

**UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE PATENT TRIAL AND APPEAL BOARD**

Anagen LLC, Petitioner

v.

Veradermics, Incorporated, Patent Owner

Case No. To Be Assigned; U.S. Patent No. 12,491,184

DECLARATION OF HOSSEIN OMIDIAN, PH.D. (EXHIBIT 1015)

I. INTRODUCTION

1. My name is Hossein Omidian; I also publish and am professionally known as Hamid Omidian. I have been retained by Fairchild Law LLC, counsel for Petitioner Anagen LLC, to provide my independent technical opinions concerning U.S. Patent No. 12,491,184 ("the '184 patent"), which names Reid Waldman as inventor and is assigned to Veradermics, Incorporated.

2. I have been asked to consider (a) the level and knowledge of a person of ordinary skill in the art ("POSITA") as of October 25, 2022, the earliest claimed priority date of the '184 patent; (b) whether the '184 specification demonstrates possession of, and enables, the subject matter claimed; and (c) whether the claimed subject matter would have been obvious to a POSITA in view of the prior art. The opinions in this declaration are my own.

3. I am being compensated at a rate of \$550 per hour for professional services, with a flat rate of \$4,000 per day for days on which I am required to be away from my office for travel, deposition, or testimony, under an engagement agreement with Petitioner and its counsel. My compensation does not depend on the outcome of this proceeding or on the content of my opinions.

4. In forming my opinions I considered the materials listed in Appendix A, my education, and my professional working experience of more than 35 years in pharmaceutical sciences, drug delivery, polymer science and technology, and formulation development.

II. QUALIFICATIONS

5. I am a Professor of Pharmaceutical Sciences at the College of Pharmacy, Nova Southeastern University, where I have served on the faculty since 2007 (Professor since 2015). I hold a Ph.D. in Polymer Engineering from Brunel University (London), and M.Sc. and B.Sc. degrees in polymer and chemical engineering from Tehran Polytechnic University. My research and teaching for more than two decades have centered on drug delivery systems (including oral, buccal, sublingual, gastro-retentive, and polymeric platforms) and on the design of hydrogels and polymeric systems for controlled and sustained drug release. I have taught graduate and professional courses in Pharmaceutics, Physical Pharmacy, Drug Delivery Technologies, Pharmaceutical Polymers, and Excipients for more than 15 years.

My previous industry work included developing oral targeted controlled-release platforms from bench to clinical trials, and I have helped with developing protocols for in-vitro, pre-clinical, and in-vivo human studies of the selected platforms. I have authored more than 450 scholarly contributions, including peer-reviewed publications, patents, books, book chapters, and conference presentations; I have served on the editorial boards of professional and scientific journals and as a delegate to the United States Pharmacopeia; and I have previously served as an expert witness in patent litigation.

6. Before joining Nova Southeastern University, I held industry positions including Principal Scientist at Abbott Laboratories and Principal Scientist, Research Manager, and Senior Scientist at Kos Pharmaceuticals, Inc., where my work included polymer synthesis, dosage-form composition, formulation analysis, and developing novel oral controlled-release platforms for trial in humans. I have also consulted on pharmaceutical technologies and formulations in patent-infringement and other intellectual-property matters.

7. A copy of my January 2026 curriculum vitae is submitted separately as Exhibit 1049.

8. Unless otherwise indicated, statements concerning my education, experience, and work are based on personal knowledge. My technical opinions are based on

the materials listed in Appendix A together with my education and professional experience. If called to testify, I could and would testify competently to those matters and opinions.

III. MATERIALS CONSIDERED

9. The materials I considered are listed in Appendix A. They include the '184 patent (Ex. 1001), its prosecution record as provided to me, the '184's two priority provisional applications (Exs. 1010, 1011), and the prior-art references identified in this declaration, including Sinclair/Samson US 2019/0269684 (Ex. 1003), Reynolds 2002 (Ex. 1004), Vañó-Galván 2021 (Ex. 1005), Fleishaker 1989 (Ex. 1006), the Loniten® label (Ex. 1007), Williams US 2010/0104639 (Ex. 1008), Biovail WO 2004/058229 (Ex. 1009), Cardinal US 2010/0159001 (Ex. 1012), Panchaprateep 2020 (Ex. 1014), Gottlieb 1972 (Ex. 1017), Lowenthal & Affrime 1980 (Ex. 1018), Beach 2021 (Ex. 1019), Sinha US 2024/0374594 (Ex. 1034) and its certified priority provisional (Ex. 1043), Follica/Barman (Ex. 1039), Bazzano WO 83/02558 (Ex. 1040), and Samson WO 2016/065426 (Ex. 1041), together with the additional references identified in Appendix A. I also reviewed Patent Owner's public February 2026 prospectus (Ex. 1048), but I do not rely on it for any opinion in this declaration.

IV. LEGAL STANDARDS PROVIDED BY COUNSEL

10. I am not an attorney. Counsel has explained the following legal frameworks, which I have applied from a technical perspective.

11. **Written description (35 U.S.C. § 112(a)).** The specification must reasonably convey to a POSITA that the inventors were in possession of the claimed invention as of the filing date. A statement of a desired result, a prediction, or a plan for future work does not by itself demonstrate possession.

12. **Enablement (35 U.S.C. § 112(a)).** The specification must teach a POSITA how to make and use the full scope of the claimed invention without undue experimentation, considering factors including the amount of direction provided, the presence of working examples, the predictability of the art, the breadth of the claims, and the quantity of experimentation required.

13. **Indefiniteness (35 U.S.C. § 112(b)).** Claims must inform a POSITA of the scope of the invention with reasonable certainty.

14. **Obviousness (35 U.S.C. § 103).** A claim is unpatentable if the differences between the claim and the prior art are such that the claimed subject matter as a whole would have been obvious to a POSITA at the relevant date, considering the scope and content of the prior art, the differences, the level of skill, motivation to combine, and whether the POSITA would have had a reasonable expectation of success, which does not require certainty. I understand that where a claimed range

overlaps ranges or values in the prior art, and where a variable is recognized as result-effective, routine optimization within known ranges is ordinarily not inventive.

V. PERSON OF ORDINARY SKILL IN THE ART

15. In my opinion, the POSITA for the '184 patent as of October 25, 2022 is a pharmaceutical scientist with an advanced degree, including a Ph.D. in pharmaceutics, polymer science, or chemical engineering, with two to three years of working experience with oral modified-release dosage forms, including hydrophilic matrices such as HPMC, lipid and hydrophobic matrices, reservoir systems, osmotic systems, and multiparticulate systems, and familiarity with pharmacokinetic principles used in formulation development, including C_{max}, T_{max}, and AUC. In the absence of an advanced degree, a POSITA can be a pharmaceutical scientist with a bachelor's or master's degree having at least five years of experience in developing oral modified-release platforms.

16. My opinions concern oral modified-release formulation science and the biopharmaceutic principles by which release from a dosage form affects systemic drug input. I do not offer opinions on therapeutic dose selection, patient management, clinical interpretation, or independently modeled clinical pharmacokinetic endpoints. Where the pharmacokinetic behavior of immediate-

release oral minoxidil bears on my analysis, I rely on values reported in the prior-art literature (¶¶ 45–46).

VI. THE '184 PATENT

17. The '184 patent claims a method of treating hair loss by orally administering a modified-release formulation of "about 4.5 mg" minoxidil that "provides" a C_{max} of about 0.25–20 ng/mL and a T_{max} of about 30–360 minutes (Claim 1, from which all 19 other claims depend). Dependent claims add, among other things, a maintained blood level of about 1–20 ng/mL for at least about 8 hours (Claim 2), five alternative release-kinetic orders (Claims 12–16), and "no cardiac effects" (Claim 19).

18. The specification's formulation work includes HPMC K4M / HPMC K200M matrix tablet prototypes at 2 mg and 10 mg (Table 8), single-stage in-vitro dissolution for those prototypes (FIGS. 2–5), and additional in-vitro dissolution data for the 030448-xxx batch series at 2.5 mg and 10 mg (Tables 9–10; FIGS. 6–7). The specification reports no measured human pharmacokinetic data from any modified-release prototype; the only human PK data reproduced is immediate-release literature data (Table 3), and certain in-vitro release curves in FIGS. 6–7 are labeled "Estimated from PBPK Slides." The specification states that "no non-clinical or clinical studies in humans have been conducted with MR oral formulations of minoxidil ... to date" (col. 65, Section 5.3) and that "No PK studies

in humans have been previously conducted with MR oral formulations of minoxidil" (col. 66, Section 5.3.2).

VII. STATE OF THE ART AS OF OCTOBER 25, 2022

19. Oral minoxidil for hair loss was old and well documented. Oral minoxidil preparations for treating alopecias, including tablets, liquids, and capsules, were disclosed as early as 1983 (Ex. 1040, Bazzano WO 83/02558, which describes weight-based dosing). By the 2010s–2020s, low-dose oral minoxidil ("LDOM") was in widespread clinical use for hair loss (Ex. 1005, Vañó-Galván 2021, involving 1,404 patients, 10 centers, and doses of 0.03–15 mg), and patent filings disclosed oral minoxidil for hair loss across fixed-dose ranges spanning the claimed "about 4.5 mg" (Ex. 1041, Samson WO 2016/065426, 0.1–20 mg for telogen effluvium, ¶ [0029]; Ex. 1034, Sinha, about 0.625 mg to about 10 mg, with sustained-, delayed-, and enteric-release oral dosage forms; see also Ex. 1003, Sinclair ¶¶ [0146], [0150], reporting conventional oral 2.5 mg and 5 mg dosing and swallowed-oral use for androgenetic alopecia). I understand from counsel that Sinha is asserted as prior art based on its certified priority provisional, Ex. 1043. I express no opinion on that legal question and address only what Exs. 1034 and 1043 disclose.

20. The pharmacokinetics of immediate-release oral minoxidil were well characterized at the doses relevant here (2.5–10 mg). Fleishaker 1989 (Ex.

1006) reported the PK of 2.5–10 mg oral doses, which the authors described as generally supporting dose-independent pharmacokinetics over the studied range, and a C_{max} of 16.8 ng/mL at 2.5 mg. Sinclair (Ex. 1003 ¶ [0146]) reported peak serum concentrations of 18.5 ng/mL (2.5 mg) and 41 ng/mL (5 mg) at approximately one hour. The Loniten® label (Ex. 1007) states plasma levels reach maximum "within the first hour," and reports an average plasma half-life of approximately 4.2 hours.

21. Modified-release technology was an established, conventional toolkit.

Modified-release dosage forms, including matrix systems, reservoir systems, osmotic systems, ion-exchange systems, swellable systems, and coated multiparticulates, had been established in pharmaceutical development and commercial practice for many years. Their conventional formulation objectives include prolonging release, reducing peak-to-trough fluctuation, lowering peak concentration, and reducing dosing frequency. Reynolds 2002 (Ex. 1004) describes routine control of release from HPMC matrix tablets. Cardinal (Ex. 1012) describes generic sustained-release oral matrix formulations. It separately identifies minoxidil in a broad list of suitable drug substances (¶ [0064]) and HPMC grades including K4M and K200M in a general polymer list (¶ [0115]); it does not disclose a minoxidil working example or a minoxidil-specific matrix using those grades. Cardinal's background also describes the general controlled-release

objectives of maintaining desired blood levels and reducing fluctuation (§ [0002]). Sinclair § [0017] lists a "lipid matrix tablet" among dosage forms for the minoxidil dose. In Sinclair's context, that listing appears among dosage forms intended for oral-mucosal delivery. I do not rely on the bare listing as teaching a swallowed, matrix-controlled modified-release architecture.

22. Developing a modified-release version of a known immediate-release drug was routine lifecycle management. When a drug is already available in immediate-release form, developing a modified-release version using established technologies of the kind at issue here (hydrophilic HPMC matrices) is a common product-development strategy for extending or improving a product portfolio. A formulation scientist would ordinarily consider known modified-release technologies to alter the input rate, extend release, reduce peak-to-trough fluctuation, or reduce dosing frequency.

VIII. OPINION 1: THE SPECIFICATION DOES NOT DEMONSTRATE POSSESSION OF THE CLAIMED FORMULATION DEFINED BY ITS IN-VIVO PK RESULT (§ 112(a) WRITTEN DESCRIPTION)

23. Claim 1 defines the invention by an in-vivo performance result: a modified-release formulation that "provides" a specified C_{max} and T_{max} at about 4.5 mg. C_{max}, T_{max}, AUC, and duration of exposure describe systemic exposure after administration; they do not identify the formulation that will produce that exposure. The same C_{max}/T_{max} may be produced by substantially different input

profiles, including continuous release, lag-then-release (delayed release), an immediate-release fraction plus sustained release, or multiphasic release. Starting from target PK values alone, a formulation scientist cannot identify a single correct formulation, or even a single correct release curve, without further information.

24. The '184 specification does not identify any formulation, at 4.5 mg or any other dose, measured to produce the claimed in-vivo envelope. Table 8 discloses compositions at 2 mg and 10 mg, and the specification reports single-stage dissolution for those prototypes in FIGS. 2–5. Tables 9–10 and FIGS. 6–7 concern a different batch series, 030448-xxx, at 10 mg and 2.5 mg; the specification does not identify which, if any, Table 8 composition corresponds to those batches. No disclosed formulation or batch is reported with any measured plasma concentration. FIGS. 6–7 show in-vitro percentage release over time, not plasma concentration, C_{max}, or T_{max}. Certain curves in those figures are labeled "Estimated from PBPK Slides," but the specification does not identify those slides or disclose the model, inputs, assumptions, or validation underlying those estimates. In-vitro dissolution is not the claimed in-vivo result, and the specification discloses no relationship, whether measured or modeled from measured inputs, connecting any disclosed composition or its in-vitro release to the claimed human exposure values. I do not suggest that a formally validated regulatory IVIVC was required.

25. In my opinion, even crediting the PBPK estimates identified only in the figure legends, the other-dose dissolution data, and the known pharmacokinetics of immediate-release minoxidil, the specification does not identify a 4.5 mg formulation, or a disclosed technical relationship, from which a POSITA would recognize that the inventors possessed a formulation producing the claimed C_{max}/T_{max} combination. My opinion is not based merely on the absence of human testing or actual reduction to practice; it is based on the absence of a disclosed structure-to-performance correlation supporting the claimed result. The disclosure identifies the intended destination; it does not demonstrate possession of a formulation that reaches it. The claimed envelope's own floor confirms the point: the specification describes no formulation, at about 4.5 mg or any dose, that it reports as producing a peak concentration at or near the recited 0.25 ng/mL floor, and it discloses no relationship between formulation variables and that value. A specification does not demonstrate possession of a claimed range when its own disclosure does not explain how the skilled artisan would reach the range's floor.

26. I have reviewed the two Veradermics provisional applications (Exs. 1010, 1011). The entire Summary of the October 25, 2022 provisional (Ex. 1010 ¶¶ [0001]–[0009]) consists of nine "In some aspects" statements without a numerical dose: ¶ [0001] recites "a daily dose of minoxidil," with no number, and ¶ [0005] likewise recites a daily dose without any number; ¶¶ [0003] and [0007] recite the

Tmax range alone; ¶¶ [0004] and [0008] recite the Cmax range alone; and no Summary aspect combines a dose with both PK windows. Ex. 1010 includes "about 4.5 mg" within undifferentiated multi-value dose lists at ¶¶ [0051], [0097], and [00131], embodiment AW at ¶ [00203], and claim 49. The December 2022 provisional (Ex. 1011 ¶¶ [0001]–[0009]) repeats the same Summary structure. From a formulation scientist's perspective, these cited disclosures do not identify the specific dose-plus-Cmax-plus-Tmax combination Claim 1 recites.

IX. OPINION 2: A TARGET PK PROFILE DOES NOT IDENTIFY A FORMULATION; REPRODUCING THE CLAIMED RESULT FROM THIS DISCLOSURE WOULD REQUIRE AN OPEN-ENDED DEVELOPMENT PROGRAM (SUPPORTING OPINIONS 1 AND 3)

27. A technical description is inadequate from a formulation perspective when it provides only a desired result, without a working formulation whose measured performance anchors it, and leaves the scientist to determine, by trial and error, which compositions and processes will achieve it. For a broad modified-release product defined by target PK values, the scientist must first choose among fundamentally different delivery platforms (hydrophilic matrices, lipid matrices, membrane reservoirs, coated multiparticulates, osmotic, ion-exchange, swellable/erodible, gastroretentive, and hybrid systems), which operate by completely different mechanisms based on different materials, different assembly, and different processing techniques.

28. Even after selecting a platform, the formulation must be determined experimentally. For an HPMC matrix alone, the relevant interacting variables include polymer substitution type and content, molecular weight and distribution, viscosity grade, concentration, particle size; drug loading and particle size; filler selection and levels; tablet diameter, thickness, shape, surface-area-to-volume ratio, porosity and solid fraction; compression conditions; granulation method and moisture; and storage history. The direction and magnitude of any one variable's effect cannot always be predicted independently of the others, and naming a commercial HPMC grade does not by itself teach which material and structure will produce a required C_{max}, T_{max}, and duration.

29. The required in-vitro dissolution behavior cannot be inferred uniquely from the target human PK result. A discriminating dissolution method must itself be selected, and testing across fast, intermediate, and slow prototypes may be needed to identify how formulation changes affect systemic exposure. The technical difficulty addressed by the '184 claims is not the general direction of change. Slower input ordinarily lowers and delays a peak. The limitations must be evaluated separately by claim. Claim 1 requires the approximately 4.5 mg dose together with its C_{max} and T_{max} ranges. Claim 2 separately adds the eight-hour blood-level limitation. Each of Claims 12 through 16 separately adds one alternative kinetic-order limitation; those alternatives are not cumulative. The

specification discloses no quantitative formulation-to-exposure relationship or controlling release-assessment method for the particular limitation added by each claim.

30. The individual techniques involved are known, and a directional screen of relatively fast, intermediate, and slow formulations followed by adjustment of standard formulation variables is routine development practice. The different question here is whether the specification provides enough guidance to satisfy the particular bounded limitation of each claim without discovering the operative formulation relationships through extensive trial and error. In my opinion, the '184 specification, which supplies prototype compositions at other doses, no measured modified-release pharmacokinetics, and no disclosed structure-release-PK relationship, does not. The general development techniques are routine; reaching each claim's particular acceptance criteria from this disclosure is not routine verification.

X. OPINION 3: CLAIMS 12–16 (RELEASE-KINETIC ORDERS)

31. Claims 12–16 recite that the formulation exhibits zero-order, pseudo-zero-order, first-order, pseudo-first-order, or second-order release. The patent does not identify a formulation-science criterion for selecting among those patterns within the context of Claim 1, and it does not provide practical guidance on how to design

a formulation that will reliably achieve any one of them at the claimed dose. The claimed kinetic orders describe results achieved, not methods for achieving them.

32. The clearest deficiencies concern Claim 12 (zero order) and Claim 16 (second order). The disclosed prototypes are HPMC hydrophilic matrix tablets, whose characteristic behavior is in the first-order, pseudo-first-order, and pseudo-zero-order regime. The "Pseudo Zero Order" and "Pseudo First Order" target curves in FIGS. 6–7 are labeled "Estimated from PBPK Slides." PBPK appears only in those figure labels; the specification text does not identify the slides or disclose the model, inputs, assumptions, or validation underlying the estimates. The only kinetic-order characterization the specification attaches to physical prototype data is the method-dependent treatment of the 10 mg prototype data discussed in ¶ 33. The specification enumerates osmotic-pump architectures only in generic, drug-agnostic passages (cols. 16–17, incorporating U.S. Pub. No. 2020/0108008 by reference) and discloses no minoxidil embodiment of them. It characterizes no embodiment as producing a constant-rate zero-order profile under a specified assessment method and interval, typically pursued with osmotic or other specially designed architectures, or second-order release, rarely a designed oral release profile, and provides no minoxidil-specific direction for achieving either at 4.5 mg. In my experience, osmotic systems are among the most established oral platforms for approximating constant-rate release, although certain multilayer, geometry-

controlled, erosion-controlled, or specially coated systems may also be designed to approach a constant release rate.

33. A related deficiency is that the specification does not fix the choices needed to assess conformance to any claimed order. It reports several dissolution procedures, but it does not designate any one procedure as controlling for claim conformance or supply a common model-fitting protocol. In particular, it identifies no controlling combination of dissolution apparatus, medium, agitation rate, sampling and assessment window, mathematical model, goodness-of-fit criterion, or rule for comparing fits. Its definitions are stated in the vocabulary of chemical reaction kinetics, using rate constants in M/sec, sec^{-1} , and $\text{M}^{-1} \text{sec}^{-1}$, without translating those expressions into a dissolution-based criterion. The "pseudo" orders are defined as species of the true orders, with pseudo-zero described as "actually a result of a first order reaction" and pseudo-first as a second-order reaction made to behave first-order, so the definitions nest rather than mark distinct boundaries. Hydrophilic-matrix profiles may fit adjacent empirical models comparably depending on the selected method and interval. The specification illustrates the problem by classifying its 10 mg prototype formulation, whose one-stage data comprise batches 030448-001 and 030448-008, as exhibiting "pseudo zero order kinetics," while describing the two-stage data, which include batch 030448-008, as showing more of a first-order release profile (cols. 97–98). From a formulation-

science perspective, a skilled formulator handed a 4.5 mg modified-release tablet and the '184 specification would lack an objective, reproducible basis for determining which of Claims 12–16 applies.

34. The dissolution record uses several materially different methods. FIG. 1 is a Phase 1 study flowchart, not a dissolution figure (Ex. 1001, col. 1, ll. 23–26). FIGS. 2–5 report single-stage dissolution in pH 7.2 phosphate buffer using USP Apparatus II at 75 rpm (col. 1, ll. 27–50). FIG. 6 reports single-stage dissolution in 900 mL of pH 6.8 phosphate buffer at 50 rpm; the figure header identifies "Baskets (50 rpm)," although the accompanying text does not identify the apparatus (FIG. 6; col. 97, ll. 61–67). FIG. 7 reports a two-stage method: 750 mL of 0.1 N HCl for hours 0–2, followed by addition of 250 mL of concentrated phosphate buffer to produce pH 6.8 for hours 2–24 (col. 98, ll. 53–60). Thus, the media, pH values, volumes, gastric-stage duration, and stage-change method are described. The two-stage description does not specify the apparatus or agitation rate, however, and it does not report a discriminating-power assessment or a model-fitting protocol. The patent states that the two-stage method produced "more of a first-order release profile with a large burst due to the acid-stage" and that minoxidil "likely has pH sensitive solubility" (col. 98, ll. 60–67). Those statements show that the observed release classification depends materially on the selected dissolution method and

that the disclosed prototypes do not behave as constant-rate systems under the gastric stage.

35. Constant-rate zero-order release is not the default behavior of a simple hydrophilic cellulose matrix of the kind disclosed. With that limitation noted, the general shape of the two-stage release profiles is similar to what is commonly seen with conventional hydrophilic matrix formulations: drug release is relatively faster during the early part of the profile and then slows as the matrix hydrates, the readily available drug is depleted, and the dosage form changes with time. Such profiles can resemble general first-order-type release behavior, with faster release initially, a decreasing release rate, and an eventual plateau. This behavior is consistent with the properties of HPMC polymers and their blends as well as similar hydrophilic polymers, which control release through a combination of hydration, swelling, diffusion, dissolution, and erosion depending on the type and amount of each water-soluble polymer alone or in combination. Because the physical structure of the matrix changes continuously during dissolution (gel thickness, diffusion path length, polymer concentration, surface area, erosion rate, and the amount of drug remaining in the matrix all change with time), it is difficult to obtain a constant release rate over a prolonged period using only a simple water-soluble cellulose matrix. For this reason, a constant-rate zero-order profile over a specified interval and under a specified assessment method should not be treated as

the default behavior of the simple HPMC-based matrix the specification discloses absent additional design controls or deliberately engineered conditions. More complex delivery systems, such as osmotic systems, multilayer tablets, or specially designed coatings, are more suitable when a nearly constant release rate over a long period is required. This observation is directed to what the specification teaches about achieving the kinetic orders Claims 12 through 16 recite; it is separate from, and consistent with, my opinion below that a zero-order profile is not necessary where the formulation objective is simply to reduce C_{max} over a relatively short modified-release period.

36. The specification's own two-stage description does not characterize the disclosed prototypes as zero-order. The specification states that the two-stage assays produced "more of a first-order release profile with a large burst due to the acid-stage" (Table 10 and FIG. 7, which include batch 030448-008) and states that minoxidil "likely has pH sensitive solubility" (Ex. 1001, col. 98, ll. 60–67). That method-dependent description is inconsistent with treating the one-stage 10 mg prototype's "pseudo zero order" label as an intrinsic property of batch 030448-008.

37. Claim 12 recites zero-order kinetics but does not specify the duration over which that order must be maintained, the dissolution method under which conformance is assessed, the mathematical transformation or model to be used, or any criterion for accepting one fit over another. The specification also does not

teach a minoxidil-specific osmotic, multilayer, or other specially designed embodiment for approaching constant release. These omissions, together with the patent's method-dependent treatment of the 10 mg prototype data described above, prevent an objective and reproducible determination of the claimed kinetic order from the disclosure.

XI. OPINION 4: OBVIOUSNESS OF THE CLAIMED SUBJECT MATTER (§ 103)

A. Motivation

38. As of October 2022, a POSITA had ample motivation to develop a modified-release oral minoxidil for hair loss. Oral minoxidil was in wide clinical use for hair loss at low doses, and its immediate-release form was known to produce an early plasma peak (T_{max} within the first hour). Modified release, specifically the hydrophilic-matrix approach the '184's own prototypes employ, is a conventional formulation option when a slower drug-input rate, a lower peak concentration, or less frequent dosing is desired. Developing a modified-release version of a drug already marketed in immediate-release form is a common lifecycle-management strategy, not an inventive departure, and the established matrix toolkit supplied conventional means to reduce C_{max} and move T_{max} later, as shown in ¶¶ 46–53.

B. The combination was conventional

39. Sinclair (Ex. 1003) discloses minoxidil for hair loss and target blood-concentration ranges for its oral-mucosal embodiments. Separately, Sinclair reports

swallowed-oral dose and serum data. I do not treat those separate disclosures as measured results from a swallowed modified-release product. Cardinal (Ex. 1012) separately identifies minoxidil among many suitable drug substances (§ [0064]) and K4M and K200M among matrix polymers (§ [0115]), while its background describes the generic controlled-release objectives of maintaining desired blood levels and reducing fluctuation (§ [0002]); it reports no minoxidil working example. Reynolds (Ex. 1004) supplies routine control of HPMC-matrix release rates. Williams (Ex. 1008) describes a different modified-release architecture: a bupropion hydrobromide core surrounded by a controlled-release membrane coating containing ethylcellulose and polyvinylpyrrolidone. Biovail (Ex. 1009) describes an SSRI modified-release matrix using METHOCEL K4M Premium CR. I rely on Williams and Biovail only for their drug-agnostic formulation teachings, not for pharmacokinetic values of their unrelated actives. Combining Sinclair's minoxidil teaching with the HPMC-matrix teachings of Reynolds, Cardinal, and Biovail was, in my opinion, within ordinary skill, with each element performing its established function. Sinha (Ex. 1034), whose certified priority provisional, Ex. 1043, is dated September 29, 2021 on its face, proposes oral minoxidil for hair loss in sustained-, delayed-, or enteric-release oral dosage forms (Ex. 1034 § [0042]) at about 0.625 mg to about 10 mg (Ex. 1034 § [0039]); corresponding hair-loss, dose, and release-form disclosures appear in Ex. 1043 §§ [0020], [0037], [0041]. I

understand from counsel that Sinha is asserted to be prior art based on Ex. 1043. I express no opinion on that legal question and address only what the documents disclose.

B.1 Per-ground support

40. Ground 4 (Sinclair + Reynolds). Sinclair supplies the drug and indication, reported swallowed-oral dosing data and clinical use (Ex. 1003 ¶¶ [0146], [0150]), and, separately, target blood-concentration ranges for its oral-mucosal embodiments. I do not treat these separate disclosures as measured results from a swallowed modified-release product. Reynolds supplies the routine HPMC-matrix methodology, demonstrated on soluble drugs (promethazine HCl, diphenhydramine HCl, propranolol HCl), with release rate empirically tunable by tablet surface-area-to-volume ratio; the effect of HPMC content is separately established in the literature Reynolds cites. Minoxidil is itself water-soluble to approximately 2 mg/mL (Ex. 1007), so the full 4.5 mg dose is expected to dissolve readily in gastrointestinal fluid. At this dose, dissolution of the minoxidil itself would not be expected to limit release; transport through the hydrated matrix would be an important rate-controlling process, the same general regime Reynolds demonstrates. Minoxidil presents a conventional reason to consider a hydrophilic matrix: it is well absorbed ($\geq 90\%$), published plasma half-life estimates span approximately 1.1 to 4.2 hours, and the prior art reports immediate-release peak

serum concentrations at the 2.5 mg and 5 mg doses that bracket the claimed 4.5 mg dose (Ex. 1003 ¶ [0146]; Ex. 1006, Table I; ¶ 46). I do not rely on a precise half-life or treat either reported estimate alone as establishing Claim 2's eight-hour limitation. Sinclair also reports a 20 ng/mL serum-concentration benchmark for hemodynamic response based on 12-hour steady-state intravenous-infusion studies (Ex. 1003 ¶ [0145]; see ¶ 46). A POSITA would have had reason to combine these teachings and would have understood from Reynolds that the matrix release rate was routinely adjustable.

41. Ground 5 (Vañó-Galván + Fleishaker + Loniten label + Sinclair + Reynolds + Beach 2021). Vañó-Galván documents pre-priority clinical LDOM use in 1,404 patients at doses of 0.03–15 mg (bracketing 4.5 mg); Fleishaker and the Loniten label supply the reported immediate-release pharmacokinetic data over the 2.5–10 mg range Fleishaker studied; Sinclair and Reynolds function as described in ¶ 40. Beach 2021 (Ex. 1019, Table I, pp. 761–62) tabulates confirmed LDOM prescriptions for central centrifugal cicatricial alopecia (n=2) and traction alopecia (n=3), documenting pre-priority clinical use of oral minoxidil in the indications of Claims 8 and 10.

42. Ground 6 (Sinclair + Follica/Barman + Williams + Biovail). Follica supplies the modified-release enumeration (Ex. 1039 ¶ [0534]) and hair-loss method context, including express recitation of central centrifugal cicatricial alopecia (¶

[0179]). Williams supplies membrane-coated modified-release architecture applied to a bupropion hydrobromide core, while Biovail supplies an SSRI modified-release matrix whose preferred release-rate-controlling polymer is METHOCEL K4M Premium CR, the same K4M hydroxypropyl methylcellulose grade used in the '184 prototypes. These are different architectures and unrelated active ingredients. I rely on Williams and Biovail only for their respective formulation teachings, not for their pharmacokinetic values (§ 39).

43. Ground 7 (Sinclair + Cardinal + Fleishaker). Cardinal supplies generic extended-release matrix teachings. In separate lists, it names minoxidil among suitable actives (Ex. 1012 § [0064]) and HPMC K4M and K200M among matrix polymers (§ [0115]), but it reports no minoxidil working example or minoxidil-specific matrix. Cardinal's background states that controlled release may maintain desired blood levels for about four to twenty-four hours and avoid immediate-release fluctuation (§ [0002]). Separately, Cardinal describes in-vitro near-linear release at gastric pH and first-order release at intestinal pH as patterns that can be adjusted through matrix components (§ [0003]). A POSITA pursuing an oral minoxidil product at about 4.5 mg would have reason to consult matrix art naming both the drug and the relevant HPMC grades. Cardinal's in-vitro teachings additionally support the achievability of near-linear and first-order release profiles,

without treating those dissolution descriptions as measured human blood-level results.

C. Dose selection

44. "About 4.5 mg" lies within fixed-dose ranges repeatedly taught for oral minoxidil in hair loss, including about 0.625 mg to about 10 mg (Exs. 1034, 1043) and 0.1–20 mg for telogen effluvium (Ex. 1041 ¶ [0029]). The art also reports specific conventional oral doses of 2.5 mg and 5 mg (Ex. 1003 ¶ [0146]; Ex. 1006; Ex. 1014), but I do not treat the separate weight-based range in Bazzano as a direct fixed-dose bracket. The patent identifies no criticality at 4.5 mg and presents 4.5 mg as one entry among more than forty enumerated values (Ex. 1001, col. 13, l. 58 to col. 14, l. 3).

D. Routine hydrophilic-matrix formulation was the conventional approach to reducing C_{max} and delaying T_{max}

45. **Approach.** In this section I address the question from the direction a formulation scientist actually works: forward, from the formulation to the pharmacokinetic result, rather than backward from the claimed values. The analysis that follows is the analysis I would perform in ordinary development practice. I do not independently model clinical pharmacokinetic endpoints or offer opinions on therapeutic dose selection, patient management, or clinical interpretation. Where the pharmacokinetic behavior of immediate-release oral

minoxidil is relevant, I rely on the values reported in the prior-art literature rather than on any pharmacokinetic calculation of my own.

46. Minoxidil's relevant properties and its reported immediate-release

pharmacokinetics. Minoxidil is a small, water-soluble molecule: the Loniten® label reports it is at least 90% absorbed from the gastrointestinal tract (Ex. 1007), and its aqueous solubility of approximately 2 mg/mL means the entire 4.5 mg dose is expected to dissolve readily in gastrointestinal fluid. Its absorption from an immediate-release dosage form is rapid: the Loniten® label reports peak plasma concentrations within the first hour (Ex. 1007); Fleishaker reports t_{max} values of 0.566, 0.389, and 0.419 hours at 2.5, 5, and 10 mg (Ex. 1006, Table I); and Sinclair reports peak serum concentrations at one hour following oral administration (Ex. 1003 ¶ [0146]). Fleishaker reports half-lives of 1.07 hours at 2.5 mg, 1.27 hours at 5 mg, and 1.34 hours at 10 mg (Ex. 1006, Table I), while the Loniten® label separately reports an average plasma half-life of 4.2 hours (Ex. 1007, Section 3, p. 2). I rely on each reported value as stated and do not independently reconcile the different study estimates. The immediate-release peak concentrations reported in the literature are 16.8 ng/mL at 2.5 mg (Ex. 1006, Table I) and, in Sinclair, 18.5 ng/mL at 2.5 mg and 41 ng/mL at 5 mg (Ex. 1003 ¶ [0146]). Sinclair explains that 12-hour steady-state intravenous infusions were used to investigate the serum concentration/hemodynamic-response relationship and states: "The serum

concentration threshold for any hemodynamic response is 20 ng/ml" (Ex. 1003 ¶ [0145]). I cite that value only as a reported concentration benchmark and do not opine that the intravenous study establishes the same clinical threshold after oral dosing. In formulation terms, minoxidil at about 4.5 mg is a highly soluble, well-absorbed, rapidly absorbed drug whose immediate-release peak was characterized in the published literature before October 2022. I do not offer a numerical interpolation to a specific immediate-release C_{max} at 4.5 mg.

47. Modified release makes dosage-form release an important rate-controlling step. For well-absorbed, highly soluble drugs, dissolution and absorption from an immediate-release dosage form are generally rapid once the drug reaches the small intestine. Gastric emptying can therefore affect C_{max} and T_{max}, including under fasted and fed conditions. A modified-release formulation adds dosage-form release as an important control on the rate at which drug becomes available for absorption. The formulation scientist can adjust polymer type, polymer concentration, viscosity, matrix structure, coating properties, excipients, and other standard variables to change that release rate. Gastric emptying nevertheless remains a potential source of variability, so I do not assume that modified release eliminates its influence.

48. Conventional hydrophilic cellulose matrices are a standard choice for a relatively short modified-release window. When the intended release period is

measured in several hours, conventional hydrophilic cellulose polymers such as HPMC polymers and their blends, as well as poly(ethylene oxide) are well-established choices. These polymers hydrate rapidly in gastrointestinal fluid and form a gel layer. Drug release can involve diffusion through that hydrated layer together with polymer swelling and erosion. For a highly soluble drug at a low loading, diffusion of dissolved drug through the hydrated gel is generally expected to predominate, while erosion may contribute progressively as the matrix changes over time. The initial hydration period can also produce a surface burst, which formulators routinely address through polymer grade and level, granulation, tablet geometry, and related variables. These are the same polymers the '184's prototypes employ (HPMC K4M and K200M, Ex. 1001, Table 8), the polymers whose release control Reynolds addresses (Ex. 1004), and the grades Cardinal names for sustained-release oral matrices (Ex. 1012).

49. Established formulation variables can be used when reducing C_{max} is specified as the formulation objective. A formulator can use established matrix variables to slow drug input, including polymer type and level, viscosity grade, matrix geometry, excipient composition, coating properties, and related dosage-form features. A conventional HPMC-based matrix that releases the drug over several hours is therefore an appropriate platform to consider when the formulation objective is to reduce C_{max} while maintaining overall absorption. I do not opine

that a particular C_{max} causes or avoids cardiovascular effects, that reducing C_{max} will produce a particular clinical outcome, or that C_{max} should be prioritized clinically over T_{max} or other PK/PD measures. Sinclair's 20 ng/mL statement is cited only in the intravenous context described in ¶ 46.

50. Routine development practice, and why it is optimization rather than discovery. In routine pharmaceutical development, formulation work does not necessarily begin by selecting a mathematical in-vitro release model such as zero-order, first-order, second-order, or Higuchi release. A common practical approach is to prepare formulations with relatively fast, intermediate, and slow release rates, evaluate their in-vitro dissolution profiles under both simulated gastric and intestinal conditions, and then determine their pharmacokinetic profiles. These formulations provide practical reference points showing how changes in formulation affect C_{max}, T_{max}, AUC, and the overall plasma concentration-time profile. The formulation can then be adjusted between the faster and slower versions to move the pharmacokinetic profile toward the specified target. In this approach, the observed in-vitro release kinetics are mainly a result of the formulation design rather than the starting objective; whether the final dissolution curve can be described as zero-order, first-order, Higuchi-type, or another model is less important than whether the formulation produces the required in-vivo performance. This iterative sequence is routine optimization rather than open-

ended discovery. I use "routine" here to describe the available development tools and directional tuning. I do not mean that those tools alone make a particular bounded C_{max}, T_{max}, eight-hour concentration, or kinetic-order result predictable without quantitative data for that endpoint.

51. Limits of simple hydrophilic matrices, and the distinction between in-vitro release and in-vivo pharmacokinetics.

Simple hydrophilic cellulose matrices do have limitations when very prolonged and tightly controlled release is required.

Because these matrices hydrate, swell, dissolve, and erode during gastrointestinal transit, other established technologies may be more suitable when release must continue well beyond the upper small intestine; these may include high-molecular-weight poly(ethylene oxide) matrices, multiparticulate systems, functional coatings, or osmotic delivery systems. The choice of formulation platform therefore depends on the intended duration and location of drug release.

Separately, an in-vitro dissolution test describes how the formulation releases drug under defined laboratory conditions, while the actual pharmacokinetic profile depends on both the formulation and biological factors such as food, gastrointestinal pH, gastric emptying, intestinal transit, fluid availability, and regional absorption. In-vitro release kinetics and in-vivo pharmacokinetics are therefore related, but they are not the same. At the claimed 4.5 mg dose, the reported aqueous solubility is ample for the dose to dissolve in ordinary

gastrointestinal fluid; dissolution of the dose itself is therefore not the limiting issue addressed by the modified-release matrix.

52. Applying this to about 4.5 mg oral minoxidil. Starting from the reported C_{max} and T_{max} of the immediate-release product, routine modified-release formulation development can be used to reduce the peak concentration and move T_{max} later through adjustment of established matrix variables. Standard formulation variables such as polymer type, polymer concentration, viscosity, matrix geometry, excipient composition, coating properties, and dosage-form design provide several ways to adjust the release profile. Minoxidil at about 4.5 mg has properties that make a hydrophilic matrix an appropriate platform to consider: it is highly soluble, at least 90% absorbed, and rapidly absorbed from an immediate-release dosage form, so release from the matrix can become an important control on the rate of systemic input. Hydrophilic cellulose matrices such as HPMC polymers and their blends are standard formulation options for slowing drug input over a relatively short modified-release period, and they are the polymers the '184's own prototypes employ. The fact that such systems may show a curved, first-order-like dissolution profile rather than a zero-order profile does not reduce their usefulness if they produce the specified pharmacokinetic outcome. None of this requires a novel formulation technology. It reflects conventional pharmaceutical development practice: start with the reported pharmacokinetic

profile of the immediate-release product, prepare formulations with faster and slower release rates, determine their in-vivo pharmacokinetic profiles, and adjust standard formulation variables toward the specified C_{max}, T_{max}, and AUC. I do not opine that every modified-release formulation would meet any particular C_{max} or T_{max} value.

53. Conclusion on reasonable expectation of success. In my opinion, a POSITA in October 2022, applying routine formulation practice to a drug whose immediate-release pharmacokinetics were already characterized in the published literature, would have reasonably expected, though not with certainty, that a conventional hydrophilic-matrix modified-release formulation of about 4.5 mg oral minoxidil could be made to reduce the peak plasma concentration and move T_{max} later relative to immediate release through routine adjustment of established matrix variables. That is the expected direction of applying conventional hydrophilic-matrix technology to slow drug input and reduce peak concentration. I do not offer an opinion on the precise plasma concentration, percentage reduction, or T_{max} that any particular formulation would produce. My opinion is limited to the direction of the effect and the ordinary nature of the formulation work.

E. Absence of a reported unexpected technical result

54. I have not identified in the '184 patent any reported modified-release minoxidil result that differs from what conventional hydrophilic-matrix technology would

have been expected to produce. The specification reports no human modified-release study from which an unexpected pharmacokinetic or tolerability result could have been shown.

XII. RECONCILIATION OF THE WRITTEN-DESCRIPTION, ENABLEMENT, AND OBVIOUSNESS OPINIONS

55. These opinions address different technical questions. As explained in ¶¶ 29–30, the established techniques and the expected direction of changing release rate were routine, while satisfying each claim's particular bounded limitations required quantitative formulation-to-exposure or release-method information the specification does not disclose. For obviousness (Opinion 4), the prior art supplied the known formulation platform, the immediate-release dose and exposure data (Fleishaker; Sinclair), generic matrix art that separately names minoxidil and the relevant HPMC grades (Cardinal), and routine methods for adjusting release (Reynolds). For written description (Opinion 1), the '184 patent identifies no specific formulation shown to achieve Claim 1's PK result, provides no measured modified-release pharmacokinetic data, and gives no disclosed relationship between formulation structure, release, and PK performance. For enablement (Opinion 3), my opinion is focused principally on Claims 12 and 16. For those claims, neither the specification nor ordinary formulation knowledge supplies an objective, reproducible route to the separately recited kinetic order at the claimed dose. Thus, the general formulation approach and direction of effect were

predictable, while the patent did not demonstrate possession of Claim 1's claimed PK result or provide an objective route to Claims 12 and 16.

XIII. CLAIM 19 ("NO CARDIAC EFFECTS"): CORROBORATION WITHIN MY DISCIPLINE

56. The published record before October 2022 documents that minoxidil is a direct-acting arteriolar vasodilator whose hemodynamic effects (reduced peripheral resistance, reflex tachycardia, fluid retention) are reported across its active dose range (Exs. 1007, 1018, 1005). From a pharmaceutical-science perspective, the '184 specification supplies no threshold, such as a blood-pressure change, heart-rate change, or other metric, by which a POSITA could determine when a measured hemodynamic response counts as "no cardiac effects" under the specification's definition of "cardiac effect" as "any effect on the heart or the vascular system." I offer this observation from the documents within my competence; I do not offer clinical-cardiology opinions.

XIV. SECONDARY CONSIDERATIONS

57. I have identified no reported unexpected result in the '184 patent or in the portions of its prosecution record I reviewed (Appendix A), and the specification itself states that no human MR study had been conducted from which such a result could have been shown (cols. 65–66). If Patent Owner presents objective evidence

of nonobviousness, I will address whether it is attributable to the claimed 4.5 mg / Cmax / Tmax combination and commensurate with the claims.

XV. CONCLUSION

58. For the reasons above, it is my opinion that: (a) the '184 specification does not demonstrate possession of the claimed modified-release formulation defined by its in-vivo PK result; (b) as to Claims 12 and 16 in particular, neither the specification nor ordinary formulation knowledge supplies an objective, reproducible route to the recited kinetic order at the claimed dose; and (c) using a conventional HPMC-matrix modified-release formulation for a known oral hair-loss drug at about 4.5 mg to reduce Cmax and delay Tmax would have been an ordinary and obvious formulation approach to a POSITA as of October 25, 2022. My opinion in subparagraph (c) is limited to the formulation approach and expected direction of effect. I do not opine that the cited formulation art, without additional quantitative PK evidence, establishes all of Claim 1's numerical Cmax and Tmax limitations.

59. I understand that any supplementation of my opinions would be subject to applicable Board rules, orders, and authorization.

Appendix A: Materials Considered

1. U.S. Patent No. 12,491,184 (Ex. 1001); file history excerpts (Exs. 1035, 1036); priority provisionals 63/419,155 and 63/433,203 (Exs. 1010, 1011)
2. Sinclair/Samson, US 2019/0269684 (Ex. 1003)
3. Reynolds 2002 (Ex. 1004)
4. Vañó-Galván 2021 (Ex. 1005)
5. Fleishaker 1989 (Ex. 1006)
6. Loniten® label, NDA 018-154 (Ex. 1007)
7. Williams, US 2010/0104639 (Ex. 1008)
8. Biovail, WO 2004/058229 (Ex. 1009)
9. Cardinal, US 2010/0159001 (Ex. 1012)
10. Bokhari 2021 (Ex. 1013); Panchaprateep 2020 (Ex. 1014)
11. Gottlieb 1972 (Ex. 1017); Lowenthal & Affrime 1980 (Ex. 1018)
12. Beach 2021 (Ex. 1019); Buhl 1990 (Ex. 1021)
13. Sinha, US 2024/0374594 (Ex. 1034), and its certified priority provisional, U.S. 63/250,009 (Ex. 1043)

14. Follica/Barman, US 2019/0381296 (Ex. 1039); Follica/Barman, US 11,207,511 (Ex. 1045)

15. Bazzano, WO 83/02558 (Ex. 1040); Samson, WO 2016/065426 (Ex. 1041)

16. Veradermics, Incorporated, prospectus, February 2026 (Ex. 1048) (reviewed; not relied upon)

I declare under penalty of perjury that the foregoing is true and correct.

Executed on 8/27/2026, at Weston, FL.

Signed by:

Hossein Omidian

69EAA28920E9488...

Hossein Omidian, Ph.D.