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.

IPR2025-00054
U.S. Patent No. 11,246,828
Issue Date: February 15, 2022

Title: ORALLY ADMINISTERED CORTICOSTEROID COMPOSITIONS

DECLARATION OF MARTYN CHRISTOPHER DAVIES

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I, Martyn Christopher Davies declare as follows:

I. INTRODUCTION

1. I submit this declaration in connection with Patent Owner's Response in the *Inter Partes* Review IPR2025-00054 (the "IPR") of claims 1-16 ("challenged claims") of U.S. Patent No. 11,246,828 (the "'828 patent"; EX1001). I have been retained by Cooley LLP, counsel for Patent Owner Ellodi Pharmaceuticals, L. P. in this matter.

A. Qualifications and Experience

2. I am an Emeritus Professor and a Pharmaceutical Consultant. I have over 35 years of experience in the field of pharmaceutical and biologic therapeutics and drug delivery fields.

3. I retired in 2017 as the Professor of Biomedical Surface Chemistry at the University of Nottingham, School of Pharmacy of Nottingham, Nottinghamshire, United Kingdom. I had held this position since 1996. I also provide consulting services for the pharmaceutical industry worldwide.

4. In 1980, I received my B.Sc. in Pharmacy from Brighton Polytechnic in the United Kingdom. I graduated first in my class with First Class Honours.

5. I was awarded a Ph.D. from the Chelsea School of Pharmacy, University of London (now Kings College, University of London) in 1985. My doctoral thesis focused on the surface energetics of hydroxypropylmethylcellulose

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and was titled "Properties of aqueous film coatings." My thesis research was under the supervision of Professor J.M. Newton.

6. In 2018, I was awarded a D.Sc. from the University of Nottingham and an Honourary Doctorate in Sciences from the University of Brighton.

7. In 1984, I was appointed as a temporary lecturer in the Department of Pharmacy at the University of Manchester, where my responsibilities included teaching physical chemistry and pharmaceutics. The following year, I was appointed to a lectureship in drug delivery in the Department of Pharmaceutical Sciences at the University of Nottingham. I was appointed as a Reader in 1991 and as a full Professor in 1996, both in Biomedical Surface Chemistry.

8. Over the course of my academic career, I have taught a range of classes, including classes in physical chemistry, pharmaceutical technology, analysis, and drug delivery, to both graduate and undergraduate students. I have trained over one hundred (100) postdoctoral and post graduate students, over twenty (20) of whom have been appointed to positions at leading international universities and many obtained important positions in the pharmaceutical industry.

9. I was Head of the Life, Health and Agricultural Sciences Division, of the Graduate School from 1995 until 1997, the Deputy Head of the School of Pharmaceutical Sciences from 1999 to 2000, and the Head of the School of

Pharmaceutical Sciences and Pharmacy School from 2000 until 2003, all at the University of Nottingham.

10. I have extensive practical experience in developing and characterizing pharmaceutical formulations. This experience comes from various sources, including conducting laboratory work with doctoral students that I have supervised, in my teaching and work at the University of Nottingham, through various industry and business partnerships and consulting roles whilst working at the Laboratory of Biophysics and Surface Analysis ("LBSA"), a research division of the University of Nottingham's School of Pharmacy that I co-founded, and in the course of performing various consulting projects through my work at Molecular Profiles Ltd. (which became Juniper Pharma Services). I have extensive experience with the formulation of tablets, capsules, and advanced drug delivery and controlled release systems that include the use and study of polymeric excipients. I have also been extensively involved in the making and characterization of many pharmaceutical preparations from 1985 to date.

11. I was well aware of the development of ODTs for the rapid dissolution of drugs in the oral cavity intended for systemic delivery. Molecular Profiles Ltd. and Juniper Pharmaceuticals also undertook testing and characterization of ODTs as part of work for external clients. We also undertook testing and characterization

on other oral delivery systems such as buccal and sublingual formulations intended for systemic delivery.

12. In my career I have been active in various national and international societies, including the Royal Pharmaceutical Society of Great Britain (where I was elected a Fellow), the Royal Society of Chemistry (where I was elected a Fellow), and the Controlled Release Society (where I was elected a Fellow). I have served as President (2011 and 2012), Vice-President (2009), and Scientific Secretary (2001) of the Controlled Release Society, the premier international society in drug delivery and controlled release.

13. I was a member of the Engineering and Physical Sciences Research Council Peer Review College, the Research Assessment Exercise 2008 Pharmacy Panel, and was a participant in the European Science Foundation Forward Look on Nanomedicine. I also was elected as a Fellow of the Academy of Pharmaceutical Sciences in the United Kingdom.

14. Over the course of my career, I have authored over 380 peer-reviewed papers, reviews, and book chapters. My work has been published in various nationally and internationally recognized journals, including the Journal of Controlled Release, the International Journal of Pharmaceutics, The Journal of Pharmaceutical Sciences, Pharmaceutical Research, Molecular Pharmaceutics, The

European Journal of Pharmaceutics and Biopharmaceutics, Expert Opinion of Drug Delivery, Gastroenterology, Langmuir, the Journal of Physical Chemistry, Analytical Chemistry, PNAS and Nature Materials. I am also a named inventor on various patents and patent applications.

15. I have presented at various national and international conferences and learned societies, including the Swedish Academy of Sciences, the Royal Society of Chemistry, the American Chemistry Society, the Controlled Release Society, and the Association of Pharmaceutical Scientists. I have presented invited seminars at various universities and research institutes including Kings College, Cambridge University, the University of Utah, and the National University of Ireland. I have also presented lectures to research groups in the pharmaceutical and chemistry industries.

16. I have sat on the editorial boards of leading international scientific journals focusing on formulation science, including the Journal of Pharmaceutical Sciences, Advanced Drug Delivery Reviews, the European Journal of Pharmaceutical Sciences, the Journal of Controlled Release, and the Journal of Biopharmaceutics and Biotechnology.

17. As mentioned earlier, I was one of the co-founders of the LBSA, which I led until 2008. The LBSA had a leading international reputation in the application

of advanced analytical tools to understand the structure and function of pharmaceutical formulations such as controlled release systems, polymeric excipients, and biomedical systems. In 2003, the LBSA was awarded the GlaxoSmithKline International Achievement Award for its internationally recognized work on the commercial exploitation of nanotechnology in pharmaceutical formulations. This was the first time that this award was given to such a group.

18. In 1997, I co-founded the private sector company Molecular Profiles Ltd. and served as the founding chairman until 2013, when the company was acquired by Columbia Laboratories and became Juniper Pharma Services, which in turn was acquired by Catalent Inc in 2018. At that time, I was appointed as an Advisor to the Board of Directors of Juniper Pharmaceuticals and Chaired and served on the Scientific Advisory Board of Juniper Pharmaceuticals. Molecular Profiles Ltd. (and then Juniper) provided customized formulation, characterization, and development across a broad range of therapies, mainly focused on small molecule Active Pharmaceutical Ingredients ("APIs"). We also provided pharmaceutical development, clinical trial manufacturing, advanced analysis, and consulting services. Molecular Profiles Ltd and then Juniper also developed, manufactured and packaged formulations for use by pharmaceutical companies in

Phase I and Phase II clinical trials.

19. In 2007 and 2011, Molecular Profiles Ltd. was awarded a Queen's Award for Enterprise in recognition of its commitment to bringing high quality, innovative science to the pharmaceutical industry.

20. In January 2018, I was appointed a Commander of the Order of the British Empire ("CBE") in Her Majesty's 2018 New Year's Honours List in recognition of my contribution to science and achievements in pharmacy and pharmaceutical research.

21. My credentials are set forth in full detail in my Curriculum Vitae which is submitted as Exhibit 2008, and incorporated here by reference.

22. I am being compensated for the time I spend working on this matter at my standard rate. My compensation does not depend in any way upon the outcome of this proceeding, and I hold no financial interest in either Dr. Falk Pharma GmbH ("Petitioner") or Ellodi Pharmaceuticals, L.P. ("Patent Owner").

23. In formulating my opinions, I have relied upon my training, knowledge, and experience in the relevant art.

B. Materials Considered

24. The analysis that I provide in this Declaration is based on my education, research, and experience, as well as the documents I have considered. In forming my

opinions, I have read and considered the claims, specification, and prosecution history of U.S. Patent No. 10,632,828 ("'828 patent"). I have reviewed the Petition for *Inter Partes* Review (and exhibits, including the Declaration of Alan F. Parr) filed by Petitioner Dr. Falk Pharma GmbH on October 24, 2024. I have also cited to or considered the following documents in my analysis below:

Exhibit No.	Description of Document
2004	Transcript of the August 29, 2025 Deposition of Alan F. Parr, Pharm.D., Ph.D. from Nos. IPR2025-00052, IPR2025-00054, and IPR2025-00055
2005	Iorgulescu, G., Saliva between normal and pathological. Important factors in determining systemic and oral health, Journal of Medicine and Life Vol. 2, No.3, July-September 2009, pp.303-307
2006	Miehkle, S. et al., A randomised, double-blind trial comparing budesonide formulations and dosages for short-term treatment of eosinophilic oesophagitis, Gut 0:1-10 (2015)
2008	*Curriculum Vitae* of Martyn Christopher Davies
2010	Clinical Trials Study, "Efficacy, Safety, and Pharmacokinetics of APT-1011 in Subjects With Eosinophilic Esophagitis (EoE)(FLUTE)," last updated Apr. 26, 2023, https://clinicaltrials.gov/study/NCT03191864?tab=results&a=11#outcome-measures
2011	Deposition of Alan F. Parr, Pharm.D., Ph.D., dated April 9, 2025
2012	"Antrum" Definition, American Medical Dictionary: A Concise and Up-to-Date Guide to Medical Terms (1998)

Exhibit No.	Description of Document
2013	M.E. Aulton (Ed.), Pharmaceutics: The Science of Dosage Form Design (2d. 2002)
2014	"Lozenge" Definition, Dennis B. Worthen (ed.), Dictionary of Pharmacy (2004)
2016	Hahm, H.A., Augsburger, L.L., Ch. 9 Orally Disintegrating Tablets and Related Tablet Formulations
2017	Ghosh, T.K. et al, Drug Delivery to the Oral Cavity Molecules to Market, Ch. 14 Quick dissolving oral dosage forms: Scientific and regulatory considerations from a clinical pharmacology and Biopharmaceutics Perspective (2005)
2018	Transcript of the August 25, 2025 deposition of Alan Parr, Pharm.D. from No. IPR2024-01197
2020	Cordova-Fraga T, Sosa M, Wiechers C, et al., Effects of anatomical position on esophageal transit time: a biomagnetic diagnostic tech-nique. World J Gastroenterol 14:5707–11 (2008)
2021	U.S. Patent No. 8,324,192
2022	Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations, Patent and Exclusivity for: N213976, Product 001 Budesonide (Eohilia) Suspension 2mg/10ml, https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=213976&Appl_type=N
2026	*Dr. Falk Pharma GMBH v. Ellodi Pharms., L.P.*, IPR2024-01197, EX1093 (P.T.A.B July 10, 2025)

II. LEGAL STANDARDS

25. In formulating my opinions and conclusions in this proceeding, I have

been provided with an understanding of the prevailing principles of U.S. patent law that govern the issues of patent validity.

A. Claim Construction

26. I understand that the purpose of claim construction is to determine what a person of ordinary skill in the art would have understood the claim terms to mean. Claim terms are generally given their ordinary and customary meaning, which is the meaning that the term would have to a person of ordinary skill in the art in question as of the effective filing date.

27. I understand that the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification. I understand that the patent specification, under the legal principles, has been described as the single best guide to the meaning of a claim term, and is thus highly relevant to the interpretation of claim terms. And I understand for terms that do not have a customary meaning within the art, the specification usually supplies the best context of understanding the meaning of those terms.

28. I further understand that other claims of the patent in question, both asserted and unasserted, can be valuable sources of information as to the meaning of a claim term. Because the claim terms are normally used consistently throughout the

patent, the usage of a term in one claim can often illuminate the meaning of the same term in other claims. Differences among claims can also be a useful guide in understanding the meaning of particular claim terms.

29. I understand that the prosecution history can further inform the meaning of the claim language by demonstrating how the inventors understood the invention and whether the inventors limited the invention in the course of prosecution, making the claim scope narrower than it otherwise would be. Extrinsic evidence, such as dictionaries, may also be consulted in construing the claim terms.

30. I understand that, in *Inter Partes* Review (IPR) proceedings, a claim of a patent shall be construed using the same claim construction standard that would be used to construe the claim in a civil action filed in a U.S. district court (which I understand is called the "*Phillips*" claim construction standard), including construing the claim in accordance with the ordinary and customary meaning of such claim as understood by one of ordinary skill in the art and the prosecution history pertaining to the patent.

31. I have been instructed by counsel to apply the "*Phillips*" claim construction standard for purposes of interpreting the claims in this proceeding, to the extent they require an explicit construction. The description of the legal principles set forth above thus provides my understanding of the "*Phillips*" standard

as provided to me by counsel.

32. Where claim construction issues arise, I have noted them in my analysis below.

B. Obviousness

33. I am also informed and understand that a claim may be rendered obvious to a person of ordinary skill in the art if the differences between the subject matter set forth in the patent claim and the prior art are such that the subject matter as a whole of the claim would have been obvious at the time the claimed invention was made.

34. I am informed and understand that obviousness is a determination of law based on various underlying determinations of fact. In particular, these underlying factual determinations include (1) the scope and content of the prior art; (2) the level of ordinary skill in the art at the time the claimed invention was made; (3) the differences between the claimed invention and the prior art; and (4) the extent of any proffered objective *indicia* of nonobviousness. I understand that the objective *indicia* which may be considered in such an analysis include commercial success of the patented invention (including evidence of industry recognition or awards), whether the invention fills a long-felt but unsolved need in the field, the failure of others to arrive at the invention, industry acquiescence and recognition, initial

skepticism of others in the field, whether the inventors proceeded in a direction contrary to the accepted wisdom of those of ordinary skill in the art, and the taking of licenses under the patent by others, among other factors.

35. I am informed and understand that to ascertain the scope and content of the prior art, it is necessary to first examine the field of the inventor's endeavor and the particular problem for which the invention was made. The relevant prior art includes prior art in the field of the invention, and also prior art from other fields that a person of ordinary skill in the art would look to when attempting to solve the problem.

36. I am informed and understand that a determination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention. Instead, it is my understanding that to render a patent claim invalid as being obvious from a combination of references, there must be some evidence within the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination in a way that would produce the patented invention.

37. I understand that there is a high standard before a party can rely on inherency to establish the existence of a claim limitation in the prior art in an obviousness analysis. Even if a certain thing may result from a given set of

circumstances, I understand that is not enough to render the result inherent. I also understand that an element can only be inherently disclosed if it is necessarily present in the prior art, not just probably or possibly present. Yet, even if an element is inherent, I understand that it is not necessarily obvious.

38. I am further informed and understand that in an obviousness analysis, neither the motivation nor the purpose of the patentee dictates. What is important is whether there existed at the time of the invention a known problem for which there was an obvious solution encompassed by the patent's claims.

39. In addition, it is my understanding that to find a patent claim invalid for obviousness, there must be a finding that each element in each limitation of the patent claim is disclosed, taught, or suggested by the asserted combination of prior-art references or elsewhere in the relevant prior art. I understand, however, that a patent claim composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. But multiple prior-art references or elements may, in some circumstances, be combined to render a patent claim obvious. I understand that I should consider whether there is an "apparent reason" or motivation to combine the prior-art references or elements in the way the patent claims. To determine whether such an "apparent reason" or motivation exists to combine the prior-art references or

elements in the way a patent claims, it will often be necessary to look to the interrelated teaching of multiple prior-art references, to the effects of demands known to the design community or present in the marketplace, and to the background knowledge possessed by a person of ordinary skill in the art.

40. I also understand that when the prior art "teaches away" from combining prior-art references or certain known elements, discovery of a successful means of combining them is more likely to be nonobvious. A prior-art reference may be said to "teach away" from a patent when a person of ordinary skill in the art, upon reading the reference, would be discouraged from following the path set out in the patent or would be led in a direction divergent from the path that was taken by the patent. Additionally, a prior-art reference may "teach away" from a claimed invention when substituting an element within that prior-art reference for a claim element would render the claimed invention inoperable.

41. I am informed and understand that a patent for a combination which only recites old elements with no change in their respective functions withdraws what is already known into the field of its monopoly and diminishes the resources available to person of ordinary skill in the field. When a patent claims a structure already known in the prior art that is altered by mere substitution of one element for another known in the field, the combination must do more than yield a predictable

result. I am informed and understand that the corollary to this principle is that when the prior art teaches away from combining known elements, discovery of a successful means of combining them is more likely to be nonobvious. Thus, the question to be answered is whether someone reading the prior art would be discouraged from following the path taken by the inventor.

42. I am further informed and understand that when an element is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill in the art can implement a predictable variation of that available element, Section 103 likely renders the invention obvious. For the same reason, I am informed and understand that if a technique has been used to improve one device or process, and a person of ordinary skill in the art would recognize that such technique would improve similar devices or processes in the same way, using the technique is obvious unless its actual application is beyond his or her skill. Following these principles often requires one to look to interrelated teachings of multiple patents; the effects of demands known to the design community present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art to determine whether there was an apparent reason to combine the known element in the manner claimed by the patent at issue. I am further informed and understand that

the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, because one can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.

43. I am further informed and understand that although the use of the "teaching, suggestion or motivation" test for combining references has not been completely rejected, the obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents. Under the correct analysis, any need or problem known in the field of endeavor at the time of the invention and addressed by the patent can provide a reason for combining the elements in the manner claimed. Finally, I am informed and understand that common sense teaches that familiar items may have obvious uses beyond their primary purposes and, in many cases, a person of ordinary skill in the art will be able to fit the teachings of multiple patents together like pieces of a puzzle.

III. OVERVIEW OF THE '828 PATENT

44. The '828 patent, titled "Orally Administered Corticosteroid Compositions," was filed as U.S. Application No. 16/821,464 on March 17, 2020 and has a priority date of October 1, 2009. It has three named inventors: Stephen Perrett, Fredric Jay Cohen, and Gopi M. Venkatesh.

45. The claims of the '828 patent are directed to orally dispersing tablets containing a topically administered corticosteroid, budesonide, that topically administers a therapeutically effective amount of a corticosteroid to inflamed tissue of the upper gastrointestinal tract for the treatment of conditions associated with inflammation of the upper portion of the gastrointestinal tract. EX1001, 1:20-35, 5:23-27. Topically depositing a therapeutically effective amount of a topically acting corticosteroid to the upper gastrointestinal tract (e.g., esophagus) is challenging, due to the constant flow of saliva and peristalsis pushing material down toward the stomach.

46. One condition, eosinophilic esophagitis (EoE), is an inflammatory condition of the esophagus. EX1001, 1:30-32. Prior treatments for EoE included corticosteroid formulations designed for inhalation that were instead applied to the back of the throat, (EX1001, 1:36-48), as well as oral administration of systemically active corticosteroids (EX1001, 1:49-57). These treatments posed undesirable side effects, including candidiasis infection and suppression of immune function, respectively. EX1001, 1:36-57.

47. The orally dispersing tablet claimed in the '828 patent solves these problems. The claims relate to a formulation comprising budesonide, which has no significant systemic glucocorticoid or mineralocorticoid activity after oral

administration (i.e. a corticosteroid that has no significant systemic activity), which disintegrates within 60 seconds to form a solution or dispersion that is swallowed, and the budesonide is released and topically deposited on the upper gastrointestinal tract, including the esophagus. EX1001, 1:63-2:7, 4:4-8. Disintegration of the tablet and dissolution (drug release) occur near simultaneously, resulting in drug deposition on the esophagus within 1-2 seconds of swallowing and before the disintegrated tablet passes to the stomach. EX2020, 5708 ("liquid [esophageal transit time] lasts approximately 1 to 2 s …"). This provides localized delivery and effective treatment for EoE that also mitigates the undesirable side effects of systemic corticosteroids used for treating EoE and candidiasis infections associated with oral corticosteroid administration. EX1001, 1:63-2:7, 4:4-8. The disintegration time is measured using the United States Pharmacopeia (USP) <701> Disintegration Test. EX1001, 10:25-32, cl. 1.

48. It would be surprising to a POSA to discover that the claimed ODT can deposit a therapeutically effective amount of a topically acting corticosteroid on the esophagus in the short period of time (~1-2 seconds) it takes the suspension to transit the esophagus and effectively treat EoE, and without causing candidiasis infections. EX2010; EX2020, 5708; *see also* EX1001, 1:41-44 (discussing oral candidiasis infections).

49. The '828 patent has 17 claims. Claim 1 is the only independent claim.

Claim 1 recites:

> 1. An orally dispersing tablet comprising:
> (i) about 0.5 mg to about 1 mg of budesonide;
>
> (ii) at least one pharmaceutically acceptable ingredient which facilitates the dispersal of the tablet in the oral cavity; and
>
> (iii) sucralose, mannitol, magnesium stearate, polyvinyl pyrrolidone, polyethylene glycol, or combinations thereof;
>
> wherein upon administration a therapeutically effective amount of budesonide is deposited topically in the upper gastrointestinal tract, and
>
> wherein the orally dispersing tablet disintegrates within 60 seconds in simulated saliva when tested using the USP <701> Disintegration Test.

Claims 2-16 depend on claim 1.

50. Claim 1 is directed towards an orally dispersing tablet comprising budesonide that disintegrates within 60 seconds. Dependent claims 14 is a method claim directed to a method for treating eosinophilic esophagitis.

A. Prosecution History

51. The '828 patent issued from U.S. Patent Application No. 16/821,464 (the "'464 Application"). EX1001, cover. Patent Owner filed the '464 Application on March 17, 2020. EX1001, cover. In a preliminary amendment, Patent Owner amended originally filed claim 1, cancelled claims 3 and 15-21, and added new

claims 23 and 24. EX1049, 292-293. The only independent claim, claim 1 recited:

> 1. (Currently Amended) An orally dispersing tablet comprising:
>
> (i) about 0.5 mg to about 1 mg of budesonide;
>
> (ii) and at least one pharmaceutically acceptable ingredient which facilitates the dispersal of the tablet in the oral cavity;
>
> (iii) sucralose, mannitol, magnesium stearate, polyvinyl pyrrolidone, polyethylene glycol, or combinations thereof;
>
> wherein upon administration a therapeutically effective amount of the corticosteroid is deposited topically in the upper gastrointestinal tract, and
>
> wherein the orally dispersing tablet disintegrates within 60 seconds in simulated saliva when tested using the USP <701> Disintegration Test.

EX1049, 292.

52. The Examiner rejected the claims for obviousness over US 2009/0131386 ("Phillips") in view of US 2009/0169620 ("Venkatesh 2009"). EX1049, 108-113. The Examiner argued that Phillips teaches solid dosage forms for the treatment of inflammation of the gastrointestinal tract and Venkatesh 2009 teaches a solid pharmaceutical composition in the form of an orally disintegrating tablet (ODT) that disintegrates within 60 seconds or less. EX1049, 108-113.

53. In response, Patent Owner cited to the Notices of Allowance for several related patents, which stated that Phillips "does not teach or suggest an orally disintegrating solid formulation composition (or an orally disintegrating tablet) that disintegrates within 60 seconds" and that Venkatesh does not cure this deficiency or teach the topical delivery of drugs. EX1049, 90-91. The Examiner withdrew the

rejection and allowed the claims. EX1049, 15.

54. Dr. Parr does not cite to the prosecution history of the '828 patent, or the Information Disclosure Statements submitted during prosecution disclosing the prior art references, in his declaration. As such, Dr. Parr does not acknowledge what the Examiner previously considered during prosecution.

IV. BACKGROUND OF THE PRIOR ART

55. In his declaration, Dr. Parr opines on the scope and content of the prior art. I address his opinions below.

V. CLAIM CONSTRUCTION

56. In his declaration, Dr. Parr opines on the construction of a number of terms in the '828 patent. I address the construction of each term below.

A. Terms Defined in the '828 Patent Specification

57. Dr. Parr states that '828 patent defines "orally disintegrating tablet", "orally dispersing tablet", or "ODT" to refer "to a solid dosage form of the present invention, which disintegrates rapidly in the oral cavity of a patient after administration, without chewing." EX1051, ¶¶ 118, 239; EX1001, 2:49-52. I agree with this definition.

58. Dr. Parr states that the '828 patent defines "about" as "used herein to refer to a numerical quantity, includes 'exactly'. For example, 'about 60 seconds' includes 60 seconds, exactly, as well as values close to 60 seconds (e.g., 50 seconds,

55 seconds, 59 seconds, 61 seconds, 65 seconds, 70 seconds, etc.). 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')." EX1051, ¶¶ 122, 245 (citing EX1001, 2:65-3:6). I agree with this definition.

59. I apply these definitions.

VI. DR. PARR'S GROUNDS LACK CREDIBLE BASIS, IGNORE CLAIM LIMITATIONS, AND MISCONSTRUE THE ASSERTED ART

60. Dr. Parr opines that the challenged claims are obvious based on two grounds: (1) 1-16 over Dohil in view of the knowledge of a POSA (ground 1); and (2) claims 1-16 over Grother in view of the FDA Guidance (ground 2). I disagree with Dr. Parr that the challenged claims would have been obvious to a POSA over any of his asserted prior art grounds. I discuss some of the errors for each ground, below.

A. Dr. Parr's Focus on Prior Art Budesonide Formulations and Uses is Irrelevant to the Claims

61. The '828 patent is directed to ODTs containing budesonide that disintegrates within 60 seconds for the treatment of conditions associated with inflammation of the upper portion of the gastrointestinal tract.

62. Over 30 pages of Dr. Parr's analysis on the scope of the prior art is

irrelevant and does not address the particular problems solved by the '828 patent or the claims of the '828 patent. Dr. Parr spends much of his analysis regarding the scope of the prior art on the prior uses of budesonide to treat inflammatory conditions of the lower gastrointestinal tract, using enterically coated budesonide, and desirability of ODTs for administering systemically active drugs. EX1051, Section VII. I note the claims of the '828 patent exclude systemically active corticosteroids. However, Dr. Parr relies on none of these references in his grounds for alleging obviousness. EX2004, 13:2-21; EX2011, 31:20-21, 41:1-15. As discussed below, a POSA would find none of the references relevant.

63. Dr. Parr spends about 12 pages on the desirability of budesonide to treat inflammation of the upper gastrointestinal tract. EX1051, ¶¶ 43-58. Importantly, none of these references discuss an orally disintegrating solid composition. Further, it is my understanding that there is no dispute that budesonide, fluticasone, or other topical corticosteroids could be used to treat inflammation of the upper gastrointestinal tract. In fact, the '828 patent describes both being used to treat EoE in the background of the invention section. EX1001, 3:33-36, 7:20-25.

64. Dr. Parr also cites to a number of references discussing various uses of budesonide in the prior art, none of which disclose an orally dispersing tablet containing budesonide, or topical deposition of budesonide on the upper

gastrointestinal tract. For example, Dr. Parr cites to Goodman & Gillman (EX1051, ¶ 43) which describes budesonide as an "enteric-release form[.]" EX1025, 1014. A POSA would understand that an "enteric-release form" refers to a coating that prevents the drug from being released until the drug passes through the stomach and into the small intestine. Thus, an enterically-coated budesonide tablet would not be deposited topically in the upper gastrointestinal tract, much less the esophagus, because these anatomical regions are before the stomach.

65. Dr. Parr also cites to Svoboda, which also uses controlled release formulations of budesonide. EX1051, ¶ 43 (citing EX1009). Svoboda explains that budesonide was originally administered in a retention enema, and was then formulated into tablets that release the budesonide in the ileum and ascending colon (i.e., the lower gastrointestinal tract), to treat inflammatory disease of the lower intestines, like Crohn's disease and ulcerative colitis. EX1009, 859-860. A POSA would understand that the Svoboda budesonide is enterically coated, as described in Goodman & Gillman (EX1025) and Budenofalk, and therefore budesonide would not be deposited topically in the upper gastrointestinal tract, much less the esophagus.

66. Dr. Parr also cites to Tan, which details a case study on administering a tablet containing budesonide to a subject with eosinophilic gastroenteritis.

EX1051, ¶ 44. The patient in Tan presented with pain in the upper abdomen and an antrum biopsy was performed for diagnosis of eosinophilic gastroenteritis. EX1010, 425. I understand an antrum biopsy to be a biopsy from the lower part of the stomach, which is below the esophagus. EX2012, 32. Tan explains that the tablet was given orally, not dissolved, and swallowed like a conventional tablet. EX1010, 425-426. Tan reports that budesonide was "absorbed mainly in the stomach and proximal small bowel." EX1010, 427. There is no discussion of oral disintegration, inflammation of the upper gastrointestinal tract, such as the esophagus, or topical deposition of the corticosteroid on the upper gastrointestinal tract (e.g., esophagus). A POSA would therefore understand that the budesonide tablet administered in Tan would not have dissolved rapidly in the mouth and budesonide was not topically deposited in the upper gastrointestinal tract, let alone the esophagus.

67. Dr. Parr then cites to a number of references that disclose using Budenofalk to treat certain inflammatory conditions of the lower gastrointestinal tract. None of the references treat EoE or inflammation of the upper gastrointestinal tract. I understand that Budenofalk contains budesonide and comes in capsule form or a rectal foam and is commercialized by Petitioner. EX1026; EX1027. It is my understanding that the capsule form is enterically coated such that the budesonide is not released until after it passes through the stomach. As such, the budesonide in

Budenofalk is not released in the upper gastrointestinal tract as required by the claims of the '828 patent. Consequently, a POSA would not find Budenofalk relevant to the claimed invention.

68. Dr. Parr cites to Kolkman as studying Budenofalk in 16 patients for ulcerative colitis. EX1051, ¶ 46. A POSA would know that ulcerative colitis occurs in the rectum and colon. Kolkman also discloses that Budenofalk is released in the intestine and colon (i.e. the lower gastrointestinal tract, not the upper gastrointestinal tract). EX1011, 590. A POSA would therefore understand from Kolkman that Budenofalk is not used to treat inflammation of the upper gastrointestinal tract, much less the esophagus.

69. Dr. Parr also cites to Siewert, which discusses the treatment of eosinophilic gastroenteritis. EX1051, ¶ 47. Siewert similarly discloses that Budenofalk is released in the small bowel and specifically states that the patient did not receive any topical corticosteroid therapy for the upper gastrointestinal tract. EX1012, 58. Thus, a POSA would understand that from Siewert that Budenofalk does not treat inflammation of the upper gastrointestinal tract, much less the esophagus.

70. Dr. Parr also cites to Elsing, which discusses the treatment of eosinophilic jejunitis. EX1051, ¶ 48. Elsing similarly discloses that Budenofalk is

released in the small bowel and specifically states that the patient had an obstruction in the small bowel that was resolved with Budenofalk, along with other steroids. EX1013, 188. Thus, a POSA would understand that from Elsing that Budenofalk does not treat inflammation of the upper gastrointestinal tract, much less the esophagus.

71. Dr. Parr also cites to Aceves 2005, Aceves 2007, and Dohil, which discuss using a viscous suspension of budesonide to treat EoE. EX1051, ¶¶ 49-57. The findings in Aceves 2005 and Aceves 2007 are cited in Dohil. EX1014; EX1015; EX1002, [0046]-[0067]. Aceves 2005 formulated budesonide in a viscous topical suspension because it is "easier to use" in young children and avoided the drawbacks of systemic steroid therapy. EX1014, 706. The results of Aceves 2005 showed that the viscous oral suspension of budesonide significantly improved patient symptoms. EX1014, 706.

72. Similarly, Aceves 2007 studied the efficacy and safety of oral viscous budesonide (OVB) in 20 patients with EoE. EX1015, 1. The results of Aceves 2007 showed that OVB improved EoE symptoms in 90% of patients. EX1015, 6. Aceves 2007 concludes that OVB is an effective and safe treatment for EoE and "ha[s] advantages over other therapies in that it is palatable, its volume (8-12 mL) provides pan-esophageal mucosal coverage, and it requires once daily administration[.]"

EX1015, 8. The results of both Aceves 2005 and Aceves 2007 are summarized in Dohil. EX1002, [0046]-[0070].

73. A POSA would understand from the disclosures in Aceves 2005, Aceves 2007, and Dohil that the viscous liquid formulation of budesonide referred to as OVB is a safe and effective treatment for EoE had several advantages over other therapies. Aceves 2005, Aceves 2007, and Dohil fail to mention any problems with OVB. Since OVB works for its intended purpose, was simple to prepare and easy to administer a POSA would have had no motivation to use a fundamentally different formulation.

74. Nothing in Aceves 2005 or Aceves 2007 suggests or implies modifying OVB to make an orally disintegrating composition containing a corticosteroid for the treatment of EoE, or that such a disintegrating composition would work considering the dramatic mechanistic and formulation differences. Dr. Parr also cites to Dohil's disclosure of a lozenge or similar tablet. EX1051, ¶ 57. I address this disclosure below.

75. None of the references Dr. Parr cites to, other than Dohil, are used as references for Petitioner's or Dr. Parr's grounds for obviousness. It's unclear why these references were cited, as there is no dispute that budesonide was known for treating inflammatory conditions of the gastrointestinal tract, including the upper

gastrointestinal tract. In my opinion, none of the cited references disclosing budesonide disclose, teach, suggest, or provide motivation to prepare an orally disintegrating composition containing budesonide, let alone provide a reasonable expectation that such a composition could topically deposit budesonide on the upper gastrointestinal tract and treat inflammation thereof. Indeed, Dr. Parr does not cite to any prior art references disclosing an orally disintegrating composition containing a topical drug to treat a condition of the upper gastrointestinal tract.

B. Dr. Parr Analysis Starts with Orally Disintegrating Tablets (ODTs) - This is Purely Hindsight

76. Regarding ODTs, Dr. Parr analysis starts by focusing on the desirability and commercial availability of ODTs. EX1051, ¶¶ 59-73. For the general knowledge of a POSA, Dr. Parr relies on the prior art disclosing ODTs and disintegration time and conditions, stating that ODTs were well-known at the time of the invention. EX1051, ¶¶ 59-60. From this point onwards, Dr. Parr's declaration relies on impermissible hindsight. In my opinion, ODTs and disintegration time would be irrelevant to a POSA seeking to formulate an effective treatment for inflammation of the upper gastrointestinal tract or EoE. Instead, a POSA would look to improving efficacy of known treatments, and consider factors such as adequately coating the inflamed area of the esophagus, contact time of the formulation with the inflamed area of the esophagus, and preventing infections in the mouth. Dr. Parr, on the other

hand, begins with the language of the claims and works backwards to make the prior art fit into his obviousness analysis.

77. I understand that there is no dispute that ODTs were available and commercialized in the prior art. The hindsight driven analysis is evidenced by the detailed discussion of ODTs to promote systemic absorption which is excluded by the claims of '828 patent. EX1001, 3:19-24 ("The term 'having no significant systemic glucocorticoid or mineralocorticoid activity', as used herein refers to 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."). Dr. Parr opines that ODTs dissolve or disintegrate in the mouth and the active ingredient is then "absorbed though the mucosa of the mouth, esophagus, or other sections of the gastrointestinal track [*sic*]." EX1051, ¶ 59. Dr. Parr goes on to cite several references which list absorption of the active ingredient through the oral mucosa and esophagus as advantages. EX1051, ¶ 72 (citing EX1019, EX1017, and EX1018). A POSA would understand that absorption of an active ingredient is necessary for systemically acting drugs only. The '828 patent, however, discloses an orally dispersing tablet containing budesonide which has no significant systemic activity. Thus, in my opinion, a POSA would not consider the advantage of using an ODT for absorption of a systemically acting drug

to be relevant to topically acting corticosteroid.

78. None of Dr. Parr's cited references disclose ODTs containing topically acting corticosteroids, or drug administered to the upper gastrointestinal tract. *See, e.g.*, Fu (EX1018, Table 2).

C. Dr. Parr Does Not Provide Support for his Conclusions

79. Dr. Parr also opines that the prior art discloses orally disintegrating solid pharmaceutical compositions containing budesonide. EX1051, ¶¶ 98-106. Dr. Parr cites to four references for support: Dohil (EX1002), Grother (EX1008), Singh (EX1035), and Cherukuri (EX1036). I disagree.

80. In my opinion, Dohil does not disclose an orally disintegrating solid pharmaceutical composition containing budesonide that disintegrates within 60 seconds.

81. Dr. Parr cites to two paragraphs in Dohil which states that budesonide can be provided in a "lozenge or other similar tablet…[that] wo[u]ld dissolve rapidly in the mouth or esophagus" or a "dissolving tablet [and] a dissolving wafer[.]" EX1051, ¶ 57 (citing EX1002, [0032], [0013]). Dohil does not exemplify or provide an enabling disclosure of a lozenge or other similar tablet, and is silent regarding the disintegration rate. In fact, Dohil does not even use the term disintegrate, as recited in the claims of the '828 patent. Dissolve and disintegrate are not the same, and are

different processes. EX2018, 21:19-22. I understand that Dr. Parr testified that dissolve and disintegrate are not the same, but he appears to equate the terms in his declaration. *Id*.

82. The remaining disclosure in Dohil, which spans approximately 110 paragraphs, is exclusively related to liquid formulations of budesonide. This is because Dohil is mainly directed to liquid compositions containing viscosity enhancing agents that improve contact of the corticosteroid with the esophagus. Dohil teaches a "simple" and "palatable" viscous liquid composition with 8-12mL volume that provides "pan-esophageal mucosal coverage" to effectively treat EoE, with only a passing reference to solid compositions. EX2011, 72:25-74:6, 61:3-9, 66:17-20, 68:10-12, 68:22-24, 70:8-12; EX1002, [0067].

83. Dohil is directed to liquid compositions of budesonide. Dohil teaches that it "is often difficult to deliver an effective dose of a corticosteroid to the targeted area of the esophagus." EX1002, [0007]. To solve this problem, Dohil teaches "[a] liquid, long-acting topical corticosteroid preparation is needed." EX1002, [0009]. Dohil also teaches using a viscosity enhancer to increase viscosity and deliver a viscous form of budesonide that coats the throat. EX1002, [0011], [0013], [0021], [0037], [0038], [0042]-[0045], [0046], [0048]-[0070]. Dohil further teaches that a large volume of the budesonide formulation is necessary to provide an effective

amount to the esophagus. EX1002, [0031], [0053], [0067] ("[OVB] may have advantages over other therapies in that…its volume (8-12ml) provides pan-esophageal mucosal coverage[.]").

84. All three examples in Dohil discuss an oral viscous liquid budesonide formulation (referred to as OVB). EX1002, [0056]-[0070]. The OVB liquid formulation is the only formulation made and tested in these examples, and the data shows that it effectively treats EoE in children. Dohil highlights several advantages of the OVB liquid formulation, including palatability and effective drug contact with the esophagus. EX1002, [0067] ("It may have advantages over other therapies in that it is palatable, its volume (8-12 ml) provides pan-esophageal mucosal coverage and it requires only once daily administration."); *id.*, [0056]-[0070].

85. In Examples 1 and 2, the patients were administered the viscous liquid formulation daily, and both patients showed improvement of EoE symptoms and complete resolution or normal appearing esophagus after treatment. EX1002, [0046]-[0047]. In Example 3, patients were given the viscous liquid formulation and 90% of patients showed improvement after treatment. EX1002, [0048], [0053], [0060]. Dohil does not mention any problems with the viscous liquid formulation. Thus, a POSA would understand Dohil as teaching that a specific, large volume (8-12mL) of a viscous liquid formulation is needed to treat EoE because it is capable

of coating the esophagus and topically delivering an effective dose of a topical corticosteroid to the esophagus. EX1002, [0067].

86. A POSA would understand a lozenge to be a solid tablet that does not contain a disintegrant, and is sucked on to continuously dissolve slowly over a period of time, as described in the art cited by Dr. Parr. EX1017, 181; *see also* EX2013, 413; EX2014, 201. Dr. Parr also admits that a typical lozenge dissolves slowly. EX2011, 62:13-15. Danckwerts, cited by Dr. Parr, also refers to lozenges or tablets formulated without disintegrants that are sucked on by patients. EX1017, 181. Thus, a POSA would understand a lozenge is not the same as an orally disintegrating tablet, because an ODT disintegrates within 60 seconds, and an ODT does not dissolve.

87. Dohil does not define "lozenge" or "dissolve rapidly" to refer to disintegration within 60 seconds as claimed. A POSA would know that lozenges are well known in the art to dissolve slowly. EX2013, 413; *see also* EX2014, 201 (defining a lozenge as a "solid preparation…intended to dissolve or disintegrate slowly"). The art also distinguishes lozenges from other ODTs. EX2016, 293 ("Despite a surge of orally disintegrating tablets in the market in the recent years, they potentially can be confused with other solid oral dosage forms that are consumed without additional water intake, including ***lozenges***, buccal tablets, and chewable tablets. Lozenges and buccal tablets are intended to dissolve slowly in the

mouth, whereas, orally disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds."); EX2017, 341 (distinguishing quick/fast/rapid/mouth-dissolving tablets and fast/quick-melting tablets from lozenges). Because lozenges are not ODTs, and lozenges dissolve slowly over several minutes whereas ODTs disintegrate within seconds, Dohil's similar tablet would also dissolve over several minutes, just like a lozenge.

88. While Dohil mentions that the "lozenge or other similar tablet…dissolve[s] rapidly," this does not lead a POSA to an ODT that disintegrates in 60 seconds. EX1002, [0032]. When read as a whole, a POSA would understand that Dohil's lozenge or similar tablet would dissolve at a rate sufficient to produce 8-12mL of liquid, which Dohil teaches is necessary for pan-esophageal coating and efficacy. EX1002, [0032], [0067]. This is reinforced by Dohil's teaching that "for children or other patients that may have difficulty with a dissolving lozenge, the lozenge may be ground or otherwise dissolved…reaching a total volume presented in embodiments herein[,]" i.e. 8-12mL. EX1002, [0032], [0067]. Placing a lozenge in the mouth results in saliva production of 4-5mL/min. EX2005, 303-304. To reach 8-12mL, a lozenge would dissolve over 2-3 minutes.

89. Neither Dohil nor Dr. Parr cite to any lozenges or similar tablets that disintegrate in 60 seconds or less. Nor was Dr. Parr able to identify fast dissolving

lozenges, let alone opine that any of the commercially available ODTs constitute lozenges or similar tablets. EX2011, 63:6-21. I also understand that Dr. Parr did not conduct any investigation into whether a fast dissolving lozenge has ever been produced or commercialized. EX2011, 63:18-21. In my opinion, a POSA would understand that a lozenge does not disintegrate rapidly like an ODT. I am also not aware of any fast or quick dissolving lozenges.

90. While Dohil mentions dissolving "rapidly," a POSA would not interpret this to mean complete disintegration within 60 seconds, as required by the claims of the '828 patent. A POSA reading Dohil and understanding the mechanism of a lozenge (*see* EX1017, 181; EX2013, 413) would understand "rapidly" to refer to refer to the initial release of some drug, but complete dissolution occurs slowly over time. Put differently, a POSA would not interpret "dissolves rapidly" to mean the entire dosage form dissolves rapidly. The process of dissolving over a several minutes may provide closer to the 8-12mL volume of viscous liquid that Dohil teaches is required to coat the esophagus and treat EoE. A POSA would understand this because a lozenge – based on the art-recognized definition – continuously dissolves slowly over time, as described in Dr. Parr's own cited references. EX1017, 181; *see also* EX2013, 413; EX2014, 201; EX2016, 293 ("Lozenges and buccal tablets are intended to dissolve slowly in the mouth"); EX2017, 341. Indeed, Dr.

Parr also admits that a typical lozenge dissolves slowly. EX2011, 62:13-15.

91. In the same paragraph as the disclosure of a lozenge, Dohil also discloses that "[b]udesonide is provided in the form of a tablet, a capsule, or, for example a gel capsule, designed for slow release and delivery to the esophagus." EX1002, [0032]. Dohil does not define slow release. In fact, Dohil does not provide any timings for the dissolving or disintegrating of the lozenge or similar tablet in the mouth. A POSA would understand from this paragraph that Dohil discloses solid dosage forms that release the budesonide slowly in the mouth as a lozenge or slow release tablet.

92. Dr. Parr cites to the FDA Guidance, which provides a specific definition for ODTs. EX1051, ¶¶ 107-110 (citing EX1005, 2). Specifically, the FDA Guidance states that ODTs are defined as "[a] solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." EX1005, 2. The FDA Guidance goes on to state that ODTs disintegrate within "approximately 30 seconds or less, when based on the United States Pharmacopeia (USP) disintegration test method or alternative[.]" *Id*. Thus, based on the FDA Guidance, a POSA would simply understand that an ODT has a specific disintegration time. The FDA Guidance does not address any particular disease, such as EoE, any particular class of drugs, such as corticosteroids, or

distinguish topically acting drugs from systemically acting drugs in ODT formulations. A POSA would therefore understand the FDA Guidance to provide a general definition of ODTs.

93. Dr. Parr also cites to Grother as disclosing a solid orally disintegrating composition of budesonide. EX1051, ¶¶ 99-101 (citing EX1008). But this is not the focus of Grother and is only arrived at through hindsight. Grother is also not directed to any topically acting corticosteroids or treating any particular disease, let alone inflammation of the upper gastrointestinal tract. EX2011, 75:5-10, 79:1-10. Grother generally discloses a new fast dispersing tablet platform that is "essentially free or absolutely free of mammalian gelatin." EX1008, Abstract. Grother describes the issues with using gelatin in formulating fast dispersing dosage forms, such as increased processing times, increased costs, and lack of homogeneity. EX1008, 2-3. Grother describes its invention as eliminating gelatin from the formulations and using modified starches instead, listing the various advantages of modified starches, such as improved stability and strength of the dosage form, allowing the use of sweeteners to improve taste, and elimination of exposure to undesirable agents. EX1008, 3. Grother describes its invention as eliminating gelatin from the formulations and using modified starches instead, listing the various advantages of modified starches, such as improved stability and strength of the dosage form,

allowing the use of sweeteners to improve taste, and elimination of exposure to undesirable agents. EX1008, 3-6.

94. Grother is not directed to any particular drug, let alone topically acting corticosteroids. Six of the eight examples disclosed in Grother do not even include a drug. EX1008, 22-32. Examples 7 and 8 include three drugs, none of which are topical corticosteroids. EX1008, 29, 31. Grother also discloses that "[a]ny drug may be used as the active ingredient in the composition of the present invention." EX1008, 15:19-20. Grother then goes on to list hundreds of drugs in multiple drug classes across six pages. EX1008, 16-21.

95. Grother does not distinguish between topically acting and systemically acting drugs in the plethora of drugs it lists. EX2011, 78:4-18. While Grother discloses corticosteroids in its list of drugs, it does not distinguish them in any way or acknowledge which ones are largely topical or which ones have significant systemic activity. EX1008, 18:15-18; EX2011, 78:4-22. Indeed, fluticasone and budesonide are listed among systemically acting corticosteroids, including hydrocortisone, prednisone, prednisolone, methylprednisolone, dexamethasone and betamethasone, which are expressly excluded from the scope of the '828 claims. *Compare* EX1001, 3:19-36, *with* EX1008, 18:15-18. The other drugs and drug classes disclosed in Grother are also predominantly systemically active drugs. A

POSA would therefore understand Grother to disclose a general ODT platform technology, for which any drug may be used as an active, but does not particularly disclose ODTs containing topical corticosteroids for the treatment of EoE.

96. Dr. Parr also remarks that one of the advantages of ODTs is the ability of the active ingredient to be absorbed through the mucosa of the gastrointestinal tract, beginning in the mouth. EX1051, ¶¶ 59, 72. A POSA would therefore be motivated to select a systemically acting drug from Grother's list of drugs for this benefit rather than a topically acting corticosteroid. This is because topically acting corticosteroids, such as fluticasone and budesonide, provide therapeutic effects from topical contact, not absorption. On the other hand, systemically acting drugs must be absorbed.

97. Dr. Parr also cites to Singh and Cherukuri for disclosing solid orally disintegrating compositions containing budesonide. EX1051, ¶¶ 102-106 (citing EX1035, EX1036). Dr. Parr does not rely on either reference as a ground for obviousness. Further, neither Singh nor Cherukuri distinguish between topical or systemic drugs in their disclosures that list numerous classes and types of drugs. Nor does either reference address any necessary contact time to a targeted area for a topically acting corticosteroid in an ODT, or how to effectively treat EoE or inflammation of the upper gastrointestinal tract. Thus, a POSA would understand

Singh and Cherukuri to be directed towards general ODT platforms.

1. Dohil Does Not Render Obvious Claims 1-17 of the '828 Patent (Ground 1)

98. Dr. Parr asserts that Dohil in view of the knowledge of a POSA renders obvious claims 1-17 of the '828 patent. However, Dr. Parr relies on nothing but hindsight-driven analysis and conclusory opinions for support.

99. From the disclosure in Dohil and the "off-label" treatments addressed in the '828 patent, a POSA would understand that liquid and aerosolized formulations were known to deliver an effective amount of a corticosteroid to the upper gastrointestinal tract. EX1002, [0006], [0046]-[0070]; EX1001, 1:36-57. Further, from Dohil, a POSA would understand that 8-12mL of viscous liquid provides pan-esophageal coverage and increases the duration of contact of the topical corticosteroid with the inflamed esophagus to effectively treat EoE. EX1002, [0031], [0053], [0067]. These formulations are a logical starting point because the delivery mechanism ensures contact of topically active budesonide with the esophagus.

100. Thus, a POSA would start with Dohil's liquid. A POSA would have no motivation to fundamentally change Dohil's liquid composition and formulate budesonide as a solid composition. In fact, Dohil teaches that solid formulations will not be as effective as the 8-12mL viscous liquid. "[OVB] may have advantages

over other therapies in that…its volume (8-12 ml) provides pan-esophageal mucosal coverage[.]" EX1002, [0067]. Because Dohil refers to a "lozenge or other similar tablet" and then states that OVB is superior to other therapies, a POSA would understand Dohil as teaching that OVB is superior to a lozenge or similar tablet. EX1002, [0032], [0067].

101. Assuming a POSA would formulate budesonide as a solid composition, it would not be an ODT that disintegrates within 60 seconds as claimed in the '828 patent. Based on Dohil's teaching that a large volume of viscous liquid (8-12mL) is necessary for pan-esophageal coating and efficacy, a POSA would therefore be motivated to provide longer disintegration times to increase volume and coating of the esophagus, such as with Dohil's lozenge which would dissolve over several minutes. A lozenge (or similar tablet) that dissolves slowly, over several minutes, such as over 2-3 minutes, would produce 8-15mL saliva containing budesonide. EX2005, 303 (the rate of saliva "increases to about 4[.]0-5[.]0 ml / min during eating, chewing and other stimulating activities."). This is consistent with the art-recognized definition of a lozenge. EX2013, 413; EX2014, 201; EX2016, 293. ODTs that disintegrate within 60 seconds would not produce Dohil's 8-12mL and would therefore be counterintuitive. A POSA would have had no motivation to modify Dohil and formulate the claimed ODT.

(a) Dohil is Directed to Liquid Formulations and Does Not Teach or Suggest Orally Dispersing Tablets that Disintegrate within 60 Seconds

102. Dr. Parr opines that Dohil discloses an orally dispersing tablet comprising budesonide that disintegrates within 60 seconds. EX1051, ¶¶ 112-123, 161-168. Dr. Parr points to Dohil's disclosure of lozenges and similar tablets that "dissolve rapidly in the mouth or esophagus[.]" EX1051, ¶ 113 (citing EX1002, [0032]). Dr. Parr goes on to argue that "[a] person of ordinary skill in the art would have understood that it was desirable for the disintegration time of Dohil's rapidly dissolving lozenge or tablet to dissolve within, for example, several seconds to about a minute[,]" as taught in the prior art and based on the FDA Guidance. EX1051, ¶¶ 161-168. Thus, according to Dr. Parr, "[a] person of ordinary skill in the art seeking to formulate budesonide into an ODT 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." EX1051, ¶ 164. This argument, however, presumes that Dohil teaches a lozenge or similar tablet that disintegrates within 60 seconds, which it does not.

103. A POSA reading Dohil would understand that Dohil's invention is an 8-12mL viscous liquid budesonide formulation (referred to in Dohil as OVB) that provides pan-esophageal coverage and effectively treats EoE. Dohil states that it

solves problems with existing formulations by formulating budesonide as a viscous liquid. EX1002, [0008]-[0009] ("A "***liquid***, long-acting topical corticosteroid preparation is needed.") (emphasis added). A POSA would therefore understand that Dohil is directed to formulating a viscous oral liquid budesonide formulation and shows that these formulations are effective for treating EoE.

104. Dohil describes various viscosity-enhancing excipients throughout its disclosure. EX1002, [0013], [0030]-[0031], [0036]-[0070]. Dohil discloses three examples administering oral viscous budesonide (OVB) to patients. EX1002, [0046]-[0070]. In Examples 1 and 2, the patients are administered the viscous liquid formulation daily and both patients showed improvement of EoE symptoms and complete resolution or normal appearing esophagus after treatment. EX1002, [0046]-[0047]. In Example 3, patients were given the viscous liquid formulation and 90% of patients showed improvement after treatment. EX1002, [0048], [0053], [0060]. From these Examples, Dohil teaches that a large volume (8-12 mL) of the budesonide formulation is necessary to provide an effective amount to the esophagus. EX1002, [0031], [0053], [0067] ("[OVB] may have advantages over other therapies in that…its volume (8-12 ml) provides pan-esophageal mucosal coverage[.]"). Dohil does not disclose any examples including a solid dosage form. A POSA would thus understand that the viscous liquid formulation was successful

in treating EoE.

105. Dohil never mentions a solid dosage form that disintegrates within 60 seconds. Dohil discloses solid compositions in only two paragraphs, as a "dissolving tablet"/"dissolving wafer" and "lozenge or other similar tablet." EX1002, [0013], [0032]. A POSA reading Dohil would understand that the first disclosure of dissolving tablets or wafers could refer to solid forms that are dissolved in water before being swallowed and is not directed to tablets that disintegrate in the mouth or esophagus, as these were well known dosage forms at the time. *See* EX1017, 181.

106. Regarding the second disclosure of a lozenge or similar tablet, a POSA would understand this is not a disclosure of an orally dissolving composition that disintegrates in 60 seconds for several reasons. EX2013, 413. Dohil does not call its "lozenge or other similar tablet" an ODT, even though ODTs were known in the art, or explicitly state that the lozenge or other similar tablet dissolves within 60 seconds. EX1002, [0032]. While Dr. Parr cites several synonyms for ODTs, nowhere does Petitioner assert that lozenges are synonymous with ODTs. EX1051, ¶¶ 62-64. A POSA would also understand that Dohil does not act as its own lexicographer to change the definition of its lozenge to mean an ODT. Second, lozenges are known in the art to dissolve over several minutes, and therefore a "similar tablet" would also dissolve over several minutes. EX2013, 413; EX2014, 201; EX2016, 293

("Lozenges and buccal tablets are intended to dissolve slowly in the mouth, whereas, orally disintegrating tablets must disperse or dissolve in the mouth quickly, within seconds."). Dr. Parr himself also acknowledges that typical lozenges dissolve slowly. EX2011, 62:13-15. As Dr. Parr has admitted, "dissolve" refers to drug release. EX2018, 21:19-22. Thus, Dohil is merely describing the initial release of drug from the lozenge which may occur rapidly after oral administration, but lozenges – by definition – dissolve completely over several minutes. EX2013, 413; EX2014, 201; EX2016, 293; EX2017, 341. Third, "dissolv[ing] slowly" is necessary to achieve the 8-12mL volume of liquid that Dohil teaches provides pan-esophageal coverage and is necessary for effective treatment of EoE. A POSA would therefore understand that the disclosure of a lozenge and similar tablet cannot be a disclosure of an orally dissolving composition that disintegrates in 60 seconds as claimed.

107. Lastly, Dohil acknowledges that its lozenge is not easily swallowed, so it is not an ODT, which Dr. Parr acknowledges, are specifically designed for ***easy swallowing***. EX1051, ¶ 67. However, Dohil explains that "for children or other patients that may have difficulty with a dissolving lozenge, the lozenge may be ground or otherwise dissolved in a small volume of water or other pharmaceutically suitable liquid[.]" EX1002, [0032]. If, as Dr. Parr contends, a lozenge is an ODT,

then these same patients, for the same reasons, could not use an ODT formulation. A POSA would therefore understand the explanation in Dohil to indicate that the lozenge or similar tablet is not an orally disintegrating composition that disintegrates within 60 seconds as claimed, because if it were, the lozenge would not need to be "ground up" or dissolved in 8-12ml of a liquid which is then swallowed to treat EoE. EX1002, [0032], [0067].

108. Dr. Parr opines that a lozenge can be formulated with a disintegrating agent. EX1051, ¶ 170. A POSA would know that lozenges do not have disintegrating agents. In fact, Danckwerts, which Dr. Parr cites in the background, contradicts Dr. Parr's position. According to Danckwerts, lozenges or tablets are manufactured "***without disintegrants*** and are intended to be sucked by patients." EX1017, 181 (emphasis added); *see also* EX2013, 413 ("Disintegrants are not used in the formulation[.]"). Danckwerts states that lozenges are "popular drug delivery system[s] for treating local mouth diseases and sore throats" which a POSA would understand is because lozenges are sucked on and dissolve slowly. EX1017, 181. Dr. Parr also stated that the disintegrants listed in Dohil are used in conventional (non-orally disintegrating) tablets. EX2011, 64:25--65:11. Thus, a POSA would understand that the lozenge or similar tablet disclosed in Dohil would be manufactured without disintegrants and intended to disintegrate slowly and

continuously releases budesonide over time, allowing for continuous treatment as the drug is swallowed over time.

109. Therefore, it is my opinion that a POSA would not understand Dohil to teach or suggest a solid orally disintegrating pharmaceutical composition for at least the reasons stated above.

(b) A POSA Would Have No Motivation to Formulate an Orally Dispersing Tablet Based on Dohil in View of the Knowledge of a POSA

110. Dr. Parr opines that a "person of ordinary skill in the art would have understood that it was desirable for the disintegration time of Dohil's rapidly dissolving lozenge or tablet to dissolve within, for example, several seconds to about a minute." EX1051, ¶ 162. I disagree. As explained above, a POSA would have understood the lozenge disclosed in Dohil to dissolve or disintegrate slowly (after an initial rapid release of budesonide) to produce 8-12 mL of liquid that achieves pan-esophageal coating for the treatment of EoE.

111. Dr. Parr also opines that a "person of ordinary skill in the art would have been motivated to follow the FDA Guidance in formulating Dohil's rapidly dissolving lozenge or tablet containing budesonide." EX1051, ¶ 164. I disagree for the following reasons.

112. Dr. Parr does not explain why a person of ordinary skill in the art would

be motivated to formulate an orally disintegrating pharmaceutical composition that dissolves in 60 seconds or less based on the disclosure in Dohil. As discussed above, Dohil teaches that the viscous liquid formulations are efficacious and superior to other treatments. EX1002, [0067] ("It may have advantages over other therapies in that it is palatable, its volume (8-12 ml) provides pan-esophageal mucosal coverage and it requires only once daily administration."). Dr. Parr fails to identify any issue with Dohil's viscous liquid formulation that would motivate a POSA to fundamentally change dosage forms to an ODT. To the contrary, Dohil's viscous liquid has several benefits, namely palatability, the ability to provide pan-esophageal coverage, and efficacy. Specifically, Dohil does not disclose any issues with dosing, compliance or stability with its liquid formulation, and the data disclosed in Dohil shows that the liquid formulation is effective in treating EoE. *See* EX2011, 72:25-74:6. As Dr. Parr acknowledges, Dohil's liquid formulation is "simple." EX2011, 61:3-9, 66:17-20, 68:10-12, 68:22-24, 70:8-12. A POSA would also understand that liquid formulations are also convenient to administer. In my opinion, a POSA would have no motivation to modify a simple, easy to administer, and effective formulation that has no recognized problems. There would be no reason for a POSA to change Dohil's "simple" and effective liquid dosage form to a more complicated and expensive to manufacture orally disintegrating composition, especially when there

is no evidence in the prior art that an orally disintegrating composition had been used to topically deposit a topically active drug to the upper gastrointestinal tract.

113. Dr. Parr characterizes Dohil's examples as a "proof of concept study" or "pilot studies" and stated that Dohil was using a simple formulation to determine if budesonide worked for EoE. EX2011, 61:3-62:3. But this statement is illogical and inconsistent with the background literature Dr. Parr cites to show that budesonide was known to be effective in treating EoE. EX2011, 61:21-62:3. As explained in the '828 patent and Dohil, budesonide was already known to be effective in treating EoE. EX1001, 1:36-48, 3:33-36; EX1002, [0067]; *see also* EX1014 (showing budesonide has previously been used to treat EoE), EX1015 (same). Thus, Dohil already invented an improved formulation, an 8-12mL viscous solution, and showed that it was effective for EoE.

114. Further, there were many commercially acceptable liquid formulations on the market and a POSA would have been able to take Dohil's "proof of concept" formulation and make a commercially viable liquid formulation for Dohil's larger clinical study. I understand that this is in fact what happened. Dohil's "proof of concept" formulation was developed as "Eohilia," a liquid budesonide composition for treating EoE sold by Takeda Pharmaceuticals, Inc. Dohil was issued as U.S. Patent No. 8,324,192 (EX2021) which is listed in the Orange Book for Eohilia

(EX2022).

115. Further, Dr. Parr does not explain why a POSA would be motivated to modify a lozenge or similar tablet such that the lozenge or similar tablet dissolves in 60 seconds or 30 seconds using the USP <701> Disintegration Test as disclosed in the FDA Guidance. Instead of offering any explanation, Dr. Parr merely states in a conclusive manner that a "person of ordinary skill in the art seeking to formulate budesonide into an ODT 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." EX1051, ¶ 164. But this is pure hindsight. Dr. Parr offers no explanation for why a POSA would be motivated to formulate an orally disintegrating composition containing budesonide that disintegrates within 60 seconds in the first place. Dr. Parr admits that Dohil discloses a "simple" liquid formulation that is effective in treating EoE and does not indicate any issues with dosing, compliance, or stability. EX2011, 72:25-74:6, 61:3-9, 66:17-20, 68:10-12, 68:22-24, 70:8-12. In my opinion, a POSA would be motivated to formulate budesonide in a liquid formulation based on Dohil.

116. If a POSA did formulate budesonide in a solid dosage form based on Dohil, a POSA reading Dohil would understand that Dohil prepares a specific volume of liquid with a high viscosity to achieve a therapeutic effect. Based on

Dohil, a POSA would understand that Dohil specifies an amount of liquid, 8-12 mL, needed to provide pan esophageal coverage to effectively treat EoE as well as enhancing the viscosity of the liquid formulation. However, the claimed orally disintegrating composition disintegrates in 60 seconds, which Dr. Parr admits would only produce 1-2 mL liquid. EX2011, 50:17-24. I understand that Dr. Parr later asserted that a lozenge would generate 4-5mL per minute. EX2026 (*Dr. Falk Pharma GMBH v. Ellodi Pharms., L.P.*, IPR2024-01197, EX1093, ¶¶41-43 (P.T.A.B. July 10, 2024); EX2005, 303-304. This is not the 8-12mL volume that Dohil teaches is required for efficacy. EX1002, [0067]. Further, based on various factors impacting saliva production of the patient (age, time of day, hydration), a POSA would understand that the amount of liquid generated in the mouth following administration of an orally disintegrating composition is unpredictable and variable, and the resulting viscosity could not be controlled as it is in Dohil's liquid formulations, lozenge, or similar tablet. Dr. Parr completely fails to address this discrepancy.

117. Dr. Parr also opines that an advantage of solid orally disintegrating pharmaceutical compositions is that they are administered orally. EX1051, ¶¶ 71-73 (citing EX1017, 172, 174-178; EX1018, 466-467; EX1019, 311). The liquid suspension in Dohil is already administered orally and therefore this is not sufficient

motivation to modify Dohil's liquid formulation. Dr. Parr goes on to argue that solid orally disintegrating pharmaceutical compositions are preferred because they promote absorption of the active through the oral mucosa. EX1051, ¶¶ 72-73 (citing EX1019, 311; EX1017, 174-178; EX1018, 466-467). The '828 patent claims budesonide, which has "no significant systemic glucocorticoid or mineralocorticoid activity." EX1001, cl. 1, 3:19-36. As defined in the '828 patent, this means that there is no "generalized effect in the body through absorption" and the amount of corticosteroid used is "selected so as to maximize the therapeutic benefit from topical administration while minimizing systemic absorption." EX1001, 3:19-24, 7:34-37. As Dr Parr points out, budesonide was known to have little to no systemic activity. EX1051, ¶¶ 43-44. Therefore this argument is also irrelevant and a POSA would not be motivated to formulate Dohil's budesonide in an ODT to "promote absorption," because budesonide is not absorbed.

(c) A POSA Would Have No Reasonable Expectation of Success in Formulating an orally dispersing tablet that Topically Deposits Topical Corticosteroids on the Upper GI Tract to Treat Inflammation or EoE

118. A POSA would not have a reasonable expectation of success in "formulating budesonide into a rapidly disintegrating lozenge or tablet that dissolved within 60 seconds using the USP <701> Disintegration Test based on Dohil's

description[,]" and effectively treat inflammation of the upper GI tract as stated by Dr. Parr. EX1051, ¶ 165. As noted above, 8-12 mL of a viscous liquid is needed to provide pan-esophageal coating and effectively treat EoE. I would not expect to get the same viscosity, volume, or contact with an orally disintegrating tablet. This is because of the stark differences in the formulation that is administered. Unlike Dohil's liquid, which is swallowed as a bolus dose, after administering the orally disintegrating composition, some of the composition disintegrates and is swallowed initially, while some remains in the mouth. A POSA could not predict from Dohil whether the resulting volume or viscosity of the dissolved tablet would topically deposit the corticosteroid in a sufficient amount to treat EoE. EX1002, [0011], [0013], [0021] ("It has been found that by administering Budesonide in oral form, in a formulation with increased fluid viscosity, that the corticosteroid was delivered to the esophagus in an effective dose to reduce the inflammation of the esophagus."). Nothing in Dohil suggests disintegration within 60 seconds would topically administer the corticosteroid to the upper gastrointestinal tract and be effective in treating EoE. Based on the disclosure in Dohil, a POSA would understand that 8-12mL of a liquid suspension of budesonide is an effective treatment for EoE with no issues of patient compliance, stability, or dosage. Dohil's lozenge or similar tablet – which as explained above, a POSA would know is sucked on by patients and

dissolves slowly over time – would produce Dohil's efficacious 8-12mL liquid. A POSA would not, however, expect an orally disintegrating composition containing a topical corticosteroid to be effective based on the disclosure in Dohil.

(d) Dohil Does Not Disclose the Claimed Doses in the Context of a Solid Composition (Claims 1[i], 15-16)

119. For the reasons discussed above, Dohil does not specifically disclose an orally disintegrating pharmaceutical composition or tablet as claimed by the '828 patent. In my opinion, Dohil also does not disclose the specific dose ranges required by claims 1 and 15-16. A POSA would understand that liquid compositions and solid compositions differ in composition and delivery mechanism (Dohil's 8-12mL that provides pan-esophageal coating vs. the claimed ODT that disintegrates in a much smaller volume of saliva) and therefore require different considerations when determining the proper dose of an active drug. Dr. Parr cites to Dohil's disclosure of the doses administered to patients in Examples 1-3. EX1051, ¶ 125. As discussed above, the patients in Examples 1-3 were given the viscous liquid formulation and a POSA would understand that doses for liquid formulations are not necessarily the same as a solid formulation. In my opinion, a POSA would not understand Dohil to disclose any dose for an ODT based on its liquid formulations.

120. As discussed above, a POSA would not have any motivation to

formulate an orally dispersing tablet based on Dohil at all, let alone with the claimed dose range. Dr. Parr fails to address reasonable expectation of success of formulating an orally dispersing tablet with the claimed doses.

(e) Dohil Does Not Teach or Suggest the Claimed Methods for Treatment (Claim 14)

121. In my opinion, Dohil does not teach or suggest the method recited in claim 14 of the '828 patent. As discussed above, Dohil does not disclose an orally dispersing tablet that disintegrates within 60 seconds. Thus, in my opinion, a POSA would understand that Dohil does not disclose the methods of treating inflammation of the upper gastrointestinal tract recited in claim 14.

122. A POSA also would not have a reasonable expectation of success in treating the treating inflammation of the upper gastrointestinal tract recited in claim 14 by administering an orally dispersing tablet that disintegrates within 60 seconds as claimed. As discussed above, Dohil teaches a liquid formulation to have a specific volume (8-12mL) of a viscous liquid formulation to achieve pan-esophageal coverage and treat EoE. EX1002, [0067] ("It may have advantages over other therapies in that it is palatable, its volume (8-12 ml) provides pan-esophageal mucosal coverage and it requires only once daily administration."). An orally disintegrating composition that disintegrates within 60 seconds or 30 seconds would not achieve the volume or viscosity that Dohil teaches provides pan-esophageal

coverage and is efficacious. It would only produce 1-4 mL saliva, which would not achieve pan-esophageal coating and would not reasonably be expected to be efficacious based on Dohil. EX2005, 303 (the rate of saliva "increases to about 4[.]0-5[.]0 ml / min during eating, chewing and other stimulating activities."). Therefore, a POSA would not reasonably expect the formulation of an orally disintegrating pharmaceutical composition based on Dohil to be effective.

2. Grother in view of the FDA Guidance Does Not Render Obvious Claims 1-17 of the '828 Patent (Ground 2)

123. Dr. Parr asserts that Grother in view of the FDA Guidance renders obvious claims 1-17 of the '828 Patent. Dr. Parr does not explain why a POSA would be motivated to arrive at the claimed invention based on the disclosures in Grother in view of the FDA Guidance. Dr. Parr's suggested motivations are conclusory and neither Grother nor the FDA Guidance provides a POSA with a reason to formulate an ODT with budesonide, because neither Grother nor the FDA Guidance suggest that an ODT can be used to topically administer budesonide to the upper GI tract (e.g., esophagus).

124. Dr. Parr never explains why a POSA would be motivated to formulate an ODT containing a topical corticosteroid for the treatment of EoE based on the disclosure in Grother. Accordingly, Dr. Parr's opinion is flawed.

(a) Grother is Directed to General ODT Formulations

125. As outlined above in Section VI.B, Grother is focused on eliminating mammalian gelatin from its disclosed "fast dispersing solid dosage forms[.]" EX1008, Abstract, 1:11-12. Grother lays out the issues with using gelatin in ODTs, and then describes its invention of eliminating gelatin from ODTs and using modified starches instead, highlighting various advantages such as improved stability and strength of the dosage form, allowing the use of sweeteners to improve taste, and elimination of exposure to undesirable agents. EX1008, 2-6. Grother's examples also disclose the success of using modified starches compared to gelatin. EX1008, 22-32. Grother is not directed towards any disease at all and discloses that "[a]ny drug may be used as the active ingredient in the composition of the present invention." EX1008, 15:19-20. A POSA would therefore understand Grother to disclose a general ODT platform, for which any drug may be used as an active. A POSA would also understand that Grother did not recognize that an ODT could be used to topically administer a corticosteroid to the upper gastrointestinal tract. Thus, a POSA would not understand the disclosure in Grother to suggest an ODT containing budesonide to topically administer the corticosteroid to the upper GI tract for the treatment of EoE.

126. Accordingly, it is my opinion that one of ordinary skill in the art would

understand that Grother in view of the FDA Guidance does not render obvious claims 1-17.

(b) A POSA Would Not Have Been Motivated to Formulate an Orally Disintegrating Solid Pharmaceutical Composition / Tablet Containing a Topical Corticosteroid for the Treatment of Inflammation of the Upper Gastrointestinal Tract Based on Grother in View of the FDA Guidance

127. Dr. Parr opines that a "person of ordinary skill in the art 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." EX1051, ¶ 248. I disagree for the following reasons.

128. As discussed above, a POSA would understand that Grother is concerned with creating an ODT formulation that eliminates mammalian gelatin from ODT formulations and works with any class of drugs. Grother does not highlight or point out any particular class of drugs for its ODT formulation. Grother list hundreds of drugs in multiple drug classes across 6 pages. EX1008, 16-21. In fact, Grother states that any drug may be used and "suitable drugs include but are not limited to those listed[.]" EX1008, 15:19-21. Although corticosteroids are listed among the hundreds of other drugs, Grother does not particularly highlight them in any way. EX1008, 18:15-18. Grother also does not distinguish between systemic

and topical drugs or acknowledge any difference between systemic and topical corticosteroids (systemic and topical corticosteroids are contained in the same list, with no distinction). As mentioned above, Grother includes topical corticosteroids among systemic corticosteroids, buried within a long list of drugs. A POSA reading Grother would have no motivation to select budesonide or fluticasone from the long list of drugs. This is particularly true where budesonide and fluticasone act topically, whereas nearly all other drugs are systemically active and must be adsorbed in the blood stream in order to provide a therapeutic effect.

129. Dr. Parr does not explain why a POSA would arbitrarily select budesonide from the hundreds of disclosed drugs based on the disclosure in Grother. Nothing in Grother or Dr. Parr's declaration identifies anything in Grother that would motivate a POSA to pick out budesonide from the hundreds of drugs listed in Grother. Dr. Parr's conclusory statement that a POSA would have been motivated to select budesonide based on Grother's disclosure is pure hindsight.

130. Dr. Parr also does not explain why a POSA would be motivated to formulate a fast dispersing dosage form containing budesonide for topical deposition on the upper gastrointestinal tract based on Grother according to the FDA Guidance. Instead of offering any explanation, Dr. Parr merely states in a conclusive manner that a "person of ordinary skill in the art seeking to formulate budesonide into an

ODT 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." EX1051, ¶ 290. But Dr. Parr offers no explanation for why a POSA would be motivated to formulate Grother's fast dispersing tablet with budesonide in the first place.

(c) A POSA Had No Reasonable Expectation of Success in Formulating an ODT Containing Budesonide or Fluticasone to Topically Deposit the Corticosteroid on the Upper Gastrointestinal Tract for the Treatment of Inflammation of the Upper Gastrointestinal Tract Based on Grother in View of the FDA Guidance

131. A POSA would also not have a reasonable expectation of success in formulating an orally disintegrating pharmaceutical composition containing budesonide or fluticasone that would topically deposit budesonide or fluticasone on the upper gastrointestinal tract based on Grother's disclosure and the FDA Guidance. Grother does not distinguish between systemic and topical drugs. A POSA would understand that formulations for administering systemic drugs, which are absorbed by the lower gastrointestinal tract, differ from formulations that topically administer the drug to a localized area to the upper gastrointestinal tract. Grother does not even recognize that a fast dispersing solid dosage form can be used for topical delivery of a drug to the upper gastrointestinal tract. As Dr. Parr acknowledges, the FDA

Guidance only provides a definition for ODTs, and thus does not remedy the deficiencies in Grother. EX2011, 56:15-21. A POSA would therefore not expect to formulate an orally disintegrating pharmaceutical composition containing a corticosteroid to topically deposit the corticosteroid on the upper gastrointestinal tract for treating inflammation of the upper gastrointestinal tract from Grother's disclosure and the FDA Guidance.

(d) Grother and the FDA Guidance Do Not Render Obvious the Claimed Doses (Claims 1[i], 15-16)

132. For the reasons discussed above, Grother and the FDA Guidance do not disclose an orally dispersing tablet containing a topical corticosteroid as claimed by the '828 patent. In my opinion, Grother also does not disclose the specific dose ranges required by claims 1 and 15-16. Dr. Parr cites to Grother's disclosure of general dosing, and that the "upper value" is generally 60 mg. EX1051, ¶ 356 (citing EX1008, 26:22-27:1). A POSA would understand that because Grother is directed to a general fast dispersing solid dosage form, the dosages disclosed in Grother relate to dosing generally, not topically active corticosteroids specifically, or topical corticosteroids that are deposited topically on the upper gastrointestinal tract. Dr. Parr also cites to various unasserted references disclosing doses for budesonide. EX1051, ¶¶ 248-249 (citing EX1014 and EX1015). None of the unasserted

references Dr. Parr cites to disclose an ODT containing budesonide, and nearly all references involve enterically coated compositions that are designed to prevent budesonide release until the drug reaches the lower gastrointestinal tract or liquid formulations. EX1051, ¶¶ 43-58. A POSA would understand that formulating an ODT to topically deposit a corticosteroid in the upper gastrointestinal tract would involve different considerations and likely different doses than enterically coated tablets and rectal foam dosage forms used for different conditions. In my opinion, a POSA would not understand Grother to disclose any dose for an ODT containing a topical corticosteroid based on its general disclosures for formulating fast dispersing solid dosage forms.

133. As discussed above, a POSA would not have any motivation to formulate an ODT containing budesonide based on Grother. Dr. Parr conclusively states that a POSA would have a reasonable expectation of success, but does not explain why or how. EX1051, ¶ 251. As discussed above, a POSA would not have had a reasonable expectation of success in formulating an ODT containing a topical corticosteroid at the claimed dose range to topically deposit the corticosteroid on the upper gastrointestinal tract based on Grother and the FDA Guidance.

(e) Grother Does Not Disclose the Claimed Methods for Treatment (Claim 14)

134. As discussed above, a POSA would not understand Grother to disclose

any disease or treatment for any disease, let alone EoE. Thus, a POSA would understand that Grother cannot disclose methods of treating EoE recited in claim 14 by administering an orally dispersing tablet.

135. There would be no reasonable expectation of success in treating the inflammation of the upper gastrointestinal tract recited in claim 14 by administering an orally dispersing tablet using the ODT platform disclosed in Grother. As discussed above, and illustrated by Dr. Parr, previous solid formulations of budesonide involved enterically coated tablets for treating inflammation of the lower gastrointestinal tract. EX1025; EX1009; EX1010; EX1011; EX1012; EX1013; EX1026; EX1027; EX1028. Dr. Parr does not cite to any evidence in Grother or the background art to show that an ODT would or could deposit a therapeutically effective amount of budesonide on the upper gastrointestinal tract to treat inflammation as required by the claims. Therefore, a POSA would not reasonably expect the formulation of an orally dispersing tablet based on Grother to be effective.

VII. OBJECTIVE INDICIA OF NONOBVIOUSNESS

136. I understand that post-filing data can used as evidence of unexpected results and efficacy for non-obviousness.

137. I understand that Petitioner, Dr. Falk, funded a study evaluating an ODT for efficacy in treating EoE. EX2006. The study indicates the ODT containing

1 mg of budesonide is therapeutically effective and well-tolerated, further supporting the non-obviousness of the claimed invention. EX2006, 8. As discussed above, and explained in the '828 patent, liquid formulations of budesonide were known to be efficacious in treating EoE and candidiasis was a known side effect. EX1002; EX1014; EX1015; EX1001, 1:41-45. A POSA would understand that Dohil teaches that 8-12 mL of a viscous liquid formulation provides pan-esophageal coating that topically delivers an effective dose of budesonide to the esophagus to treat EoE. EX1002, [0067]. As a result, a POSA would not have expected an orally dispersing tablet that dispersed in the mouth within 60 seconds to be efficacious because it would not produce 8-12 mL (as discussed above in Section VI.C.1.c). Further, a POSA would have known that oral budesonide administration causes candidiasis, and the longer budesonide was held in the mouth, the greater the chance of candidiasis developing. A POSA would have thus been further deterred from developing any dosage form that would be held in the mouth and increased the time budesonide resided in the mouth for the risk of increased prevalence on candidiasis.

138. Petitioner's study compared the claimed orally dispersing tablet to a 5 ml viscous solution containing budesonide (dosed twice a day, for a total of 10 ml viscous solution), such as the one disclosed in Dohil. EX2006, 2. The study found that "interestingly," patients who received the tablet of 1 mg of budesonide twice

daily achieved remission, similar to patients who received the viscous solution of 2 mg of budesonide twice daily. EX2006, 8. The study concluded that "no additional benefit could be shown for the higher dose of[budesonide tablet] 2 mg twice daily used in our study compared with previous studies examining viscous suspensions." *Id*. Based on the known efficacy of the viscous liquid formulations of budesonide, administered twice a day at a volume of 5 ml, for a total of 10 ml, or 8-12 ml as disclosed in Dohil, a POSA would not have expected an ODT that produces only 1-2 ml of solution and uses half the budesonide dose to be efficacious in providing the necessary pan-esophageal coverage in order to effectively treat EoE.

139. Further, the incidence of candidiasis remained the same across all study groups. EX2006, 7. The study noted that this was similar to previous studies on topical corticosteroids for EoE. EX2006, 8. A POSA would have found this unexpected, as the orally dispersing tablet would have been held in the mouth for longer than the liquid formulation and increased budesonide contact in the mouth, resulting in more fungal infections. A POSA would therefore not have thought an orally dispersing tablet containing budesonide would have been efficacious or well tolerated for the treatment of EoE.

VIII. RESERVATION OF RIGHTS

140. The opinions and analyses in this report are based on currently available

documents and information. Accordingly, I reserve my right to supplement and amend my opinions if additional information becomes available. Similarly, this report may be supplemented by testimony.

141. I also reserve the right to adjust or supplement my analyses in light of any rebuttal or alternative opinion advanced by the Petitioner.

IX. CONCLUSION

142. In my opinion, claims 1-16 of the '828 patent are not invalid in light of the prior art grounds asserted by Dr. Parr.

143. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001.

Dated: September 9, 2025

Respectfully submitted,

Martyn Christopher Davies