why a POSA would combine the references in the manner outlined in the Petition. This is because Petitioner begins with the claims of the '598 patent instead of beginning with the disclosures in the prior art which effectively treat EoE. Petitioner's conclusory statements fall far short of any rational underpinning of why a POSA would have been motivated to combine the references, or had any reasonable expectation of success, and the Petition's analysis is therefore deficient.

Further, Venkatesh516 is not available as prior art against claims 24 and 26, without considering the Certificate of Correction, or any of the claims once the Certificate of Correction is granted. Because Venkatesh516 is the only reference cited against claim 26, and Venkatesh516 is not available as prior art against this claim, Petitioner has failed to establish *prima facie* obviousness at least for claim 26.

Accordingly, Petitioner has not carried its burden to show that it is reasonably likely to prevail on any Grounds it challenges against the '598 patent. Correction of claim 1 moots a number of Petitioner's asserted Grounds. Petitioner's remaining grounds are flawed for applying incorrect law, impermissible hindsight, and deficient analysis on obviousness. The Board should deny institution.

II. BACKGROUND

A. Treatment of EoE

Eosinophilic esophagitis (“EoE” or “EE”) is an inflammatory condition of the esophagus. EX1001, 1:35-37. It is a painful disease, and symptoms include vomiting, dysphagia, and abdominal pain, among others. EX1033, 1216; EX1001, 1:37-40; EX1002, [0003]. Treating EoE is incredibly difficult. EX1033, 1216, 1223; EX1001, 1:41-62; EX1002, [0006]-[0007]. Prior treatments for EoE included a “strict elemental diet” and systemic corticosteroids. EX1033, 1216; EX1001, 1:54-62; EX1002, [0006]. Both of these treatments posed problems, however, as strict elemental diets had significant compliance issues and systemic corticosteroids caused immune suppression and stunted children’s growth. EX1033, 1216-1217, 1219, 1223; EX1001, 1:41-62; EX1002, [0005]-[0007]; EX2007, ¶¶51-53.

Other treatments for EoE included the use of topical corticosteroid, such as fluticasone propionate or budesonide, which must be deposited on the inflamed tissue of the esophagus to be effective. *See generally* EX1001; EX1033; EX1002. By 2009 it was known that depositing an effective dose of the corticosteroid to the target area of the esophagus is challenging, because of the anatomical location, constant flow of saliva down the esophagus, and peristalsis pushing liquid and the therapeutics down the esophagus toward the stomach. EX2007, ¶51; EX1001, 1:41-62; EX1002, [0007]. Another complication with administering oral topical

corticosteroids is candidiasis infections (also known as oral thrush). EX1001, 1:46-48; EX1033, 1216-1217, 1219. Prior to the '598 patent, only two types of formulations were shown to effectively deliver topical corticosteroids to the esophagus. EX1001, 1:41-62; EX1002; EX1014; EX1015; EX1033; EX1065; EX1066. One method for administering a topical corticosteroid to the esophagus was through a metered inhaler, where the aerosolized corticosteroid was swallowed instead of inhaled. EX1001, 1:41-53; *see also* EX1033, 1217; EX1065, 4; EX1066, 1382. To prevent a candidiasis infection and keep the drug from washing away from the esophagus, patients were instructed “to rinse their mouth immediately after administration and not to swallow food or water for two hours after administration[,]” respectively. EX1001, 1:41-53; *see also* EX1033, 1217. Aqueous solutions containing the topical corticosteroid, such as those described in Aceves 2005, Aceves 2007, and Dohil, were another way to apply the topical corticosteroid to the esophagus. *See generally* EX1014; EX1015; EX1002. To promote contact of the corticosteroid with the esophagus, patients receiving these aqueous solutions were also instructed not to swallow food or water for at least 30 minutes after administration to not wash the drug away. *See generally* EX1014; EX1015; EX1002. The aqueous solution containing budesonide described in Aceves 2005, Aceves

2007, and Dohil is now sold as Eohilia, marketed by Takeda Pharmaceuticals¹. EX2031, 2.

B. Orally Disintegrating Tablets (ODTs) and Lozenges

Prior to the '598 patent, ODTs had not been used to topically administer any drug to the esophagus. EX2007, ¶54; EX2011, 18:5-13. ODTs were known to effectively deliver systemically acting drugs to patients. *See generally* EX1017, EX1018, EX1019. One of the main advantages of ODTs was easier administration of systemic drugs for children and elderly patients so these patient populations did not need to swallow a tablet whole. EX1017, 173-174; EX1018, 434; EX1019, 311. By allowing the tablet to disintegrate in the patient's mouth, systemic drugs were easily swallowed and delivered to the gut for systemic absorption. EX1017, 173-174; EX1018, 434; EX1019, 311. Because the ODT disintegrates in the mouth, taste-masking technologies were developed for use with ODTs to prevent drug release in the mouth and still allow for systemic absorption with an immediate release profile. EX1018, 434; EX1019, 310-311; EX1020; EX1111. As of 2009, commercially available ODTs consisted of ODT products comprising systemically acting drugs. Pet., 12-14; EX1017, 178-180; EX1018, 438-439; EX1019, 312.

¹ Dohil (EX1002) was issued as U.S. Patent No. 8,324,192 (EX2021) which is listed in the Orange Book for Eohilia. EX2022.

The FDA Guidance provides a specific definition for ODTs, namely that ODTs are “solid oral preparations that disintegrate rapidly in the oral cavity, with an in-vitro disintegration time of approximately 30 seconds or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative (see section IV).” EX1005, 2. The FDA Guidance further clarifies that applicants use the USP <701> Disintegration Test. EX1005, 3. However, there is no discussion of using ODTs to topically administer corticosteroids to the esophagus or topically treating inflammatory conditions of the upper gastrointestinal tract. EX2007, ¶126.

Lozenges were also well-known by 2009 and were recognized as a distinct and separate oral dosage form from ODTs. EX1017, 178, 181 (distinguishing quick-disintegrating tablets from lozenges); EX2016, 293 (“Despite a surge of orally disintegrating tablets in the market in the recent years, they potentially can be confused with other solid oral dosage forms that are consumed without additional water intake, including lozenges, buccal tablets, and chewable tablets.”); EX2017, 341 (distinguishing quick/fast/rapid/mouth-dissolving tablets and fast/quick-melting tablets from lozenges); EX1104, 676 (describing a “variety of presentations for tablets” and distinguishing “rapidly disintegrating” tablets and lozenges). Further, USP <1151>, titled Pharmaceutical Dosage Forms, distinguishes lozenges from ODTs. *Compare* EX2034, 1289 (describing lozenges) *with* EX2034, 1303 (describing ODTs).

One of the main distinctions is that lozenges, by definition, dissolve slowly over time – i.e., over several minutes. EX2016, 293 (“Lozenges and buccal tablets are intended to dissolve *slowly* in the mouth, whereas, orally disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds.”) (emphasis added); EX2013, 413; *see also* EX2014, 201 (defining a lozenge as a “solid preparation...intended to dissolve or disintegrate *slowly*”) (emphasis added).

C. Hardness

Tablet hardness is the tablet’s breaking force or resistance to breakage in a specific plane. EX1104, 676; EX1106, 882. A number of manual hardness testers have been manufactured since the mid-1900s, such as the Monsanto, or Stokes, Strong-Cobb, and Pfizer hardness testers. EX1106, 883. These testers, however did not always give equivalent results due to inherent variation in the testers themselves and operator variation. EX1106, 883; EX1107, 928; EX1104, 676. Thus, these manual hardness testers were no longer used by 2009. EX1106, 883. The most commonly used apparatus as of 2009 was the automated, or electrically operated, Schleuniger apparatus. EX1106, 883. Automated testers eliminated the variability in results associated with the manual testers. EX1106, 883; EX1104, 676. A comparison study from 2005 also showed that 16 testers from three different manufacturers, Schleuniger, Pharma Test, and Erweka, showed a deviation in hardness value of about 10% on average when compared to each other. *See generally*

EX2032. While some variation among automated testers may still exist, USP <1217> instructs routine calibration and consistent procedures to ensure accurate and consistent results. EX1104, 677. USP <1217> also provides guidance and procedures to ensure proper calibration and testing across hardness testers. EX1104, 677-678. Thus, as of the filing date of the '598 patent, a POSA would have used automated hardness testers, calibrated it according to USP guidelines, and expected consistent results across automated hardness testers. EX2007, ¶¶81-83.

III. THE LEVEL OF ORDINARY SKILL IN THE ART

In this proceeding only, Patent Owner generally accepts Petitioner's proposed level of ordinary skill in the art. *See* Pet., 22-23.

IV. CLAIM CONSTRUCTION

In this proceeding only, Patent Owner generally accepts Petitioner's proposed constructions. *See* Pet., 23-24.

V. THE '598 PATENT (EX1001)

The '598 patent is directed to ODTs containing a topically active corticosteroid, selected from budesonide or fluticasone propionate, that topically administers a therapeutically effective amount of a corticosteroid to inflamed tissue of the upper gastrointestinal tract for the treatment of conditions associated with inflammation of the upper portion of the gastrointestinal tract. EX1001, 1:25-40, 5:15-38, 7:25-36, cl. 1. As explained in Section II.A, topically depositing a

therapeutically effective amount of a topically acting corticosteroid to the upper gastrointestinal tract (e.g., esophagus) is challenging, due to the constant flow of saliva, peristalsis, and gravity pushing material down toward the stomach. EX1033, 1217, 1219, 1223; EX1001, 1:41-62; EX1002, [0006]-[0007]; EX2007, ¶51. Prior treatments for EoE included corticosteroid formulations designed for inhalation that were instead applied to the back of the throat, (EX1001, 1:41-53; EX1033, 1217), as well as oral administration of systemically active corticosteroids (EX1033, 1216; EX1001, 1:54-62; EX1002, [0006]). These treatments posed undesirable side effects, including candidiasis infection and suppression of immune function, respectively. EX1001, 1:46-48; EX1033, 1216-1217, 1219.

Despite these challenges, Patent Owner developed the first ODT for topical treatment of EoE. The ODT and method of treatment claimed in the '598 patent solves these problems by formulating an ODT with a topical corticosteroid, which has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration (i.e., a topically active corticosteroid). EX1001, 3:25-42, cl. 1. The ODT disintegrates within 60 seconds to form a solution or dispersion that is swallowed, and the corticosteroid is released and budesonide is topically deposited on the upper gastrointestinal tract, including the esophagus. EX1001, 5:15-32. Disintegration of the tablet and dissolution (drug release) occur near simultaneously, resulting in drug deposition on the esophagus within 1-2 seconds of swallowing and

before the disintegrated tablet passes to the stomach. EX1001, 5:15-32, cl. 1; EX2020, 5708 (“liquid [esophageal transit time] lasts approximately 1 to 2 s”). This mechanism of localized delivery mitigates the undesirable side effects of systemic corticosteroids used for treating EoE and candidiasis infections associated with oral corticosteroid administration. EX1001, 2:3-12, 4:7-17.

Patent Owner also surprisingly discovered that the claimed ODT can deposit a therapeutically effective amount of a topically acting corticosteroid on the esophagus in the short period of time (~1-2 seconds) it takes the suspension to transit the esophagus and effectively treat EoE, without causing candidiasis infections. *See generally* EX2010; EX2020, 5708. It is surprising that the claimed pharmaceutical composition mitigates candidiasis since an orally disintegrating composition would remain in the oral cavity longer than formulations designed for inhalation that are instead applied to the back of the throat or liquid formulations. EX2003, 188; *see also* EX2010, 89.

VI. PROSECUTION OF THE '598 PATENT

The '598 patent issued from U.S. Application No. 17/569,047 (the “'047 Application”), and claims priority to U.S. Provisional Patent Application No. 61/247,642 (the “'642 Provisional Application”). EX1001, cover. Patent Owner filed the '047 Application on January 5, 2022. EX1001, cover. During prosecution, the Examiner rejected the pending claims for non-statutory double patenting over

U.S. Patent Nos. 8,771,729 (the “’729 patent” or “Perrett”) and 9,486,407 (the “’407 patent”). EX1096, 172-176. The Examiner also rejected the pending claims for statutory double patenting over U.S. Patent No. 11,266,598. EX1096, 177. Patent Owner overcame the non-statutory double patenting rejections by filing a terminal disclaimer to the ’729 and ’407 patents. EX1096, 165-167. Patent Owner stated in its response to the Examiner’s rejection that it is not “acquiescing to the merits of the rejection[.]” EX1096, 157.

Patent Owner also amended the claims in response to the statutory double patenting rejection. EX1096, 151-158. Specifically, Patent Owner amended the dosage recited in claim 1, and added the hardness and friability limitations:

1. (Currently Amended) An orally disintegrating tablet comprising:
 - (i) about ~~[[1]]~~0.5 mg to about 6 mg of ~~fluticasone propionate~~ a corticosteroid selected from fluticasone propionate or budesonide; and
 - (ii) at least one disintegrant;wherein upon administration a therapeutically effective amount of ~~fluticasone propionate~~ the corticosteroid is deposited topically in the ~~upper gastrointestinal tract~~ esophagus, and wherein the orally ~~dispersing-disintegrating~~ tablet disintegrates within 60 seconds when tested using the USP <701> Disintegration Test, and
wherein the orally disintegrating tablet has a hardness of 4-48 N or a friability of not more than 1%.

EX1096, 151. Patent Owner pointed to the ’598 patent specification generally and Example 1 for support for these amendments. EX1096, 156. Patent Owner also

submitted an Information Disclosure Statement (“IDS”), which included Petitioner’s Petition for *Inter Partes* Review of the ’729 patent and all exhibits. EX1096, 144.

The Examiner subsequently issued a Notice of Allowance. EX1096, 75-82. In the Notice of Allowance, the Examiner stated:

The closest prior art is Singh *et al.* (US 7,122,198) []. Singh *et al.* teach a fast dissolving composition (Abstract), in the form of a compressed tablet which when orally administered dissolves or disperses in the mouth within one minute (Col. 2, lines 30-36 and Col. 24, lines 2-6). The drugs include glucocorticoids such as budesonide (Col. 16, lines 56-58). However, Singh *et al.* do not teach or suggest that their fast dissolving tablet contains about 0.5 mg to about 6 mg of budesonide, the deposition of the corticosteroid in the esophagus, or that the hardness of the tablet is 4-48 N or the friability of not more than 1 %, as recited in instant claim 1.

EX1096, 80. The Examiner further concluded that a prior art search

did not uncover a reference that teaches an orally disintegrating tablet comprising about 0.5 mg to about 6 mg of a corticosteroid selected from fluticasone propionate or budesonide and at least one disintegrant wherein the corticosteroid is deposited in the esophagus, and the tablet has a hardness of 4-48 N or a friability of not more than 1%, as recited in the instant claims.

EX1096, 80. On January 22, 2025, Patent Owner submitted a Request for Continued Examination (“RCE”) and filed an IDS. EX1096, 50-57. In the IDS, Patent Owner

submitted papers from related *inter partes* review petitions challenging the claims of four patents related to the '598 patent. EX1096, 50-55. Specifically, Patent Owner provided Patent Owner's Preliminary Response submitted in IPR2024-01197 regarding the '729 patent, and petitions in IPR2025-00052 challenging U.S. Patent No. 10,632,069, IPR2025-00054 challenging U.S. Patent No. 11,246,828, and IPR2025-0055 challenging the '407 patent. EX1096, 50-55. The same Petitioner here submitted the petitions in the related IPR proceedings, asserting the same references, including Dohil, Grother, Venkatesh988, and the FDA Guidance. *See* IPR2024-01197; IPR2025-00052; IPR2025-00054; IPR2025-00055 (collectively, the "related IPRs"). Importantly, in addition to submitting the IPR petitions, Patent Owner also submitted Dohil, Grother, Venkatesh988, and the FDA Guidance in IDS filings throughout prosecution prior to allowance and the RCE². EX1096, 43, 50-55, 143, 144, 304. On February 6, 2025, Patent Owner filed another IDS, which included the Board's institution decision in IPR2024-01197, relating to the '729 patent. EX1096, 43.

² Patent Owner submitted Dohil and Venkatesh988 in an IDS on August 11, 2022, before Petitioner had filed the first of many petitions attacking Patent Owner's patents.

On March 24, 2025, the Examiner subsequently issued another Notice of Allowance. EX1096, 12-18. The Examiner maintained her reasons for allowance, again citing to Singh as the closest prior art and stating that she uncovered no prior art reference that teaches the instant claims. EX1096, 16. The Examiner also acknowledged the January 22, 2025 and February 6, 2025 IDS's, and found that the filings

did not change the previous determination of patentability since the references do not teach an orally disintegrating tablet comprising about 0.5 mg to about 6 mg of a corticosteroid selected from fluticasone propionate or budesonide and at least one disintegrant wherein the corticosteroid is deposited in the esophagus, and the tablet has a hardness of 4-48 N or a friability of not more than 1%, as recited in the instant claims.

EX1096, 16. Thus, the Examiner considered Petitioner's arguments asserting Dohil, Grother, Venkatesh988, and the FDA Guidance which refers to USP<701>. made in IPR2024-01197, IPR2025-00052, IPR2025-00054, and IPR2025-00055.

The '598 patent issued on May 6, 2025. EX1001, cover. On October 14, 2025, Patent Owner filed a Request for a Certificate of Correction to correct an obvious typographical error. EX2001. Specifically, Patent Owner seeks to correct inadvertent errors in the claims that recite a hardness value of "4-48 N" to "8-48 N." EX2001, 1-2. As explained in Patent Owner's Request, the errors are clerical or typographical in nature, are of minor character, and do not constitute new matter or require

reexamination, as the only hardness value disclosed in the specification is “8-48 N.” EX2001, 1-2.

VII. PETITIONER’S GROUNDS 1-4 FAIL

A. The Board’s Stay of Patent Owner’s Request for Certificate of Correction Should be Lifted

As discussed above, Patent Owner filed a Certificate of Correction to fix an obvious typographical error in claim 1 of the ’598 patent. EX2001. On December 18, 2025, the Board stayed Patent Owner’s Request. Paper 7. While the Board may exercise exclusive jurisdiction over a patent pre-institution, it is not obligated to do so. 37 C.F.R. § 42.3; *see also ipDataTel, LLC v. ICN Acquisition, LLC*, IPR2018-01822, Paper 19 at 7 n.4, 14-17 (P.T.A.B. April 22, 2019). The Board has routinely declined exercising its optional jurisdiction where they have yet to make a decision on institution. *See, e.g., Samsung Elecs. Co. v. Anonymous Media Rsch. Holdings LLC*, IPR2024-01350, Paper 19 at 22-23 (P.T.A.B. March 21, 2025) (deciding whether to exercise its jurisdiction over patent owner’s certificate of correction until *after* making a decision on institution); *Askeladden L.L.C. v. Encoditech, LLC*, IPR2017-00452, Paper 7 at 3-4 (P.T.A.B. March 31, 2017) (declining to stay patent owner’s request for certificate of correction prior to the institution decision, finding that “[s]hould trial be instituted, it is in the interest of the parties and the public that the corrected claim be the subject of our final written decision.”). Further, it is “the Director—not the Board—[that] will evaluate the merits of the patentee’s petition,

including whether the mistake is of ‘minor character’ or ‘occurred in good faith.’ *See* 35 U.S.C. § 255.” *Honeywell Int’l*, 939 F.3d at 1349. The Board should allow the Director to evaluate Patent Owner’s Request on the merits prior to a decision on institution so that the typographical error is corrected and the Board can evaluate Petitioner’s and Patent Owner’s arguments on the corrected basis.

B. Patent Owner’s Request for a Certificate of Correction Renders Grounds 1 and 2 Moot

Patent Owner has submitted a Request for a Certificate of Correction to correct the limitation to read a “hardness of 8-48 N.” EX2001. This obviates Petitioner’s § 112 arguments, as there is written description and enablement support in the specification of the ’598 patent for a “hardness of 8-48 N.” Pet., 24-37; EX1001, 17:40-18:24.

As explained in the Request for Certificate of Correction, Patent Owner amended the claims to, among other things, recite the hardness limitations to overcome a statutory double patenting rejection. EX2001, 1. In its Remarks Made in Amendment, Patent Owner pointed to Example 1 for support of the amendments. EX1096, 156. Example 1 is the only place a hardness value is disclosed in the ’598 patent, which recites a hardness of 8-48 N. EX1001, 18:6-17. Thus, the file history is clear that Patent Owner intended to amend the claims to recite “8-48 N” and inadvertently introduced a mere typographical error reciting “4-48 N” instead.

Based on Patent Owner's Request for Certificate of Correction, which will correct the typographical error introduced during prosecution of the '598 patent, Petitioner's arguments in Grounds 1 and 2 are moot. EX2001. With respect to Ground 1, Petitioner argues that there is no written description for a hardness value below 8 N. Pet., 24-28. Regarding Ground 2, Petitioner argues that the claims are not enabled for a hardness value below 8 N. Pet., 28-33. Once corrected, however, the claims will not recite a hardness value below 8 N, obviating both of Petitioner's arguments with respect to written description and enablement. EX2001. *See ipDataTel*, IPR2018-01822, Paper 19 at 7 n.4, 14-17(denying institution in part because the asserted grounds no longer addressed the language of the claims based on changes to the claims made by a Certificate of Correction issued after the Petition but prior to the institution decision.)

Further, there is certainly written description support for a hardness of 8-48 N in the '598 patent specification, and Petitioner does not argue otherwise. EX1001, 18:7-17. As described in further detail below, the '598 patent also enables a POSA to arrive at the claimed ODT having a hardness of 8-48 N. Thus, Grounds 1-2 are moot, and the Petitioner fails to show it is more likely that any of the challenged claims are unpatentable based on Grounds 1-2.

C. Petitioner Has Not Shown a Likelihood of Succeeding on the Merits for Grounds 3-4

In Grounds 3 and 4, Petitioner asserts that the claims are not enabled and are indefinite, respectively, because a POSA would not be in possession of the full scope of the claims. Pet., 34-40. For both Grounds, Petitioner argues that because the '598 patent does not teach a POSA how to measure the claimed hardness, and there are multiple ways to measure hardness, the claims must not be enabled and indefinite. Pet., 34-40. Petitioner is wrong.

The hardness of a tablet is an important consideration during formulation development and is routinely measured. EX1104, 676. Petitioner cites to a number of different hardness testers sold since the mid-1900s. Pet., 34, 38. As explained in Section II.C, however, by 2009 the most commonly used hardness testers were automated, which eliminated the variability inherent in the manual testers, such as Monsanto/Stokes, Strong-Cobb, and Pfizer. EX1106, 883; EX1104, 676. USP <1217> further instructs routine calibration and offers guidance to ensure consistent and accurate results when using automated testers. EX1104, 677-678. As Petitioner admits, the USP is a recognized authority in the pharmaceutical field, and a POSA would have followed the USP's recommendations. Pet., 57-58, 76-77. Thus, by 2009, a POSA would have known to use an automated hardness tester, and routinely calibrate it for consistent results. EX1004, 677; EX2007, ¶84. The USP also

discloses that changing testing units is possible, as long as comparison tests are run. EX1104, 677. A POSA would therefore know that the hardness value across different testing methods will yield comparable results. EX2007, ¶84. As described in further detail below, the '598 patent did not need to describe the precise hardness tester used, because such hardness testers were well known and yielded equivalent results. *See Spectra-Physics*, 827 F.2d at 1534; *Koito Mfg.*, 381 F.3d at 1156.

Further, a comparison study of hardness testers concluded that hardness values deviate among testers by about 10%. EX2032, 112-115. While a POSA would be aware that the hardness testers may not produce precisely uniform results among testers (EX1107, 928), the corrected claimed range of 8-48 N accounts for measurement variations between testers. EX2007, ¶85. Petitioner's cited references do not demonstrate anything different or support a finding of non-enablement or indefiniteness. *Pet.*, 34-40. The USP (EX1104), Remington (EX1106), and Lee (EX1107) all disclose that hardness testers have some variation, however the variation does not result in materially different hardness values. *See* EX2032, 112-115. Sietz (EX1108) is a reference from 1965, and uses manual testers, which does not represent the state of the art by 2009.

1. The Claims of the '598 Patent Are Enabled

Petitioner's entire argument for non-enablement centers around the assertion that a POSA would not be able to practice the invention without undue

experimentation. Pet., 35-37. As explained above, measuring hardness of tablets was routine and well-known in the field as of 2009. Further, as Petitioner admits, the '598 specification provides a working example of formulating a tablet with a hardness of 8-48 N. Pet., 35; EX1001, 17:40-18:23. Petitioner complains that the specification does not teach or provide guidance as to how to measure the hardness. As the Federal Circuit has explained, however, “[a] patent need not teach, and preferably omits, what is well known in the art.” *Spectra-Physics*, 827 F.2d at 1534 (citation omitted); *Koito Mfg.*, 381 F.3d at 1156 (finding the claimed invention enabled where certain details were omitted from the specification because they were standard in the industry, and stating that “[t]his Court has repeatedly explained that a patent applicant does not need to include in the specification that which is already known to and available to one of ordinary skill in the art.”). As explained above, measuring hardness is routine and Patent Owner was not obligated to explain the process for testing hardness in the specification of the '598 patent. Because a POSA would know the parameters for measuring hardness from USP <1217>, there would be no need for undue experimentation to practice the claims of the '598 patent. EX2007, ¶¶86-88; EX1104, 676-678. Further, the face of the '598 patent cites to Dr. Schleuniger, “Key factors influencing measured tablet hardness,” *Pharmatron*; 2011, 5 pages.” EX1001, 4. The publication identifies the design requirements that should be met for consistent results, and identifies a specific model, MultiTest50. *See*

generally EX2033. Thus, a POSA reading the '598 patent in its entirety would understand that the hardness of the claimed ODT is measured using an automated tester. EX2007, ¶¶86-88.

2. The '598 Patent is Not Indefinite

Petitioner misapplies the law in its assertion that because there are multiple hardness testers, there are multiple ways to measure hardness and a POSA would not be reasonably certain of the scope of the '598 patent claims. Pet., 39. On the contrary, there are not competing or multiple methodologies for measuring hardness. As explained above, measuring hardness is a routine test during formulation of tablets. EX1004, 677. While multiple hardness testers are available, a POSA would know to follow a consistent methodology for acquiring the hardness value, as provided in USP <1217>. EX1104, 677; EX2007, ¶89. USP <1217> instructs that (1) the platens should be parallel, polished and perpendicular to the direction of movement; (2) the loading rate should be constant (20 N); the tablet should be oriented such that compression occurs across the diameter of the tablet; and (4) the test results should be expressed in standard units and readable within 1 N. EX1104, 676-677. As Petitioner admits, the USP is a recognized authority in the pharmaceutical field, and a POSA would have followed the USP's recommendations. Pet., 57-58, 76-77.

This is not a case like *Dow* where the possible methodologies involve a different set of parameters and steps. *Dow Chem. Co. v. Nova Chems. Corp.*, 803 F.3d 620 (Fed. Cir. 2015). Nor is this case similar to *Teva*, where the molecular weight could be determined by three different measurements and give three different results. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335 (Fed. Cir. 2015). Rather, hardness testers follow a set methodology to determine the breaking force of a tablet and the breaking force is not determined through different types of measurements. EX1104, 677. Breaking force measurements are the same and provide equivalent results across automated hardness testers that were the standard in the art at time. EX1104, EX2032. Thus, Petitioner has not shown that the claims of the '598 patent are indefinite.

VIII. PATENT OWNER'S REQUEST FOR A CERTIFICATE OF CORRECTION RENDERS GROUNDS 5-6 MOOT

Petitioner relies on Perrett (EX1109) for anticipation and obviousness, stating that because the '598 patent cannot claim priority to the '642 Provisional Application, Perrett is prior art. Pet., 41. This stems from the obvious typographical error in the claims discussed above regarding the recited hardness value. EX2001. When informed of this error, Patent Owner filed a Request for Certificate of Correction to fix the typographical error on October 14, 2025. As such, the '598 patent is entitled to an October 1, 2009 priority date. EX2001. The Board has stayed

Patent Owner's Request. Paper 7. As explained above in Section VII.A, the Board's stay should be lifted so the Director can evaluate Patent Owner's Request on the merits before the institution decision is due.

Once the Certificate of Correction is issued, the '598 patent should be evaluated based on the changes made in the Certificate of Correction. *See ipDataTel, LLC*, IPR2018-01822, Paper 19 at 7 n.4, 14-17 (denying institution in part by evaluating the claims based on changes to the claims made by a Certificate of Correction issued after the Petition but prior to the institution decision); *Edwards Lifesciences Corp. v. Evalve, Inc.*, IPR2019-01285, Paper 19 at 6, 8 (P.T.A.B. Jan. 9, 2020) (denying institution because a Certificate of Correction filed after the Petition but issued before the institution decision changed the priority date of the patent to a date that predated the applied prior art); *Parsons Xtreme Golf, LLC v. Taylor Made Golf Co.*, IPR2018-00657 at Paper 14 at 3, 11 (P.T.A.B. Aug. 14, 2018) (denying institution in part because a Certificate of Correction issued after the Petition but before the institution decision changed the priority date of the patent to a date that predated the applied prior art). Because the '598 patent will be entitled to priority of the '642 Provisional Application, Perrett cannot anticipate the '598 patent, or render it obvious, making both Grounds 5 and 6 moot.

IX. OVERVIEW OF THE REMAINING ASSERTED REFERENCES

A. Dohil – Liquid Formulations for Treating EoE

U.S. Publication No. 2007/0111978 to Dohil (EX1002) is titled “Viscous Budesonide For The Treatment Of Inflammatory Diseases Of The Gastrointestinal Tract.” EX1002, cover. Dohil is directed to treating EoE using *liquid* pharmaceutical compositions comprising corticosteroids to alleviate inflammation of the esophagus. EX1002, [0002]-[0013]. Dohil discloses that it “is often difficult to deliver an effective dose of corticosteroid to the targeted area of the esophagus.” EX1002, [0007]. To accomplish esophageal delivery, Dohil teaches that “[a] liquid, long-acting topical corticosteroid preparation is needed.” EX1002, [0009]. Dohil specifically designed a liquid formulation of sufficient volume and a defined viscosity to deliver a corticosteroid to the esophagus to treat EoE. *See e.g.* EX1002, [0011]. Specifically, Dohil teaches that its liquid compositions are formulated with a viscosity enhancer to deliver to the esophagus a viscous liquid containing budesonide that coats the esophagus. EX1002, [0011], [0013], [0021], [0038], [0042]-[0045], [0046], [0048]-[0070]. Dohil also teaches that 8-12mL of liquid is necessary to provide an effective amount of the corticosteroid to the esophagus. EX1002, [0031], [0053], [0067] (“[OVB] may have advantages over other therapies in that...its volume (8-12ml) provides pan-esophageal mucosal coverage...”). Dohil discloses three examples, all of which discuss an oral viscous liquid budesonide

formulation, referred to as OVB. EX1002, [0056]-[0070]. The OVB liquid formulation is the only formulation made and tested in these examples, and the data shows that it effectively treats EoE in children. EX1002, [0056]-[0070]. Dohil highlights several advantages of the OVB liquid formulation, including palatability and effective drug contact with the esophagus. EX1002, [0067] (“It may have advantages over other therapies in that it is palatable, its volume (8-12ml) provides pan-esophageal mucosal coverage and it requires only once daily administration.”); *id.*, [0056]-[0070]. More specifically, in Examples 1 and 2, the patients were administered the viscous liquid formulation daily, and both patients showed improvement of EoE symptoms and complete resolution or normal appearing esophagus after treatment. EX1002, [0046]-[0047]. In Example 3, patients were given the viscous liquid formulation and 90% of patients showed improvement after treatment. EX1002, [0048], [0053], [0060]. Dohil does not mention any problems with the viscous liquid formulation. EX2007, ¶118. Thus, Dohil describes its invention as a “simple” and “palatable” liquid composition formulated with 8-12mL volume, which improves contact of the corticosteroid with the esophagus and provides “pan-esophageal mucosal coverage” to effectively treat EoE. EX1002, [0067]; *see also* EX2011, 72:25-74:6, 61:3-9, 66:17-20, 68:10-12, 68:22-24, 70:8-12.

Only three paragraphs in Dohil refer to a solid dosage form. EX1002, [0032], [0013], [0037]. In paragraph 0032, Dohil discloses a “lozenge or other similar tablet” that “wo[u]ld dissolve rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus.” EX1002, [0032]. Dohil does not exemplify or provide an enabling disclosure of a lozenge or other similar tablet, and is silent regarding any disintegration rate of the lozenge or similar tablet. EX1002, [0032]. Indeed, Dohil does not even use the term disintegrate at all in its disclosure. Dohil also teaches that “for children or other patients that may have difficulty with a dissolving lozenge, the lozenge may be ground or otherwise dissolved...reaching a total volume presented in embodiments herein[,]” i.e. 8-12mL. EX1002, [0032], [0067]. The remaining 110 paragraphs out of 113 paragraphs in Dohil describe the liquid composition. EX1002.

Dohil issued as U.S. Patent No. 8,324,192 (EX2021) on December 4, 2012. EX2021, cover. Dohil’s patent is listed in the Orange Book as covering Eohilia, an oral suspension comprising budesonide for the treatment of EoE. EX2022; EX2031.

B. Grother – General ODT Platform

International Publication No. WO2000/044351 to Grother is titled “Fast Dispersing Dosage Forms Free Of Gelatin” and is directed to a new fast dispersing tablet platform for any drug that is “essentially free or absolutely free of mammalian gelatin.” EX1008, Abstract. To this end, Grother describes the issues with using gelatin in formulating fast dispersing dosage forms, such as increased processing

times, increased costs, and lack of homogeneity. EX1008, 2-3. Grother describes its invention as eliminating gelatin from the formulations and using modified starches instead, listing the various advantages of modified starches, such as improved stability and strength of the dosage form, allowing the use of sweeteners to improve taste, and elimination of exposure to undesirable agents. EX1008, 3-6; *see also* EX2007, ¶127.

Grother discloses that “[a]ny drug may be used as the active ingredient in the composition of the present invention.” EX1008, 15:19-20. Grother then goes on to list hundreds of drugs in multiple drug classes across six pages. EX1008, 16-21; EX2007, ¶128. One of the drug classes Grother includes is corticosteroids, and includes budesonide in its list, but does not distinguish between topically acting and systemically acting drugs in the plethora of drugs it lists. EX1008, 18:15-18. The other drugs and drug classes disclosed in Grother are also predominantly systemically active drugs. EX1008, 16-21; EX2007, ¶¶128-129. Grother also discloses eight examples of its formulation, six of which do not even include a drug. EX1008, 22-32; EX2007, ¶128. Examples 7 and 8 include three drugs, none of which are topically acting corticosteroids. EX1008, 29, 31; EX2007, ¶128.

C. Kararli – Fast-Melt Tablet for Systemically Acting Drug

International Publication No. WO 2002/15884 to Kararli is titled “Rapidly Disintegrating Oral Formulation Of a Cyclooxygenase-2 Inhibitor.” EX1110,

Abstract. Kararli is directed to “orally deliverable pharmaceutical compositions containing a selective cyclooxygenase-2 inhibitory drug[.]” EX1110, 1:4-8. Kararli describes certain challenges in formulating cyclooxygenase-2 inhibitory drugs into “fast-melt tablets[.]” such as difficulties in preparing such compositions with blend uniformity due to the properties of cyclooxygenase-2 inhibitory drugs, like low solubility. EX1110, 5:24-6:9. Karali’s fast-melt composition is “molded” “without wet granulating, to form a moldable blend; and a step of shaping the unit-dose quantity of the moldable blend in a mold to form the molded article.” EX1110, 9:3-18. Thus, Kararli discloses its invention as providing a tablet for treatment of a cyclooxygenase-2 mediated condition, that does not require wet granulation, which prevents the problems arising from the properties of cyclooxygenase-2 inhibitory drugs, such as blend non-uniformity. EX1110, 6:11-7:13.

Nowhere does Kararli disclose treatment of EoE, or treatment of any disorder with a topical drug, much less a topical corticosteroid such as fluticasone propionate or budesonide.

D. FDA Guidance – Defines the Disintegration Time for ODTs

The FDA Guidance is not directed to specific formulations for topical delivery of drugs to the esophagus or treating inflammation of the esophagus. *See* EX2011, 56:15-21; *see also* EX2007, ¶126. The FDA Guidance simply provides a definition for ODTs. Specifically, the FDA Guidance states that ODTs are defined as “[a] solid

dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.” EX1005, 2. The FDA Guidance goes on to state that ODTs disintegrate within “approximately 30 seconds or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative[.]” *Id.* The FDA Guidance does not discuss or even recognize that an ODT can be used to topically administer a topically acting drug to the esophagus.

E. Venkatesh988 and Venkatesh516 – Taste-Masking Drug Particles to Prevent Contact in the Mouth

U.S. Publication No. 2005/0232988 to Venkatesh (“Venkatesh988”) is titled “Orally Disintegrating Tablets and Methods of Manufacture” and is generally directed to taste-masking bitter drugs that are administered using an ODT. EX1020, [0013]; *see also* EX2011, 90:13-92:18, 93:12-16, 94:4-25. Venkatesh988 teaches that taste-masking involves coating with a drug with a water-insoluble polymer, like ethylcellulose, to prevent the drug from being released in saliva and contacting the oral cavity. EX1020, [0009], [0018], [0022], [0027]. Venkatesh988 also discloses cellulose acetate phthalate and hydroxypropyl methylcellulose phthalate as suitable polymers for taste-masking, which are pH-responsive polymers used for enterically coating drugs, so the drug is released after it passes through the stomach. EX1020, [0027]; EX2015, 191, 476. Thus, Venkatesh988’s taste-masking prevents the drug

from topically contacting the oral cavity and, because of the proximity of the esophagus to the oral cavity, taste-masking would also prevent the drug from contacting the esophagus. EX1020, [0009], [0013], [0018], [0022], [0027]. Consequently, taste-masking prevents a therapeutically effective amount of a drug from being deposited topically on the esophagus and a taste-masked drug would not treat EoE.

International Publication No. 2009/006516 to Venkatesh (“Venkatesh516”) is titled “Orally Disintegrating Tablet Composition Of Lamotrigine” and is directed to taste-masked particles of lamotrigine for treatment of epilepsy and mood disorders. EX1111, Abstract, 1:8-10, 2:6-3:7, 7:11-25, 13:8-14:9, Figs. 1, 2, 6. As an initial matter, Venkatesh516 is not prior art to the ’598 patent. As discussed in Section VI, Patent Owner has requested correction of an obvious typographical error regarding the recited hardness values. Once the correction is made, all claims will be entitled the earliest priority date of October 1, 2009. *See* Section V.II.A-B, VIII. Venkatesh516 was published on January 8, 2009. The October 1, 2009 effective filing date is within one year of Venkatesh516’s January 8, 2009 publication date. Further, Gopi Venkatesh is an inventor of the ’598 patent and Venkatesh516 and both the ’598 patent and Venkatesh516 were owned by Eurand, Inc. as of October 1, 2009. Therefore, Venkatesh516 is not available as prior art under § 102 (pre-AIA).

Even without this correction, at least claims 24 and 26 have an earliest effective filing date of October 1, 2009. *See Lucent Techs., Inc., v. Gateway, Inc.*, 543 F.3d 710, 718 (Fed. Cir. 2008) (“Patent claims are awarded priority on a claim-by-claim basis based on the disclosure in the priority applications.”) (citations omitted). Specifically, Petitioner’s asserted grounds for lack of written description and enablement, as well as indefiniteness, relate only to the “hardness of 4-48 N.” Pet., 24-37. However, at least claims 24 and 26 do not require or encompass a tablet hardness of 4-48 N. Claim 1 recites tablet hardness and friability, alternatively, as two possible properties of the claimed ODT. EX1001, cl. 1 (“...the orally disintegrating tablet has a hardness of 4-48 N *or* a friability of not more than 1%”) (emphasis added). Dependent claims 24 and 26, both of which depend directly on claim 1, recite only tablet friability values of the ODT. Because these claims depend on claim 1, the claims must further limit claim 1. Thus, under the doctrine of claim differentiation, claims 24 and 26 are interpreted as not including 4-48 N. Consequently, claims 24 and 26 have an earliest effective filing date of October 1, 2009³.

³ This effective filing date is earlier than the publication date of Perrett (EX1109), so Perrett is not available as § 102 (pre-AIA) prior art to these claims.

For the same reasons stated above, Venkatesh516, which is cited for teaching friability, is not prior art to claims 24 and 26. Venkatesh516 was published on January 8, 2009. The October 1, 2009 effective filing date for claims 24 and 26 is within one year of Venkatesh516's January 8, 2009 publication date, and Gopi Venkatesh is an inventor of both the '598 patent and Venkatesh516. Therefore, the invention recited in at least claims 24 and 26 was not described in a printed publication more than one year prior to the effective filing date, and Venkatesh516 is not available as prior art under § 102 (pre-AIA).

Moreover, as discussed above for Venkatesh988, Venkatesh516's taste-masking prevents a therapeutically effective amount of a drug from being deposited topically in the esophagus. Further, Venkatesh516 is directed to the release and systemic absorption of lamotrigine. *See generally* EX1111. Figures 1 and 2 show the drug release profile of lamotrigine, indicating 100% of the drug is released in about 15 minutes in the gut, i.e. *after* passing through the esophagus. EX1111, Fig. 1 (showing 100% drug release in ~15 min, corresponding to drug release in the gut), Fig. 2 (showing 100% drug release in ~15 min). Figure 6 further shows that the taste-masked ODT has a bioequivalent pharmacokinetic profile compared to a conventional immediate release formulation, confirming that the term "immediate release" refers to release in the gut for systemic absorption. EX1111, Figure 6, *see also* 2:9-11, 5:9-14, 5:18-29 ("[ODT] substantially disintegrates in the oral cavity of

a patient and provides a lamotrigine release profile which is substantially the same as the lamotrigine release profile of an immediate release lamotrigine composition” and “[t]hus, an ODT composition of the present invention which has a dissolution profile, plasma concentration-time profile, $C_{\max}$, or $AUC_{(0-24)}$, or any combination or subcombination of these parameters, which is substantially the same as a non-ODT immediate release lamotrigine composition”).

X. STARTING WITH AN ODT WHEN SOLVING THE PROBLEM OF DELIVERING TOPICALLY ACTING CORTICOSTEROID TO THE ESOPHAGUS IS IMPERMISSIBLE HINDSIGHT

Petitioner argues that an ODT containing budesonide and/or fluticasone was known in the art. Pet., 17-18. This is incorrect and based on impermissible hindsight. As discussed for Grounds 7-12, below, Petitioner’s cited art does not actually teach or suggest using an ODT that disintegrates within 60 seconds to topically administer a therapeutically effective amount of corticosteroid to the esophagus.

Petitioner does not analyze the art as a POSA, because Petitioner is not focused on finding a treatment for EoE. Petitioner starts with the presumption that a POSA would be motivated to formulate an ODT that disintegrates within 60 seconds as measured with the USP <701> Disintegration Test, not identifying a formulation that would topically deposit a therapeutically effective amount of a topical corticosteroid to the esophagus. *See* Pet., 9-11, 17-18. This is evident from Petitioner’s reliance on ODTs used to administer systemic drugs to the gut. Pet., 9-

11. Perhaps the most striking evidence of Petitioner’s hindsight-driven analysis is its expert’s admission in related proceedings that he was not aware of any prior art orally disintegrating composition used to deliver a topically acting drug to the esophagus. EX2011, 18:5-13 (“Q[:] Are you aware of any drugs that have been developed as an ODT for topical administration of the esophagus? A[:] No, I do not). This is the epitome of hindsight. “The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time.” *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1138 (Fed. Cir. 1985).

In contrast to the Petition, a POSA trying to treat inflammation of the esophagus would have begun by first identifying formulations that were shown to deliver drugs to the esophagus and were effective for treating inflammation of the esophagus. EX2007, ¶109. As described above in Section II.A, there are significant challenges in effectively treating EoE. *See* EX1002, [0007] (“It is often difficult to deliver an effective dose of corticosteroid to the targeted area of the esophagus.”). Petitioner fails to appreciate these challenges, such as the need to prevent candidiasis infection and keeping the drug from washing away from the esophagus. EX1001, 1:41-53; *see also* EX1033, 1217 (studying fluticasone propionate for treatment of EoE and instructing patients not to swallow for 30 minutes after taking the medication). Thus, a POSA would have these challenges in mind when developing a formulation for treating EoE. EX2007, ¶¶109-11.

Out all of the prior art references⁴ cited in the Grounds, only Dohil discusses treatments for EoE. As discussed above, Dohil teaches that 8-12mL of a viscous liquid is effective to treat EoE. Dohil specifically teaches that solid formulations are inferior because it will not achieve pan-esophageal coverage (“[OVB] may have advantages over other therapies in that...its volume (8-12ml) provides pan-esophageal mucosal coverage....” EX1002, [0067].) Because Dohil refers to a “lozenge or other similar tablet” and then states that OVB is superior to other therapies, a POSA would understand Dohil as teaching that OVB is superior to a lozenge or similar tablet because it provides the necessary esophageal coverage for effective treatment of EoE. EX1002, [0032], [0067]; EX2007, ¶134.

Because a POSA would understand from Dohil that liquid formulations were capable of delivering an effective amount of a corticosteroid to the esophagus (EX1002, [0006], [0046]-[0070]; EX1001, 1:41-62) and that 8-12mL of viscous liquid provides pan-esophageal coverage and increases the duration of contact of the topical corticosteroid with the inflamed esophagus to effectively treat EoE, a POSA would be motivated to start with a liquid formulation. EX1002, [0031], [0053], [0067]. These liquid formulations are a logical starting point because the delivery mechanism ensures contact of a topically active corticosteroid with the esophagus

⁴ Perrett is not prior art to the '598 patent, as discussed in Section VII, above.

(EX1002, [0067]), as opposed to an ODT, which, as of 2009, had only been used to administer systemically active drugs to the stomach for absorption. Pet., 9-14; EX1017, 178-180; EX1018, 438-439; EX1019, 312. Thus, a POSA would start with Dohil's liquid. EX2007, ¶¶156-157. This is reinforced by the fact that Dohil's OVB formulation was indeed developed as "Eohilia," a liquid budesonide composition for treating EoE sold by Takeda Pharmaceuticals, Inc. EX2022. A POSA would therefore have no motivation to fundamentally change Dohil's liquid composition and formulate budesonide as a solid composition, given the challenges of treating EoE with a topical corticosteroid and the fact that Dohil itself discloses that its OVB formulation is superior to solid formulations. EX1001, 1:41-53; EX1002, [0067]; EX2007, ¶¶158-159.

Even assuming a POSA would formulate budesonide or fluticasone as a solid composition, it would not be an ODT that disintegrates within 60 seconds as claimed in the '598 patent. EX2007, ¶160. Based on Dohil's teaching that a large volume of viscous liquid (8-12mL) is necessary for pan-esophageal coating and efficacy, and the risk of the drug washing away from the esophagus before effectively treating the inflammation, a POSA would be motivated to provide longer disintegration times to increase volume and coating of the esophagus, such as with Dohil's lozenge which would dissolve over several minutes. EX1001, 1:41-53; EX1002, [0067]; EX2007, ¶160. A lozenge (or similar tablet) that dissolves slowly, over several minutes, would

produce Dohil's 8-12mL volume. EX2005, 303 (the rate of saliva "increases to about 4[.]0-5[.]0 ml / min during eating, chewing and other stimulating activities."). This is consistent with the art-recognized definition of a lozenge. *Supra* Section II.B; EX2013, 413; EX2014, 201; EX2016, 293. ODTs that disintegrate within 60 seconds would not produce Dohil's 8-12mL and would therefore be counterintuitive. EX2007, ¶160. Thus, Petitioner's presumption that a POSA would begin with an ODT when determining how to effectively formulate a topical corticosteroid for treatment of EoE is pure hindsight and wrong.

XI. PETITIONER'S GROUNDS 7-9 FAIL

A. Petitioner Fails to Demonstrate that Dohil Discloses an ODT to Topically Deposit a Corticosteroid on the Esophagus and Treat EoE

In Grounds 7-9, Petitioner relies on Dohil in view of Kararli, the FDA Guidance, and the USP to challenge claims 1-4, 9, 13-14, 18-20, 22-25, and 31-32, Dohil in view of Kararli, the FDA Guidance, the USP, and Vekatesh988 to challenge claims 5-8 and 15-16, and Dohil in view of Kararli, the FDA Guidance, the USP, and Venkatesh516 to challenge claims 26-28 and 34. As discussed in more detail below, a POSA had no motivation to modify Dohil and formulate the claimed ODT. This is because Dohil teaches a lozenge, which is known in the art to dissolve "slowly" and would produce the 8-12mL of viscous liquid needed to provide pan-esophageal coverage and effectively treat EoE. EX1002, [0067].

Petitioner relies on Kararli for its disclosure on the hardness limitation, along with USP <1217>, but Kararli cannot fill the gaps in Dohil. Pet., 57-59. Kararli is directed to a fast-melt tablet comprising a selective cyclooxygenase-2 inhibitory drug, not an ODT that topically deposits a corticosteroid in the esophagus. EX1110, 1:4-8. Venkatesh988 also does not cure the deficiencies in Dohil because Venkatesh988's particles are coated with a water-insoluble or pH-responsive polymer for the purpose of taste-masking, and the taste-mask coating would prevent the corticosteroid from being topically deposited on the upper gastrointestinal tract. EX1020, [0009], [0018], [0022], [0027]; EX2007, ¶¶149-153. Venkatesh516 similarly discloses taste-masked particles and is directed to formulating an ODT comprising a systemically absorbed drug. EX1111, 1:8-10, 2:6-3:7, 7:11-30, 13:8-14:32, Figs. 1, 2, 6-8. Thus, Petitioner's Grounds 7-9 fail and claims 1-9, 13-16, 18-20, 22-28, 31-32, and 34 are patentable.

1. Dohil Does Not Suggest or Teach ODTs as Required by Claims 1-9, 13-16, 18-19, and 34

Petitioner argues that Dohil discloses an ODT comprising a corticosteroid that disintegrates within 60 seconds. Pet., 51-59. Petitioner points to Dohil's disclosure of "a lozenge or other similar tablet" that "wo[u]ld dissolve rapidly in the mouth or esophagus[.]" Pet., 54-55 (citing EX1002, [0032]). Petitioner goes on to argue that "[i]t was obvious to formulate Dohil's rapidly dissolving lozenge or tablet to

disintegrate within 60 seconds” using the USP <701> Disintegration Test based on the FDA Guidance. Pet., 55. According to Petitioner, “[a] POSA seeking to formulate budesonide into an orally disintegrating pharmaceutical composition would be highly motivated to follow the FDA Guidance that such a composition should disintegrate within 30 seconds or less when tested using the USP <701> Disintegration Test.” Pet., 56. This argument presumes that a POSA would be motivated to make an ODT based on the disclosure in Dohil, which is not true.

As explained above in Section IX.A, Dohil’s invention is an 8-12mL OVB formulation that provides pan-esophageal coverage and effectively treats EoE, and all three examples administer the viscous liquid formulation and treat EoE. EX1002, [0013], [0030], [0031], [0036]-[0070]. Dohil does not disclose any examples using a solid dosage form. Dohil never mentions a solid dosage form that disintegrates within 60 seconds. Dohil discloses solid compositions in only two paragraphs, as a “dissolving tablet”/“dissolving wafer” and “lozenge or other similar tablet.” EX1002, [0013], [0032]. A POSA would understand the first disclosure of dissolving tablets or wafers to refer to solid forms that are dissolved in water before oral administration and not tablets that disintegrate in the mouth, as solid dosage forms that are dissolved in water before oral administration were well known at the time. *See* EX1017, 181; EX2007, ¶139.

Regarding the second disclosure of a lozenge or similar tablet, this does not refer to an ODT that disintegrates in 60 seconds for several reasons. First, Dohil does not call its lozenge or other similar tablet an ODT, even though ODTs were known in the art, or explicitly state that the lozenge or other similar tablet dissolves within 60 seconds. EX1002, [0032]; *supra* Section II.B. While Petitioner cites several synonyms for ODTs, nowhere does Petitioner assert that lozenges are synonymous with ODTs. Pet., 10-11. Thus, Dohil also does not act as its own lexicographer to change the definition of its lozenge to mean an ODT.

Further, as explained in Section II.B, the art distinguishes lozenges from ODTs. *See* EX2016, 293 (“Despite a surge of orally disintegrating tablets in the market in the recent years, they potentially can be confused with other solid oral dosage forms that are consumed without additional water intake, including *lozenges*, buccal tablets, and chewable tablets. Lozenges and buccal tablets are intended to dissolve *slowly* in the mouth, whereas, orally disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds.”) (emphasis added); EX2017, 341 (distinguishing quick/fast/rapid/mouth-dissolving tablets and fast/quick-melting tablets from lozenges); *see also* EX2034 (USP <1151>), 1289 (describing lozenges), 1303 (describing ODTs).

Second, lozenges do not disintegrate within 60 seconds in the USP <701> test. Indeed, in related proceedings, Petitioner’s expert has admitted that a typical lozenge

dissolves slowly. EX2011, 62:13-15. Neither Petitioner nor its expert have been able to identify any lozenge in the prior art that disintegrates within 60 seconds here or in related proceedings. EX2011, 62:13-15; *Dr. Falk Pharma GmbH v. Ellodi Pharms., L.P.*, IPR2024-01197, Paper 20 (Petitioner’s Reply Brief) at 6-9 (identifying no **lozenge** that dissolves rapidly); *see also id.*, Paper 28 (PO’s Corrected Surreply), 5-9. Instead, lozenges are known in the art to dissolve over several minutes EX2013, 413; EX2014, 201; EX2016, 293 (“Lozenges and buccal tablets are intended to dissolve slowly in the mouth, whereas, orally disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds.”). Because a lozenge disintegrates over several minutes (not in 60 seconds as claimed), a POSA would understand that a “similar tablet” would also disintegrate over several minutes. EX2007, ¶140. Thus, a POSA would not consider Dohil’s reference to a lozenge or similar tablet to refer to an ODT.

The use of the phrase “dissolve rapidly” does not change the well-understood definition of a lozenge. As Petitioner’s expert has admitted, “dissolve” refers to drug release, not disintegration. EX2018, 21:19-22. Thus, Dohil is merely describing the initial release of drug from the lozenge which may occur rapidly after oral administration, but lozenges – by definition – dissolve or disintegrate completely over several minutes. EX2013, 413; EX2014, 201; EX2016, 293; EX2017, 341; EX2007, ¶140.

Third, the process of dissolving slowly over a several minutes would be more likely to provide the 8-12mL volume of viscous liquid that Dohil teaches is required to coat the esophagus and treat EoE compared to an ODT. EX1002, [0067] (“It may have advantages over other therapies in that it is palatable, its volume (8-12ml) provides pan-esophageal mucosal coverage and it requires only once daily administration.”); EX2007, ¶140. This is reinforced by Dohil’s teaching to dissolve or grind up a lozenge in 8-12mL to treat EoE (“for children or other patients that may have difficulty with a dissolving lozenge, the lozenge may be ground or otherwise dissolved...reaching a total volume presented in embodiments herein[,]” i.e. 8-12mL. EX1002, [0032], [0067]). Interpreting Dohil to teach disintegration within 60 seconds reads a disclosure into Dohil a disclosure that simply is not there. Petitioner therefore starts with the claim language of the ’598 patent and attempts to force Dohil’s disclosure to fit into the claims of the ’598 patent.

The Petition also acknowledges ODTs are specifically designed for *easy swallowing*. Pet., 9-10 (citing EX1018, 434). However, Dohil teaches that its lozenge is not easily swallowed, so it is not an ODT. In particular, Dohil provides alternative administration instructions: “for children or other patients that may have *difficulty with a dissolving lozenge*, the lozenge may be ground or otherwise dissolved...reaching a total volume presented in the embodiments herein” i.e., 8-12mL. EX1002, [0032] (emphasis added). If, as Petitioner contends, a lozenge is an

ODT, then these same patients, for the same reasons, could not use an ODT formulation. On the contrary, however, this disclosure confirms Dohil's lozenge *is not* an ODT that would rapidly disintegrate because if it were, the lozenge would not need to be "ground up" or dissolved in 8-12ml of a liquid which is then swallowed to treat EoE. EX1002, [0032], [0067]; EX2007, ¶141.

Petitioner also argues that a lozenge can be formulated with a disintegrating agent. Pet., 53-54. Petitioner's own reference, Danckwerts (EX1017), expressly contradicts this argument. Danckwerts teaches that lozenges are manufactured "*without disintegrants* and are intended to be sucked by patients." EX1017, 181 (emphasis added); *see also* EX2013, 413 ("Disintegrants are not used in the formulation..."). As acknowledged by Petitioner's expert in related proceedings, the mere reference to a disintegrant does not teach or suggest an orally disintegrating composition because conventional (non-orally disintegrating) tablets include disintegrants. EX2011, 64:25-65:2-11; EX2007, ¶142.

Thus, Dohil does not teach or suggest an orally disintegrating tablet that disintegrates within 60 seconds for at least the reasons stated above.

a. Kararli Does Not Cure the Deficiencies in Dohil

Petitioner relies on Kararli, and the USP, for its argument that a POSA would be motivated to formulate an ODT with a hardness of 4-48 N as claimed in the '598 patent. Pet., 57-59. As explained in Section IX.C, Kararli is directed to "fast-melt

tablets” comprising cyclooxygenase-2 inhibitory drugs. EX1110, 1:4-8; EX1110, 5:24-6:9.

A POSA would understand that Kararli is not directed to an ODT that deposits a therapeutically effective amount of a topical corticosteroid on the esophagus. EX2007, ¶¶144-148. As an initial matter, “fast-melt tablets” are not ODTs. EX2017, 341 (distinguishing fast-melting tablet from ODT). Further, unlike the ODT described and claimed in the ’598 patent, Kararli’s fast-melt composition does not contain granulated particles and is not pressed into a tablet using a tableting press. EX1110, 9:3-18 (describing that the fast-melt composition is molded, “without wet granulating, to form a moldable blend; and a step of shaping the unit-dose quantity of the moldable blend in a mold to form the molded article.”). In contrast, the claimed ODT is prepared by wet granulation, and the resulting granulated mass is pressed into a tablet to produce a hardness of 8-48 N. EX1001, 17:41-58 (“A Glatt GPCG-3 fluid-bed apparatus equipped with a top spray granulation bowl is charged with the pre-blend....and granulated by spraying purified water.”). A POSA would understand that the composition of the tablet and the process used to make tablet contribute to hardness. EX1107, 927-928; EX1108, 1356-1357; EX2007, ¶147. Because of the different composition and process, a POSA would not consider Kararli to teach or suggest hardness for an ODT containing a corticosteroid. EX2007, ¶147.

A POSA would rather understand Kararli to specifically disclose a fast-melt tablet comprising cyclooxygenase-2 inhibitory drug and not teaching or suggesting that an ODT with the claimed hardness that can be used to topically administer a therapeutically effective amount of a corticosteroid to the esophagus for the treatment of EoE. EX2007, ¶¶144-148. Petitioner conclusively states that a POSA would have been motivated to follow Kararli and the USP to achieve the claimed hardness, but does not support this statement with any reasoning or expert testimony. Pet., 58. Rather, Petitioner merely points to the USP as background knowledge and reinforcement of the teachings in Kararli. Pet., 57-59. Specifically, Petitioner points to USP <1216> and <1217> on friability and hardness, respectively, as important indicators for tablet strength. Pet., 57-59. Neither chapter of the USP, however, instructs a POSA to turn to Kararli for its disclosures on hardness and Petitioner fails to explain why a POSA would rely on Kararli's teachings to achieve the ODT claimed in the '598 patent. Thus, Petitioner's reliance on Kararli is impermissible hindsight as it has no relevance to the claims in the '598 patent.

XII. VENKATESH988 AND VENKATESH516 DO NOT CURE THE DEFICIENCIES IN DOHIL

Petitioner asserts in Ground 8 that claims 5-8 and 15-16 are unpatentable over Dohil, Kararli, the FDA Guidance, the USP, and Venkatesh988 and in Ground 9 that claims 26-28 and 34 are unpatentable over Dohil, Kararli, the FDA Guidance, the

USP, and Venkatesh516. Pet., 61-68. As described above in Section IX.E, Venkatesh516 is not prior art to the '598 patent, and Ground 9 fails for this reason alone.

Further, a POSA would not have been motivated to combine Venkatesh988 or Venkatesh516 with the formulation in Dohil, because both Venkatesh988's and Venkatesh516's taste-masking prevents the drug from contacting the mouth and esophagus, whereas Dohil is directed to achieving contact of corticosteroids with the esophagus to treat EoE. EX1020, [0009], [0018], [0022], [0027]; EX1111, Abstract, 1:8-10, 2:6-3:7, 7:11-25, 13:8-14:9, Figs. 1, 2, 6. Petitioner continues to rely on impermissible hindsight.

As explained in Section II.B, ODTs were known to deliver systemically absorbed drugs to patients, and therefore taste-masking technologies were developed for use with ODTs to prevent drug release in the mouth and still allow for systemic absorption with an immediate release profile. EX1018, 434; EX1019, 310-311; EX1020; EX1111. As explained in Section IX.E, this "immediate release" is described in Venkatesh516 as complete drug release in the gut, *after* the esophagus. EX1111, Fig. 1 (showing 100% drug release in ~15 min, corresponding to drug release in the gut and FDA Guidance for immediate release formulations), Fig. 2 (showing 100% drug release in ~15 min, corresponding to drug release in the gut and FDA Guidance for immediate release formulations), and Fig. 6 (showing taste-

masked ODT has a bioequivalent pharmacokinetic profile compared to a conventional immediate release formulation), 2:9-11, 5:9-14, 5:18-29. Venkatesh988 also discloses that 12% or less of the drug is released in 5 minutes after administration, further supporting the fact that Venkatesh988 and Venkatesh516 are directed to systemically acting drugs, and taste-masking could not be used to administer a therapeutically effective amount of a corticosteroids to the esophagus. EX1020, [0035]-[0060] (Examples 2-7).

Neither Petitioner nor its expert explain why a POSA would be motivated to look to Venkatesh988 or Venkatesh516. Instead, Petitioner merely states that a POSA would have been motivated to manufacture Dohil's lozenges according to Venkatesh988 and Venkatesh516. Pet., 61-68. Petitioner is wrong. A POSA developing a formulation to deposit a corticosteroid to the esophagus would have no motivation to combine Dohil with Venkatesh988 or Venkatesh516, because the combinations would undermine Dohil's intended purpose of administering a corticosteroid to the esophagus (taste-masking would prevent a corticosteroid from contacting the esophagus). EX2007, ¶¶149-153. A POSA would not remove either Venkatesh988's or Venkatesh516's taste-masking because this would undermine both references' intended purpose of preventing contact of bitter or poor tasting drugs with the mouth. EX1020, [0009], [0018], [0022], [0027]; EX1111, Abstract, 1:8-10, 2:6-3:7, 7:11-25, 13:8-14:9. "[A] proposed modification [is] inappropriate

for an obviousness inquiry when the modification render[s] the prior art reference inoperable for its intended purpose.” *In re Fritch*, 972 F.2d 1260, 1265 n.12 (Fed. Cir. 1992); *see also In re Ratti*, 270 F.2d 810, 813 (C.C.P.A. 1959) (rejecting “suggested combination of references” that “would require ... a change in the basic principles under which the [primary reference] was designed to operate.”); *Plas-Pak Indus., Inc. v. Sulzer Mixpac AG*, 600 F. App’x 755, 758-760 (Fed. Cir. 2015) (nonprecedential) (affirming the Board’s decision in finding certain claims not unpatentable over obviousness as petitioner’s contention that a first reference rendered the claims obvious fundamentally altered the operating principle of the prior art). Because Petitioner’s arguments regarding the alleged motivation to combine Dohil with Venkatesh988 are conclusory and do not explain any benefit to combining the references, they must be rejected. *See In re Magnum Oil Tools Int’l, Ltd.*, 829 F.3d 1364, 1380 (Fed. Cir. 2016) (declaring that “a petitioner cannot employ mere conclusory statements”); EX2007, ¶¶149-153.

1. Dohil Provides No Motivation to Formulate an ODT for the Treatment of EoE

Petitioner asserts that “[i]t was desirable for the disintegration time of rapidly dissolving solid compositions to vary ‘from several seconds to about a minute’” and that it would have been obvious to formulate Dohil’s lozenge or similar tablet to disintegrate within 60 seconds in view of the FDA Guidance. Pet., 55 (citing

EX1018, 434). The claims of the '598 patent recite depositing a therapeutically effective amount of the corticosteroid on the esophagus. As explained in Section II.A, the prior art acknowledged the difficulties of delivering an effective dose of the corticosteroid to the esophagus. EX1002, [0007]; EX1001, 1:41-62. Petitioner does not address what would motivate a POSA to formulate a tablet to disintegrate within 60 seconds when trying to deposit a therapeutically effective amount of the corticosteroid on the esophagus or how such a disintegrate rate would address the challenges in depositing a therapeutically effective amount of the corticosteroid on the esophagus.

A Petition must demonstrate “that a skilled artisan would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so.” *In re Cyclobenzaprine*, 676 F.3d 1063, 1068-69 (Fed. Cir. 2012) (citation omitted). As discussed above in Section IX.A, Dohil’s liquid formulation is palatable and simple, and, most importantly, effective for treating EoE. EX1002, [0067]. An ODT is significantly more complicated and expensive to manufacture than Dohil’s liquid and there is no evidence in the prior art that an ODT had been used to topically deposit a topically active drug to the upper gastrointestinal tract. EX2007, ¶156.

The Petition fails to identify any issue with Dohil’s viscous liquid formulation that would motivate a POSA to fundamentally change dosage forms to an ODT.

EX2007, ¶¶134, 156. Further, as Petitioner's expert admitted in his deposition testimony in related proceedings, Dohil does not disclose any issues with dosing, compliance or stability with its OVB, and the data disclosed in Dohil shows that OVB is effective in treating EoE. EX2011, 72:25-74:6. Without a recognized problem, a POSA had no motivation to change Dohil's effective liquid dosage form to an ODT. EX2007, ¶156. It is only through impermissible hindsight, guided by the teachings of the '598 patent, that a POSA would disregard Dohil's effective liquid formulation, and formulate an ODT that disintegrates within 60 seconds based on Dohil. EX2007, ¶¶156-159. To the contrary, Dohil's viscous liquid has several benefits, namely palatability, the ability to provide pan-esophageal coverage, and efficacy. EX1002, [0067]; EX2007, ¶¶156-159. "The invention must be viewed not with the blueprint drawn by the inventor, but in the state of the art that existed at the time." *Interconnect Planning*, 774 F.2d at 1138. An obviousness combination is only legitimate if the petition provides an "explanation as to how or why the references would be combined to arrive at the claimed invention," failing which "we are left with only hindsight bias that *KSR* warns against." *Metalcraft of Mayville, Inc. v. The Toro Co.*, 848 F.3d 1358, 1367 (Fed. Cir. 2017) (citation omitted). Petitioner and its expert fail to provide such an explanation, instead jumping to the conclusion that a POSA would seek to formulate budesonide in an ODT that disintegrates within 60 seconds based on the passing references of a lozenge in Dohil. *See supra* Section X.

To fabricate a motivation, Petitioner's expert characterized Dohil's examples as a "proof of concept study" or "pilot studies" and stated that Dohil was using a simple formulation to determine if budesonide worked for EoE in related proceedings. EX2011, 61:3-62:3. But this statement is illogical and inconsistent with the background literature Petitioner's expert cited to show that budesonide was known to be effective in treating EoE. EX2011, 61:3-62:3; *see also* Pet., 15-17. As explained in the '598 patent and Dohil, budesonide was already known to be effective in treating EoE. EX1001, 1:41-53, 3:39-42; EX1002, [0067]; *see also* EX1014 (showing budesonide has previously been used to treat EoE), EX1015 (same). Further, Dohil's liquid formulation proved to be commercially viable, as Eohilia. EX2022; EX2031. Thus, Dohil already invented an improved formulation, an 8-12mL viscous solution, and showed that it was effective for EoE.

Petitioner ignores Dohil's liquid formulation and focuses on Dohil's mention of a lozenge. As discussed above in Section II.B, lozenges are not ODTs because lozenges dissolve "slowly" to continuously release a drug (EX2013, 413; EX2014, 201; EX2016, 293; EX2017, 341). Petitioner and its expert fail to explain why a POSA would be motivated to modify a lozenge or similar tablet to disintegrate within 30 seconds using the USP <701> Disintegration Test as disclosed in the FDA Guidance. Modifying a lozenge to disintegrate within 30 seconds based on the FDA Guidance would render the lozenge and similar tablet unsatisfactory for its intended

purpose or change the principal operation, because it would no longer dissolve slowly to continuously deliver the corticosteroid to the esophagus over several minutes as the lozenge dissolves. EX2007, ¶¶160-161; *see* MPEP § 2143.01 (V) (“If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, there may be no suggestion or motivation to make the proposed modification”) (citing *In re Gordon*, 733 F.2d 900, 221, USPQ 1125 (Fed. Cir. 1984)); *see also* MPEP § 2143.01 (VI) (“If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.”) (citing *In re Ratti*, 270 F.2d 810, 813, 123 USPQ 349, 352 (C.C.P.A. 1959)).

Further, as explained above in Section X, an ODT that disintegrates within 60 seconds would not produce 8-12mL of liquid and would not be expected to provide pan-esophageal coverage discussed in Dohil, and thus a POSA would not be motivated to pursue an ODT. EX1002, [0067]. In a related proceeding, *Dr. Falk Pharma GmbH v. Ellodi Pharma., L.P.*, IPR2024-01197, Petitioner’s expert testified that an ODT that disintegrates within 60 seconds would only produce about 1-2mL of liquid. EX2011, 50:17-24. Petitioner’s expert then back tracked and argued that a lozenge would generate 4-5mL per minute and could be effective to treat EoE. *Dr. Falk Pharma GmbH v. Ellodi Pharms., L.P.*, IPR2024-01197, Paper

20 at 10-11 (P.T.A.B July 14, 2025); EX2005, 303-304. Petitioner's expert provided no support for this argument in that proceeding, or here. Nonetheless, this is not the 8-12mL volume that Dohil teaches is required for efficacy. EX1002, [0067]. Put differently, an ODT that disintegrates within 60 or 30 seconds would not produce Dohil's 8-12mL of liquid that provides pan-esophageal coverage. EX2007, ¶160. A POSA therefore would not be motivated to modify Dohil to formulate an ODT that disintegrates within 60 or 30 seconds. *Id.* Instead, a POSA would have been motivated to have longer disintegration times to produce 8-12mL and provide pan-esophageal coverage. *Id.*; see *DePuy Spine, Inc. v. Medtronic Sofamor Danek, Inc.*, 567 F.3d 1314, 1326-27 (Fed. Cir. 2009) ("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[,]" i.e., where a prior art reference "teaches away" from the proposed modification) (citation omitted); EX2007, ¶¶154-161.

2. No Reasonable Expectation of Success in Arriving at the Claimed Invention

Petitioner conclusively asserts that a POSA would have had a reasonable expectation of success formulating an ODT that disintegrates within 60 seconds or 30 seconds and topically deposits the corticosteroid on the esophagus based on Dohil

and Petitioner's allegation that formulating such compositions would have been routine at the time of the '598 patent. Pet., 56-57.

Prior to the '598 patent and its parent applications, an ODT had never been used to deposit a topically acting drug with no significant systemic activity on the upper gastrointestinal tract (e.g., esophagus) to treat a disease of the upper gastrointestinal tract. Indeed, Petitioner's expert was not able to identify a single prior art ODT containing a topically acting drug that deposited the drug topically on the upper gastrointestinal tract. EX2011, 17:8-15. What has never been done cannot be routine.

Further, as explained above, Dohil teaches that 8-12mL of a viscous liquid is needed to provide pan-esophageal coverage and effectively treat EoE. EX1002, [0067]. Unlike Dohil's liquid formulation, which is swallowed as an 8-12mL bolus dose, a POSA would know that when an ODT is administered orally, it disintegrates in the small volume of saliva produced in that short period of time and is swallowed. A POSA could not predict based on Dohil's disclosure whether the resulting volume or viscosity of the dissolved tablet would provide pan-esophageal coverage and effectively treat EoE. EX2007, ¶162. Nothing in Dohil suggests that an ODT that disintegrates within 60 seconds would topically administer the corticosteroid to the upper gastrointestinal tract and effectively treat EoE. *Id.* On the other hand, as

explained above, because Dohil's lozenge or similar tablet dissolves slowly over several minutes, it would produce Dohil's efficacious 8-12mL liquid.

Petitioner's assertions for reasonable expectation of success in combination with Kararli, Venkatesh988, and Venkatesh 516 fare even worse. Petitioner conclusively states that a POSA would have had a reasonable expectation of success in formulating Dohil's lozenge according to the hardness value disclosed in Kararli to achieve the claimed ODT. Pet., 58. Petitioner, however, fails to address the differences in composition and tableting process disclosed in Kararli, which affect the hardness of a tablet. EX1110, 1:4-8, 5:24-6:9, 9:3-18. In particular, as explained above in Section XI.A.1.a, Kararli is directed to a fast-melt composition, not an ODT, comprising cyclooxygenase-2 inhibitory drug that is not topically acting. EX1110, 1:4-8; EX1110, 5:24-6:9; EX2017, 341. Further, Kararli's compositions do not contain granulated particles and are not pressed into a tablet using a tableting press. EX1110, 9:3-18. In contrast, the claimed ODT is prepared by wet granulation, and then pressed into a tablet to produce a hardness of 8-48 N. EX1001, 17:41-18:5. Petitioner fails to address these difference and explain how a POSA would successfully arrive at the claimed ODT based on Kararli's disclosures. EX2007, ¶163.

Petitioner's only argument regarding Venkatesh988 is that it discloses successfully manufacturing orally disintegration compositions and so a POSA would

have had a reasonable expectation of success in formulating the claimed ODT. Pet., 62-65. Petitioner fails to address the fact that Venkatesh988 is directed to taste-masking of bitter drug particles in ODTs in general, which prevents the drug from contacting the oral cavity. EX1020, [0002], [0009], [0013]-[0015], [0018]; *see also* EX2011, 90:13-92:18, 93:12-16, 94:4-25. Venkatesh988's taste-masking also prevents topical administration of the active ingredient on the upper gastrointestinal tract. EX2007, ¶164. Petitioner fails to address Venkatesh988's taste-masking, much less articulate a reasonable expectation to remove this essential feature from Venkatesh988's composition and still achieving a pleasant tasting formulation.

Finally, Petitioner does not even attempt to argue that a POSA would have a reasonable expectation of success with respect to Venkatesh516, and barely addresses expectation of success in the Grounds. Pet., 66. Petitioner does not acknowledge that Venkatesh516 is directed to taste-masking systemically acting drugs. EX1111, Abstract, 1:8-10, 2:6-3:7, 7:11-25, 13:8-14:9, Figs. 1, 2, 6. Petitioner also does not explain how or why a POSA would have success in formulating Dohil's lozenge according to the disclosures in Venkatesh516 to achieve the claimed ODT. EX2007, ¶164

3. Dohil Does Not Disclose the Claimed Doses in the Context of a Tablet (Claims 1[i], 2-3, 22, and 34)

Dohil also does not disclose the specific dose ranges required by claims 1[i],

2-3, 22 and 34. Liquid compositions and solid compositions differ in composition and delivery mechanism (Dohil's 8-12mL that provides pan-esophageal coating vs. the claimed ODT that disintegrates in a much smaller volume of saliva) and therefore require different considerations when determining the proper dose of an active drug. EX2017, 344-348. Petitioner cites to Dohil's disclosure of the doses administered to patients in Examples 1-3. Pet., 53. But the patients in Examples 1-3 were given the viscous liquid formulation. EX1002, [0046]-[0070]. Dohil does not explain, and Petitioner does not address, the difference in formulation or the fact that doses for liquid compositions are not necessarily the same as a solid compositions. EX2017, 344-348. Indeed, Petitioner has cited no evidence that the dosage of a topical acting drug in a liquid formulation is always the same as the dose of the same drug used in an ODT. Pet., 53. Dohil therefore does not disclose any dose for an ODT based on its liquid compositions or teach a POSA how to extrapolate from a liquid to a solid. EX2007, ¶¶165-166. In fact, the art cannot teach this because the '598 patent and its parent applications are the first example of an ODT topically administering a topically acting drug to the esophagus.

Petitioner fails to address a reasonable expectation of success of formulating an orally dispersing tablet with the claimed doses.

4. Dohil Does Not Teach or Suggest the Claimed Methods for Treatment (Claims 20-22, and 31-32)

Similarly, Dohil does not teach or suggest the method recited in claims 20-22, and 31-32 of the '598 patent. As discussed above, Dohil does not teach or suggest an ODT that disintegrates within 60 seconds and therefore cannot disclose a method of treating eosinophilic esophagus recited in claims 20-22, and 31-32. Section XI.A.1.

There would also be no reasonable expectation of success in treating eosinophilic esophagus recited in claims 20-22, and 31-32 by administering an ODT that disintegrates within 60 seconds as claimed, because there is no reasonable expectation of successfully administering a therapeutically effective amount of a corticosteroid to the upper gastrointestinal tract using an ODT. Dohil teaches that a specific volume (8-12mL) of a viscous liquid formulation is required to achieve pan-esophageal coverage and treat EoE. EX1002, [0067] (“It may have advantages over other therapies in that it is palatable, its volume (8-12ml) provides pan-esophageal mucosal coverage and it requires only once daily administration.”). As discussed above in Section XI.A.1, an ODT that disintegrates within 60 seconds or 30 seconds would not achieve the volume that Dohil teaches provides pan-esophageal coverage and is efficacious. It would only produce 2-5mL saliva, which would not achieve pan-esophageal coating and would not reasonably be expected to be efficacious

based on Dohil. EX2005, 303 (the rate of saliva “increases to about 4[.]0-5[.]0 ml / min during eating, chewing and other stimulating activities.”). Therefore, there would be no reasonable expectation of success. EX2007, ¶¶167-168.

XIII. PETITIONER’S GROUNDS 10-12 FAIL

A. Grother and the FDA Guidance do Not Render the Claimed ODT Obvious

In Grounds 10-12, Petitioner relies on Grother in view of Kararli, the FDA Guidance, and the USP to challenge claims 1-4, 9, 11, 13-14, 18-25, 29, and 31-32, Venkatesh988 to challenge claims 5-8, 10, 12, 15-17, and 30, and Venkatesh516 to challenge claims 26-28 and 33-34. A POSA had no motivation or reasonable expectation of success in formulating the claimed ODT to treat inflammation (e.g., EoE), because none of Grother, Kararli, the FDA Guidance, or the USP suggest that an ODT can topically deposit a topical/non-systemic drug on the upper gastrointestinal tract. EX2007, ¶¶169-175. Neither Venkatesh988 nor Venkatesh516 cure these deficiencies because both Venkatesh988’s and Venkatesh516’s drug particles are coated with a taste-masking layer, which prevents the corticosteroid from being topically deposited on the upper gastrointestinal tract. EX2007, ¶¶176-178. Thus, Petitioner’s Grounds 10-12 fail and claims 1-25 and 29-32 are patentable.

1. Grother and the FDA Guidance are General References and Do Not Teach or Suggest the ODT as Required by Claims 1-19, 23-25, and 29-30

Petitioner argues that Grother discloses fast dispersing dosage forms that contain budesonide and fluticasone. Pet., 69-81 Petitioner points to Grother's disclosure that "[a]ny drug may be used as the active ingredient in the composition of the present invention," which includes budesonide and fluticasone. Pet., 69 (citing EX1008, 15:19-20, 18:15-18). As laid out above in Section IX.B, Grother is not directed to any disease, but rather focused on eliminating mammalian gelatin from its disclosed fast dispersing solid dosage forms. EX2011, 75:5-10, 79:1-10; EX1008, Abstract. A POSA would therefore understand that Grother discloses a general ODT platform for which any drug could be used as an active ingredient. EX1008, 15:19-20; EX2007, ¶171.

While Grother lists corticosteroids among hundreds of drugs, Grother also does not highlight the topical corticosteroids it lists or distinguish between systemically acting drugs from topically acting drugs with no systemic activity. EX2011, 78:4-18. To the contrary, Grother comingles topically acting corticosteroids with systemically acting corticosteroids that are excluded by the claims. *Compare* EX1001, 3:39-42, 7:25-30 *with* EX1008, 18:15-18.

Petitioner arbitrarily cites to Grother's disclosure of corticosteroids, specifically fluticasone and budesonide, but does not acknowledge that Grother does

not distinguish between topically acting and systemically acting drugs in the plethora of drugs it lists. Pet., 70; EX1008, 18:15-18; EX2011, 78:4-8. Indeed, budesonide is listed among systemically acting corticosteroids, which are expressly excluded from the scope of the '598 patent, including hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone and betamethasone. *Compare* EX1001, 3:39-42, 7:25-30, *with* EX1008, 18:15-19. The other drugs and drug classes disclosed in Grother are also predominantly systemically active drugs. EX1008, 16-21; EX2007, ¶¶128-129. Moreover, Petitioner remarks that one of the advantages of ODTs is the ability of the active ingredient to be absorbed through the mucosa of the gastrointestinal tract, beginning in the mouth. Pet., 9-10. In other words, Petitioner admits that improving systemic adsorption is an advantage of the ODT. *Id.* A POSA would therefore be motivated to select a **systemically** acting drug from Grother's list of drugs for this benefit rather than a topically acting corticosteroid. EX2007, ¶¶130, 179-182. This is because topically acting corticosteroids, such as fluticasone and budesonide, provide therapeutic effects from topical contact, not absorption through the mucosa of the gastrointestinal tract, beginning in the mouth. EX2007, ¶¶130, 179-182. Notably, Grother does not teach or suggest that its fast dispersing dosage form is capable of topically depositing a topically acting drug on the upper gastrointestinal tract. EX2011, 75:5-10; 79:1-10. Thus, nothing in Grother points to formulating an ODT with a topical corticosteroid, let alone budesonide or

fluticasone, for the treatment of inflammation of the upper gastrointestinal tract or EoE. A POSA would thus understand that Grother did not recognize, and therefore did not teach or suggest, that orally disintegrating compositions could be used to topically administer budesonide or fluticasone to the upper gastrointestinal tract or esophagus for the treatment of EoE. EX2007, ¶¶179-182.

The FDA Guidance does not cure this deficiency in Grother. Rather, as explained above and as acknowledged by Petitioner's expert, the FDA Guidance merely provides a definition of ODTs. EX2011, 56:15-21. The FDA Guidance does not address any particular disease, such as EoE, any particular class of drugs, such as corticosteroids, or recognize the use of ODT to topically deposit topically acting drugs on the upper gastrointestinal tract. EX2011, 55:14-23. All the FDA Guidance does, therefore, is provide a POSA with the general definition of ODTs. EX2011, 56:15-21. The generalized disclosures in Grother and the FDA Guidance therefore cannot disclose the required claim limitations of the '598 patent. EX2007, ¶¶169-172.

a. Kararli Does Not Cure the Deficiencies in Grother

Petitioner relies on Kararli, and the USP, for its argument that a POSA would be motivated to formulate an ODT with a hardness of 4-48 N as claimed in the '598 patent. Pet., 75-77. As explained in Section IX.C, Kararli is directed to "fast-melt tablets" comprising cyclooxygenase-2 inhibitory drugs. EX1110, 1:4-8; EX1110,

5:24-6:9. For the same reasons that Kararli does not cure the deficiencies in Dohil for Grounds 7-9, Kararli also does not cure the deficiencies in Grother for Grounds 10-12.

First, as explained above in Section XI.A.1.a, the “fast-melt tablets” taught in Kararli are not ODTs. EX2017, 341 (distinguishing fast-melting tablet from ODT). Second, Kararli’s tablets do not contain granulated particles and are not pressed into a tablet using a tableting press, unlike the claimed ODT. EX1110, 9:3-18; EX1001, 17:41-18:5. As explained in Section XI.A.1.a., because of the different composition and process, a POSA would not consider Kararli to teach or suggest hardness for an ODT containing a corticosteroid. EX1107, 927-928; EX1108, 1356-1357; EX2007, ¶¶173-175.

Petitioner conclusively states that a POSA would have been motivated to follow Kararli and the USP to achieve the claimed hardness, but does not support this statement with any reasoning or expert testimony. Pet., 76. Rather, Petitioner merely points to the USP as background knowledge and reinforcement of the teachings in Kararli. Pet., 76-77. Specifically, Petitioner points to USP <1216> and <1217> on friability and hardness, respectively, as important indicators for tablet strength. Pet., 76-77. Neither chapter of the USP, however, instructs a POSA to turn to Kararli for its disclosures on hardness and Petitioner fails to explain why a POSA would rely on Kararli’s teachings in combination with Grother to achieve the ODT

claimed in the '598 patent. Thus, Petitioner's reliance on Kararli is impermissible hindsight as it has no relevance to the claims in the '598 patent.

b. Venkatesh988 and Venkatesh516 Do Not Cure the Deficiencies in Grother

Petitioner asserts in Ground 11 that claims 5-8, 10, 12, 15-17, and 30 are unpatentable over Grother, Kararli, the FDA Guidance, the USP, and Venkatesh988. Petitioner further asserts in Ground 12 that claims 26-28 and 33-34 are unpatentable over Grother, Kararli, the FDA Guidance, the USP, and Venkatesh516. As described above in Section IX.E, Venkatesh516 is not prior art to the '598 patent, and Ground 12 fails for this reason alone.

As set out above, a POSA had no motivation to formulate an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet containing a topical corticosteroid that is topically deposited on the upper gastrointestinal tract based on the disclosure in Grother, Kararli, the FDA Guidance, and the USP. Neither Venkatesh988 nor Venkatesh516 cure these deficiencies, because a POSA also would not have been motivated to combine the teachings in Venkatesh988 or Venkatesh516 with the formulation in Grother and the FDA Guidance to arrive at the claimed invention. Petitioner continues to rely on impermissible hindsight. EX2007, ¶¶176-178.

As explained above, in Section XI.A.1.b, Venkatesh988 is not directed to a particular disease, the delivery of corticosteroids, or topical delivery of drugs. Instead, Venkatesh988 is directed generally to taste-masking of bitter drug particles administered using an ODT, as confirmed by Petitioner's expert. EX2011, 90:13-92:18, 93:12-16, 94:4-25; EX1020, [0013]. Similarly, Venkatesh516 discloses taste-masked drug particles and ODT formulations comprising systemically acting drugs, which provide immediate release of the drug in the gut over the course of 15 minutes or more. EX1111, Abstract, 1:8-10, 2:6-3:7, 7:11-25, 13:8-14:9, Figs. 1, 2, 6. Based on the disclosure of taste-masking alone, a POSA would not consider Venkatesh988 or Venkatesh516 to be relevant to the claims of the '598 patent and would not be motivated to combine Venkatesh988 or Venkatesh516 with Grother and the FDA Guidance, and arrive at the claimed invention. Moreover, for the same reasons discussed in Section XI.A.1.b, Petitioner fails to address Venkatesh988's and Venkatesh516's taste-masking, much less articulate a motivation to remove this essential feature from either references' disclosed ODT.

Neither Petitioner nor its expert explain why a POSA would be motivated to look to Venkatesh988 or Venkatesh516. Instead, Petitioner merely states that a POSA would have been motivated to manufacture Grother's fast dispersing solid dosage form according to Venkatesh988 or Venkatesh516. Pet., 81-86. Because Petitioner's arguments regarding the alleged motivation to combine Grother with

Venkatesh988 and Venkatesh516 are conclusory and do not explain any benefit to combining the references, they must be rejected. *See In re Magnum*, 829 F.3d at 1380 (declaring that “a petitioner cannot employ mere conclusory statements”). A POSA had no expectation of success based on Grother alone or in combination with Venkatesh988 or Venkatesh516.

Petitioner does not even attempt to explain why a POSA would have a reasonable expectation of success in formulating an orally disintegrating pharmaceutical composition containing budesonide or fluticasone that would topically deposit budesonide or fluticasone on the upper gastrointestinal tract based on Grother’s disclosure and the FDA Guidance. The most Petitioner can offer is that formulating orally disintegrating pharmaceutical compositions were routine at the time of the ’598 patent. Pet., 82. But Petitioner’s expert was not able to identify a single prior art ODT containing a topically acting drug that was deposited topically to the upper gastrointestinal track. EX2011, 17:8-15. Grother fails to recognize that an ODT can topically deposit a topically acting drug, such as a corticosteroid, to the upper gastrointestinal tract. EX2007, ¶171. As Petitioner’s expert acknowledges, the FDA Guidance only provides a definition for ODTs, and thus does not remedy the deficiencies in Grother. EX2011, 56:15-21. Therefore, Petitioner failed to provide any actual evidence that a POSA would arrive at the claimed invention with a reasonable expectation of success.

A POSA would understand that formulations for administering systemic drugs, which are absorbed by the lower gastrointestinal tract, differ from formulations that topically administer the drug to a localized area to the upper gastrointestinal tract. EX2007, ¶177. A POSA would therefore not reasonably expect to successfully formulate an orally disintegrating pharmaceutical composition containing a corticosteroid to topically deposit the corticosteroid on the upper gastrointestinal tract for treating inflammation of the upper gastrointestinal tract from Grother's disclosure and the FDA Guidance. EX2007, ¶¶176-178, 183.

Venkatesh988 and Venkatesh516 do not cure the deficiencies in Grother. Petitioner relies on conclusory assertions that a POSA would have a reasonable expectation of success based on the process disclosed in Venkatesh988 and Venkatesh516. Pet., 82-83, 85-86. Again, Petitioner does not attempt to explain how a POSA would have a reasonable expectation of success in arriving at the claimed invention based on Venkatesh988's or Venkatesh516's process, which coats the drug with a water-insoluble or pH-responsive taste-masking layer so that the drug does not contact the mouth or the upper gastrointestinal tract, or why a POSA would have a reasonable expectation of success in removing this essential feature from Venkatesh988's composition and still achieve a pleasant tasting formulation.

Because Venkatesh988's and Venkatesh516's taste-masking layer would prevent a corticosteroid from contacting the upper gastrointestinal tract, there is no

reasonable expectation of formulating an orally disintegrating composition to topically deposit a topically acting corticosteroid on the upper gastrointestinal tract to treat EoE based on Grother, Kararli, the FDA Guidance, and either Venkatesh988 or Venkatesh516. EX2007, ¶178.

2. No Motivation to Formulate the Claimed ODT Based on Grother in view of the FDA Guidance – No Recognition That an ODT Could Topically Deposit a Corticosteroid on the Upper Gastrointestinal Tract

Petitioner again uses impermissible hindsight to support its conclusory arguments for motivation to combine. As explained above, a POSA would have understood Grother to disclose a general ODT platform that is not directed to any disease or particular drug, and does not teach or suggest using an ODT to topically deposit a topically active drug on the upper gastrointestinal tract. Section XII.A.1; EX2007, ¶180. Similarly, a POSA would understand the FDA Guidance to supply a definition for ODTs, and not teach or suggest using an ODT to topically deposit a topically active drug on the upper gastrointestinal tract. EX2007, ¶¶180-182; EX2011, 56:15-21. Petitioner argues that a POSA “would have been motivated to select budesonide or fluticasone as an active ingredient in Grother’s fast dispersing solid dosage form based on Grother’s express disclosure to do so.” Pet., 70. Petitioner asserts that this would not require a “leap of inventiveness.” Pet., 70 (citing *Boston Sci. Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982, 991 (Fed. Cir. 2009)).

Petitioner misstates the law. The law actually states that “[d]isparate embodiments in one reference can only be combined if they are a ‘predictable variation’ of each other that does not ‘require a leap of inventiveness.’” *Apple Inc. v. Corephotonics, Ltd.*, No. IPR2018-01348, 2019 WL 3714167, at *2 (P.T.A.B. Aug. 5, 2019) (Paper 11) (quoting *Boston Sci. Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982 (Fed. Cir. 2009)). But the drugs in Grother are not predictable variations.

Grother cites hundreds of drugs across six pages. EX1008, 16-21. While corticosteroids are listed, Grother does not highlight them in any way or distinguish between systemic and topical corticosteroids. EX1008, 18:15-18. Rather, systemic and topical corticosteroids are contained in the same list, with no distinction. *Id.* The drugs in Grother span a vast variety of drug classes, from analgesics to vaccines and stimulants, the overwhelming majority of which are systemically active and are absorbed through the lower gastrointestinal tract. *Id.* at 16-21. Petitioner does not and cannot argue that the various drugs listed in Grother are “predictable variations” of each other. This is particularly true where budesonide and fluticasone act topically, whereas nearly all other drugs listed are systemically active and must be absorbed in the blood stream in order to provide a therapeutic effect. EX1008, 16-21; EX1033, 1216, 1223; EX1001, 1:41-62; EX2007, ¶180. Because of the wide array of drugs disclosed, and the lack of guidance on formulating an ODT with a topically acting drug for topical deposition on the upper gastrointestinal tract, the

Petitioner's arbitrary selection of budesonide or fluticasone cannot be a "predictable variation," and Patent Owner's claims involve a leap of inventiveness. EX2007, ¶¶180-182.

It is clear that Petitioner has arbitrarily picked budesonide and fluticasone from Grother's non-limiting list simply because these drugs are recited in the claims of the '598 patent. EX2007, ¶181. The "rationale ... that a person of ordinary skill would 'pick and choose' features from various embodiments of [a single reference], simply because they are in the same [reference], is insufficient to demonstrate a reasonable likelihood of prevailing on this challenge[.]" *LG Display Co. v. Innovative Display Techs. LLC*, Case IPR2014-01362, Paper 12 at 13 (P.T.A.B. Mar. 2, 2015).

Petitioner's reliance on the FDA Guidance does not provide the requisite motivation that is absent from Grother. Instead of offering any explanation, Petitioner recites that a "POSA seeking to formulate budesonide into an orally disintegrating pharmaceutical composition would be highly motivated to follow the FDA Guidance that such a composition should disintegrate within 60 seconds when tested using the USP <701> Disintegration Test." Pet., 74. As discussed above in Section X, Petitioner does not explain why a POSA would be motivated to formulate fluticasone or budesonide in an ODT that disintegrates within 60 seconds using the USP <701> Disintegration Test for topical deposition of budesonide on the upper

gastrointestinal tract in the first place. The FDA Guidance does not remedy this deficiency because the FDA Guidance is silent regarding topical corticosteroids, topical deposition of any active on the upper gastrointestinal tract, or topical treatment of inflammation of the upper gastrointestinal tract. *See generally* EX1005. The Petitioner's conclusory statements must be rejected. "To satisfy its burden of proving obviousness, a petitioner cannot employ mere conclusory statements. The petitioner must instead articulate specific reasoning, based on evidence of record, to support the legal conclusion of obviousness." *In re Magnum*, 829 F.3d at 1380.

Because Grother fails to recognize that ODTs can be used to topically administer a therapeutically effective amount of a topical drug to the upper gastrointestinal tract, and the FDA Guidance is silent regarding topical corticosteroids and topical treatment of the upper gastrointestinal tract, a POSA would not have been motivated to formulate an ODT with budesonide or fluticasone as asserted by Petitioner's argument. EX2007, ¶¶179-183. For this reason, Grounds 10-12 must fail.

3. Grother and the FDA Guidance Do Not Render Obvious the Claimed Doses (Claims 1[i], 2-3, 10, 12, 21-22, and 29-30)

Grother does not disclose the specific dose ranges required by claims 1[i], 2-3, 10, 12, 21-22, and 29-30. Petitioner cites to Grother's disclosure of general dosing, and that the "upper value" is generally 60 mg. Pet., 70 (citing EX1008, 26:22-27:1).

The dosages disclosed in Grother relate to dosing generally, not topically active corticosteroids specifically, and certainly not for a corticosteroid that is topically deposited on the upper gastrointestinal tract to treat inflammation or EoE. EX1008, 26:22-27:1; EX2007, ¶¶184-185. Petitioner cites to references discussing budesonide in a liquid formulation or fluticasone in a metered inhaler. Pet., 70-71 (citing EX1014; EX1015; EX1002; EX1033; EX1034). A POSA would understand that formulating an ODT to topically deposit a corticosteroid in the upper gastrointestinal tract would involve different considerations and likely different doses than liquid formulations, as well as metered inhalers meant for swallowing. EX2017, 344-348; EX2007, ¶¶184-185. Petitioner fails to explain how Grother discloses the claimed doses for an orally disintegrating solid pharmaceutical composition or orally disintegrating tablet containing a topical corticosteroid based on its general disclosures. EX2007, ¶¶184-185.

As discussed above, a POSA would not have any motivation or reasonable expectation of success to formulate an orally dispersing tablet containing a topical corticosteroid with the claimed doses based on Grother. Petitioner's expert conclusively states that a POSA would have a reasonable expectation of success, but does not explain why or how. Pet., 71. For at least this reason, Petitioner's arguments must be rejected. *See In re Magnum*, 829 F.3d at 1380 (declaring that "a petitioner cannot employ mere conclusory statements").

4. Grother Does Not Disclose the Claimed Methods for Treatment (Claims 20-22 and 31-32)

Grother does not disclose the method disclosed in claims 20-22 and 31-32 of the '598 patent. As discussed above in Section XII.A.1, Grother does not disclose any disease and therefore cannot disclose methods of treating inflammation of the upper gastrointestinal tract recited in claims 20-22 and 31-32 by administering an ODT. Thus, Petitioner has failed to establish *prima facie* obviousness for these claims, because all claim limitations are not taught by the asserted references.

There would also be no reasonable expectation of success in treating eosinophilic esophagitis recited in claims 20-22 and 31-32 by administering an orally dispersing tablet. As illustrated through Petitioner's evidence, previous solid formulations of budesonide largely involved enterically coated tablets for treating inflammation of the lower gastrointestinal tract. Pet., 15-16 (citing EX1025, EX1009, EX1010, EX1011, EX1012, EX1013, EX1026, EX1027, EX1028). There is no evidence in Grother, or the background art, that an ODT would or even could deposit a therapeutically effective amount of a topical corticosteroid on the esophagus to treat eosinophilic esophagitis as required by the claims. Therefore, there would be no reasonable expectation of success.

XIV. OBJECTIVE INDICIA OF NONOBVIOUSNESS

Secondary considerations also establish that the claims of the '598 patent are not obvious as of the priority date, including unexpected results.

A. Unexpected Results

Patent Owner's clinical trials show that ODTs containing 1.5 mg and 3 mg of fluticasone are therapeutically effective and well-tolerated, further supporting the non-obviousness of the invention. *See generally* EX2002. As discussed above, Dohil teaches that 8-12mL of a viscous liquid formulation provides pan-esophageal coating and delivers an effective dose of budesonide to the esophagus to treat EoE, whereas the claimed ODT would not produce 8-12mL. EX1002, [0067]. Consequently, a POSA would not have expected an ODT that disintegrated in the mouth within 60 seconds to be efficacious.

However, a clinical study funded by Petitioner comparing the claimed ODT to Dohil's liquid showed that the ODT was equally efficacious, even at half the corticosteroid dose, which is surprising and unexpected. EX2006. Petitioner's study compared the claimed orally dispersing tablet to a 5ml viscous solution containing budesonide (dosed twice a day, for a total of 10ml viscous solution), such as the one disclosed in Dohil. EX2006, 2. The study found that "[i]nterestingly," patients who received the tablet of 1 mg of budesonide twice daily achieved remission, similar to patients who received the viscous solution of 2 mg of budesonide twice daily. EX2006, 8. The study concluded that "no additional benefit could be shown for the higher dose of . . . budesonide [tablet] (2 mg twice daily) used in our study compared with previous studies examining viscous suspensions." *Id.* Based on the known

efficacy of the viscous liquid formulations of budesonide, administered twice a day at a volume of 5ml, for a total of 10ml, or 8-12ml as disclosed in Dohil, a POSA would not have expected an ODT that produces only 1-2ml of solution and uses half the budesonide dose to be efficacious in providing the necessary pan-esophageal coverage in order to effectively treat EoE. EX2011, 50:17-24; EX2005, 303.

Further, a POSA would have known that oral corticosteroid administration causes candidiasis, and the longer the corticosteroid is held in the mouth, the greater the chance of candidiasis developing. EX1001, 1:46-48; EX1033, 1216-1217, 1219. A POSA would have been deterred from developing an ODT that would be held in the mouth longer than a liquid (which is swallowed immediately) because it would have been expected to increase the rate of candidiasis infections. Surprisingly, Patent Owner's study found that patients who received 1.5 and 3 mg of fluticasone once daily achieved remission, with low rates of candidiasis, compared to patients receiving fluticasone twice daily. EX2002, 2491. Also surprisingly, patients receiving 1.5 and 3 mg of fluticasone once daily showed equal or superior improvement in clinical symptoms compared to twice daily treatment. EX2002, 2491-2493.

XV. CONCLUSION

For the foregoing reasons, Petitioner has failed to establish that the challenged claims of the '598 patent are unpatentable. Patent Owner respectfully requests the Board find the challenged claims patentable over the grounds in the Petition.

Date: December 26, 2025

Respectfully submitted,

Cooley LLP
ATTN: Patent Group
1299 Pennsylvania Ave., NW
Suite 700
Washington D.C. 20004
Tel: (202) 776-2982
Fax: (202) 842-7887

BY: /Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390
Counsel for Patent Owner

CERTIFICATE OF COMPLIANCE WITH WORD COUNT

Pursuant to 37 C.F.R. § 42.24(d), I certify that this response complies with the type-volume limits of 37 C.F.R. § 42.24(c)(1) because it contains 17,612 words, according to the word-processing system used to prepare this petition, excluding the parts of this response that are exempted by 37 C.F.R. § 42.24(c) (including the table of contents, a table of authorities, an exhibits list, a listing of facts, a certificate of service or this certificate of word count, or appendix of exhibits).

Date: December 26, 2025

Respectfully submitted,

Cooley LLP
ATTN: Patent Group
1299 Pennsylvania Ave., NW
Suite 700
Washington D.C. 20004
Tel: (202) 776-2982
Fax: (202) 842-7887

BY: /Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390
Counsel for Patent Owner

**CERTIFICATION OF SERVICE
UNDER 37 C.F.R. §§ 42.6(e), 42.105(a)**

I, Sanya Sukduang, hereby certify that on December 26, 2025, the foregoing **PATENT OWNER'S PRELIMINARY RESPONSE AND EXHIBITS 2002–2003, 2005–2008, 2010–2018, 2020–2022, 2026, 2031–2034** pursuant to 37 C.F.R. § 42.8 were served electronically via email on the following counsel of record for Petitioner as follows:

Nathanael Luman
Eric S. Furman
Philip J. Minnick
KNOBBE, MARTENS, OLSON, & BEAR, LLP
2nrl@knobbe.com
2esf@knobbe.com
2pjm@knobbe.com
BoxFalkPharma@knobbe.com

DATED: December 26, 2025

/Sanya Sukduang/
Sanya Sukduang
Reg. No. 46,390