

Filed October 24, 2024

On behalf of **Dr. Falk Pharma GMBH**

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

DR. FALK PHARMA GMBH,

Petitioner

v.

ELLODI PHARMACEUTICALS, L.P.,

Patent Owner

Case No. IPR2025-00055

Patent No. 9,486,407

**PETITION FOR *INTER PARTES* REVIEW OF
U.S. PATENT NO. 9,486,407**

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LIST OF EXHIBITS

Exhibit No.	Description
1001	U.S. Patent No. 9,486,407 to Perrett et al.
1002	U.S. Publication No. 20070111978 to Dohil et al.
1003	EP2482822B1 that was revoked by the European Patent Office
1004	The Opposition Division of the European Patent Office decision revoking EP2484822B1 with auxiliary requested claims
1005	“Guidance for Industry: Orally Disintegrating Tablets,” U.S. Food & Drug Administration, Center for Drug Evaluation and Research (CDER), 2008.
1006	Notice of Publication of FDA Guidance for Industry on Orally Disintegrating Tablets, Federal Register, Vol. 73, No. 242 at 76366, December 16, 2008.
1007	“DRAFT Guidance for Industry: Orally Disintegrating Tablets,” U.S. Food & Drug Administration, Center for Drug Evaluation and Research (CDER), 2007.
1008	International Publication No. WO2000044351 to Grother et al.
1009	Svoboda et al., “Oral formulations of budesonide: a novel treatment for inflammatory bowel disease,” <i>Drugs of Today</i> , 44:857-863 (2008) at 857.
1010	Tan et al., “Eosinophilic gastroenteritis treated with non-enteric-coated budesonide tablets,” <i>European Journal of Gastroenterology & Hepatology</i> , 13:425-427 (2001)
1011	Kolkman et al., “Evaluation of oral budesonide in the treatment of active distal ulcerative colitis,” <i>Drugs of Today</i> , 40:589-601 (2004)
1012	Siewert et al., “Eosinophilic gastroenteritis with severe protein-losing enteropathy: Successful treatment with budesonide,” <i>Digestive and Liver Disease</i> , 38:55-59 (2006)

Exhibit No.	Description
1013	Elsing et al., “Budesonide for the treatment of obstructive eosinophilic jejunitis,” Z. Gastroenterology, 45:187-189 (2007).
1014	Aceves et al., “Topical viscous budesonide suspension for treatment of eosinophilic esophagitis,” Journal of Allergy and Clinical Immunology 116:705-706 (2005)
1015	Aceves et al., “Oral Viscous Budesonide: A potential new therapy for eosinophilic esophagitis in children,” American Journal of Gastroenterology, 102:1-9 (2007)
1016	The United States Pharmacopeia, USP 32, 2009 at pages 262-263 “<701> Disintegration”
1017	Danckwerts, “Intraoral Drug Delivery: A Comparative Review,” American Journal of Drug Delivery, 1:171-186 (2003).
1018	Fu et al., “Orally fast disintegrating tablets: developments, technologies, taste-masking and clinical studies,” Critical Reviews in Therapeutic Drug Carrier Systems, 21:433-475 (2004)
1019	Shukla et al., “Mouth Dissolving Tablets I: An overview of formulation technology,” Scientia Pharmaceutica, 77:309-326 (2009) (March 6, 2009)
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1021	RESERVED
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1025	Goodman & Gilman’s: The Pharmacological Basis of Therapeutics, 11th edition, eds. Brunton, Lazo, Parker, 2005
1026	Budenofalk® Brochure (2005)

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1027	Budenofalk® Advertisement (2007)
1028	Dr. Falk Pharma Brochure (2008)
1029	<i>Curriculum Vitae</i> of Alan F. Parr, Pharm.D., Ph.D.
1030	RESERVED
1031	Prosecution history excerpts from U.S. Application No. 12/896,005, which issued as U.S. 8,771,729
1032	Prosecution history excerpts from U.S. Application No. 15/816,154, which issued as U.S. 10,632,069
1033	Teitlebaum et al., Eosinophilic esophagitis in children: Immunopathological analysis and response to fluticasone propionate,” <i>Gastroenterology</i> 122:1216-1225 (2002)
1034	Noel et al., “Clinical and immunopathologic effects of swallowed fluticasone for eosinophilic esophagitis,” <i>Clinical Gastroenterology and Hepatology</i> 2:568-575 (2004)
1035	U.S. Patent No. 7,122,198 to Singh et al.
1036	U.S. Patent No. 7,229,641 Cherukuri et al.
1037	RESERVED
1038	Ellodi Response to the Grounds of Opposition filed by Dr. Falk Pharma GmbH in opposition proceedings in EP2484822B1
1039	Prosecution history excerpts from U.S. Application No. 17/236,295, which issued as U.S. 11,266,598
1040	RESERVED
1041	Conway, “Solid dosage forms,” Chapter 4.1 in <i>Pharmaceutical Manufacturing Handbook: Production and Processes</i> , ed. Gad, pages 235-265 (2008)

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1049	Prosecution history excerpts from U.S. Application No. 15/816,154, which issued as U.S. 11,246,828
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1053	Declaration of Alan F. Parr, Pharm.D., Ph.D. supporting IPR petition of U.S. 9,486,407
1054	Wen, “Adsorption at solid surfaces: pharmaceutical applications,” in Encyclopedia of Pharmaceutical Technology, Third Edition, ed. Swarbrick, pages 34-45 (2007)
1055	Physical Pharmacy: Physical Chemical Principles in the Pharmaceutical Sciences, Fourth Edition, eds. Martin et al. (1993)

Dr. Falk Pharma GmbH (“Petitioner”) requests *inter partes* review (“IPR”) of claims 1-42 (“the challenged claims”) of U.S. 9,486,407 (“the ’407 patent”), which is assigned to Ellodi Pharmaceuticals, L.P. (“Patent Owner” or “Ellodi”).

Dr. Falk Pharma is concurrently filing IPR petitions challenging Ellodi’s U.S. Patent Nos. 10,632,069, 11,246,828, and 11,260,061. Also, Dr. Falk Pharma recently filed a petition challenging Ellodi’s U.S. 8,771,729 in IPR2024-01197, to which Ellodi has not yet filed a Preliminary Response and the PTAB has not yet issued an Institution Decision. All of these patents claim orally disintegrating solid pharmaceutical compositions that are obvious over the prior art and should be cancelled.

I. INTRODUCTION

Dr. Falk Pharma is an undisputed innovator in the fields of gastroenterology and hepatology. It has earned the respect of the medical and pharmaceutical formulation communities through its many educational outreach programs and seminars. The company’s first hepatological formulation, Hepatofalk[®], was launched in 1960 in Freiburg, Germany. By 2009, Dr. Falk Pharma had launched eight additional formulations having important gastroenterological and hepatological indications in 63 countries. The company’s newest product, Jorveza[®], is an innovative budesonide formulation that is approved for treating eosinophilic esophagitis in Europe. Dr. Falk

Pharma is working with the FDA to allow U.S. patients to receive the benefits of Jorveza[®].

In contrast, Patent Owner Ellodi does not have any products on the market in Europe, the U.S., or anywhere else. Ellodi has, however, acquired ownership of certain U.S. and European patents, including the '407 patent and its European equivalent, EP2482822. Ellodi sought to preclude Jorveza[®] from being used by European patients based on EP2482822. This forced Dr. Falk Pharma to initiate opposition proceedings at the European Patent Office, which resulted in the complete revocation of all of Ellodi's original and auxiliary claims. The '407 patent claims are equivalent to the revoked European claims, and the USPTO should likewise cancel all of Ellodi's claims.

The '407 patent improperly removes from the public the claimed orally disintegrating solid pharmaceutical compositions containing a topically administered corticosteroid (such as budesonide or fluticasone) that disintegrates within 60 seconds. Such compositions were not inventive in the relevant 2009 time period.

Orally disintegrating solid pharmaceutical compositions were well-known by 2009. These compositions rapidly disperse in a patient's saliva in the oral cavity. The released active ingredient can be topically absorbed through the mucosa of the gastrointestinal track. Such compositions are especially desirable for patients who have difficulty swallowing tablets and capsules.

By 2009, there were over 40 commercially available orally disintegrating solid compositions marketed in the U.S. During this time period, many believed it was only a matter of time before the majority of orally administered drugs would be formulated as an orally disintegrating pharmaceutical composition.

The prevalence of orally disintegrating solid pharmaceutical compositions led to the FDA issuing guidelines and recommendations to the pharmaceutical industry in 2008. The FDA guidelines recommended that orally disintegrating solid pharmaceutical compositions should disintegrate rapidly in a patient's mouth, and also have an *in-vitro* disintegration time of approximately 30 seconds or less when tested according to the USP <701> Disintegration Test. The ordinarily skilled artisan was highly motivated to comply with the FDA's guidelines to obtain regulatory approval for an orally disintegrating formulation.

The Dohil prior art reference discloses an orally disintegrating solid pharmaceutical composition containing budesonide that renders obvious the challenged claims. The Grother prior art reference emphasizes the obviousness of the challenged claims because, like Dohil, it also discloses orally disintegrating solid pharmaceutical compositions containing budesonide as well as other corticosteroids such as fluticasone. These references present compelling evidence of obviousness. The Board should institute trial and hold that all claims from the '407 patent are unpatentable over the prior art.

II. BACKGROUND REGARDING THE '407 PATENT

The '407 patent is entitled “Orally administered corticosteroid compositions.” EX1001 Title. It claims priority to a provisional application filed October 1, 2009. The '407 patent issued with 42 claims, of which only claims 1 and 35 are independent claims. The claims are directed to orally disintegrating solid pharmaceutical compositions of a corticosteroid that disintegrate within 60 seconds when deposited in the upper gastrointestinal tract or a method of treating an inflammatory condition using such a pharmaceutical. Claim 35 is representative and recites:

35. An orally disintegrating solid pharmaceutical composition comprising

- [i] less than or equal to about 20 mg of a topically administrable corticosteroid and
- [ii] at least one excipient,
- [iii] wherein the solid pharmaceutical composition has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration,
- [iv] wherein the solid pharmaceutical composition disintegrates within 60 seconds when tested using the USP <701> Disintegration Test, and
- [v] upon administration the corticosteroid is deposited topically in the upper gastrointestinal tract.

EX1001 21:1-14.¹

Claim 1 is directed to “[a] method of treating an inflammatory condition of the gastrointestinal tract” using a pharmaceutical composition that is substantively identical to claim 35. *Id.* 18:50-62.

III. LEVEL OF ORDINARY SKILL

A person of ordinary skill in the art (“POSA”) related to the ’407 patent would have a Ph.D., another advanced degree, or its equivalent, in areas related to pharmaceuticals, chemistry, biology, medicine, or a related discipline, and 2-3 years of experience in formulation development. Alternatively, a POSA would have a lesser degree in those fields, with at least five or more years of experience in formulation development. The POSA would also have had access to a medical doctor with a specialty in gastroenterology, and other individuals with expertise related to the above subjects. EX1053 ¶30.

IV. STATE OF THE PRIOR ART

A. Budesonide

Budesonide is a potent, locally acting anti-inflammatory glucocorticoid that was known to treat a wide spectrum of inflammatory diseases. EX1025 1014-1015;

¹ Bracketed labels are added for convenient referencing to the limitations of claims 1 and 35. The ’407 patent claims are reproduced in Appendix A.

EX1009 857. Budesonide was considered to be a desirable drug for treating inflammation of the gastrointestinal tract because it is “a locally acting corticosteroid with a high first-pass effect, which minimizes systemic side effects.” EX1010 425.

Dr. Falk Pharma launched an orally administered capsule formulation of budesonide known as Budenofalk® in 1998. EX1026 1, 60; EX1027; EX1028 7. By 2009, nearly 1 million treatment cycles of Budenofalk® had been used by patients to treat Crohn’s disease and collagenous colitis. Budenofalk® also treated ulcerative colitis, eosinophilic gastroenteritis, and obstructive eosinophilic jejunitis. EX1011 589-590; EX1012 55; EX1013 187; EX1053 ¶¶47-52.

In 2005 and 2007, Aceves et al. reported that a viscous suspension of budesonide was orally administered as a topical formulation to successfully treat eosinophilic esophagitis (EOE or EE). EX1014 706; EX1015 1, 6, 8. Clinicians from the Aceves team filed a patent application describing the topical administration of budesonide, which published as US20070111978, EX1002 (“Dohil”). Dohil discloses at least two types of formulations of budesonide:

- (1) a viscous oral suspension of budesonide, *id.* ¶¶[0021], [0030], [0046]-[0070], and
- (2) a solid oral lozenge or tablet that dissolves rapidly in the mouth or esophagus, *id.* ¶¶[0032], [0013], [0037].

Dohil's lozenge or tablet "dissolve[s] rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus." *Id.* ¶¶0032]; EX1053 ¶¶53-62.

B. Orally disintegrating pharmaceutical compositions

Orally disintegrating solid pharmaceutical compositions were well-known by 2009. A patient's saliva causes an orally disintegrating pharmaceutical composition to disintegrate in the oral cavity, which allows the active ingredient contained in the composition to dissolve or disperse in the saliva and become absorbed through the mucosa of the mouth, esophagus, or other sections of the gastrointestinal track. EX1018 Abstract; EX1017 173-174.

The prior art uses several terms to refer to orally disintegrating solid pharmaceutical compositions, such as "fast disintegrating tablets (FDTs)," EX1018 Abstract, "quick-disintegrating/dissolving tablet[s]," EX1017 178, and "mouth dissolving drug delivery systems (MDDDS)," EX1019 Abstract. Such terms were often used interchangeably in the literature to refer to solid orally disintegrating pharmaceutical compositions. EX1018 434 ("The FDT is also known as fast melting, fast dispersing, rapid dissolve, rapid melt, and/or quick disintegrating tablet."); EX1017 178; EX1019 310.

"All FDTs approved by the [FDA] are classified as orally disintegrating tablets." EX1018 434. The FDA defines "orally disintegrating tablets" as "[a] solid dosage form containing medicinal substances which disintegrates rapidly, usually

within a matter of seconds, when placed upon the tongue.” EX1005 2; EX1053 ¶¶63-68.

1. Improved patient compliance

Many patients were known to have difficulty swallowing tablets and gelatin capsules. Dysphagia, or difficulty in swallowing, “is common in about 35% of the general population.” EX1018 433-34; EX1019 310. Patients who have difficulty swallowing medications may have a high incidence of noncompliance with taking their medications. “Lack of patient compliance is probably the most important factor that results in suboptimal therapeutic outcome for patients.” EX1017 172. Difficulties with patient compliance can be significantly improved by formulating active ingredients in an orally disintegrating solid pharmaceutical composition. EX1053 ¶¶69-73.

“Solid dosage forms that can be dissolved or suspended with water in the mouth for easy swallowing are highly desirable for the pediatric and geriatric population, as well as other patients who prefer the convenience of readily administered dosage forms.” EX1018 434. Such solid dosage forms desirably disintegrate “in less than 1 minute, but it is preferred to have disintegration as soon as possible.” *Id.* 435; EX1017 178 (“Whatever mechanism is used, the drug delivery systems all disintegrate in the patient’s mouth within a minute without the need of water or chewing.”).

Solid orally disintegrating pharmaceutical compositions can advantageously promote absorption of active ingredients through the oral mucosa, pharynx, and esophagus. EX1019 310-11; EX1018 466-67. This allows transmucosal delivery through oral or esophageal mucosa that beneficially “avoid[s] long-term parenteral therapy.” EX1017 172; EX1053 ¶¶74-77.

2. Commercial orally disintegrating pharmaceutical compositions

By 2009, there were several commercially available solid orally disintegrating pharmaceutical formulations on the market. Exemplary commercially available formulations included the Zydis[®] fast-dissolving wafer, the WOWTab[®] (With-Out-Water tablet), the Flash Dose[®] tablet, and OraSolv[®]. EX1017 178-181; EX1018 436-37. Drugs that were formulated into marketed orally disintegrating compositions were compiled into the following table:

TABLE 2. Examples of Commercially Available, Preapproval, or Submitted Orally Disintegrating Tablet Products

Brand name	Active ingredient	Application	Company	Technology
Claritin® RediTabs®	Loratadine	Antihistamine	Schering Corporation	Zydis®
Feldene Melt®	Piroxicam	NSAID	Pfizer	
Maxalt®-MLT®	Rizatriptan benzoate	Migraine	Merck	
Pepcid® ODT	Famotidine	Anti-ulcer	Merck	
Zyprexa®	Olanzapine	Psychotic disorders	Eli Lilly	
Zofran® ODT®	Ondansetron	Anti-emetic	Glaxo Smith Kline	
Risperdal® M-Tab™	Risperidone	Schizophrenia	Janssen	
Zubrin™(pet drug)	Tepoxalin	Canine NSAID	Schering Corporation	
Zelapar™	Selegiline	Parkinson's disease	Elan / Amarin Corporation	
Klonopin® Wafers	Clonazepam	Sedation	Roche	
Children's Dimetapp® ND	Loratadine	Allergy	Wyeth Consumer Healthcare	
Imodium Instant Melts	Loperamide HCl	Anti-diarrheal	Janssen	
Propulsid® Quicksolv®	Cisapride monohydrate	Gastrointestinal prokinetic agent	Janssen	Quicksolv®
Tempra Quicklets Tempra FirsTabs	Acetaminophen	Analgesic	Bristol-Myers Squibb	OraSolv®
Remeron® SolTab®	Mirtazapine	Anti-depression	Organon Inc.	
Triaminic® Softchews®	Various combinations	Pediatric cold, cough and allergy	Novartis Consumer Health	
Zomig-ZMT® and Rapimelt®	Zolmitriptan	Anti-migraine	AstraZeneca	DuraSolv®
Alavert®	Loratadine	Allergy	Wyeth Consumer Healthcare	
NuLev®	Hyoscyamine sulfate	Anti-ulcer	Schwarz Pharma	
Kemstro™	Baclofen	Anti-spastic analgesic	Schwarz Pharma	
Benadryl® Fastmelt®	Diphenhydramine citrate	Allergy, sinus pressure relief	Pfizer	WOWTAB®
Nasea OD	Ramosetron HCl	Anti-emetic	Yamanouchi	
Gaster D	Famotidine	Anti-ulcer	Yamanouchi	
Excedrin® QuickTabs	Acetaminophen	Pain reliever	Bristol-Myers Squibb	QuickTabs™
Ralivia FlashDose®	Tramadol HCl	Analgesics	Biovail	FlashDose®
Zolpidem ODT	Zolpidem tartrate	Sleep disorders	Biovail	
Fluoxetine ODT	Fluoxetine	Anti-depression	Biovail	
Nurofen® Flashtab®	Ibuprofen	NSAID	Boots Healthcare	Flashtab®
Hyoscyamine Sulfate ODT	Hyoscyamine sulfate	Anti-ulcer	ETHEX Corporation	OraQuick
Cibalginadue FAST	Ibuprofen	NSAID	Novartis Consumer Health	Ziplets™

EX1018 438-439.

By 2009, a POSA had “no doubt that the need for these [orally disintegrating pharmaceutical] systems is real, and many classes of drugs could benefit from this noninvasive type of delivery.” EX1017 183. Based on “the many benefits of FDTs [fast disintegrating tablets],” it was thought that it was “only a matter of time until a

majority of oral formulations are prepared in FDT forms.” EX1018 469; EX1053 ¶¶78-86.

C. Solid Orally Disintegrating Compositions Of Budesonide

The formulation of budesonide as an orally disintegrating solid pharmaceutical composition that would dissolve rapidly was disclosed in at least four prior art references.

First, Dohil’s disclosure of budesonide formulated into a solid oral lozenge or tablet that dissolves rapidly in the mouth or esophagus is discussed above. *Supra* Section IV.A; EX1002 ¶¶[0032], [0013], [0037].

Second, Grother discloses “fast dispersing solid dosage forms that preferably dissolve in the oral cavity within sixty (60), more preferably within thirty (30), most preferably within ten (10) seconds.” EX1008 Abstract; *id.* 13:19-22. Grother discloses a fast dispersing dosage form comprising an active ingredient, a modified starch, and a matrix forming agent. *Id.* 12:10-19, 15:19-20. Grother discloses several types of drugs suitable for its fast dispersing dosage form, *id.* 16:1-21:15, including corticosteroids, such as fluticasone and budesonide, *id.* 18:15-18.

Third, Singh discloses “fast dissolving tablets,” EX1035 1:20-23, 2:37-49, that preferably “dissolves or disperses in the mouth within one minute,” *id.* 2:29-36. Singh discloses groups of drugs that can be employed in the tablets, *id.* 3:16-19:54, including glucocorticoids such as budesonide, *id.* 16:56-17:14.

Fourth, Cherukuri discloses “a rapid-melt composition” that preferably is “a gastrointestinal therapeutic.” EX1036 1:15-20, 9:6-10. Cherukuri’s rapid-melt composition “disintegrates quickly in the mouth of the mammal,” preferably “in less than 20 seconds.” *Id.* 14:50-56. Cherukuri discloses several classes of active ingredients suitable for the rapid-melt composition, *id.* 7:51-11:52, including fluticasone and budesonide, *id.* 9:64-67; EX1053 ¶¶87-95.

D. FDA Guidance

In December of 2008, the FDA published its guidance for the pharmaceutical industry regarding orally disintegrating tablets. EX1005. The FDA Guidance explains that orally disintegrating tablets are designed to disintegrate or dissolve rapidly without the need to swallow or chew for the benefit of patients with impaired swallowing. *Id.* 1.

The FDA Guidance defines orally disintegrating tablets as “[a] solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.” *Id.* 2. The FDA Guidance further clarifies that orally disintegrating tablets 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.” *Id.* 2. The Guidance recommends “that applicants use

the USP method for disintegration testing,” *id.* 3, specifically “USP 29, <701> Disintegration, pp.2670-2672.” *Id.* 3 n.3; EX1016; EX1053 ¶¶96-99.

V. THE EPO REVOKED ELLODI’S CLAIMS

The USPTO is not the first office to adjudicate the obviousness of Ellodi’s composition claims. In an opposition proceeding, the European Patent Office (EPO) determined that Dohil rendered obvious substantively identical claims in EP2482822. EX1004 ¶¶33-36.9; EX1003. Of particular relevance, the EPO held claim 1 of Ellodi’s Auxiliary Request 5 (AR5) was obvious over Dohil.² A side-by-side comparison of claim 35 of the ’407 patent and EPO AR5 is shown below:

U.S. 9,486,407 Claim 35	EP2482822 (AR5) Claim 1
35. An orally disintegrating solid pharmaceutical composition comprising	1. An orally dispersing tablet comprising
less than or equal to about 20 mg of a topically administrable corticosteroid and	less than or equal to 20 mg of budesonide or a solvate or ester thereof, and
at least one excipient, wherein: the solid pharmaceutical composition has no	at least one pharmaceutically acceptable ingredient which

² As noted in the EPO decision, Auxiliary Request 5 (AR5) was previously filed as Auxiliary Request 3(II) (AR3(II)). EX1004 ¶33. The claims appended to the EPO decision retained their prior labeling. Thus, AR5 claims are on page 27 under the heading “Claims – Auxiliary Request 3(II).” *Id.* page 27.

U.S. 9,486,407 Claim 35	EP2482822 (AR5) Claim 1
significant systemic glucocorticoid or mineralocorticoid activity after oral administration,	facilitates the dispersal of the tablet in the oral cavity,
wherein the solid pharmaceutical composition disintegrates within 60 seconds when tested using the USP <701> Disintegration Test, and upon administration the corticosteroid is deposited topically in the upper gastrointestinal tract.	wherein the tablet is suitable for topical administration of budesonide in the upper gastrointestinal tract, and wherein said tablet disintegrates within 60 seconds in simulated saliva fluid when tested using the USP <701> Disintegration Test.

EX1001 21:1-13; EX1004 ¶33, page 27. Claim 35 of the '407 patent is substantively identical to EPO AR5 claim 1 when the “topically administrable corticosteroid” recited by '407 patent claim 35 is the budesonide as recited in, e.g., '407 patent claim 37. EX1001 9:11-18.

In holding that Dohil renders obvious claim 1 of AR5, the EPO determined that Dohil is “the closest prior art as it is also directed to oral dosage forms comprising corticosteroids for the topical treatment of the upper GI tract, e.g., of the esophagus.” EX1004 ¶36.1 (citing EX1002 ¶¶[0010]-[0013]). The EPO explained that “the dosage forms disclosed in [Dohil] [0032] represent the closest starting point to the claimed subject-matter, as the dosage form in [0032] and the claimed ODT [orally dispersing tablet] have the same release mechanism.” *Id.* ¶36.3.

The EPO determined that Dohil “clearly describes a lozenge or similar tablet, which rapidly dissolves in the mouth,” and includes “an excipient which facilitates their dispersion and dissolution.” EX1004 ¶¶26.4-26.5; EX1002 ¶[0032]. Dohil explicitly mentions solid compositions “as suitable dosage forms for the topical treatment of the upper GI tract.” EX1004 ¶36.2. Dohil discloses orally disintegrating solid pharmaceutical compositions “comprising less than or equal to 20 mg of budesonide.” EX1004 ¶¶26.6-26.8; EX1002 ¶¶[0015], [0032].

The EPO determined that a POSA putting Dohil’s disclosure into practice would have arrived at the claimed disintegration time of within 60 seconds because orally dispersing tablets (ODTs) were well-known dosage forms and their disintegration time could be modulated to obtain a desired therapeutic effect as follows:

ODTs are well-known dosage forms and belong to the common technical knowledge of the skilled formulator. The skilled person is aware that their disintegration time can be modulated in order to obtain the desired therapeutic effect. Therefore, the claimed disintegration time is regarded as one of the options available to the skilled person when putting into practice the general disclosure of [0032] of [Dohil].

EX1004 ¶36.8. The EPO held that “a budesonide ODT showing a disintegration time within 60 seconds in simulated saliva fluid when tested using the USP <701> Disintegration Test is an obvious solution to the problem” of providing a budesonide

orally dispersible tablet. EX1004 ¶¶36.8. The USPTO should reach the same conclusion in this proceeding.

VI. RELIEF REQUESTED

Petitioner requests cancellation of claims 1-42 of the '407 patent as obvious over the asserted prior art.

A. The Asserted References Are Prior Art

The earliest claimed priority date for the '407 patent is October 1, 2009. The asserted references are all prior art to the '407 patent:

Exhibit	Reference	Date	Art Type
1002	Dohil	Published: 05/17/2007	§102(b)
1008	Grother	Published: 08/03/2000	§102(b)
1005	FDA Guidance	Published: 12/16/2008	§102(a) ³
1020	Venkatesh	Published: 10/20/2005	§102(b)

³ See EX1006 for 12/16/2008 publication date. Also, on 04/09/2007, the FDA published substantively identical draft guidance for the industry. *Id.*; EX1007. To the extent Ellodi attempts to swear behind the 2008 FDA Guidance, Dr. Parr has mapped the disclosures of the 2007 Draft FDA Guidance to the claims. *See, e.g.*, EX1053 ¶¶127, 157, 214.

B. Grounds of Unpatentability

IPR is requested for the following grounds of unpatentability:

Ground	Reference(s)	Basis	Challenged Claims
1	Dohil in view of the knowledge of a POSA	§103	1-4, 16-19, 21-23, 35-39
2	Grother in view of the FDA Guidance	§103	1-4, 16-19, 21, 23-25, 27-42
3	Dohil and Venkatesh in view of the knowledge of a POSA	§103	5-15, 20
4	Grother, the FDA Guidance, and Venkatesh	§103	5-15, 20, 26

The petition is supported by the expert declaration of Dr. Alan F. Parr, Pharm.D., Ph.D. EX1053.

VII. CLAIM CONSTRUCTION

All claim terms not specifically construed in this petition have been accorded their plain and ordinary meaning under a *Phillips*-type construction.

The '407 patent defines “having no significant systemic glucocorticoid or mineralocorticoid activity” as “corticosteroid compositions which do not provide a generalized effect in the body through absorption into the circulation, but do provide local effects through topical contact with a diseased tissue.” EX1001 3:16-21.

The '407 patent defines “adhesive agent” as “agents which promote adhesion of the corticosteroid to biological surfaces, and includes, but is not limited to bio-adhesive agents.” EX1001 3:4-7.

The '407 patent defines “orally disintegrating tablet”, “orally dispersing tablet”, or “ODT” as “a solid dosage form of the present invention, which disintegrates rapidly in the oral cavity of a patient after administration, without chewing.” EX1001 2:46-49. This definition is equivalent to that adopted by the FDA. EX1005 2; EX1053 ¶162.

The '407 patent defines “intimately associated” as describing “the spatial relationship between two or more components of a composition refers to components [*sic*] that are intimately mixed, such as for example in mixtures, coatings and matrices.” EX1001 3:11-15.

The '407 patent defines “sugar alcohols” as “hydrogenated forms of carbohydrates in which the carbonyl group (i.e., aldehyde or ketone) has been reduced to a primary or secondary hydroxyl group.” EX1001 13:30-32. “Non-limiting examples of suitable sugar alcohols... include e.g. arabitol, isomalt, erythritol, glycerol, lactitol, mannitol, sorbitol, xylitol, maltitol, and mixtures thereof.” *Id.* 13:33-37.

The '407 patent states that “[t]he term ‘saccharide’ is synonymous with the term ‘sugars’ includes monosaccharides such as glucose, fructose, the lactose, and

ribose; and disaccharides such as sucrose, lactose, maltose, trehalose, and cellobiose.” EX1001 13:37-41.

The ’407 patent states that “[t]he term ‘about’, as used herein to refer to a numerical quantity, includes ‘exactly’. ... When the term ‘about’ is used in reference to a range of values, the term ‘about’ refers to both the minimum and maximum value of the range (e.g., ‘about 1-50 μm ’ means ‘about 1 μm to about 50 μm ’).” EX1001 2:62-3:3.

Patent Owner’s lexicography governs, and Petitioner adopts and applies each of these definitions.

VIII. GROUND 1: DOHIL IN VIEW OF THE KNOWLEDGE OF A POSA

Dohil discloses an orally disintegrating solid composition having the same ingredients claimed by the ’407 patent. This section introduces Dohil, and then explains how Dohil in view of the knowledge of a POSA renders obvious claims 1-4, 16-19, 21-23, and 35-39 of the ’407 patent. Petitioner will first address the independent composition (claim 35) and method (claim 1) claims, followed by the dependent claims.

A. Dohil

Dohil discloses a budesonide formulation “provided in the form of a lozenge which may be dissolved in the mouth, thus reaching and coating the esophagus.” EX1002 ¶[0032]. Dohil explains that the lozenge “or other similar tablet” will

“dissolve rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus.” *Id.* Exemplary dosage amounts of budesonide in Dohil’s formulation include “1-2 mg or 2-3 mg.” *Id.* ¶[0015]; EX1053 ¶102.

B. Claim 35

Dohil discloses orally disintegrating solid compositions that render obvious all limitations of claim 35.

1. Preamble

The preamble of claim 35 recites: “[a]n orally disintegrating solid pharmaceutical composition.”

If the preamble were limiting, Dohil discloses the recited orally disintegrating solid pharmaceutical composition. For example, Dohil discloses that “[b]udesonide is provided in the form of a *lozenge which may be dissolved in the mouth*, thus reaching and coating the esophagus. The lozenge or other similar tablet, capsule, or other solid, would *dissolve rapidly in the mouth* or esophagus to produce a solution that can then coat the esophagus.” EX1002 ¶[0032].⁴ Dohil further discloses “[b]udesonide, in the form of a *dissolving tablet*.” *Id.* ¶[0013]; *id.* ¶[0037] (disclosing “dissolving tablets”); EX1053 ¶¶106-107.

Dohil’s lozenges and tablets are solid pharmaceutical compositions that dissolve rapidly in the mouth without chewing and meet the preamble. Indeed, the

⁴ All emphases supplied unless otherwise noted.

EPO determined that Dohil’s “dosage forms described in [0032] of [Dohil] at least overlap the ODT [orally dispersing tablet] addressed in claim 1.” EX1004 ¶26.4.

2. **Limitation 35[i]**

Limitation 35[i] recites “less than or equal to about 20 mg of a topically administrable corticosteroid.”

Dohil discloses that “[b]udesonide is provided in the form of a lozenge which may be dissolved in the mouth.” EX1002 ¶[0032]. Budesonide is a topically administrable corticosteroid, as admitted by the ’407 patent. EX1001 3:30-33 (disclosing budesonide as an exemplary corticosteroid that “provide[s] local effects through topical contact with a diseased tissue,” *id.* 20-21), 7:24-26 (compositions “comprise budesonide”); *supra* Section IV.A.

Dohil further discloses that “[i]n certain embodiments, 1-2 mg or 2-3 mg of corticosteroid per day is administered to said individual.” EX1002 ¶[0015]; *id.* ¶¶[0031], [0058] (“0-1 mg/day, 1-2 mg/day... or 5-6 mg/day of... for example, Budesonide, are administered”). Dohil’s patients were actually dosed with topically administered budesonide at 0.5, 1, and 2 mg/day. *Id.* ¶¶[0058], [0053], Table 1. “In one illustrative example, the dose is provided once a day.” *Id.* ¶[0031]. Dohil thus discloses a lozenge or tablet containing a daily dose of budesonide containing, e.g., 0.5mg, 1mg, 2mg, and/or 3mg. EX1053 ¶¶109-113.

Dohil therefore discloses limitation 35[i], which was previously confirmed by the EPO. EX1004 ¶26.6 (“Therefore, when reading the disclosure of [0032] in light of the teaching of [0015], the skilled person understands that the orally dispersing tablet disclosed therein comprises at most 3 mg budesonide”).

3. Limitation 35[ii]

Limitation 35[ii] recites “at least one excipient.”

Dohil discloses that “[b]udesonide is provided in the form of a lozenge” or “other similar tablet” which will “dissolve rapidly in the mouth or esophagus.” EX1002 ¶[0032]. Dohil discloses “[p]harmaceutical preparations for oral use may be obtained by combining the corticosteroids with solid excipients” to obtain tablets, and discloses “[s]uitable excipients.” EX1002 ¶[0037]; *id.* ¶[0014]. Tablets contain excipients. EX1041 239 (“In addition to the active ingredients, solid oral dosage forms will also contain a range of substances called excipients.”); EX1053 ¶¶115-119.

Dohil therefore discloses limitation 35[ii], which the EPO’s ruling confirms. EX1004 ¶26.4 (“the skilled person would understand that the tablets addressed in [0032] of [Dohil] necessarily require an excipient which facilitates their dispersion and dissolution”).

4. Limitation 35[iii]

Limitation 35[iii] recites “wherein the solid pharmaceutical composition has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration.”

The ’407 patent admits that budesonide has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration. EX1001 3:16-32 (“Exemplary corticosteroids... include... budesonide....”). Budesonide must have no significant systemic glucocorticoid or mineralocorticoid activity for dependent claim 37 (which recites “budesonide”) to properly depend from claim 35.

Dohil teaches the corticosteroid used in its formulations should “ha[ve] a low bioavailability” to “result in decreased systemic side effects and complications.” EX1002 ¶[0041]. Dohil teaches that budesonide undergoes “rapid hepatic metabolism.” EX1002 ¶[0065]. The rapid hepatic metabolism of budesonide was known to beneficially result in no systemic activity such that it does not provide a generalized effect via absorption into the circulation. EX1009 857; EX1025 1014-15; EX1053 ¶¶122-124. Thus, a POSA would have known that the rapid hepatic metabolism of budesonide would result in no significant systemic glucocorticoid or mineralocorticoid activity after oral administration in Dohil’s rapidly dissolving lozenges and tablets.

Dohil therefore discloses limitation 35[iii], which the EPO proceeding confirms. EX1038 ¶4.10 (“‘Budesonide’ is an anti-inflammatory corticosteroid that can be administered topically and has a very low systemic effect.”).

5. Limitation 35[iv]

Limitation 35[iv] recites “wherein the solid pharmaceutical composition disintegrates within 60 seconds when tested using the USP <701> Disintegration Test.”

Dohil discloses that “[t]he lozenge or other similar tablet, capsule, or other solid, would dissolve rapidly in the mouth or esophagus to produce a solution that can then coat the esophagus.” EX1002 ¶[0032]. It was desirable for the disintegration time of rapidly dissolving solid compositions to vary “from several seconds to about a minute.” EX1018 434; EX1053 ¶¶126-127.

It would have been obvious to formulate Dohil’s rapidly dissolving lozenge or tablet to disintegrate within 60 seconds when tested using the USP <701> Disintegration Test in view of the knowledge of the POSA. The knowledge of the POSA is represented by, for example, the FDA’s Guidance for Industry on orally disintegrating tablets. The FDA Guidance explains that orally disintegrating tablets “disintegrate[] rapidly, usually within a matter of seconds.” EX1005 2. The FDA recommends that such compositions have “*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).” *Id.* 2. The FDA Guidance “recommend[s] that applicants use the USP method for disintegration testing,” *id.* 3, specifically “**USP 29, <701> Disintegration**” *id.* 3 n.3.

A POSA would have been motivated to follow the FDA Guidance in formulating Dohil’s rapidly dissolving lozenge or tablet containing budesonide. The FDA Guidance provides the agency’s thinking and recommendations on the topic of rapidly disintegrating oral pharmaceutical compositions. *Id.* 1. The FDA regulates the use of pharmaceutical compositions in the United States. Dohil’s formulations were intended to “be used in therapy for human patients,” EX1002 ¶[0028], and the initial testing of its formulations was conducted within the United States, *id.* ¶[0049]. 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. EX1053 ¶128; *Allergan, Inc. v. Sandoz Inc.*, 726 F.3d 1286, 1291-92 (Fed. Cir. 2013) (“[t]he potential for FDA approval also may properly be considered, as it was here, in determining whether one of ordinary skill would be motivated to develop a drug product”).

A POSA would have had a reasonable expectation of success in doing so based on Dohil’s detailed description of how to formulate budesonide into a rapidly disintegrating lozenge or tablet. EX1002 ¶¶[0027]-[0041] (section entitled

“Formulation”). Formulating orally disintegrating pharmaceutical compositions that dissolve within “several seconds to about a minute” would have been a routine exercise by 2009. EX1018 434; EX1005 2. There were many commercially available orally disintegrating systems and products available by 2009, which would have bolstered the POSA’s expectation of success. EX1017 179-181; EX1018 436-439; EX1053 ¶129.

Dohil in view of the knowledge of a POSA renders obvious limitation 35[iv], which the EPO’s ruling confirms as follows:

[A] budesonide ODT [orally dispersing tablet] showing a disintegration time within 60 seconds in simulated saliva fluid when tested using the USP <701> Disintegration Test is an obvious solution to the problem. ... ODTs are well-known dosage forms and belong to the common technical knowledge of the skilled formulator. The skilled person is aware that their disintegration time can be modulated in order to obtain the desired therapeutic effect. Therefore, the claimed disintegration time is regarded as one of the options available to the skilled person when putting into practice the general disclosure of [0032] of [Dohil].

EX1004 ¶36.8.

6. Limitation 35[v]

Limitation 35[v] recites “upon administration the corticosteroid is deposited topically in the upper gastrointestinal tract.”

Upon administration of Dohil’s lozenge or tablet, it “dissolve[s] rapidly in the mouth or esophagus to produce a solution” of budesonide that is deposited topically in the upper gastrointestinal tract by “coat[ing] the esophagus.” EX1002 ¶[0032]. Dohil repeatedly discloses that its formulations are designed to topically deposit budesonide in the “upper gastrointestinal tract,” *id.* ¶[0010], such as “to the esophagus,” *id.* ¶¶[0013], [0037], [0041]; EX1053 ¶¶131-132.

Dohil therefore discloses limitation 35[v], which the EPO proceeding confirms. EX1004 ¶36.1 (“The OD agrees with the parties in the choice of [Dohil] as the closest prior art as it is also directed to oral dosage forms comprising corticosteroids for the topical treatment of the upper GI tract, e.g. of the esophagus (*see* [0010][0013]).”).

Dohil in view of the knowledge of a POSA therefore renders obvious claim 35.

C. Claim 1

Independent claims 1 and 35 are highly similar. Claim 1 is directed to a method of treating an inflammatory condition using the pharmaceutical composition recited by claim 35.

1. Preamble

The preamble of claim 1 recites: “[a] method of treating an inflammatory condition of the gastrointestinal tract.”

If the preamble were limiting, Dohil discloses the recited method. Dohil discloses using its formulations to treat inflammation of the gastrointestinal tract as follows:

The methods of the present invention are useful, for example, for preventing and *alleviating the symptoms and inflammation of eosinophilic esophagitis... esophageal inflammation* secondary to caustic/irritant ingestion, persistent/recurrent esophageal strictures of any cause and including caustic/irritant ingestion, pill-induced esophagitis, systemic diseases, congenital diseases, Epidermolysis bullosa, and post-surgery inflammation. The present methods are also useful for preventing or *alleviating symptoms and inflammation associated with other diseases or conditions of the gastrointestinal tract, for example, the upper gastrointestinal tract*, where it is beneficial to target a particular target site, rather than provide systemic therapy.

EX1002 ¶[0010]; *id.* ¶¶[0011], [0015]; EX1053 ¶¶135-136.

The EPO determined that Dohil is “directed to oral dosage forms comprising corticosteroids for the topical treatment of the upper GI tract, e.g., of the esophagus (see [0010]-[0013]).” EX1004 ¶36.1.

2. Limitation 1[i]

Limitation 1[i] recites “administering to an individual in need thereof a pharmaceutical composition.”

Dohil discloses administering a pharmaceutical composition. EX1002 ¶¶[0011], [0015], [0021]; EX1053 ¶¶138-139. The EPO determined that Dohil's compositions "are intended for daily administration." EX1004 ¶26.6.

3. Limitations 1[ii]-1[vi]

Dohil renders obvious limitations 1[ii]-1[vi]⁵ for reasons discussed, *supra*, at Sections VIII.B.2-6, regarding limitations 35[i]-35[v]. Dohil in view of the knowledge of a POSA renders obvious claim 1. EX1053 ¶¶140-154.

D. Claims 2 and 36

Claim 2 depends from claim 1. Claim 36 depends from claim 35. Both claims require that the composition "disintegrates within 30 seconds."

Dohil discloses a budesonide lozenge or tablet that "dissolve[s] rapidly in the mouth." EX1002 ¶[0032]. A POSA would have been motivated to formulate Dohil's rapidly dissolving lozenge or tablet to disintegrate within 30 seconds with a reasonable expectation of success. *Supra* Section VIII.B.5. Indeed, the FDA recommended that such compositions have "an *in-vitro* disintegration time of approximately 30 seconds or less," EX1005 2, using the "USP 29, <701> Disintegration" test. *Id.* 3 n.3; EX1053 ¶157. Dohil renders obvious claims 2 and 36.

⁵ The claims are reproduced in Appendix A.

E. Claims 3 and 37

Claim 3 depends from claim 1. Claim 37 depends from claim 35. Both claims recite that “said corticosteroid is selected from the group consisting of budesonide...”

Dohil discloses that “[b]udesonide is provided in the form of a lozenge which may be dissolved in the mouth.” EX1002 ¶¶[0032], ¶[0013] (“Budesonide, in the form of a dissolving tablet, a dissolving wafer....”); EX1053 ¶160. Dohil renders obvious claims 3 and 37.

F. Claim 4

Claim 4 requires the composition of claim 1 to be “in the form of an orally disintegrating tablet (ODT).”

Dohil discloses budesonide formulated as a lozenge or tablet that “*dissolve[s] rapidly in the mouth* or esophagus.” EX1001 ¶[0032]; *id.* [0013] (disclosing solid “dissolving tablet” and “dissolving wafer”). A POSA would understand that Dohil’s lozenges and tablets that dissolve rapidly in the oral cavity do so without chewing. EX1053 ¶¶163-165; EX1005 1; *supra* Section IV.B. Dohil renders obvious claim 4, which the EPO’s ruling confirms. EX1004 ¶26.3-4 (“the dosage forms described in [0032] at least overlap the ODT [orally dispersing tablet] in claim 1”).

G. Claims 16-17 and 38

Claim 16 depends from claim 1 and “further compris[es] an adhesive agent.”

Claim 17 depends from claim 16 and recites “the adhesive agent is selected from the group consisting of... polyvinylpyrrolidone... sodium carboxymethylcellulose, [and] hydroxypropyl cellulose....”

Claim 38 depends from claim 35 and “further compris[es] an adhesive agent.”

The '407 patent admits that suitable adhesive agents include polyvinylpyrrolidone, sodium carboxymethylcellulose, and hydroxypropyl cellulose. EX1001 10:40-57.

Dohil discloses that its tablets are beneficially “formulated with at least one excipient to deliver a viscous form of the corticosteroid to the esophagus.” EX1002 ¶[0013]. Such excipients promote adhesion of the corticosteroid to the esophagus, which meets the claimed “adhesive agent.” EX1053 ¶¶170-171. Dohil’s excipients “may be, for example, selected from the group consisting of... hydroxypropylmethyl-cellulose, *sodium carboxymethyl-cellulose (CMC)*, and *polyvinylpyrrolidone (PVP: povidone)*.” EX1002 ¶[0014]; *id.* ¶[0037] (“Suitable excipients are, in particular... *hydroxypropylmethyl-cellulose*, *sodium carboxymethyl-cellulose (CMC)*, and/or *polyvinylpyrrolidone (PVP: povidone)*.”). Dohil renders obvious claims 16, 17 and 38.

H. Claim 18

Claim 18 depends from claim 1 and recites “further comprising a disintegrant selected from the group consisting of crospovidone....”

The '407 patent admits that crospovidone is “cross-linked PVP [polyvinylpyrrolidone].” EX1001 8:65-9:3, 13:21-25.

Dohil teaches “[i]f desired, disintegrating agents may be added, such as the *cross-linked polyvinylpyrrolidone*, agar, or alginic acid or a salt thereof such as sodium alginate.” EX1002 ¶[0037]; EX1053 ¶¶174-176. Dohil renders obvious claim 18.

I. Claims 19 and 39

Claim 19 depends from claim 1. Claim 39 depends from claim 35. Both claims recite an excipient “selected from the group consisting of... sorbitol... lactose, sucrose....”

Dohil discloses that “[s]uitable excipients are, in particular, fillers such as sugars, including *lactose*, *sucrose*... or *sorbitol*....” EX1002 ¶[0037]; *id.* ¶[0014] (“[t]he excipient may be, for example, selected from the group consisting of *lactose*, *sucrose*... *sorbitol*....”); EX1053 ¶179. Dohil renders obvious claims 19 and 39.

J. Claims 21 and 23

Claim 21 depends from claim 16 and further requires “the adhesive agent and corticosteroid are intimately associated.”

Claim 23 depends from claim 21 and recites “the corticosteroid is disposed on the surface of said adhesive agent.”

Dohil discloses the claimed adhesive agent because its tablets are beneficially “formulated with at least one excipient to deliver a viscous form of the corticosteroid to the esophagus.” EX1002 ¶[0013]. The excipient promotes adhesion of budesonide to the esophagus. *Supra* Section VIII.G. Dohil further discloses “combining the corticosteroids with solid excipients, *optionally grinding a resulting mixture, and processing the mixture of granules...* to obtain tablets or dragee cores.” EX1002 ¶[0037]. The process of grinding the corticosteroid with an excipient creates an intimate mixture that meets the claimed intimate association and disposes the corticosteroid over the surface of the excipient. Dohil renders obvious claims 21 and 23. EX1053 ¶¶183-186; EX1054 35; EX1055 382-83.

K. Claim 22

Claim 22 depends from claim 21 and requires “the corticosteroid is surrounded or encapsulated by the adhesive agent.”

Dohil discloses that the “[d]ragee cores are provided with suitable coatings,” that include the adhesive excipient “polyvinylpyrrolidone.” EX1002 ¶[0039]. The dragee core contains the corticosteroid and is surrounded by the coating of the adhesive polyvinylpyrrolidone excipient. EX1053 ¶¶188-189. Dohil renders obvious claim 22.

IX. GROUND 2: GROTHER IN VIEW OF THE FDA GUIDANCE

Grother discloses an orally disintegrating solid composition having the same ingredients claimed by the '407 patent. A POSA would have been motivated to follow the FDA Guidance in formulating Grother's orally disintegrating solid composition to disintegrate within 60 seconds using the USP <701> Disintegration Test with a reasonable expectation of success. This section introduces Grother, and then explains how Grother in view of the FDA Guidance renders obvious claims 1-4, 16-19, 21, 23-25, 27-42 of the '407 patent.

A. Grother

Grother discloses “fast dispersing solid dosage forms that preferably dissolve in the oral cavity within sixty (60), more preferably within thirty (30), most preferably within ten (10) seconds.” EX1008 Abstract. Grother's fast dispersing dosage form comprises an active ingredient, a modified starch, and a matrix forming agent as follows:

There is disclosed a fast dispersing solid dosage form designed to release an active ingredient rapidly in the oral cavity characterized in that said dosage form is essentially free of mammalian gelatin and comprises:

- at least one active ingredient;
- at least one modified starch at a concentration of from 20 to 90% by weight of said solid dosage form; and
- at least one matrix forming agent;

wherein said solid dosage form is obtainable by removing a solvent from a mixture comprising said active ingredient, said modified starch and said matrix forming agent.

EX1008 12:10-19. Grother discloses that “[a]ny drug may be used as the active ingredient in the composition of the present invention,” *id.* 15:19-20, including budesonide, *id.* 18:15-18; EX1053 ¶191.

B. Claim 35

Grother in view of the FDA Guidance discloses orally disintegrating solid compositions that render obvious all limitations of claim 35.

1. Preamble

The preamble of claim 35 recites: “[a]n orally disintegrating solid pharmaceutical composition.”

If the preamble were limiting, Grother discloses the recited orally disintegrating solid pharmaceutical composition. For example, Grother discloses “a fast dispersing solid dosage form designed to release an active ingredient rapidly in the oral cavity.” EX1008 12:10-19; *id.* 1:10-11, 3:18-20, 32:10. Grother discloses “fast dispersing solid dosage forms that preferably dissolve in the oral cavity within sixty (60), more preferably within thirty (30), most preferably within ten (10) seconds.” *Id.* Abstract; *id.* 13:19-22; EX1053 ¶195.

2. Limitation 35[i]

Limitation 35[i] recites “less than or equal to about 20 mg of a topically administrable corticosteroid.”

Grother discloses that “the active ingredient is generally present in an amount from 0.2 to 95%, normally 1 to 20%, by weight of the composition of the dried dosage form.” EX1008 21:16-18. Grother discloses that 60 mg is generally the “upper value” per dosage form. *Id.* 26:22-27:1. Grother discloses specific examples of 10 mg and 12.5 mg of active ingredient per dosage form. *Id.* 29, Table I.

Grother discloses that “[a]ny drug may be used as the active ingredient in the composition of the present invention,” EX1008 15:19-20, including corticosteroids, such as fluticasone and budesonide, *id.* 18:15-18; EX1053 ¶¶197-198. A POSA would have been motivated to select budesonide as an active ingredient in Grother’s fast dispersing solid dosage form based on Grother’s express disclosure to do so. *Boston Scientific Scimed, Inc. v. Cordis Corp.*, 554 F.3d 982, 991 (Fed. Cir. 2009) (“Combining two embodiments disclosed adjacent to each other in a prior art patent does not require a leap of inventiveness”). In addition, budesonide was a well-known corticosteroid with desirable anti-inflammatory activity. *Supra* Section IV.A. EX1053 ¶199. The ’407 patent admits that budesonide is a topically administrable corticosteroid. EX1001 3:25-32.

It was generally known that dosages of budesonide in solid oral tablets desirably ranged from 3-9 mg. For example, Budenofalk® contained 3 mg of budesonide in each dosage unit. EX1026 8. Entocort EC tablets contained 3 mg of budesonide. EX1009 859. Other tablets contained 4.5 mg, 6 mg, 9 mg of budesonide. *Id.* Dohil discloses topically administrable budesonide formations containing, e.g., 1-2 mg and 5-6 mg per dosage unit. EX1002 ¶¶[0058], [0015], Table 1. Based on Grother's instruction that its compositions should normally have 1-20% by weight active ingredient and the general knowledge in the art that topically administrable formulations of budesonide typically contain, e.g., 3 mg of budesonide, a POSA would have been motivated to formulate budesonide in Grother's compositions at, e.g., 3 mg, with a reasonable expectation of success. EX1053 ¶¶200-201. Grother therefore renders obvious a pharmaceutical composition that comprises less than or equal to about 20 mg of a topically administrable corticosteroid.

3. Limitation 35[ii]

Limitation 35[ii] recites “at least one excipient.”

Grother's fast dispersing solid dosage forms comprise a “matrix forming agent.” EX1008 Abstract, 3:18-22, 12:10-19. The matrix forming agent is a “crystal forming excipient.” *Id.* 27:7-10; *id.* 3:13-14, 32:12-14.

Grother discloses that “[t]he preferred matrix forming agent is mannitol.” *Id.* 13:12; *id.* 14:16-21. “Most commercial ODTs have been developed using mannitol as the bulk excipient of choice.” EX1041 261; EX1053 ¶¶203-207. The ’407 patent admits that mannitol was “typically used in disintegrating tablet formulations.” EX1001 8:47-55. Grother therefore discloses at least one excipient.

4. Limitation 35[iii]

Limitation 35[iii] recites “wherein the solid pharmaceutical composition has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration.”

The ’407 patent admits that budesonide has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration. EX1001 3:16-32.

Grother discloses the use of budesonide as the active ingredient in its composition. EX1008 15:19-20, 18:15-18. Budesonide has a rapid hepatic metabolism that was known to beneficially result in no systemic activity such that it does not provide a generalized effect via absorption into the circulation. EX1009 857; EX1025 1014-15; EX1053 ¶¶210-211. Grother therefore discloses a solid pharmaceutical composition having no significant systemic glucocorticoid or mineralocorticoid activity after oral administration.

5. Limitation 35[iv]

Limitation 35[iv] recites “wherein the solid pharmaceutical composition disintegrates within 60 seconds when tested using the USP <701> Disintegration Test.”

Grother discloses “fast dispersing solid dosage forms that preferably dissolve in the oral cavity within sixty (60), more preferably within thirty (30), most preferably within ten (10) seconds.” EX1008 Abstract; *id.* 13:19-22 (“the term ‘fast dispersing dosage form (FDDF)’ refers to compositions which disintegrate/disperse within 1 to 60 seconds, preferably 1 to 30 seconds, more preferably 1 to 10 seconds and particularly 2 to 8 seconds, of being placed in the oral cavity.”).

It would have been obvious to formulate budesonide in Grother’s fast dispersing solid dosage form to disintegrate within 60 seconds when tested using the USP <701> Disintegration Test in view of the FDA Guidance for Industry on orally disintegrating tablets. The FDA Guidance recommended that orally disintegrating formulations should have “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 “recommend[s] that applicants use the USP method for disintegration testing,” *id.* 3, specifically “USP 29, <701> Disintegration,” *id.* 3 n.3.

A POSA would have been motivated to follow the FDA Guidance in formulating Grother’s fast dispersing solid dosage form containing budesonide. The FDA Guidance provides the agency’s recommendations on the topic of orally disintegrating pharmaceutical compositions. *Id.* 1. The FDA regulates the use of pharmaceutical compositions in the United States. Grother’s formulations were intended to “enhance patient compliance.” EX1008 32:5-7. 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. EX1053 ¶¶213-215; *Allergan*, 726 F.3d at 1291-92.

A POSA would have had a reasonable expectation of success in doing so based on Grother’s description of how to formulate active ingredients into a fast dispersing solid dosage form. *See, e.g.*, EX1008 13:18-15:20. Formulating orally disintegrating pharmaceutical compositions that dissolve within “several seconds to about a minute” would have been a routine exercise by 2009. EX1018 434; EX1005 2. The numerous commercially available orally disintegrating systems and products available by 2009 would have bolstered the POSA’s expectation of success. EX1017 179-181; EX1018 436-439; EX1053 ¶¶216-217. The EPO determined that orally disintegrating tablets were “well-known dosage forms and belong to the common technical knowledge of the skilled formulator” such that “[t]he skilled

person is aware that their disintegration time can be modulated in order to obtain the desired therapeutic effect.” EX1004 ¶36.8.

Grother in view of the FDA Guidance therefore renders obvious a solid pharmaceutical composition that disintegrates within 60 seconds when tested using the USP <701> Disintegration Test.

6. Limitation 35[v]

Limitation 35[v] recites “upon administration the corticosteroid is deposited topically in the upper gastrointestinal tract.”

Grother discloses “a pharmaceutical composition for oral administration in the form of a fast dispersing dosage form *designed to release an active ingredient rapidly in the oral cavity.*” EX1008 3:18-20; *id.* 1:10-11 (“This invention relates to a pharmaceutical composition for oral administration in the form of a fast dispersing dosage form.”), 13:19-22, 32:10. A POSA would understand that oral administration of budesonide in the form of a fast dispersing dosage form would release budesonide rapidly in the oral cavity, which will topically deposit budesonide in the oral cavity of the upper gastrointestinal tract. EX1053 ¶¶219-220. Grother therefore discloses topical deposition of a corticosteroid in the upper gastrointestinal tract. Grother in view of the FDA Guidance renders obvious claim 35.

C. Claim 1

1. Preamble

The preamble of claim 1 recites “[a] method of treating an inflammatory condition of the gastrointestinal tract.”

If the preamble were limiting, Grother renders it obvious. Grother teaches formulating its fast dispersing solid dosage form with “budesonide,” which was a known “corticosteroid.” EX1008 18:15-18. Budesonide was known to be a potent, locally acting anti-inflammatory glucocorticoid that was desirable for treating inflammation of the gastrointestinal tract. *Supra* Section IV.A. In particular, budesonide was known to successfully treat several inflammatory conditions of the gastrointestinal tract, including inflammation of the esophagus (such as eosinophilic esophagitis), as well as Crohn’s disease, collagenous colitis, ulcerative colitis, eosinophilic gastroenteritis, and obstructive eosinophilic jejunitis. *Supra* Section IV.A; EX1014 706 (treating eosinophilic esophagitis); EX1015 1, 6, 8 (treating eosinophilic esophagitis); EX1002 ¶¶[0010], [0011], [0015] (treating inflammation of the esophagus, including eosinophilic esophagitis); EX1026 1 (treating Crohn’s disease and collagenous colitis); EX1011 589-590 (treating ulcerative colitis); EX1012 55 (treating eosinophilic gastroenteritis); EX1013 187 (treating obstructive eosinophilic jejunitis); EX1053 ¶¶223-229.

2. Limitation 1[i]

Limitation 1[i] recites “administering to an individual in need thereof a pharmaceutical composition.”

Grother discloses administering a pharmaceutical composition. EX1008 1:10-11, 3:18-22, 32:10; EX1053 ¶231.

3. Limitations 1[ii]-1[vi]

Grother and the FDA Guidance render obvious limitations 1[ii]-1[vi] for reasons discussed, *supra*, at Section IX.B.2-6, regarding limitations 35[i]-35[v]. Grother and the FDA Guidance render obvious claim 1. EX1053 ¶¶232-247.

D. Claims 2 and 36

Claim 2 depends from claim 1. Claim 36 depends from claim 35. Both claims require that the composition “disintegrates within 30 seconds.”

Grother discloses “fast dispersing solid dosage forms that preferably dissolve in the oral cavity within sixty (60), *more preferably within thirty (30)*, most preferably within ten (10) seconds.” EX1008 Abstract; *id.* 13:19-22 (disclosing “compositions which disintegrate/disperse within 1 to 60 seconds, *preferably 1 to 30 seconds*, more preferably 1 to 10 seconds and particularly 2 to 8 seconds, of being placed in the oral cavity”).

A POSA would have been motivated to formulate Grother’s fast dispersing dosage form to disintegrate within 30 seconds with a reasonable expectation of

success. *Supra* Section IX.B.5. The FDA recommended that such compositions have “*an in-vitro disintegration time of approximately 30 seconds or less,*” EX1005 2, using the “USP 29, <701> Disintegration” test. *Id.* 3 n.3; EX1053 ¶¶250-251. Grother and the FDA Guidance render obvious claims 2 and 36.

E. Claims 3 and 37

Claim 3 depends from claim 1. Claim 37 depends from claim 35. Both claims recite that “said corticosteroid is selected from the group consisting of budesonide...”

Grother discloses the use of budesonide as the active ingredient in its composition. EX1008 15:19-20, 18:15-18; EX1053 ¶254. Grother in view of the FDA Guidance renders obvious claims 3 and 37. *Supra* Section IX.B.2.

F. Claim 4

Claim 4 requires the composition of claim 1 to be “in the form of an orally disintegrating tablet (ODT).”

Grother discloses “fast dispersing solid dosage forms that preferably dissolve in the oral cavity within sixty (60), more preferably within thirty (30), most preferably within ten (10) seconds.” EX1008 Abstract; *id.* 13:19-22. A POSA would understand that Grother’s fast dispersing solid dosage forms that dissolve rapidly within the oral cavity do so without chewing. *Supra* Section IV.B; EX1005

1; EX1053 ¶¶256-259. Grother in view of the FDA Guidance renders obvious claim 4.

G. Claims 16-17 and 38

Claim 16 depends from claim 1 and further comprises “an adhesive agent.”

Claim 17 depends from claim 16 and recites “wherein the adhesive agent is selected from the group consisting of... polyvinylpyrrolidone, methylcellulose, sodium carboxymethylcellulose, [and] hydroxypropyl cellulose....”

Claim 38 depends from claim 35 and “further compris[es] an adhesive agent.”

Grother discloses that “[t]he fast dispersing dosage form according to the invention may also contain, in addition to the active ingredient and modified starch, *other matrix forming agents* and secondary components.” EX1008 14:7-9. Grother’s matrix forming agent include *carboxymethylcelluloses* or *polyvinylpyrrolidone*, *id.* 14:9-15, and the ’407 patent admits that sodium carboxymethylcellulose and polyvinylpyrrolidone are adhesive agents, EX1001 10:42-46. “One or more matrix forming agents may be incorporated into the solution or suspensions prior to solidification.” EX1008 14:22-23. Thus, Grother discloses a solid pharmaceutical composition comprising carboxymethylcelluloses or polyvinylpyrrolidone, which a POSA would understand meets the claimed “adhesive agent.” EX1053 ¶¶263-266. Grother in view of FDA Guidance renders obvious claims 16, 17 and 38.

H. Claim 18

Claim 18 depends from claim 1 and further comprises “a disintegrant selected from the group consisting of... sodium starch glycolate....”

Grother’s fast dispersing dosage form comprises “at least one modified starch.” EX1008 12:10-19. Grother’s modified starch includes oxidized starches containing carboxyl groups and crosslinked starches, *id.* 5:10-6:5, which beneficially “may be used as the primary structure forming agent in FDDF’s [fast dispersing dosage forms] to form physically robust products while maintaining the desired rapid dispersion characteristics of the products,” *id.* 4:2-4. Sodium starch glycolate is a commercially available disintegrant made by carboxymethylation and crosslinking. A POSA understood that sodium starch glycolate was included in Grother’s disclosure of modified starches. EX1053 ¶¶268-270. Grother in view of the FDA Guidance renders obvious claim 18.

I. Claims 19 and 39

Claim 19 depends from claim 1. Claim 39 depends from claim 35. Both claims recite an excipient “selected from the group consisting of mannitol... lactose....”

Grother discloses that “[m]atrix forming agents suitable for use in the present invention include sugars such as *mannitol*, dextrose, *lactose*....” EX1008 14:16-21. “One or more matrix forming agents may be incorporated into the solution or

suspensions prior to solidification.” *Id.* 14:22-23; EX1053 ¶¶273-274. Grother in view of FDA Guidance renders obvious claims 19 and 39.

J. Claims 21 and 23

Claim 21 depends from claim 16 and further recites “wherein the adhesive agent and the corticosteroid are intimately associated.”

Claim 23 depends from claim 16 and recites “the corticosteroid is disposed on the surface of said adhesive agent.”

Grother discloses that the “solid dosage form is obtainable by removing a solvent from a mixture comprising said active ingredient, said modified starch and said matrix forming agent.” EX1008 12:17-19; *id.* Abstract, 13:8-11. Grother’s matrix forming agent includes carboxymethylcelluloses, *id.* 14:9-15, and the ’407 patent admits that sodium carboxymethylcellulose is an adhesive agent, EX1001 10:23-39. The process of mixing the active ingredient with the matrix forming agent and modified starch creates an intimate mixture that meets the claimed intimate association and disposes the active ingredient over the surface of the matrix forming adhesive agent. EX1053 ¶¶277-280. Grother in view of the FDA Guidance renders obvious claims 21 and 23.

K. Claim 24

Claim 24 depends from claim 4 and recites “the ODT comprises a lyophilized matrix, wherein the lyophilized matrix comprises the corticosteroid in combination with at least one excipient.”

Grother discloses that “the solid dosage forms according to the invention are obtainable by removing a solvent, such as water, from a mixture comprising an active ingredient, a modified starch and a matrix forming agent via freeze drying.” EX1008 Abstract; *id.* 13:15-16, 32:14-15. “The resulting tablet has an open porous matrix that dissolves rapidly on contact with saliva.” *Id.* 32:15-17. A POSA understood that freeze drying Grother’s mixture containing a modified starch and a matrix forming agent is a lyophilization process that forms a lyophilized matrix with at least one excipient. EX1053 ¶¶283-284.

Grother and the FDA Guidance render obvious claim 24.

L. Claim 25

Claim 25 depends from claim 24 and recites “the ODT is in the form of a wafer or film.”

It was well known to a POSA that orally disintegrating tablets were beneficially provided in the form of a film. For example, the Zydis® fast-dissolving wafer was developed in the late 1970s. EX1017 178. Dohil discloses budesonide in the form of “a dissolving wafer.” EX1002 ¶[0013]. A wafer has a relatively large

surface area compared to a tablet of the same weight, and the large surface area increases the amount of surface that comes into contact with saliva in a patient's mouth thereby providing beneficial dissolution. EX1053 ¶286. Grother and the FDA Guidance render obvious claim 25.

M. Claims 27-29 and 40

Claim 27 depends from claim 1 and further requires “at least one antifungal agent.”

Claim 28 depends from claim 27 and recites “wherein the antifungal agent is selected from the group consisting of... benzimidazole antifungals, imidazole antifungals... triazole antifungals, thiazole antifungals...”

Claim 29 depends from claim 28 and recites “wherein the antifungal agent is selected from the group consisting of... clotrimazole, fluconazole, itraconazole... nystatin...”

Claim 40 depends from claim 35 and further requires “at least one antifungal agent.”

Grother discloses that the fast dispersing solid dosage form comprises “*at least one* active ingredient.” EX1008 12:13, 34 (claim 1). The “*at least one* active ingredient” informs the POSA that Grother's fast dispersing solid dosage form includes two active ingredients. EX1053 ¶¶291-292. Grother discloses that “[a]ny drug may be used as the active ingredient in the composition of the present

invention,” EX1008 15:19-20, including “*Anti-fungal agents*: amphotericin, butoconazole nitrate, *clotrimazole*, econazole nitrate, *fluconazole*, flucytosine, griseofulvin, *itraconazole*, ketoconazole, miconazole, natamycin, *nystatin*, sulconazole nitrate, terbinafine HCl, terconazole, tioconazole, undecenoic acid,” *id.* 17:1-4. Grother in view of the FDA Guidance renders obvious claims 27-29 and 40.

N. Claims 30-32 and 41

Claim 30 depends from claim 1 and further comprises “at least one antiviral agent.”

Claim 31 depends from claim 30 and requires “the antiviral agent is selected from the group consisting of interferons....”

Claim 32 depends from claim 31 and requires “the antiviral agent is selected from the group consisting of acyclovir... famciclovir... idoxuridine... trifluridine... valaciclovir....”

Claim 41 depends from claim 35 and further comprises “at least one antiviral agent.”

Grother discloses that the fast dispersing solid dosage form comprises “at least one active ingredient.” EX1008 12:13, 34 (claim 1). The “at least one active ingredient” informs the POSA that Grother’s fast dispersing solid dosage form includes two active ingredients. EX1053 ¶¶298-299. Grother discloses that “[a]ny drug may be used as the active ingredient in the composition of the present

invention,” EX1008 15:19-20, including “***Proteins, peptides and recombinant drugs***: insulin... ***interferons*** (especially Alpha-2 interferon for treatment of common colds). . . .” *id.* 20:22-21:3.

Grother discloses that its solid dosage forms include drugs designed to prevent or reduce the symptoms of “herpes” and “herpes simplex.” *Id.* 19:18-20:21. Drugs that were known to prevent or reduce symptoms of herpes in solid orally disintegrating compositions include acyclovir, idoxuridine, trifluridine, valacyclovir, and famcyclovir. EX1025 1246-1256; EX1035 14:25-37; EX1036 10:55-61. A POSA would have been motivated to include these drugs in Grother’s solid orally disintegrating pharmaceutical composition based on Grother’s instruction to include anti-herpetic drugs and because those drugs were known to be anti-herpetic in such compositions. EX1053 ¶¶300-301. Grother in view of the FDA Guidance renders obvious claims 30-32 and 41.

O. Claims 33-34 and 42

Claim 33 depends from claim 4 and requires between about 0.01mg and 20mg fluticasone.

Claim 34 depends from claim 4 and requires between about 0.05-3.0 mg fluticasone.

Claim 42 depends from claim 35 and requires between about 0.01 mg and 20 mg fluticasone.

As discussed regarding limitation 35[i], Grother discloses that “[t]he precise quantity of active ingredient will depend on the drug selected. However, the active ingredient is generally present in an amount from 0.2 to 95%, normally 1 to 20%, by weight of the composition of the dried dosage form.” EX1008 21:16-18. Grother also discloses that “[a]ny drug may be used as the active ingredient in the composition of the present invention,” *id.* 15:19-20, including “fluticasone,” *id.* 18:15-18.

A POSA would have been motivated to select fluticasone as an active ingredient in Grother’s fast dispersing solid dosage form based on Grother’s express disclosure to do so. Also, fluticasone was a well-known corticosteroid with desirable anti-inflammatory activity. EX1033 1216-17; EX1034 568; EX1053 ¶¶305-309. The ’407 patent admits that fluticasone is a topically administrable corticosteroid. EX1001 3:30-33.

It was generally known that dosages of fluticasone for topical administration desirably ranged from, e.g., 0.044-0.44 mg (EX1033 1217) and 0.44-1.32 mg (EX1034 573 & Table 1); EX1053 ¶¶307-310. Based on Grother’s instruction that its compositions should normally have 1-20% by weight active ingredient and the general knowledge that topical administration of fluticasone typically ranged from 0.044-1.32 mg, a POSA was motivated to formulate fluticasone in Grother’s

compositions at, e.g., 0.44 mg, with an expectation of success. Grother in view of the FDA Guidance therefore renders obvious claims 33, 34 and 42.

X. GROUND 3: DOHIL AND VENKATESH IN VIEW OF THE KNOWLEDGE OF A POSA

This section introduces Venkatesh, and then explains how Dohil and Venkatesh in view of the knowledge of a POSA renders obvious dependent claims 5-15 and 20 of the '407 patent.

A. Venkatesh

Dr. Gopi M. Venkatesh is listed as a co-inventor on the '407 patent and US2005/0232988 (EX1020, “Venkatesh”).

Venkatesh discloses “orally disintegrating tablets and a method for their manufacture.” EX1020 ¶[0001]. Venkatesh discloses that “[m]ore particularly [the invention] relates to an orally disintegrating tablet made up of rapidly dispersing microgranules and taste-masked microcapsules.” *Id.* Venkatesh’s orally disintegrating tablet rapidly disintegrates in the buccal cavity within “preferably less than 60 seconds.” *Id.* ¶[0016]. Venkatesh’s orally disintegrating tablets can be formulated using “any therapeutic active agent indicated for oral administration.” *Id.* ¶[0025].

B. Claim 5

Claim 5 depends from claim 4 and recites “the ODT comprises drug particles and rapidly dispersing granules, the drug particles comprise the corticosteroid, the

rapidly dispersing granules comprise a disintegrant, the excipient is a sugar alcohol, a saccharide, or a mixture thereof, and the drug particles are disposed over the surface of the rapidly dispersing granules.”

A POSA was motivated to formulate budesonide in an orally disintegrating tablet based on Dohil as discussed above regarding claim 4. *Supra* Section VIII.F. Dohil discloses budesonide ODTs formulated with mannitol and sorbitol as sugar alcohol excipients. EX1002 ¶¶[0014], [0037]. Mannitol was the bulk excipient of choice for ODTs. EX1041 261.

Dohil discloses “[i]f desired, *disintegrating agents* may be added, such as the cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate.” EX1002 ¶[0037]. It was known that the rapid dissolution of a lozenge or tablet would be desirably aided by at least one disintegrating agent. EX1018 446-47; EX1030 ¶¶109-111. Dohil discloses “combining the corticosteroids with solid excipients, *optionally grinding a resulting mixture, and processing the mixture of granules...* to obtain tablets or dragee cores.” EX1002 ¶[0037]. The process of grinding the budesonide corticosteroid with a disintegrating agent excipient would dispose budesonide particles over the surface of the granules. EX1053 ¶¶320-323.

Venkatesh discloses “an orally disintegrating tablet made up of rapidly dispersing microgranules and taste-masked microcapsules” of drug particles.

EX1020 ¶[0001]; *id.* ¶¶[0018], [0025] (microcapsule drug particles). Venkatesh discloses that “this invention relates to pharmaceutical compositions comprising rapidly dispersing microgranules of a disintegrant and sugar alcohol or a saccharide.” *Id.* ¶[0014]; *id.* ¶¶[0018], [0021]-[0022], [0028] (“sugar alcohol” and “saccharide”). Venkatesh therefore discloses orally disintegrating tablets comprising drug particles and rapidly dispersing microgranules comprising a disintegrant, a sugar alcohol and/or saccharide.

Venkatesh discloses that its ODT is “produced by mixing microgranules” with “one or more taste-masked microcapsules and other excipients.” *Id.* ¶[0018]; *id.* ¶¶[0019]-[0025]. The process of mixing the rapidly dispersing microgranules and the microcapsules of drug particles disposes the drug particles over the surface of the microgranules. EX1053 ¶¶185, 324-327.

The POSA would have been motivated for the budesonide in Dohil’s tablet to comprise drug particles and the disintegrant to be rapidly dispersing granules, and to include a sugar alcohol and/or saccharide excipient based on Venkatesh. Venkatesh teaches that formulating orally disintegrating tablets to have drug particles, rapidly-dispersing microgranules, and a sugar alcohol and/or saccharide beneficially “avoid[ed] gritty mouthfeel,” EX1020 ¶[0012], to assist with providing a “smooth creamy mouthfeel (no grittiness),” *id.* ¶[0002]; EX1053 ¶328.

The POSA had an expectation of success based on Venkatesh. Venkatesh teaches that its formulations “don’t require a special pharmaceutical production technique and can be simply and easily produced by a normal equipment.” EX1020 ¶[0018]; EX1053 ¶¶329-330. Dohil and Venkatesh therefore render obvious claim 5.

C. Claim 6

Claim 6 depends from claim 5 and recites “the drug particles have an average particle size of less than about 400 μm , the rapidly dispersing granules have an average particle size of less than about 300 μm , and the disintegrant and the sugar alcohol, the saccharide, or mixture thereof have an average particle size of less than about 30 μm .”

Venkatesh discloses drug particles that advantageously have “an average particle size of 200 μm and can be effectively taste masked by coacervation by phase separation to produce taste-masked particles with optimum size distribution” and provide “a smooth creamy mouthfeel.” EX1020 ¶[0015]; *id.* ¶[0015] (exemplary “average particle diameter less than about 50 μm , preferably less than about 25 μm ”), ¶[0015].

Venkatesh discloses that the rapidly dispersing granules “typically” have an “average particle size of not more than 300 μm .” EX1020 ¶[0020]. A small particle size assists with mouthfeel. *Id.* ¶¶[0019], [0009], [0025].

Venkatesh discloses “rapidly dispersing microgranules of a disintegrant and sugar alcohol or a saccharide whose average particle size is not more than 30 μm ,” which is advantageous in “effectively taste-mask[ing] by coacervation.” EX1020 ¶[0014]; *id.* ¶[0018] (“preferably not more than 20 μm ”), ¶[0028].

A POSA was motivated to formulate budesonide in an orally disintegrating tablet based on Dohil, and also having drug particles with a particle size less than 400 μm , rapidly dispersing granules with a particle size less than 300 μm , and a disintegrant and sugar alcohol and/or saccharide with a particle size less than 30 μm based on Venkatesh to avoid a gritty texture and improve mouthfeel with an expectation of success. EX1053 ¶¶332-336. Dohil and Venkatesh render obvious claim 6.

D. Claim 7

Claim 7 depends from claim 5 and recites “the drug particles have an average particle size of less than about 4 μm , the rapidly dispersing granules have an average particle size of less than about 300 μm , and the disintegrant and sugar alcohol, the saccharide, or mixture thereof have an average particle size of less than about 30 μm .”

Venkatesh discloses that drug particles have an “average particle diameter less than about 50 μm , preferably less than about 25 μm .” EX1020 ¶[0015]. Venkatesh’s

ranges of “less than 50 μm ,” and preferably “less than 25 μm ” overlap with the range of “less than about 4 μm ” recited by claim 7, which is prima facie obvious.

As discussed for claim 6, Venkatesh discloses rapidly dispersing granules having an average particle size less than about 300 μm , and a disintegrant, sugar alcohol, and/or saccharide having an average particle size less than 30 μm . *Supra* Section X.C.

A POSA was motivated to formulate budesonide in an orally disintegrating tablet based on Dohil, and also having drug particles with a particle size less than 4 μm , rapidly dispersing granules with a particle size less than 300 μm , and a disintegrant, sugar alcohol, and/or saccharide with a particle size less than 30 μm based on Venkatesh to avoid a gritty texture and improve mouthfeel with a reasonable expectation of success. EX1053 ¶¶338-341. Dohil and Venkatesh render obvious claim 7.

E. Claim 8

Claim 8 depends from claim 5 and recites “the corticosteroid is disposed over the surface of the excipient, the rapidly dispersing granules have an average particle size of less than about 300 μm , and the disintegrant and the sugar alcohol, the saccharide, or mixture thereof have an average particle size of less than about 30 μm .”

Dohil discloses “combining the corticosteroids with solid excipients, *optionally grinding a resulting mixture, and processing the mixture of granules...* to obtain tablets or dragee cores.” EX1002 ¶[0037]. The process of grinding the corticosteroid with excipients would dispose the corticosteroid over the surface of the excipient. EX1053 ¶¶343-344.

As discussed for claim 7, Dohil and Venkatesh render obvious rapidly dispersing granules having a particle size less than 300 µm, and a disintegrant, sugar alcohol, and/or the saccharide having a particle size less than 30 µm. *Supra* Section X.D. Dohil and Venkatesh render obvious claim 8.

F. Claim 9

Claim 9 depends from claim 5 and recites “the ODT further comprises microcrystalline cellulose and a pharmaceutically acceptable sweetener, flavorant, and/or colorant, and wherein the excipient is the sugar alcohol.”

Dohil discloses the use of sucralose in its ODT formulations of budesonide. EX1002 ¶¶[0014], [0037]. Dohil discloses that “[a]ppropriate excipients may also, for example, include those that render the dissolving tablet palatable.” *Id.* ¶[0037]. The POSA was well-aware that, “[a]fter FDTs [fast disintegrating tablets] disintegrate/dissolve in the saliva, the drug in FDTs remains in the oral cavity until it is swallowed.” EX1018 459. ODTs were therefore known to advantageously

include sweeteners to improve the tablet's taste and palatability. EX1019 314; EX1053 ¶¶346-347.

Venkatesh teaches that microcrystalline cellulose beneficially imparts resilient characteristics to orally disintegrating tablets. EX1020 ¶[0021] (“granulating a bitter active pharmaceutical ingredient and optionally one or more pharmaceutically acceptable diluents such as mannitol, lactose and microcrystalline cellulose with at least one polymeric binder such as modified starch and hydroxypropylmethylcellulose with a viscosity of 100 cps or higher, which imparts resilient, characteristics to the dried granules”); EX1053 ¶¶348-350.

As discussed for claim 5, Dohil and Venkatesh disclose that the excipient should be a sugar alcohol. *Supra* Section X.B. Dohil and Venkatesh therefore render obvious claim 9.

G. Claims 10 and 13

Claim 10 depends from claim 5. Claim 13 depends from claim 9. Both claims recite “the sugar alcohol is selected from the group consisting of mannitol, xylitol, sorbitol, maltol, maltitol, and combinations thereof.”

Dohil discloses budesonide ODTs formulated with mannitol and sorbitol as sugar alcohol excipients. EX1002 ¶¶[0014], [0037]. Mannitol was the bulk excipient of choice for ODTs. EX1041 261; EX1053 ¶¶353-356.

Venkatesh discloses that “[t]he dispersible microgranules comprise a sugar alcohol such as mannitol.” EX1020 ¶¶[0032], [0047]. Venkatesh further discloses that “[t]he sugar alcohol may be selected from the group consisting of mannitol, sorbitol, xylitol, maltitol and the like...” *Id.* ¶[0028]. Dohil and Venkatesh render claims 10 and 13 obvious.

H. Claims 11 and 14

Claim 11 depends from claim 5. Claim 14 depends from claim 9. Both claims recite “the saccharide is selected from the group consisting of lactose, sucrose, maltose, and combinations thereof.”

Dohil discloses budesonide ODTs using lactose and sucrose as saccharide excipients. EX1002 ¶¶[0014], [0037].

Venkatesh discloses that “this invention relates to pharmaceutical compositions comprising rapidly dispersing microgranules of a disintegrant and sugar alcohol or a saccharide.” EX1020 ¶[0014]; *id.* ¶[0018], ¶[0028]. Venkatesh further discloses that “the saccharide may be selected from the group consisting of lactose, sucrose,....” *Id.* ¶[0028]; EX1053 ¶¶359-362. Dohil and Venkatesh render claims 11 and 14 obvious.

I. Claims 12 and 15

Claim 12 depends from claim 5. Claim 15 depends from claim 9. Both claims recite “the disintegrant is selected from the group consisting of crospovidone,

sodium starch glycolate, crosslinked carboxymethyl cellulose, low-substituted hydroxypropylcellulose, and combinations thereof.”

The '407 patent admits that crospovidone is “cross-linked PVP [polyvinylpyrrolidone].” EX1001 8:65-9:3, 13:21-25; *id.* 12:7 (“polyvinylpyrrolidone (PVP)”).

Dohil teaches “[i]f desired, disintegrating agents may be added, such as the *cross-linked polyvinylpyrrolidone*, agar, or alginic acid or a salt thereof such as sodium alginate.” EX1002 ¶[0037].

Venkatesh discloses that the “disintegrant is selected from the group consisting of crospovidone (crosslinked PVP), sodium starch glycolate, crosslinked Sodium carboxymethyl cellulose, calcium silicate and low substituted hydroxypropyl cellulose.” EX1020 ¶[0029]; *id.* ¶[0020]; EX1053 ¶¶365-368. Dohil and Venkatesh render obvious claims 12 and 15.

J. Claim 20

Claim 20 depends from claim 1 and recites “the orally disintegrating solid pharmaceutical composition is substantially free of lubricant.”

A POSA would have been motivated to formulate Dohil’s rapidly dissolving lozenge or tablet with budesonide as an anti-inflammatory active ingredient to be substantially free of lubricant based on Venkatesh.

Venkatesh discloses “orally disintegrating tablets,” EX1020 ¶[0001], that are compatible with “any therapeutic active agent indicated for oral administration,” *id.* ¶[0025]. Budesonide is a therapeutic active agent indicated for oral administration. *Supra* Section IV.A.

Venkatesh discloses manufacturing orally disintegrating tablets by “compress[ion] in a tablet press equipped with an externally lubricating system to pre-lubricate dies and punches ***and the tablet formulation otherwise being free of lubricant.***” EX1020 ¶[0017]; *id.* ¶¶[0008], [0018]. This technique uses “a conventional rotary tablet press equipped with an external lubrication system to pre-lubricate the dies and punches.” *Id.* ¶[0024].

The ’407 patent uses the same language as Venkatesh in stating that a “rotary tablet press equipped with an external lubrication system to pre-lubricate the dies and punches” was “conventional” in the prior art. EX1001 16:41-43, 17:7-9. The ’407 patent admits that using “an externally lubricating system to pre-lubricate dies and punches, thereby provid[es] a tablet formulation otherwise free of lubricant.” *Id.* 16:11-13, 17:34-36.

A POSA would have been motivated to manufacture Dohil’s rapidly dissolving lozenge or tablet using conventional punch and die surfaces with an external lubricating system to provide lozenges and tablets that are substantially free of lubricant. Such conventional manufacturing was desirable to mass produce

lozenges and tablets with a reasonable expectation of success, as evidenced by Venkatesh. EX1053 ¶¶370-374. Dohil and Venkatesh render obvious claim 20.

XI. GROUND 4: GROTHER, FDA GUIDANCE AND VENKATESH

This section explains how Grother, the FDA Guidance, and Venkatesh render obvious dependent claims 5-15, 20, and 26 of the '407 patent.

A. Claim 5

A POSA would have been motivated to formulate budesonide in an orally disintegrating tablet based on Grother for reasons discussed above regarding claim 4. *Supra* Section IX.F. Grother discloses mannitol as its preferred matrix forming excipient, which is a sugar alcohol. *Supra* Section IX.B.3. Grother discloses a disintegrant in its formulations. *Supra* Section IX.H.

Grother discloses that “[a] further technique is to dose a non-aqueous solution of the active ingredient onto preformed placebo FDDF [fast dispersing dosage form] units.” EX1008 27:11-14. This technique advantageously strengthens the structure of the fast dispersing dosage form. *Id.* 27:7-14. Grother therefore discloses a formulation of budesonide where the budesonide is disposed over the surface of a preformed placebo fast dispersing dosage form comprising a disintegrant. EX1053 ¶382.

Venkatesh discloses “an orally disintegrating tablet made up of rapidly dispersing microgranules and taste-masked microcapsules” of drug particles.

EX1020 ¶[0001]; *id.* ¶¶[0018], [0025] (microcapsule drug particles). Venkatesh discloses that “this invention relates to pharmaceutical compositions comprising rapidly dispersing microgranules of a disintegrant and sugar alcohol or a saccharide.” *Id.* ¶[0014]; *id.* ¶¶[0018], [0021]-[0022], [0028]. Venkatesh therefore discloses orally disintegrating tablets comprising drug particles and rapidly dispersing microgranules comprising a disintegrant, a sugar alcohol and/or saccharide.

Venkatesh discloses that its ODT is “produced by mixing microgranules” with “one or more taste-masked microcapsules and other excipients.” *Id.* ¶[0018]; *id.* ¶¶[0019]-[0025]. The process of mixing the rapidly dispersing microgranules and the microcapsules of drug particles disposes the drug particles over the surface of the microgranules. EX1053 ¶¶383-386.

The POSA would have been motivated for the budesonide in Grother’s formulations to comprise drug particles and the disintegrant to be rapidly dispersing granules, and to include a sugar alcohol and/or saccharide excipient based on Venkatesh. Venkatesh teaches that formulating orally disintegrating tablets to have drug particles, rapidly-dispersing microgranules, and a sugar alcohol and/or saccharide beneficially “avoid[ed] gritty mouthfeel,” EX1020 ¶[0012], to assist with providing a “smooth creamy mouthfeel (no grittiness),” *id.* ¶[0002]; EX1053 387.

The POSA had a reasonable expectation of success based on Venkatesh and its teaching that such formulations “don't require a special pharmaceutical production technique and can be simply and easily produced by a normal equipment.” EX1020 ¶[0018]; EX1053 ¶¶379-388. Grother, the FDA Guidance, and Venkatesh renders obvious claim 5.

B. Claim 6

Venkatesh discloses drug particles that advantageously have “an average particle size of 200 μm and can be effectively taste masked by coacervation by phase separation to produce taste-masked particles with optimum size distribution” and provide “a smooth creamy mouthfeel.” EX1020 ¶[0015].

Rapidly dispersing granules “typically” have an “average particle size of not more than 300 μm .” EX1020 ¶[0020]. A small particle size assists with mouthfeel. *Id.* ¶¶[0019], [0009], [0025].

Venkatesh discloses “rapidly dispersing microgranules of a disintegrant and sugar alcohol or a saccharide whose average particle size is not more than 30 μm ,” which is advantageous in “effectively taste-mask[ing] by coacervation.” EX1020 ¶[0014]; *id.* ¶[0018], ¶[0028].

A POSA would have been motivated to formulate budesonide in an orally disintegrating tablet based on Grother, and also having drug particles with a particle size less than 400 μm , rapidly dispersing granules with a particle size less than 300

μm, and a disintegrant and sugar alcohol and/or saccharide with a particle size less than 30 μm based on Venkatesh to avoid a gritty texture and improve mouthfeel with a reasonable expectation of success. EX1053 ¶¶390-394. Grother, the FDA Guidance, and Venkatesh render obvious claim 6.

C. Claim 7

Venkatesh discloses that the drug particles have an “average particle diameter less than about 50 μm, preferably less than about 25 μm.” EX1020 ¶[0015]. Venkatesh’s ranges of “less than 50 μm,” and preferably “less than 25 μm” overlap with the range of “less than about 4 μm” recited by claim 18, which is prima facie obvious.

As discussed for claim 6, Venkatesh discloses rapidly dispersing granules having an average particle size less than about 300 μm and a disintegrant, sugar alcohol, and/or saccharide having an average particle size less than 30 μm. *Supra* Section XI.B.

A POSA would have been motivated to formulate budesonide in an orally disintegrating tablet based on Grother, and also having drug particles with a particle size less than 4 μm, rapidly dispersing granules with a particle size less than 300 μm, and a disintegrant, sugar alcohol, and/or saccharide with a particle size less than 30 μm based on Venkatesh to avoid a gritty texture and improve mouthfeel with a

reasonable expectation of success. EX1053 ¶¶396-398. Grother, the FDA Guidance, and Venkatesh render obvious claim 7.

D. Claim 8

Grother discloses that “[a] further technique is to dose a non-aqueous solution of the active ingredient onto preformed placebo FDDF [fast dispersing dosage form] units.” EX1008 27:11-14. This technique advantageously strengthens the structure of the fast dispersing dosage form. *Id.* 27:7-14. Grother therefore discloses a formulation of budesonide where the budesonide is disposed over the surface of a preformed placebo fast dispersing dosage form comprising an excipient. EX1053 ¶¶400-402.

As discussed for claim 7, Grother and Venkatesh render obvious rapidly dispersing granules having a particle size less than 300 µm, and a disintegrant, sugar alcohol, and/or saccharide having a particle size less than 30 µm. *Supra* Section XI.C. Grother, the FDA Guidance, and Venkatesh render obvious claim 8.

E. Claim 9

Grother discloses that excipients for orally disintegrating tablets were known to “include microcrystalline cellulose, corn starch and lactose.” EX1008 10:9-10. Grother discloses the use of sweeteners in its formulations. *Id.* 15:7-8. The POSA was well-aware that ODTs are designed to dissolve in the oral cavity. EX1018 459.

ODTs were therefore known to advantageously include sweeteners to improve taste and palatability. EX1019 314; EX1053 ¶¶404-409.

Grother discloses mannitol as its preferred matrix forming excipient. *Supra* Section IX.B.3. Grother discloses a disintegrant. *Supra* Section IX.H.

Venkatesh teaches that microcrystalline cellulose imparts resilient characteristics to orally disintegrating tablets. EX1020 ¶[0021]. As discussed for claim 5, Venkatesh discloses that the excipients should be a sugar alcohol. *Supra* Section XI.A. Grother, the FDA Guidance, and Venkatesh renders obvious claim 9.

F. Claims 10 and 13

Grother discloses mannitol as its preferred matrix forming excipient. *Supra* Section IX.B.3.

Venkatesh discloses that “[t]he dispersible microgranules comprise a sugar alcohol such as mannitol.” EX1020 ¶¶[0032], [0028], [0047]; EX1053 ¶¶412-415.

Grother, the FDA Guidance, and Venkatesh render claims 10 and 13 obvious.

G. Claims 11 and 14

Grother discloses that “[m]atrix forming agents suitable for use in the present invention include sugars such as... lactose...”. EX1008 14:16-17.

Venkatesh discloses that “this invention relates to pharmaceutical compositions comprising rapidly dispersing microgranules of a disintegrant and sugar alcohol or a saccharide.” *Id.* ¶[0014]; *id.* ¶[0018], ¶[0028]. Venkatesh

discloses that “the saccharide may be selected from the group consisting of lactose, sucrose....” *Id.* ¶[0028]; EX1053 ¶¶418-421.

Grother, the FDA Guidance, and Venkatesh render claims 11 and 14 obvious.

H. Claims 12 and 15

Grother’s fast dispersing dosage form comprises “at least one modified starch.” EX1008 12:10-19. Grother’s modified starch includes oxidized starches containing carboxyl groups and crosslinked starches, *id.* 5:10-6:5, which beneficially “may be used as the primary structure forming agent in FDDF’s [fast dispersing dosage forms] to form physically robust products while maintaining the desired rapid dispersion characteristics of the products,” *id.* 4:2-4. Sodium starch glycolate is a commercially available disintegrant made by carboxymethylation and crosslinking. A POSA understood that sodium starch glycolate was included in Grother’s disclosure of modified starches. EX1053 ¶¶424-426.

Venkatesh discloses that the disintegrant includes sodium starch glycolate. EX1020 ¶[0029]; EX1053 ¶¶427-429. Grother, the FDA Guidance, and Venkatesh render obvious claims 12 and 15.

I. Claim 20

A POSA would have been motivated to formulate Grother’s fast dispersing dosage form with budesonide and be substantially free of lubricant.

Venkatesh discloses manufacturing orally disintegrating tablets “with an externally lubricating system to pre-lubricate dies and punches *and the tablet formulation otherwise being free of lubricant.*” EX1020 ¶[0017]; *id.* ¶¶[0008], [0018]. This uses “a conventional rotary tablet press equipped with an external lubrication system to pre-lubricate the dies and punches.” *Id.* ¶[0024].

A POSA was motivated to manufacture Grother’s dosage form using conventional punch and die surfaces with an external lubricating system to provide tablets that are substantially free of lubricant. Such manufacturing was desirable to mass produce such dosage forms. EX1053 ¶¶431-436. Grother, the FDA Guidance, and Venkatesh render obvious claim 20.

J. Claim 26

It was known that orally disintegrating tablets were beneficially formed into a film. *Supra* Section IX.L; EX1017 178; EX1002 ¶[0013]; EX1053 ¶438. Claim 26 is obvious.

XII. 325(D) DOES NOT APPLY

This petition is not subject to discretionary denial under *Advanced Bionics, LLC v. MED-EL Elektromedizinische Geräte GmbH*, IPR2019-01469, Paper 6 (PTAB 2020) (precedential).

A. Advanced Bionics Step 1 Is Inapplicable

This Petition is based on two different primary references: Dohil and Grother. Neither reference was made of record during prosecution of the '407 patent. When references were not previously presented, “the first prong of the *Advanced Bionics* framework is not satisfied and we need not consider the second prong.” *Yita LLC v. MacNeil IP LLC*, IPR023-00172, Paper 12 at 47 (PTAB 2023).

This Petition is further based on two secondary references: the FDA Guidance and Venkatesh. The FDA Guidance was not made of record during prosecution. Venkatesh is cited in the specification of the '407 patent. EX1001 8:14-19, 16:62-63.⁶ This Petition relies on Venkatesh only to address certain dependent claims. The Grounds 1 and 2 challenges to independent claims 1 and 35 do not rely on Venkatesh. Thus, Grounds 1 and 2 are not based on previously presented art, and the combination of references for the select dependent claims in Grounds 3 and 4 were not previously presented.

⁶ A different patent publication, US2009/0169620, having Gopi Venkatesh as an inventor was cited by the Examiner during prosecution of the parent U.S. 8,771,729. EX1031 19, 41-42, 47-54, 79, 85-96. That publication is from a different family than the Venkatesh of present Grounds 3-4.

The Examiner applied a Dohil equivalent in rejecting a later related application to the '407 patent. EX1032 6-7, 20-27, 51-57. It was also discussed during a single interview that involved two later related applications. EX1039 30; EX1049 99. Dohil, however, was not made of record during prosecution of the present '407 patent. This Petition also relies on Grother in view of the FDA Guidance. Neither of those references were made of record during prosecution of the '407 patent, or any of its progeny patents, and therefore present an entirely new and independent ground. *Advanced Bionics* step 1 is inapplicable.

B. Advanced Bionics Step 2 Compels Institution

There is no colorable 325(d) challenge for Ground 2 based on Grother in view of the FDA Guidance. Even accepting for the other grounds that Dohil and Venkatesh were “previously presented,” the Office “erred in a manner material to the patentability of the challenged claims” by not applying rejections based on the Grounds in this Petition. *Advanced Bionics*, Paper 6 at 8-9.

The later related application where a Dohil equivalent was applied issued before the EPO revoked Ellodi’s relevant European claims. The Examiner did not have the benefit of the EPO’s decision, which determined that “a budesonide ODT showing a disintegration time within 60 seconds in simulated saliva fluid when tested using the USP <701> Disintegration Test is an obvious solution to the problem” of providing a budesonide orally dispersible tablet. EX1004 ¶36.8. The

interview where the Dohil equivalent was discussed also took place before the EPO revoked Ellodi's claims.

The Examiner did not have the FDA Guidance during prosecution and therefore overlooked the specific teachings of the FDA Guidance that are representative of the POSA's knowledge that orally disintegrating compositions should have an *in-vitro* disintegration time of approximately 30 seconds or less based on the USP <701> Disintegration Test. EX1005 3. This knowledge directly addresses the limitation the Examiner asserted was missing from the prior art during examination. EX1031 6-7, 19.

The Examiner did not have the benefit of this Petition mapping the references to Patent Owner's claims and Dr. Parr's accompanying expert declaration explaining the POSA's understanding of the references. Where, as here, references were "not extensively evaluated during examination and [were] not the basis for a rejection," and Petitioner "present[s] a sufficient showing that the Examiner overlooked disclosures" that invalidate the claims, "the Office erred in a manner material" to patentability. *Apple Inc. v. Telefonaktiebolaget LM Ericsson*, IPR2022-00457, Paper 7 at 8 (PTAB 2022). This Petition presents compelling challenges to patentability that warrant institution.

XIII. NO SECONDARY CONSIDERATIONS

There is no evidence of secondary considerations. Should Ellodi make allegations regarding secondary considerations, Petitioner will respond.

XIV. MANDATORY NOTICES, STANDING, AND PAYMENT

Pursuant to 37 C.F.R. §42.8(a)(1), the mandatory notices identified in 37 C.F.R. §42.8(b) are provided below as part of this Petition.

A. Real Party-In-Interest (37 C.F.R. §42.8(b)(1))

Dr. Falk Pharma GmbH is the real party in interest. Petitioner is aware of no other entities that have a financial interest in, or could be substantially affected by the outcome of, this proceeding.

B. Related Matters (37 C.F.R. §42.8(b)(2))

Petitioner is aware of the following judicial proceedings that could affect or be affected by this proceeding:

- *Ellodi Pharmaceuticals, LP v. Dr. Falk Pharma GmbH*, Case No. 24-cv-1392 (E.D. Va);
- *Ellodi Pharmaceuticals, LP v. Dr. Falk Pharma GmbH*, Düsseldorf Regional Court, Case No. 4b O 43/24, Patent Litigation Chamber, Werdener Str. 1, 40227 Düsseldorf, Germany.

Petitioner is aware of the following U.S. patents and patent applications related to the '407 patent:

- 61/247,642 filed on October 1, 2009;
- 12/869,005 filed on October 1, 2010, now U.S. patent number 8,771,729
- 14/311,732 filed on June 23, 2014, now U.S. patent number 9,387,167;
- 15/205,390 filed on July 8, 2016, now U.S. patent number 9,849,084;
- 15/816,154 filed on November 17, 2017, now U.S. patent number 10,632,069;
- 16/821,464 filed on March 17, 2020, now U.S. patent number 11,246,828;
- 17/236,295 filed April 21, 2021, now U.S. patent number 11,266,598;
- and
- 17/569,047 filed on January 5, 2022.

C. Lead and Backup Counsel (37 C.F.R. §42.8(b)(3))

Petitioner provides the following designation of counsel, all of whom are included in Customer No. 20,995 identified in Petitioner's Power of Attorney.

Lead Counsel	Back-up Counsel
Nathanael Luman (Reg. No. 63,160) 2nrl@knobbe.com Knobbe, Martens, Olson, & Bear, LLP <u>Postal and Hand-Delivery Address:</u> 3579 Valley Centre Drive, Suite 300 San Diego, CA 92130 Telephone: 858-707-4000 Facsimile: 858-707-4001	Eric S. Furman (Reg. No. 45,664) Phillip J. Minnick (Reg. No. 81,223) 2esf@knobbe.com 2pjm@knobbe.com Knobbe, Martens, Olson, & Bear, LLP <u>Postal and Hand-Delivery Address:</u> 3579 Valley Centre Drive, Suite 300 San Diego, CA 92130 Telephone: 858-707-4000 Facsimile: 858-707-4001

D. Service Information (37 C.F.R. §42.8(b)(4))

Please direct all correspondence to lead counsel and back-up counsel at the addresses shown above. Petitioner also consents to electronic service by email to BoxFalkPharma@knobbe.com.

XV. PAYMENT OF FEES

The Office may charge the §42.15(a) fee and any additional fees that may be due to Deposit Account No. 11-1410. Review of forty-two claims is requested.

XVI. REQUIREMENTS FOR REVIEW

Petitioner certifies that the '407 patent is available for IPR and that it is not barred or estopped from requesting this IPR.

XVII. CONCLUSION

Claims 1-42 of the '407 patent are unpatentable and should be canceled.

IPR Petition – Patent No. 9,486,407

Dr. Falk Pharma GmbH v. Ellodi Pharmaceuticals, L.P.

Dated: October 24, 2024 Respectfully submitted,

By: /Nathanael Luman/

Nathanael Luman (Reg. No. 63,160)

KNOBBE MARTENS OLSON & BEAR, LLP

Attorney for Petitioner Dr. Falk Pharma GmbH

APPENDIX A

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 1	
Preamble	A method of treating an inflammatory condition of the gastrointestinal tract comprising
[i]	administering to an individual in need thereof a pharmaceutical composition comprising
[ii]	less than or equal to 20 mg of a topically administrable corticosteroid and
[iii]	at least one excipient,
[iv]	wherein: the composition has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration,
[v]	the pharmaceutical composition disintegrates within 60 seconds when tested using the USP <701> Disintegration Test, and
[iv]	upon administration the corticosteroid is deposited topically in the upper gastrointestinal tract.
Claim 2	
--	The method of claim 1, wherein said pharmaceutical composition disintegrates within 30 seconds when tested using the USP <701> Disintegration Test.
Claim 3	
--	The method of claim 1, wherein said corticosteroid is selected from the group consisting of budesonide, fluticasone, flunisolide, ciclesonide, mometasone, beclomethasone, and salts, solvates and esters thereof.

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 4	
--	The method of claim 1, wherein the pharmaceutical composition is in the form of an orally disintegrating tablet (ODT).
Claim 5	
--	The method of claim 4, wherein the ODT comprises drug particles and rapidly dispersing granules, the drug particles comprise the corticosteroid, the rapidly dispersing granules comprise a disintegrant, the excipient is a sugar alcohol, a saccharide, or a mixture thereof, and the drug particles are disposed over the surface of the rapidly dispersing granules.
Claim 6	
--	The method of claim 5, wherein the drug particles have an average particle size of less than about 400 μm , the rapidly dispersing granules have an average particle size of less than about 300 μm , and the disintegrant and the sugar alcohol, the saccharide, or mixture thereof have an average particle size of less than about 30 μm .
Claim 7	
--	The method of claim 5, wherein the drug particles have an average particle size of less than about 4 μm , the rapidly dispersing granules have an average particle size of less than about 300 μm , and the disintegrant and sugar alcohol, the saccharide, or mixture thereof have an average particle size of less than about 30 μm .
Claim 8	
--	The method of claim 5, wherein the corticosteroid is disposed over the surface of the excipient, the rapidly dispersing granules have an average particle size of less than about 300 μm , and the disintegrant and the sugar alcohol, the saccharide, or mixture thereof have an average particle size of less than about 30 μm .

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 9	
--	The method of claim 5, wherein the ODT further comprises microcrystalline cellulose and a pharmaceutically acceptable sweetener, flavorant, and/or colorant, and wherein the excipient is the sugar alcohol.
Claim 10	
--	The method of claim 5, wherein the sugar alcohol is selected from the group consisting of mannitol, xylitol, sorbitol, maltol, maltitol, and combinations thereof.
Claim 11	
--	The method of claim 5, wherein the saccharide is selected from the group consisting of lactose, sucrose, maltose, and combinations thereof.
Claim 12	
--	The method of claim 5, wherein the disintegrant is selected from the group consisting of crospovidone, sodium starch glycolate, crosslinked carboxymethyl cellulose, low-substituted hydroxylpropylcellulose, and combinations thereof.
Claim 13	
--	The method of claim 9, wherein the sugar alcohol is selected from the group consisting of mannitol, xylitol, sorbitol, maltol, maltitol, and combinations thereof.
Claim 14	
--	The method of claim 9, wherein the saccharide is selected from the group consisting of lactose, sucrose, maltose, and combinations thereof.

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 15	
--	The method of claim 9, wherein the disintegrant is selected from the group consisting of crospovidone, sodium starch glycolate, crosslinked carboxymethyl cellulose, low-substituted hydroxylpropylcellulose, and combinations thereof.
Claim 16	
--	The method of claim 1, further comprising an adhesive agent.
Claim 17	
--	The method of claim 16, wherein the adhesive agent is selected from the group consisting of sucrose aluminum sulfate complex, chitosan and derivatives thereof, polyvinylpyrrolidone, methylcellulose, sodium carboxymethylcellulose, hydroxypropyl cellulose, cross-linked or uncross-linked polyacrylates, cross-linked polyacrylates, acidic cross-linked or uncross-linked polyacrylates, polyacrylic acid homopolymers or copolymers, aminoalkyl methacrylate copolymers, methacrylic acid/methylmethacrylate copolymer, alkylacrylate/alkylmethacrylate copolymers, ammoniomethacrylate copolymers, carbomer homopolymers or copolymers, hydrophilic polysaccharide gums, maltodextrins, cross-linked alginate gums, polycarboxylated vinyl polymers, pectins, xanthan gums, alginic acid, modified alginic acids, and combinations thereof.
Claim 18	
--	The method of claim 1, further comprising a disintegrant selected from the group consisting of crospovidone, sodium starch glycolate, crosslinked carboxymethyl cellulose, low-substituted hydroxylpropylcellulose, mannitol, xylitol, sorbitol, maltol, maltitol, lactose, sucrose, maltose, and combinations thereof.

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 19	
--	The method of claim 1, wherein the excipient is selected from the group consisting of mannitol, xylitol, sorbitol, maltol, maltitol, lactose, sucrose, maltose, cyclodextrin, and combinations thereof.
Claim 20	
--	The method of claim 1, wherein the orally disintegrating solid pharmaceutical composition is substantially free of lubricant.
Claim 21	
--	The method of claim 16, wherein the adhesive agent and the corticosteroid are intimately associated.
Claim 22	
--	The method of claim 21, wherein said corticosteroid is surrounded or encapsulated by the adhesive agent.
Claim 23	
--	The method of claim 21, wherein the corticosteroid is disposed on the surface of said adhesive agent.
Claim 24	
--	The method of claim 4, wherein the ODT comprises a lyophilized matrix, wherein the lyophilized matrix comprises the corticosteroid in combination with at least one excipient.
Claim 25	
--	The method of claim 24, wherein the ODT is in the form of a wafer or film.

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 26	
--	The method of claim 5, wherein the ODT is in the form of a wafer or film.
Claim 27	
--	The method of claim 1, further comprising at least one antifungal agent.
Claim 28	
--	The method of claim 27, wherein the antifungal agent is selected from the group consisting of mitotic inhibitor antifungals, pyrimidine analog antifungals, polyene antifungals, benzimidazole antifungals, imidazole antifungals, polyene antifungals, triazole antifungals, thiazole antifungals, allylamine antifungals, echinocandin antifungals, and uncategorized antifungals.
Claim 29	
--	The method of claim 28, wherein the antifungal agent is selected from the group consisting of anidulafungin, caspofungin, clotrimazole, fluconazole, itraconazole, micafungin, nystatin, posaconazole, and voriconazole.
Claim 30	
--	The method of claim 1, further comprising at least one antiviral agent.
Claim 31	
--	The method of claim 30, wherein the antiviral agent is selected from the group consisting of interferons, nucleoside and nucleotide reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors, protease inhibitors, integrase inhibitors, fusion inhibitors, maturation inhibitors, purine analogs, pyrimidine analogs, and uncategorized antiviral drugs.

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 32	
--	The method of claim 31, wherein the antiviral agent is selected from the group consisting of aciclovir, brivudine, docosanol, famciclovir, ganciclovir, idoxuridine, penciclovir, trifluridine, tromantadine, valaciclovir, and valganciclovir.
Claim 33	
--	The method of claim 4, wherein the orally disintegrating tablet comprises about 0.01 to about 20 mg fluticasone.
Claim 34	
--	The method of claim 4, wherein the orally disintegrating tablet comprises about 0.05-3.0 mg fluticasone.
Claim 35	
Preamble	An orally disintegrating solid pharmaceutical composition comprising
[i]	less than or equal to about 20 mg of a topically administrable corticosteroid and
[ii]	at least one excipient,
[iii]	wherein: the solid pharmaceutical composition has no significant systemic glucocorticoid or mineralocorticoid activity after oral administration,
[iv]	wherein the solid pharmaceutical composition disintegrates within 60 seconds when tested using the USP <701> Disintegration Test, and
[v]	upon administration the corticosteroid is deposited topically in the upper gastrointestinal tract.

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 36	
--	The orally disintegrating solid pharmaceutical composition of claim 35, wherein said orally disintegrating solid pharmaceutical composition disintegrates within 30 seconds.
Claim 37	
--	The orally disintegrating solid pharmaceutical composition of claim 35, wherein said corticosteroid is selected from the group consisting of budesonide, fluticasone, flunisolide, ciclesonide, mometasone, beclomethasone, and salts, solvates and esters thereof.
Claim 38	
--	The orally disintegrating solid pharmaceutical composition of claim 35, further comprising an adhesive agent.
Claim 39	
--	The orally disintegrating solid pharmaceutical composition of claim 35, wherein the excipient is selected from the group consisting of mannitol, xylitol, sorbitol, maltol, maltitol, lactose, sucrose, maltose, cyclodextrin, and combinations thereof.
Claim 40	
--	The orally disintegrating solid pharmaceutical composition of claim 35, further comprising at least one antifungal agent.
Claim 41	
--	The orally disintegrating solid pharmaceutical composition of claim 35, further comprising at least one antiviral agent.

Listing of Challenged Claims from U.S. Patent No. 9,486,407	
Claim 42	
--	The orally disintegrating solid pharmaceutical composition of claim 35, wherein the orally disintegrating tablet comprises about 0.01 to about 20 mg fluticasone.

CERTIFICATE OF COMPLIANCE

Pursuant to 37 C.F.R. § 42.24(d), the undersigned certifies that this PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,486,407 contains 13,914 words according to the word-processing program used to prepare this paper. The foregoing word count complies with the 14,000 word type-volume limit specified by 37 C.F.R. § 42.24(a)(1).

Dated: 24 October 2024

By: /Nathanael Luman/

Nathanael Luman (Reg. No. 63,160)

KNOBBE MARTENS OLSON & BEAR, LLP

CERTIFICATE OF SERVICE

The undersigned hereby certifies that on the date below a copy of this PETITION FOR *INTER PARTES* REVIEW OF U.S. PATENT NO. 9,486,407, PETITIONER’S POWER OF ATTORNEY, AND EXHIBITS 1001-1020, 1025-1029, 1031-1036, 1038-1039, 1041, 1049, 1053-1055 were served by FedEx on the Patent Owner at the correspondence address of record for the subject patent as follows:

91543 - Cooley LLP / Eurand
ATTN: Patent Group
1299 Pennsylvania Avenue, Suite 700
Washington, DC 20004
UNITED STATES

Dated: 24 October 2024

By: /Nathanael Luman/

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