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1288329

THE UNITED STATES OF AMERICA

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UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

November 16, 2023

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APPLICATION NUMBER: 63/433,203

FILING DATE: *December 16, 2022*

RELATED PCT APPLICATION NUMBER: *PCT/US23/35920*

THE COUNTRY CODE AND NUMBER OF YOUR PRIORITY APPLICATION, TO BE USED FOR FILING ABROAD UNDER THE PARIS CONVENTION, IS *US63/433,203*



Certified by

Kathi

Performing the Functions and Duties of the
Under Secretary of Commerce
for Intellectual Property
and Director of the United States
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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	148262-000510
		Application Number	
Title of Invention	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL		
The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76. This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.			

Secrecy Order 37 CFR 5.2:

☐	Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)
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Inventor Information:

Inventor	1	<button>Remove</button>		
Legal Name				
Prefix	Given Name	Middle Name	Family Name	Suffix
	Reid		WALDMAN	
Residence Information (Select One) • US Residency Non US Residency Active US Military Service				
City	West Hartford	State/Province	CT	Country of Residence
				US
Mailing Address of Inventor:				
Address 1	85 Memorial Road #415			
Address 2				
City	West Hartford	State/Province	CT	
Postal Code	06107	Country	US	
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button.				
<button>Add</button>				

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).			
☐ An Address is being provided for the correspondence information of this application.			
Customer Number	185628		
Email Address	ip.pitt@us.dlapiper.com	<button>Add Email</button>	<button>Remove Email</button>

Application Information:

Title of the Invention	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL		
Attorney Docket Number	148262-000510	Small Entity Status Claimed	☒
Application Type	Provisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	0	Suggested Figure for Publication (if any)	N/A

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Application Data Sheet 37 CFR 1.76	Attorney Docket Number	148262-000510
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Title of Invention	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)

☐ **Request Not to Publish.** I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application **has not and will not be** the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.

Please Select One:	☒ Customer Number	☐ US Patent Practitioner	☐ Limited Recognition (37 CFR 11.9)
Customer Number	185628		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status		Remove	
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the Add button. Add			

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	148262-000510
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Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)ⁱ the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Application Number	Country ⁱ	Filing Date (YYYY-MM-DD)	Access Code ^j (if applicable)

Additional Foreign Priority Data may be generated within this form by selecting the **Add** button.

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	148262-000510
	Application Number	
Title of Invention	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL	

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	148262-000510
	Application Number	
Title of Invention	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL	

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant	1	Remove
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If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.

[Clear](#)

☒ Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
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Person to whom the inventor is obligated to assign.	Person who shows sufficient proprietary interest
---	--

If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:

Name of the Deceased or Legally Incapacitated Inventor:

If the Applicant is an Organization check here. ☒

Organization Name	Veradermics Incorporated
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Mailing Address Information For Applicant:

Address 1	85 Memorial Rd #415		
Address 2			
City	West Hartford	State/Province	CT
Country	US	Postal Code	06107
Phone Number		Fax Number	
Email Address			

Additional Applicant Data may be generated within this form by selecting the Add button. [Add](#)

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76	Attorney Docket Number	148262-000510
	Application Number	
Title of Invention	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL	

Assignee	1
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Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.

[Remove](#)If the Assignee or Non-Applicant Assignee is an Organization check here. ☐

Prefix	Given Name	Middle Name	Family Name	Suffix

Mailing Address Information For Assignee including Non-Applicant Assignee:

Address 1				
Address 2				
City		State/Province		
Country i		Postal Code		
Phone Number		Fax Number		
Email Address				

Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button.

[Add](#)**Signature:**[Remove](#)

NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). However, if this Application Data Sheet is submitted with the **INITIAL** filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).

This Application Data Sheet **must** be signed by a patent practitioner if one or more of the applicants is a **juristic entity** (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, **all** joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of **all** joint inventor-applicants.

See 37 CFR 1.4(d) for the manner of making signatures and certifications.

Signature	/Marissa S. Kuzirian/		Date (YYYY-MM-DD)	2022-12-16	
First Name	Marissa S.	Last Name	Kuzirian	Registration Number	78983

Additional Signature may be generated within this form by selecting the Add button.

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Application Data Sheet 37 CFR 1.76		Attorney Docket Number	148262-000510
		Application Number	
Title of Invention	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL		

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL

SUMMARY

[0001] In some aspects, the techniques described herein relate to a pharmaceutical formulation for oral administration, including a daily dose of minoxidil, wherein the pharmaceutical formulation is a modified release formulation.

[0002] In some aspects, the techniques described herein relate to a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

[0003] In some aspects, the techniques described herein relate to a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a Tmax of about 30 to about 360 minutes.

[0004] In some aspects, the techniques described herein relate to a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a Cmax of about 0.25 ng/ml to about 20 ng/ml.

[0005] In some aspects, the techniques described herein relate to a method of treating hair loss, including administering to a subject in need thereof a daily dose of a composition including a modified release formulation of minoxidil.

[0006] In some aspects, the techniques described herein relate to a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

[0007] In some aspects, the techniques described herein relate to a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a Tmax of about 30 to about 360 minutes.

[0008] In some aspects, the techniques described herein relate to a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a Cmax of about 0.25 ng/ml to about 20 ng/ml.

[0009] In some aspects, the techniques described herein relate to a kit including, a slow modified release vehicle including oral minoxidil.

DETAILED DESCRIPTION

[0010] This disclosure is not limited to the particular systems, devices and methods described, as these may vary. The terminology used in the description is for the purpose of describing the particular versions or embodiments only, and is not intended to limit the scope. Such aspects of the disclosure be embodied in many different forms; rather, these embodiments are provided so that this disclosure will be thorough and complete, and will fully convey its scope to those skilled in the art.

[0011] The present disclosure is not to be limited in terms of the particular embodiments described in this disclosure, which are intended as illustrations of various aspects. Many modifications and variations can be made without departing from its spirit and scope, as will be apparent to those skilled in the art. Functionally equivalent methods and apparatuses within the scope of the disclosure, in addition to those enumerated herein, will be apparent to

those skilled in the art from the foregoing descriptions. Such modifications and variations are intended to fall within the scope of the appended claims. The present disclosure is to be limited only by the terms of the appended claims, along with the full scope of equivalents to which such claims are entitled. It is to be understood that this disclosure is not limited to particular methods, reagents, compounds, compositions or biological systems, which can, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting.

[0012] As used in this document, the singular forms “a,” “an,” and “the” include plural references unless the context clearly dictates otherwise. Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art. Nothing in this disclosure is to be construed as an admission that the embodiments described in this disclosure are not entitled to antedate such disclosure by virtue of prior invention. As used in this document, the term “comprising” means “including, but not limited to.”

[0013] While various compositions, methods, and devices are described in terms of "comprising" various components or steps (interpreted as meaning "including, but not limited to"), the compositions, methods, and devices can also "consist essentially of" or "consist of" the various components and steps, and such terminology should be interpreted as defining essentially closed-member groups.

[0014] With respect to the use of substantially any plural and/or singular terms herein, those having skill in the art can translate from the plural to the singular and/or from the singular to the plural as is appropriate to the context and/or disclosure. The various singular/plural permutations may be expressly set forth herein for sake of clarity.

[0015] It will be understood by those within the art that, in general, terms used herein, and especially in the appended claims (for example, bodies of the appended claims) are generally intended as “open” terms (for example, the term “including” should be interpreted as “including but not limited to,” the term “having” should be interpreted as “having at least,” the term “includes” should be interpreted as “includes but is not limited to,” etc.). It will be further understood by those within the art that if a specific number of an introduced claim recitation is intended, such an intent will be explicitly recited in the claim, and in the absence of such recitation no such intent is present. For example, as an aid to understanding, the following appended claims may contain usage of the introductory phrases “at least one” and “one or more” to introduce claim recitations. However, the use of such phrases should not be construed to imply that the introduction of a claim recitation by the indefinite articles “a” or “an” limits any particular claim containing such introduced claim recitation to embodiments containing only one such recitation, even when the same claim includes the introductory phrases “one or more” or “at least one” and indefinite articles such as “a” or “an” (for example, “a” and/or “an” should be interpreted to mean “at least one” or “one or more”); the same holds true for the use of definite articles used to introduce claim recitations. In addition, even if a specific number of an introduced claim recitation is explicitly recited, those skilled in the art will recognize that such recitation should be interpreted to mean at least the recited number (for example, the bare recitation of “two recitations,” without other modifiers, means at least two recitations, or two or more recitations). Furthermore, in those instances where a convention analogous to “at least one of A, B, and C, etc.” is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (for example, “a system having at least one of A, B, and C” would include but not be limited to systems that have A alone, B alone, C alone, A

and B together, A and C together, B and C together, and/or A, B, and C together, etc.). In those instances where a convention analogous to “at least one of A, B, or C, etc.” is used, in general such a construction is intended in the sense one having skill in the art would understand the convention (for example, “a system having at least one of A, B, or C” would include but not be limited to systems that have A alone, B alone, C alone, A and B together, A and C together, B and C together, and/or A, B, and C together, etc.). It will be further understood by those within the art that virtually any disjunctive word and/or phrase presenting two or more alternative terms, whether in the description, claims, or drawings, should be understood to contemplate the possibilities of including one of the terms, either of the terms, or both terms. For example, the phrase “A or B” will be understood to include the possibilities of “A” or “B” or “A and B.”

[0016] In addition, where features or aspects of the disclosure are described in terms of Markush groups, those skilled in the art will recognize that the disclosure is also thereby described in terms of any individual member or subgroup of members of the Markush group.

[0017] All percentages, parts and ratios are based upon the total weight of the compositions and all measurements made are at about 25 °C, unless otherwise specified.

[0018] As will be understood by one skilled in the art, for any and all purposes, such as in terms of providing a written description, all ranges disclosed herein also encompass any and all possible subranges and combinations of subranges thereof. Any listed range can be easily recognized as sufficiently describing and enabling the same range being broken down into at least equal halves, thirds, quarters, fifths, tenths, etc. As a non-limiting example, each range discussed herein can be readily broken down into a lower third, middle third and upper third, etc. As will also be understood by one skilled in the art all language such as “up to,” “at least,” and the like include the number recited and refer to ranges which can be subsequently broken down

into subranges as discussed above. Finally, as will be understood by one skilled in the art, a range includes each individual member. Thus, for example, a group having 1-3 cells refers to groups having 1, 2, or 3 cells. Similarly, a group having 1-5 cells refers to groups having 1, 2, 3, 4, or 5 cells, and so forth.

[0019] Where a range of values is provided, it is intended that each intervening value between the upper and lower limit of that range and any other stated or intervening value in that stated range is encompassed within the disclosure. For example, if a range of 1 μm to 8 μm is stated, it is intended that 2 μm , 3 μm , 4 μm , 5 μm , 6 μm , and 7 μm are also explicitly disclosed, as well as the range of values greater than or equal to 1 μm and the range of values less than or equal to 8 μm .

[0020] The term “about,” as used herein, refers to variations in a numerical quantity that can occur, for example, through measuring or handling procedures in the real world; through inadvertent error in these procedures; through differences in the manufacture, source, or purity of compositions or reagents; and the like. Typically, the term “about” as used herein means greater or lesser than the value or range of values stated by 1/10 of the stated values, e.g., $\pm 10\%$. The term “about” also refers to variations that would be recognized by one skilled in the art as being equivalent so long as such variations do not encompass known values practiced by the prior art. Each value or range of values preceded by the term “about” is also intended to encompass the embodiment of the stated absolute value or range of values. Whether or not modified by the term “about,” quantitative values recited in the present disclosure include equivalents to the recited values, e.g., variations in the numerical quantity of such values that can occur, but would be recognized to be equivalents by a person skilled in the art. Where the context of the disclosure indicates otherwise, or is inconsistent with such an interpretation, the above-stated interpretation

may be modified as would be readily apparent to a person skilled in the art. For example, in a list of numerical values such as "about 49, about 50, about 55, "about 50" means a range extending to less than half the interval(s) between the preceding and subsequent values, e.g., more than 49.5 to less than 52.5. Furthermore, the phrases "less than about" a value or "greater than about" a value should be understood in view of the definition of the term "about" provided herein.

[0021] The terms "administer," "administering," and "administration" as used herein refer to either directly administering a compound (also referred to as an agent of interest) or pharmaceutically acceptable salt of the compound (agent of interest) or a composition to a subject.

[0022] The term "adverse effect" as use herein refers to undesired harmful effect resulting from the administration of a pharmaceutical formulation. An adverse effect can be selected from peripheral edema, tachycardia, hypotension, lightheadedness, and hirsutism. An "adverse effect" can also be referred to as a side effect.

[0023] The term "animal" as used herein includes, but is not limited to, humans and non-human vertebrates such as wild, domestic, and farm animals.

[0024] The term "cardiac condition" as used herein refers to any condition related to the heart or vascular system. A cardiac condition can be selected heart disease, hypotension (including orthostatic hypotension), chronic congestive heart failure, cardiomyopathy, tachyarrhythmia (including atrial fibrillation, premature ventricular contractions, supraventricular tachycardia, ventricular fibrillation, etc.), renal disease, preexisting pulmonary hypertension, and chronic congestive heart failure not secondary to hypertension.

[0025] The term "cardiac effect" as used herein refers to any effect on the heart or the vascular system as a result of the administration of a pharmaceutical formulation. A cardiac

effect can be a hemodynamic change in blood pressure. A cardiac effect can be selected from tachycardia, hypotension, premature ventricular contractions, and other tachyarrhythmias.

[0026] The terms “clinical significance” or “clinically significant” as used herein refer to the practical importance of a treatment effect on daily life.

[0027] The term “composition” as used herein refers to a combination or a mixture of two or more different ingredients, components, or substances.

[0028] The term “daily” as used herein refers to administration within a single day.

[0029] The term “disorder” as used herein refers to an abnormal condition of the human or animal body or of one of its parts that impairs normal functioning, is typically manifested by distinguishing signs and symptoms, and causes the human or animal to have a reduced duration or quality of life. The term “disorder” can be used interchangeably with the terms “disease,” “condition,” or “illness,” unless otherwise indicated.

[0030] The term “excipients” as used herein encompasses carriers and diluents, meaning a material, composition or vehicle, such as a liquid or solid filler, diluent, excipient, solvent or encapsulating material involved in carrying or transporting a pharmaceutical, cosmetic or other agent across a tissue layer such as the stratum corneum or stratum spinosum.

[0031] The term “hair loss” as used herein refers to excessive hair loss. Hair loss can be from the scalp. Hair loss can be male pattern hair loss, female pattern hair loss, hereditary hair loss, telogen effluvium, anagen effluvium, alopecia areata, cicatricial alopecia (including central centrifugal cicatricial alopecia, lichen planopilaris, frontal fibrosing alopecia, etc.), or traction alopecia.

[0032] The term “hair regrowth” as used herein refers to the growth of hair to restore hair after hair loss. Hair regrowth can be measured with commonly accepted measurements

including a target area hair count (TAHC) and pattern hair loss specific grading systems (e.g. Hamilton Norwood scale, Sinclair scale, Ludwig scale, etc.).

[0033] The term “improvement” as used herein refers to a state that is better than another state.

[0034] The term “modified release” as used herein refers to pharmaceutical compositions that do not otherwise release the entirety of the active ingredient immediately. For example, it may release the active ingredient at a sustained or controlled rate over an extended period of time, or may release the active ingredient after a lag time after administration, or may be used optionally in combination with an immediate release composition. Modified release includes extended release, sustained release, controlled release, and delayed release. The term “extended release” or “sustained release” as used herein is a dosage form that makes a drug available over an extended period of time after administration relative to a dose delivered in an entirely immediate release form. The term “delayed release” as used herein is a dosage form that releases a drug at a time other than immediately upon administration. The terms “orally” and “oral” and “oral administration” as used herein refer to the route of administration where a substance is taken through the mouth.

[0035] The term “pharmaceutical formulation” as used herein refers to a substance that contains a combination of excipients and an active pharmaceutical ingredient to create a medicinal product. As used herein, the term “pharmaceutical agent” or “compound” refers to a chemical entity or biological product, or combination of chemical entities or biological products, administered to a person to treat or prevent or control a disease or condition. The chemical entity or biological product is preferably, but not necessarily a low molecular weight compound, but may also be a larger compound, for example, an oligomer of nucleic acids, amino acids, or

carbohydrates including without limitation proteins, oligonucleotides, ribozymes, DNazymes, glycoproteins, siRNAs, lipoproteins, aptamers, and modifications and combinations thereof.

[0036] The term “pharmacokinetics” as used herein refers to the movement of a drug within a body and the elimination of a drug from a body. The term “pharmacokinetic profile” as used herein refers to the measurements of the pharmacokinetic properties of a drug, a compound, or a formulation. A pharmacokinetic profile the following measurements: half-life, C_{max}, T_{max} and area under the plasma concentration- time curve (AUC). The term “half-life” as used herein refers to the time required for a drug, a compound, or a formulation to be reduced to half of the initial amount. The term “plasma concentration versus time” as used herein refers to the measurement of the concentration of the active ingredient in the plasma over time. The term “C_{max}” as used herein refers to maximum serum concentration that a drug, a compound, or a formulation achieves after administration of a single dose. The term “T_{max}” as used herein refers to the time it takes for a drug, a compound, or a formulation to reach the maximum concentration after administration of a single dose. The term “AUC” as used herein refers to the total drug exposure in the plasma over time.

[0037] The term “skin” as used herein refers to the thin layer of tissue forming the natural outer covering of the body of a person or animal. The skin is made of the epidermis and dermis. The term “scalp” as used herein refers to the skin on a patient’s head.

[0038] The term “steady state” as used here in refers to when the quantity of drug eliminated in the unit of time equals the quantity of the drug that reaches the systemic circulation in the unit of time. The term “steady state blood level” as used herein refers to the time when the amount of drug in the blood is constant. This occurs when the amount of the drug being absorbed is the same amount being cleared from the body when a drug is being administered repeatedly.

[0039] The term "subject" and "patient" are interchangeable and may be taken to mean any living organism which may be treated with compounds of the present invention. As such, the terms "patient" and "subject" may include, but is not limited to, any non-human mammal, primate or human. In some embodiments, the "patient" or "subject" is a mammal, such as mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, primates, or humans. In some embodiments, the patient or subject is an adult, child or infant. In some embodiments, the patient or subject is a human.

[0040] The term "subtherapeutic" or "subtherapeutically effective amount" of a compound or composition is a dose or concentration of a drug that is lower than what is usually prescribed to treat a disease effectively.

[0041] As used herein, the term "therapeutic" or "therapeutic agent" or "pharmaceutically active agent" or "active agent" means an agent utilized to treat, combat, ameliorate, prevent or improve an unwanted condition or disease of a patient.

[0042] A "therapeutically effective amount" or "effective amount" of a compound or composition is a predetermined amount calculated to achieve the desired effect, i.e., to inhibit, block, or reverse the activation, migration, or proliferation of cells. The activity contemplated by the present methods includes both medical therapeutic and/or prophylactic treatment, as appropriate. The specific dose of a compound administered according to this invention to obtain therapeutic and/or prophylactic effects will, of course, be determined by the particular circumstances surrounding the case, including, for example, the compound administered, the route of administration, and the condition being treated. The compounds are effective over a wide dosage range. However, it will be understood that the effective amount administered will be determined by the physician in the light of the relevant circumstances including the condition to

be treated, the choice of compound to be administered, and the chosen route of administration, and therefore the above dosage ranges are not intended to limit the scope of the invention in any way. A therapeutically effective amount of compound of this invention is typically an amount such that when it is administered in a physiologically tolerable excipient composition, it is sufficient to achieve an effective systemic concentration or local concentration in the tissue.

[0043] The term "treat," "treated," or "treating" as used herein refers to both therapeutic treatment and prophylactic or preventative measures, wherein the object is to reduce the frequency of, or delay the onset of, symptoms of a medical condition, enhance the texture, appearance, color, sensation, or hydration of the intended tissue treatment area of the tissue surface in a subject relative to a subject not receiving the compound or composition, or to otherwise obtain beneficial or desired clinical results. For the purposes of this invention, beneficial or desired clinical results include, but are not limited to, reversal, reduction, or alleviation of symptoms of a condition; diminishment of the extent of the condition, disorder or disease; stabilization (*i.e.*, not worsening) of the state of the condition, disorder or disease; delay in onset or slowing of the progression of the condition, disorder or disease; amelioration of the condition, disorder or disease state; and remission (whether partial or total), whether detectable or undetectable, or enhancement or improvement of the condition, disorder or disease. Treatment includes eliciting a clinically significant response without excessive levels of side effects. Treatment also includes prolonging survival as compared to expected survival if not receiving treatment.

[0044] In some embodiments, the compounds and methods disclosed herein can be utilized with or on a subject in need of such treatment, which can also be referred to as "in need thereof." As used herein, the phrase "in need thereof" means that the subject has been identified

as having a need for the particular method or treatment and that the treatment has been given to the subject for that particular purpose.

[0045] By hereby reserving the right to proviso out or exclude any individual members of any such group, including any sub-ranges or combinations of sub-ranges within the group, that can be claimed according to a range or in any similar manner, less than the full measure of this disclosure can be claimed for any reason. Further, by hereby reserving the right to proviso out or exclude any individual substituents, structures, or groups thereof, or any members of a claimed group, less than the full measure of this disclosure can be claimed for any reason. Throughout this disclosure, various patents, patent applications and publications are referenced. The disclosures of these patents, patent applications and publications are incorporated into this disclosure by reference in their entireties in order to more fully describe the state of the art as known to those skilled therein as of the date of this disclosure. This disclosure will govern in the instance that there is any inconsistency between the patents, patent applications and publications cited and this disclosure.

[0046] Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art. Nothing in this disclosure is to be construed as an admission that the embodiments described in this disclosure are not entitled to antedate such disclosure by virtue of prior invention.

PHARMACEUTICAL FORMULATION

[0047] Embodiments described herein are directed to a pharmaceutical formulation for oral administration, comprising a daily dose of minoxidil, wherein the pharmaceutical formulation is a modified release formulation.

[0048] In some embodiments, the pharmaceutical formulation described herein further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof. In some embodiments, the pharmaceutical formulation further comprises medrogestone, cetirizine, setipiprant, valproic acid, and combinations thereof.

[0049] In any embodiment of the pharmaceutical formulation described herein, the non-steroid anti-androgen is selected from flutamide, clascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof. In any embodiment, the 17 α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof. In any embodiment, the 19-norprogesterone derivative is nomegestrol acetate. In any embodiment, 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof. In any embodiment, the 17 α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof. In any embodiment, the 5-alpha reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof. In any embodiment, the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof. In any embodiment, the GnRH analog is a GnRH agonist wherein the GnRH agonist is selected from goserelin, buserelin,

leuporelin, and combinations thereof. In any embodiment, the GnRH analog is a GnRH antagonist wherein the GnRH antagonist is cetrorelix. In any embodiment, the prostaglandin F2 α analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof. In any embodiment, the prostamide is bimatoprost. In any embodiment, the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof. In any embodiment, the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof. In any embodiment, the prostaglandin E2 analog is sulprostone. In any embodiment, the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof. In any embodiment, the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof. In any embodiment, the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof. In any embodiment, the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.

[0050] In some embodiments of the pharmaceutical formulation described herein, the modified release formulation is selected from an extended release formulation, a sustained release formulation, a controlled release formulation, or a delayed release formulation. In some embodiments, the modified release formulation may release the minoxidil a pharmaceutically acceptable salt thereof at a sustained or controlled rate over an extended period of time, or may release it after a lag time after administration. For example, it may be released from the composition 4 hours after administration, 8 hours after administration, 12 hours after

administration, 16 hours after administration, or 24 hours after administration. Modified release formulations include extended release, sustained release, a controlled release formulation, and delayed release compositions. In some examples, the modified release compositions may release about 10% in about 2 hours, about 20% in 2 hours, about 40% in about 2 hours, about 50% in about 2 hours, about 10% in about 3 hours, about 20% in 3 hours, about 40% in about 3 hours, about 50% in about 3 hours, about 10% in about 4 hours, about 20% in 4 hours, about 40% in about 4 hours, about 50% in about 4 hours, about 10% in about 6 hours, about 20% in 6 hours, about 40% in about 6 hours, or about 50% in about 6 hours.

[0051] In some embodiments of the pharmaceutical formulation described herein, the extended release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration. In some embodiments of the pharmaceutical formulation described herein, the extended release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 18 hours after the oral administration. In some embodiments described herein, the extended release formulation releases about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 98% of the daily dose of minoxidil within about 12 to about 18 hours after the oral administration, or any range within these values.

[0052] In some embodiments of the pharmaceutical formulation described herein, the controlled release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration. In some embodiments, the controlled-release formulation releases about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 98% of the daily dose of minoxidil within about 12 hours after the oral administration, or any range within these values.

[0053] In some embodiments of the pharmaceutical formulation described herein, the delayed release formulation releases the daily dose of minoxidil within about 6 hours after the oral administration. In some embodiments, the delayed release formulation releases the daily dose of minoxidil in multiple distinct releases each within about 18 hours after the oral administration.

[0054] In some embodiments of the pharmaceutical formulation described herein, the minoxidil is in a therapeutically effective amount. In some embodiments, the one or more active agents are in a therapeutically effective amount. In some embodiments, the pharmaceutical formulation comprises minoxidil in a subtherapeutic amount. In some embodiments, the pharmaceutical formulation comprises one or more active agents in a subtherapeutic amount. In some embodiments, the pharmaceutical formulation comprises minoxidil and one or more active agents wherein the minoxidil and the one or more active agents are each in subtherapeutic amounts.

[0055] In some embodiments of the pharmaceutical formulation described herein, the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.5 mg to about 2.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.625 mg to about 7.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg. In some embodiments, the daily dose of minoxidil is about 0.25 mg to about 20 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.125 mg to about 100 mg. In some embodiments, the daily dose of minoxidil is about 2.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.125 mg, about 0.25 mg, about 5 mg, about 0.625 mg, about 0.75 mg, about 1 mg, about 1.25 mg, about 1.5 mg, about 2 mg, about 2.5 mg, about 3

mg, about 3.5 mg, about 4 mg, about 4.5 mg, about 5 mg, about 5.5 mg, about 6 mg, about 6.5 mg, about 7 mg, about 7.5 mg, about 8 mg, about 9 mg, about 10 mg, about 12 mg, about 15mg, about 18 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, about 100 mg, or any range within these values.

[0056] In some embodiments of the pharmaceutical formulation described herein, the daily dose of minoxidil is administered to a subject in an amount of about 0.00625 mg/kg/day to about 0.375 mg/kg/day. In some embodiments, the daily dose of the minoxidil is about 0.00625 mg/kg/day to about 0.5 mg/kg/day. In some embodiments, the daily dose of the minoxidil is about 0.00625 mg/kg/day, about 0.0125 mg/kg/day, about 0.025 mg/kg/day, about 0.0375 mg/kg/day, about 0.05 mg/kg/day, about 0.0625 mg/kg/day, about 0.075 mg/kg/day, about 0.0875 mg/kg/day, about 0.1 mg/kg/day, about 0.125 mg/kg/day, about 0.25 mg/kg/day, about 0.5 mg/kg/day, or any range within these values.

[0057] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation is administered only once daily. In some embodiments, the pharmaceutical formulation is administered at least once daily. In some embodiments, the pharmaceutical formulation is administered four times per day. In some embodiments, the pharmaceutical formulation is administered three times per day. In some embodiments, the pharmaceutical formulation is administered two times per day.

[0058] In some embodiments of the pharmaceutical formulation described herein, the oral administration of the daily dose of minoxidil results in a steady state blood level of the minoxidil of about 1 ng/ml to about 20 ng/ml. In some embodiments, the steady state blood level of the daily dose of minoxidil is maintained for at least about 12 hours.

[0059] In some embodiments of the pharmaceutical formulation described herein, the oral administration of the daily dose minoxidil results in a C_{max} of about 0.25 ng/ml to about 20 ng/ml. In some embodiments, the oral administration of the daily dose minoxidil results in a C_{max} that is devoid of cardiac effects.

[0060] In some embodiments of the pharmaceutical formulation described herein, the oral administration of the daily dose of minoxidil results in a T_{max} of about 30 to about 360 minutes. In some embodiments, the oral administration of the daily dose of minoxidil results in a delayed release that results in a T_{max} between both 30 to 360 minutes and between 390 minutes and 1080 minutes.

[0061] In some embodiments of the pharmaceutical formulation described herein, the oral administration of the daily dose of modified release minoxidil results in an AUC that is greater than an equivalent dose of an immediate release formulation.

[0062] Embodiments described herein are directed to a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

[0063] In some embodiments, the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5- α reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F₂ α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D₂ receptor antagonist, a prostglandin E₂ analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication,

a supplement, and combinations thereof. In some embodiments, the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[0064] Embodiments described herein are directed to a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a T_{max} of about 30 to about 360 minutes.

[0065] In some embodiments, the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof. In some embodiments, the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[0066] Embodiments described herein are directed to a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a C_{max} of about 0.25 ng/ml to about 20 ng/ml.

[0067] In some embodiments, the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication,

a supplement, and combinations thereof. In some embodiments, the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[0068] In some embodiments of the pharmaceutical formulation described herein, the oral administration results in a half-life of the daily dose of minoxidil of about 4 hours to about 24 hours. In some embodiments, the oral administration results in a half-life of the daily dose of minoxidil of about 4 hours, about 5 hours, about 6 hours, about 7 hours, about 8 hours, about 9 hours, about 10 hours, about 12 hours, about 14 hours, about 16 hours, about 18 hours, about 20 hours, about 22 hours, about 24 hours, or any range within these values.

[0069] In some embodiments of the pharmaceutical formulation described herein, the subject has a minoxidil plasma concentration versus time curve with a Tmax of about 30 to about 360 minutes.

[0070] In some embodiments, the pharmaceutical formulation is an inert solid vehicle, or matrix, in which a drug is uniformly suspended, including in the form of tablets or small beads. In some embodiments, the matrix is a gelling material including gelatin, methylcellulose, gum tragacanth, Veegum, and alginic acid. In some embodiments, the matrix is a polymer including polylactic acid copolymer, polyacrylate, methacrylate, polyester, ethylene—vinyl acetate copolymer (EVA), polyglycolide, polylactide, and silicone. In some embodiments, the modified release formulation is a slow-release pellet, bead, or granule. In some embodiments, the modified release formulation is an extended release tablet where the solubility of a drug is modified for extended release. In some embodiments, the extended release tablet is formed by using the nonionized base or acid form of the drug. In some embodiments, the extended release tablet is formed by granulating the drug with excipients (including stearic acid, castor wax, high-molecular-weight polyethylene glycol (Carbowax), glyceryl monostearate, white wax, spermaceti

oil, magnesium stearate and hydrogenated vegetable oil (Sterotex)) to decrease the aqueous solubility of the drug. In some embodiments, the modified release formulation is an ion-exchange preparation whereby an anionic or cationic drug is complexed with an oppositely charged ionic resin to form an insoluble nonabsorbable resin–drug complex.

[0071] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation further comprises one or more pharmaceutically acceptable excipients. Examples of pharmaceutically acceptable excipients that may be present in the composition include but are not limited to fillers/vehicles, solvents/co-solvents, preservatives, antioxidants, suspending agents, surfactants, antifoaming agents, buffering agents, chelating agents, sweeteners, flavoring agents, binders, extenders, disintegrants, diluents, lubricants, fillers, wetting agents, glidants, and combinations thereof.

[0072] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation can further comprise one or more exemplary fillers. Examples of exemplary fillers include cellulose and cellulose derivatives such as microcrystalline cellulose; starches such as dry starch, hydrolyzed starch, and starch derivatives such as corn starch; cyclodextrin; sugars such as powdered sugar and sugar alcohols such as lactose, mannitol, sucrose and sorbitol; inorganic fillers such as aluminum hydroxide gel, precipitated calcium carbonate, carbonate, magnesium aluminometasilicate, dibasic calcium phosphate; and sodium chloride, silicon dioxide, titanium dioxide, titanium oxide, dicalcium phosphate dihydrate, calcium sulfate, alumina, kaolin, talc, or combinations thereof. Fillers may be present in the composition from about 20 wt% to about 65 wt%, about 20 wt% to about 50 wt%, about 20 wt% to about 40 wt%, about 45 wt% to about 65 wt%, about 50 wt% to about 65 wt%, or about 55 wt% to about 65 wt% of the total weight of the composition, or any value between these ranges.

[0073] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation further comprises one or more disintegrants. Examples of disintegrants include starches, alginic acid, crosslinked polymers such as crosslinked polyvinylpyrrolidone, croscarmellose sodium, potassium starch glycolate, sodium starch glycolate, clays, celluloses, starches, gums, or combinations thereof. Disintegrants may be present in the composition from about 1 wt% to about 10 wt%, about 1 wt% to about 9 wt%, about 1 wt% to about 8 wt%, about 1 wt% to about 7 wt%, about 1 wt% to about 6 wt%, or about 1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[0074] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation further comprises one or more binders, including but not limited to celluloses such as hydroxypropylcellulose, methyl cellulose, and hydroxypropylmethylcellulose; starches such as corn starch, pregelatinized starch, and hydroxypropyl starch; waxes and natural and synthetic gums such as acacia, tragacanth, sodium alginate; synthetic polymers such as polymethacrylates and polyvinylpyrrolidone; and povidone, dextrin, pullulane, agar, gelatin, tragacanth, macrogol, or combinations thereof. Binders may be present in the composition from about 0.5 wt% to about 5 wt%, about 0.5 wt% to about 4 wt%, about 0.5 wt% to about 3 wt%, about 0.5 wt% to about 2 wt%, or about 0.5 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[0075] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation further comprises one or more wetting agents, including but not limited to oleic acid, glyceryl monostearate, sorbitan mono-oleate, sorbitan monolaurate, triethanolamine oleate, polyoxyethylene sorbitan mono-oleate, polyoxyethylene sorbitan monolaurate, sodium oleate, sodium lauryl sulfate, poloxamers, poloxamer 188, polyoxyethylene

ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, polyethylene glycol fatty acid esters, polyoxyethylene hardened castor oil, polyoxyethylene alkyl ethers, polysorbates, cetyl alcohol, glycerol fatty acid esters (for example, triacetin, glycerol monostearate, etc.), polyoxymethylene stearate, sodium lauryl sulfate, sorbitan fatty acid esters, sucrose fatty acid esters, benzalkonium chloride, polyethoxylated castor oil, and combinations thereof. Wetting agents may be present in the composition from about 0.1 wt% to about 1 wt%, about 0.1 wt% to about 2 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 4 wt%, or about 0.1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[0076] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation further comprises one or more lubricants, including but not limited to stearic acid, magnesium stearate, calcium hydroxide, talc, corn starch, sodium stearyl fumarate, alkali-metal and alkaline earth metal salts, waxes, boric acid, sodium benzoate, sodium acetate, sodium chloride, leucine, polyethylene glycol (PEG), a methoxypolyethylene glycol, propylene glycol, sodium oleate, glyceryl behenate, glyceryl palmitostearate, glyceryl benzoate, magnesium lauryl sulfate, sodium lauryl sulfate, and combinations thereof. Lubricants may be present in the composition from about 0.1 wt% to about 5 wt%, about 0.1 wt% to about 4 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 2 wt%, or about 0.1 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[0077] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation further comprises one or more glidants, including but not limited to colloidal silicon dioxide, talc, sodium lauryl sulfate, native starch, and combinations thereof. Glidants may be present in the composition from about 0.05 wt% to about 1 wt%, about 0.05

wt% to about 0.9 wt%, about 0.05 wt% to about 0.8 wt%, about 0.05 wt% to about 0.5 wt%, or about 0.05 wt% to about 0.1 wt% of the total weight of the composition, or any value between these ranges.

[0078] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation is a tablet and further comprises a top coat, such as hydroxypropyl-methylcellulose coating or polyvinyl alcohol coating, and are available under the trade name Opadry, such as Opadry White, Opadry II (Opadry is a registered trademark of BPSI Holdings LLC, Wilmington, DE, USA). Top coats may be present in the composition from about 1 wt% to about 10 wt%, about 1 wt% to about 9 wt%, about 1 wt% to about 8 wt%, about 1 wt% to about 7 wt%, about 1 wt% to about 6 wt%, or about 1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[0079] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation can further comprise one or more preservative agents. Examples of preservative agents include sodium benzoate, paraoxybenzoic acid esters, methyl, ethyl, butyl, and propyl parabens, chlorobutanol, benzyl alcohol, phenylethylalcohol, dehydroacetic acid, sorbic acid, benzalkonium chloride (BKC), benzethonium chloride, phenol, phenylmercuric nitrate, thimerosal, or combinations thereof. Preservative agents can be included in the liquid dosage form. The preservative agents can be in an amount sufficient to extend the shelf-life or storage stability, or both, of the liquid dosage form. Preservatives may be present in the composition from about 0.05 wt% to about 1 wt%, about 0.05 wt% to about 0.9 wt%, about 0.05 wt% to about 0.8 wt%, about 0.05 wt% to about 0.5 wt%, or about 0.05 wt% to about 0.1 wt% of the total weight of the composition, or any value between these ranges.

[0080] In some embodiments of the pharmaceutical formulation described herein, the pharmaceutical formulation can further comprise one or more flavoring agents. Examples of flavoring agents include synthetic flavor oils and flavoring aromatics and/or natural oils, extracts from plants leaves, flowers, fruits, and so forth and the like or any combinations thereof. Additional examples include cinnamon oil, oil of wintergreen, peppermint oils, clove oil, bay oil, anise oil, eucalyptus, thyme oil, cedar leaf oil, oil of nutmeg, oil of sage, oil of bitter almonds, and cassia oil and the like or any combinations thereof. Also useful as flavors are vanilla, citrus oil, including lemon, orange, grape, lime and grapefruit, and fruit essences, including apple, banana, pear, peach, strawberry, raspberry, cherry, plum, pineapple, apricot, strawberry flavor, tutti-fruity flavor, mint flavor, or any combinations thereof. Flavoring agents may be present in the composition from about 0.1 wt% to about 5 wt%, about 0.1 wt% to about 4 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 2 wt%, or about 0.1 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[0081] The pharmaceutical formulation can generally be in any physical form suitable for use in treating a subject. These forms can be referred to as a unit dosage form, such as an individual pill or tablet. In some examples, the pharmaceutical compositions can be formulated as tablets, capsules, granules, powders, liquids, suspensions, gels, syrups, slurries, suppositories, patches, nasal sprays, aerosols, injectables, implantable sustained-release formulations, or mucoadherent films. In some examples, the pharmaceutical formulation may be formed as a tablet, a bi-layer tablet, a capsule, a multiparticulate, a drug coated sphere, a matrix tablet, or a multicore tablet. A physical form can be selected according to the desired method of treatment.

[0082] Pharmaceutical formulation can be manufactured by various conventional methods such as conventional mixing, dissolving, granulating, dragee-making, levigating,

emulsifying, encapsulating, entrapping, or lyophilizing processes. Pharmaceutical formulations can be formulated in a conventional manner using one or more physiologically acceptable carriers, diluents, excipients or auxiliaries that facilitate processing of the active agent into preparations that can be used pharmaceutically. Proper formulation can be selected upon the oral route of administration chosen.

[0083] In some embodiments, the pharmaceutical formulation is a core tablet, or a tablet within a tablet, whereby the inner core is used for the slow-drug-release component, and the outside shell contains a rapid-release dose of drug. In some embodiments, pharmaceutical formulation is achieved via microencapsulation whereby microscopic drug particles are encapsulated with a special coating material, such as ethylcellulose. In some embodiments, the pharmaceutical formulation is an osmotic drug delivery system in the form of a tablet which contains an outside semipermeable membrane and an inner core filled with a mixture of drug and osmotic agent (salt solution). In some embodiments, the pharmaceutical formulation is a gastroretentive system that can remain in the gastric region for several hours and prolong the gastric residence time of a drug. In some embodiments, the pharmaceutical formulation is a combination of any of the above-described embodiments.

[0084] For oral administration, the pharmaceutical formulation can combine minoxidil with another pharmaceutical agent with one or more pharmaceutically acceptable carriers well known in the art. Such carriers facilitate formulation as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. For oral solid formulations such as, for example, powders, capsules and tablets, suitable excipients include fillers such as sugars, such as lactose, sucrose, mannitol and sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum

tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP); granulating agents; and binding agents. If desired, disintegrating agents may be added, such as the cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. If desired, solid dosage forms may be sugar-coated or enteric-coated using standard techniques.

[0085] For oral liquid preparations such as, for example, suspensions, elixirs and solutions, suitable carriers, excipients or diluents include water, glycols, oils, alcohols, etc. Additionally, flavoring agents, preservatives, coloring agents and the like can be added. For buccal administration, the compositions may take the form of tablets, lozenges, etc. formulated in conventional manner.

[0086] In some examples, modified release formulations may comprise a matrix selected from microcrystalline cellulose, sodium carboxymethylcellulose, hydroxyalkylcelluloses such as hydroxy propyl methylcellulose and hydroxypropylcellulose, polyethylene oxide, alkylcelluloses such as methylcellulose and ethylcellulose, polyethylene glycol, polyvinylpyrrolidone, cellulose acetate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl acetate phthalate, polyalkylmethacrylates, polyvinyl acetate and mixtures thereof.

METHODS OF TREATING HAIR LOSS

[0087] Embodiments described herein are directed to a method of treating hair loss, comprising administering to a subject in need thereof a daily dose of a composition comprising a modified release formulation of minoxidil.

[0088] In some embodiments of the method described herein, the composition further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof. In some embodiments, the composition further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[0089] In any embodiment of the method described herein, the non-steroid anti-androgen is selected from flutamide, clascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof. In any embodiment, the 17 α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof. In any embodiment, the 19-norprogesterone derivative is nomegestrol acetate. In any embodiment, 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof. In any embodiment, the 17 α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof. In any embodiment, the 5-alpha reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof. In any embodiment, the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof. In any embodiment, the GnRH analog is a GnRH agonist wherein the GnRH agonist is selected from goserelin, buserelin, leuprorelin, and

combinations thereof. In any embodiment, the GnRH analog is a GnRH antagonist wherein the GnRH antagonist is cetrorelix. In any embodiment, the prostaglandin F2 α analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof. In any embodiment, the prostamide is bimatoprost. In any embodiment, the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof. In any embodiment, the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof. In any embodiment, the prostaglandin E2 analog is sulprostone. In any embodiment, the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof. In any embodiment, the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof. In any embodiment, the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof. In any embodiment, the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.

[0090] In some embodiments of the method described herein, the composition is administered orally. In some embodiments, the minoxidil is in an orally dissolving tablet.

[0091] In some embodiments of the method described herein, the modified release formulation is an extended release formulation, a controlled release formulation, or a delayed release formulation.

[0092] In some embodiments of the method described herein, the extended release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration. In some embodiments of the pharmaceutical formulation

described herein, the extended release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 18 hours after the oral administration. In some embodiments described herein, the extended release formulation releases about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 98% of the daily dose of minoxidil within about 12 to about 18 hours after the oral administration, or any range within these values.

[0093] In some embodiments of the method described herein, the controlled release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration. In some embodiments, the controlled-release formulation releases about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 98% of the daily dose of minoxidil within about 12 hours after the oral administration, or any range within these values.

[0094] In some embodiments of the method described herein, the delayed release formulation releases the daily dose of minoxidil within about 6 hours after the oral administration. In some embodiments, the delayed release formulation releases the daily dose of minoxidil in multiple distinct releases each within about 18 hours after the oral administration.

[0095] In some embodiments of the method described herein, the subject in need thereof is diagnosed with hairloss. In some embodiments, the hair loss is selected from male pattern hair loss, female pattern hair loss, hereditary hair loss, telogen effluvium, alopecia areata, central centrifugal cicatricial alopecia, lichen planopilaris, or traction alopecia.

[0096] In some embodiments of the method described herein, the administering results in hair regrowth. In some embodiments, the administering results in hair regrowth within about 1 months to about 12 months. In some embodiments, the administering results in hair regrowth

within about 6 months. In some embodiments, the administering results in hair regrowth within about 4 months. In some embodiments, the administering results in hair regrowth within about 3 months. In some embodiments, the administering results in hair regrowth within about 1 month, about 2 months, about 3 months, about 4 months, about 5 months, about 6 months, about 7 months, about 8 months, about 9 months, about 10 months, about 11 months, about 12 months, or any range within these values. In some embodiments, the administering results in an increased improvement in hair growth as compared to administration of an immediate-release dosage form of minoxidil.

[0097] Use of the described methods and pharmaceutical formulations can result in a reduction or elimination of disease, symptom, or other undesired property in a subject relative to a control population (for example, without treatment by the described methods and materials). The reduction can generally be reduced by any amount. For example, the reduction can be at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 96%, at least about 97%, at least about 98%, at least about 99%, and in an ideal situation, about 100% reduction (complete elimination of disease, symptom, virus concentration, or other undesired property).

[0098] In some embodiments of the method described herein, the subject is diagnosed with at least one cardiac condition selected from heart disease, chronic congestive heart failure, cardiomyopathy, tachyarrhythmia, renal disease, preexisting pulmonary hypertension, and chronic congestive heart failure not secondary to hypertension.

[0099] In some embodiments of the method described herein, the subject is taking at least one of the following for treatment of the at least one cardiac condition, an anti-

hypertensive, an ace-inhibitor, an angiotensin receptor blocker, a direct renin inhibitor, a loop diuretic, a thiazide diuretic, a calcium channel blocker, a beta blocker, an anti-arrhythmic, and a diuretic.

[00100] In some embodiments of the method described herein, the pharmaceutical formulation is administered only once daily. In some embodiments, the pharmaceutical formulation is administered at least once daily. In some embodiments, the pharmaceutical formulation is administered four times per day. In some embodiments, the pharmaceutical formulation is administered three times per day. In some embodiments, the pharmaceutical formulation is administered two times per day.

[00101] In some embodiments of the method described herein, the composition is administered daily for at least about 3 months with substantially no adverse effects and substantially no cardiac effects. In some embodiments, the composition is administered daily for at least 4 months with substantially no adverse effects and substantially no cardiac effects. In some embodiments, the composition is administered daily for at least 6 months with substantially no adverse effects and substantially no cardiac effects. In some embodiments, the composition is administered daily for at least 1 year with substantially no adverse effects and substantially no cardiac effects. In some embodiments, the composition is administered daily indefinitely with substantially no adverse effects and substantially no cardiac effects.

[00102] In some embodiments of the method described herein, administering results in substantially no cardiac effects. In some embodiments, the cardiac effects are selected from tachycardia, hypotension, premature ventricular contractions, and other tachyarrhythmias.

[00103] In some embodiments of the method described herein, administering results in hair regrowth with substantially no clinically significant hemodynamic changes in blood

pressure. In some embodiments, administering results in hair regrowth with substantially no cardiac effects. In some embodiments, the daily dose of minoxidil results in substantially no cardiac effects or hemodynamic effects as compared to administration of an immediate-release oral minoxidil used to treat hypertension. In some embodiments, the daily dose of minoxidil results in substantially no cardiac effects as compared to administration of an immediate-release oral minoxidil used to treat hypertension.

[00104] In some embodiments of the method described herein, the daily dose amount of minoxidil results in fewer cardiac effects or hemodynamic effects as compared to administration of an amount of an immediate-release oral minoxidil used to treat hypertension. In some embodiments, the cardiac effects are selected from tachycardia, hypotension, premature ventricular contractions, and other tachyarrhythmias.

[00105] In some embodiments of the method described herein, the daily dose of minoxidil is about 25% to about 500% of the amount of the immediate-release oral minoxidil used to treat hypertension. In some embodiments, the daily dose of minoxidil is about 10% to about 90% of the amount of the immediate-release oral minoxidil used to treat hypertension. In some embodiments, the daily dose of minoxidil is about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, about 125%, about 150%, about 175%, about 200%, about 225%, about 250%, about 275%, about 300%, about 325%, about 350%, about 375%, about 400%, about 425%, about 450%, about 475%, about 500% of the amount of the immediate-release oral minoxidil used to treat hypertension, or any range within these values.

[00106] In some embodiments of the method described herein, the minoxidil is in a therapeutically effective amount. In some embodiments, the one or more active agents are in a therapeutically effective amount. In some embodiments, the pharmaceutical formulation comprises minoxidil in a subtherapeutic amount. In some embodiments, the pharmaceutical formulation comprises one or more active agents in a subtherapeutic amount. In some embodiments, the pharmaceutical formulation comprises minoxidil and one or more active agents wherein the minoxidil and the one or more active agents are each in subtherapeutic amounts.

[00107] In some embodiments of the method described herein, the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.5 mg to about 2.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.625 mg to about 7.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg. In some embodiments, the daily dose of minoxidil is about 0.25 mg to about 20 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.125 mg to about 100 mg. In some embodiments, the daily dose of minoxidil is about 2.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.125 mg, about 0.25 mg, about 5 mg, about 0.625 mg, about 0.75 mg, about 1 mg, about 1.25 mg, about 1.5 mg, about 2 mg, about 2.5 mg, about 3 mg, about 3.5 mg, about 4 mg, about 4.5 mg, about 5 mg, about 5.5 mg, about 6 mg, about 6.5 mg, about 7 mg, about 7.5 mg, about 8 mg, about 9 mg, about 10 mg, about 12 mg, about 15mg, about 18 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, about 100 mg, or any range within these values.

[00108] In some embodiments of the method described herein, the daily dose of minoxidil is administered to a subject in an amount of about 0.00625 mg/kg/day to about 0.375 mg/kg/day. In some embodiments, the daily dose of the minoxidil is about 0.00625 mg/kg/day to about 0.5 mg/kg/day. In some embodiments, the daily dose of the minoxidil is about 0.00625 mg/kg/day, about 0.0125 mg/kg/day, about 0.025 mg/kg/day, about 0.0375 mg/kg/day, about 0.05 mg/kg/day, about 0.0625 mg/kg/day, about 0.075 mg/kg/day, about 0.0875 mg/kg/day, about 0.1 mg/kg/day, about 0.125 mg/kg/day, about 0.25 mg/kg/day, about 0.5 mg/kg/day, or any range within these values.

[00109] In some embodiments of the method described herein, the minoxidil is in an amount of about 0.625 mg four times per day.

[00110] In some embodiments of the method described herein, the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration.

[00111] In some embodiments of the method described herein, the oral administration of the daily dose minoxidil results in a C_{max} of about 0.25 ng/ml to about 20 ng/ml. In some embodiments, the oral administration of the daily dose minoxidil results in a C_{max} that is devoid of cardiac effects.

[00112] In some embodiments of the method described herein, the subject has a minoxidil plasma concentration versus time curve with a T_{max} of about 30 to about 360 minutes. In some embodiments, the oral administration of the daily dose of minoxidil results in a delayed release that results in a T_{max} between both 30 to 360 minutes and between 390 minutes and 1080 minutes.

[00113] In some embodiments of the method described herein, the oral administration of the daily dose of modified release minoxidil results in an AUC that is greater than an equivalent dose of an immediate release formulation.

[00114] In some embodiments of the method described herein, the oral administration results in a half-life of the daily dose of minoxidil of about 4 hours to about 24 hours. In some embodiments, the oral administration results in a half-life of the daily dose of minoxidil of about 4 hours, about 5 hours, about 6 hours, about 7 hours, about 8 hours, about 9 hours, about 10 hours, about 12 hours, about 14 hours, about 16 hours, about 18 hours, about 20 hours, about 22 hours, about 24 hours, or any range within these values.

[00115] Embodiments described herein are directed to a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

[00116] In some embodiments of the method described herein, the composition further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5- α reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof. In some embodiments, the composition further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00117] Embodiments described herein are directed to a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a Tmax of about 30 to about 360 minutes.

[00118] In some embodiments of the method described herein, the composition further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiolactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof. In some embodiments, the composition further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00119] Embodiments described herein are directed to a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a Cmax of about 0.25 ng/ml to about 20 ng/ml.

[00120] In some embodiments of the method described herein, the composition further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiolactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an

alopecia areata medication, a supplement, and combinations thereof. In some embodiments, the composition further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00121] In some embodiments of the method described herein, the modified release formulation is an inert solid vehicle, or matrix, in which a drug is uniformly suspended, including in the form of tablets or small beads. In some embodiments, the matrix is a gelling material including gelatin, methylcellulose, gum tragacanth, Veegum, and alginic acid. In some embodiments, the matrix is a polymer including polylactic acid copolymer, polyacrylate, methacrylate, polyester, ethylene—vinyl acetate copolymer (EVA), polyglycolide, polylactide, and silicone. In some embodiments, the modified release formulation is a slow-release pellet, bead, or granule. In some embodiments, the modified release formulation is an extended release tablet where the solubility of a drug is modified for extended release. In some embodiments, the extended release tablet is formed by using the nonionized base or acid form of the drug. In some embodiments, the extended release tabled is formed by granulating the drug with excipients (including stearic acid, castor wax, high-molecular-weight polyethylene glycol (Carbowax), glyceryl monostearate, white wax, spermaceti oil, magnesium stearate and hydrogenated vegetable oil (Sterotex)) to decrease the aqueous solubility of the drug. In some embodiments, the modified release formulation is an ion-exchange preparation whereby an anionic or cationic drug is complexed with an oppositely charged ionic resin to form an insoluble nonabsorbable resin–drug complex.

[00122] In some embodiments of the method described herein, the modified release formulation further comprises one or more pharmaceutically acceptable excipients. Examples of pharmaceutically acceptable excipients that may be present in the composition include but are

not limited to fillers/vehicles, solvents/co-solvents, preservatives, antioxidants, suspending agents, surfactants, antifoaming agents, buffering agents, chelating agents, sweeteners, flavoring agents, binders, extenders, disintegrants, diluents, lubricants, fillers, wetting agents, glidants, and combinations thereof.

[00123] In some embodiments of the method described herein, the modified release formulation can further comprise one or more exemplary fillers. Examples of exemplary fillers include cellulose and cellulose derivatives such as microcrystalline cellulose; starches such as dry starch, hydrolyzed starch, and starch derivatives such as corn starch; cyclodextrin; sugars such as powdered sugar and sugar alcohols such as lactose, mannitol, sucrose and sorbitol; inorganic fillers such as aluminum hydroxide gel, precipitated calcium carbonate, carbonate, magnesium aluminometasilicate, dibasic calcium phosphate; and sodium chloride, silicon dioxide, titanium dioxide, titanium oxide, dicalcium phosphate dihydrate, calcium sulfate, alumina, kaolin, talc, or combinations thereof. Fillers may be present in the composition from about 20 wt% to about 65 wt%, about 20 wt% to about 50 wt%, about 20 wt% to about 40 wt%, about 45 wt% to about 65 wt%, about 50 wt% to about 65 wt%, or about 55 wt% to about 65 wt% of the total weight of the composition, or any value between these ranges.

[00124] In some embodiments of the method described herein, the modified release formulation further comprises one or more disintegrants. Examples of disintegrants include starches, alginic acid, crosslinked polymers such as crosslinked polyvinylpyrrolidone, croscarmellose sodium, potassium starch glycolate, sodium starch glycolate, clays, celluloses, starches, gums, or combinations thereof. Disintegrants may be present in the composition from about 1 wt% to about 10 wt%, about 1 wt% to about 9 wt%, about 1 wt% to about 8 wt%, about

1 wt% to about 7 wt%, about 1 wt% to about 6 wt%, or about 1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[00125] In some embodiments of the method described herein, the modified release formulation further comprises one or more binders, including but not limited to celluloses such as hydroxypropylcellulose, methyl cellulose, and hydroxypropylmethylcellulose; starches such as corn starch, pregelatinized starch, and hydroxypropyl starch; waxes and natural and synthetic gums such as acacia, tragacanth, sodium alginate; synthetic polymers such as polymethacrylates and polyvinylpyrrolidone; and povidone, dextrin, pullulane, agar, gelatin, tragacanth, macrogol, or combinations thereof. Binders may be present in the composition from about 0.5 wt% to about 5 wt%, about 0.5 wt% to about 4 wt%, about 0.5 wt% to about 3 wt%, about 0.5 wt% to about 2 wt%, or about 0.5 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[00126] In some embodiments of the method described herein, the modified release formulation further comprises one or more wetting agents, including but not limited to oleic acid, glyceryl monostearate, sorbitan mono-oleate, sorbitan monolaurate, triethanolamine oleate, polyoxyethylene sorbitan mono-oleate, polyoxyethylene sorbitan monolaurate, sodium oleate, sodium lauryl sulfate, poloxamers, poloxamer 188, polyoxyethylene ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, polyethylene glycol fatty acid esters, polyoxyethylene hardened castor oil, polyoxyethylene alkyl ethers, polysorbates, cetyl alcohol, glycerol fatty acid esters (for example, triacetin, glycerol monostearate, etc.), polyoxymethylene stearate, sodium lauryl sulfate, sorbitan fatty acid esters, sucrose fatty acid esters, benzalkonium chloride, polyethoxylated castor oil, and combinations thereof. Wetting agents may be present in the composition from about 0.1 wt% to about 1 wt%, about 0.1 wt% to about 2 wt%, about 0.1

wt% to about 3 wt%, about 0.1wt% to about 4 wt%, or about 0.1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[00127] In some embodiments of the method described herein, the modified release formulation further comprises one or more lubricants, including but not limited to stearic acid, magnesium stearate, calcium hydroxide, talc, corn starch, sodium stearyl fumarate, alkali-metal and alkaline earth metal salts, waxes, boric acid, sodium benzoate, sodium acetate, sodium chloride, leucine, polyethylene glycol (PEG), a methoxypolyethylene glycol, propylene glycol, sodium oleate, glyceryl behenate, glyceryl palmitostearate, glyceryl benzoate, magnesium lauryl sulfate, sodium lauryl sulfate, and combinations thereof. Lubricants may be present in the composition from about 0.1 wt% to about 5 wt%, about 0.1 wt% to about 4 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 2 wt%, or about 0.1 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[00128] In some embodiments of the method described herein, the modified release formulation further comprises one or more glidants, including but not limited to colloidal silicon dioxide, talc, sodium lauryl sulfate, native starch, and combinations thereof. Glidants may be present in the composition from about 0.05 wt% to about 1 wt%, about 0.05 wt% to about 0.9 wt%, about 0.05 wt% to about 0.8 wt%, about 0.05 wt% to about 0.5 wt%, or about 0.05 wt% to about 0.1 wt% of the total weight of the composition, or any value between these ranges.

[00129] In some embodiments of the method described herein, the modified release formulation is a tablet and further comprises a top coat, such as hydroxypropyl-methylcellulose coating or polyvinyl alcohol coating, and are available under the trade name Opadry, such as Opadry White, Opadry II (Opadry is a registered trademark of BPSI Holdings LLC, Wilmington, DE, USA). Top coats may be present in the composition from about 1 wt% to about 10 wt%,

about 1 wt% to about 9 wt%, about 1 wt% to about 8 wt%, about 1 wt% to about 7 wt%, about 1 wt% to about 6 wt%, or about 1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[00130] In some embodiments of the method described herein, the modified release formulation can further comprise one or more preservative agents. Examples of preservative agents include sodium benzoate, paraoxybenzoic acid esters, methyl, ethyl, butyl, and propyl parabens, chlorobutanol, benzyl alcohol, phenylethylalcohol, dehydroacetic acid, sorbic acid, benzalkonium chloride (BKC), benzethonium chloride, phenol, phenylmercuric nitrate, thimerosal, or combinations thereof. Preservative agents can be included in the liquid dosage form. The preservative agents can be in an amount sufficient to extend the shelf-life or storage stability, or both, of the liquid dosage form. Preservatives may be present in the composition from about 0.05 wt% to about 1 wt%, about 0.05 wt% to about 0.9 wt%, about 0.05 wt% to about 0.8 wt%, about 0.05 wt% to about 0.5 wt%, or about 0.05 wt% to about 0.1 wt% of the total weight of the composition, or any value between these ranges.

[00131] In some embodiments of the method described herein, the modified release formulation can further comprise one or more flavoring agents. Examples of flavoring agents include synthetic flavor oils and flavoring aromatics and/or natural oils, extracts from plants leaves, flowers, fruits, and so forth and the like or any combinations thereof. Additional examples include cinnamon oil, oil of wintergreen, peppermint oils, clove oil, bay oil, anise oil, eucalyptus, thyme oil, cedar leaf oil, oil of nutmeg, oil of sage, oil of bitter almonds, and cassia oil and the like or any combinations thereof. Also useful as flavors are vanilla, citrus oil, including lemon, orange, grape, lime and grapefruit, and fruit essences, including apple, banana, pear, peach, strawberry, raspberry, cherry, plum, pineapple, apricot, strawberry flavor, tutti-fruity

flavor, mint flavor, or any combinations thereof. Flavoring agents may be present in the composition from about 0.1 wt% to about 5 wt%, about 0.1 wt% to about 4 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 2 wt%, or about 0.1 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[00132] In some embodiments of the method described herein, the modified release formulation can generally be in any physical form suitable for use in treating a subject. These forms can be referred to as a unit dosage form, such as an individual pill or tablet. In some examples, the pharmaceutical compositions can be formulated as tablets, capsules, granules, powders, liquids, suspensions, gels, syrups, slurries, suppositories, patches, nasal sprays, aerosols, injectables, implantable sustained-release formulations, or mucoadherent films. In some examples, the pharmaceutical formulation may be formed as a tablet, a bi-layer tablet, a capsule, a multiparticulate, a drug coated sphere, a matrix tablet, or a multicore tablet. A physical form can be selected according to the desired method of treatment.

[00133] In some embodiments of the method described herein, the modified release formulation can be manufactured by various conventional methods such as conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes. Modified release formulations can be formulated in a conventional manner using one or more physiologically acceptable carriers, diluents, excipients or auxiliaries that facilitate processing of the active agent into preparations that can be used pharmaceutically. Proper formulation can be selected upon the oral route of administration chosen.

[00134] In some embodiments, the modified release formulation is a core tablet, or a tablet within a tablet, whereby the inner core is used for the slow-drug-release component, and the outside shell contains a rapid-release dose of drug. In some embodiments, the modified

release formulation is achieved via microencapsulation whereby microscopic drug particles are encapsulated with a special coating material, such as ethylcellulose. In some embodiments, the modified release formulation is an osmotic drug delivery system in the form of a tablet which contains an outside semipermeable membrane and an inner core filled with a mixture of drug and osmotic agent (salt solution). In some embodiments, the modified release formulation is a gastroretentive system that can remain in the gastric region for several hours and prolong the gastric residence time of a drug. In some embodiments, the modified release formulation is a combination of any of the above-described embodiments.

[00135] In some embodiments of the method described herein, for oral administration, the modified release formulation can combine minoxidil with another pharmaceutical agent with one or more pharmaceutically acceptable carriers well known in the art. Such carriers facilitate formulation as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. For oral solid formulations such as, for example, powders, capsules and tablets, suitable excipients include fillers such as sugars, such as lactose, sucrose, mannitol and sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP); granulating agents; and binding agents. If desired, disintegrating agents may be added, such as the cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. If desired, solid dosage forms may be sugar-coated or enteric-coated using standard techniques.

[00136] For oral liquid preparations such as, for example, suspensions, elixirs and solutions, suitable carriers, excipients or diluents include water, glycols, oils, alcohols, etc. Additionally, flavoring agents, preservatives, coloring agents and the like can be added. For

buccal administration, the compositions may take the form of tablets, lozenges, etc. formulated in conventional manner.

[00137] In some embodiments of the method described herein, the modified release formulations may comprise a matrix selected from microcrystalline cellulose, sodium carboxymethylcellulose, hydroxyalkylcelluloses such as hydroxy propyl methylcellulose and hydroxypropylcellulose, polyethylene oxide, alkylcelluloses such as methylcellulose and ethylcellulose, polyethylene glycol, polyvinylpyrrolidone, cellulose acetate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl acetate phthalate, polyalkylmethacrylates, polyvinyl acetate and mixtures thereof.

KIT

[00138] Embodiments described herein are directed to a kit comprising a slow modified release vehicle comprising oral minoxidil.

[00139] In some embodiments of the kit described herein, the slow modified release vehicle further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof. In some embodiments, the slow modified release vehicle further comprises medrogestone, cetirizine, setipiprant, valproic acid, and combinations thereof.

[00140] In any embodiment of the kit described herein, the non-steroid anti-androgen is selected from flutamide, clascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof. In any embodiment, the 17 α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof. In any embodiment, the 19-norprogesterone derivative is nomegestrol acetate. In any embodiment, 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof. In any embodiment, the 17 α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof. In any embodiment, the 5-alpha reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof. In any embodiment, the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof. In any embodiment, the GnRH analog is a GnRH agonist wherein the GnRH agonist is selected from goserelin, buserelin, leuprorelin, and combinations thereof. In any embodiment, the GnRH analog is a GnRH antagonist wherein the GnRH antagonist is cetrorelix. In any embodiment, the prostaglandin F2 α analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof. In any embodiment, the prostamide is bimatoprost. In any embodiment, the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof. In any embodiment, the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof. In any embodiment, the prostaglandin E2 analog is sulprostone. In any embodiment, the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof. In any embodiment, the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib,

deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof. In any embodiment, the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof. In any embodiment, the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.

[00141] In some embodiments of the kit described herein, the kit comprises an information sheet. In some embodiments, the information sheet comprises instructions for selecting an oral dosage form based on a body weight of a patient. In some embodiment, the information sheet comprises instructions for selecting a daily dose of minoxidil.

[00142] In some embodiments of the kit described herein, the information sheet comprises a warning of adverse effects. In some embodiments, the adverse effects are selected from peripheral edema and hirsutism.

[00143] In some embodiments of the kit described herein, the minoxidil is administered only once daily. In some embodiments, the minoxidil is administered at least once daily. In some embodiments, the minoxidil is administered four times per day. In some embodiments, the minoxidil is administered three times per day. In some embodiments, the minoxidil is administered two times per day.

[00144] In some embodiments of the kit described herein, the slow modified release vehicle releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration. In some embodiments of the pharmaceutical formulation described herein, the extended release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 18 hours after the oral administration. In some embodiments described

herein, the slow modified release vehicle releases about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 98% of the daily dose of minoxidil within about 18 hours after the oral administration, or any range within these values.

[00145] In some embodiments of the kit described herein, the minoxidil is in a therapeutically effective amount. In some embodiments, the one or more active agents are in a therapeutically effective amount. In some embodiments, the pharmaceutical formulation comprises minoxidil in a subtherapeutic amount. In some embodiments, the pharmaceutical formulation comprises one or more active agents in a subtherapeutic amount. In some embodiments, the pharmaceutical formulation comprises minoxidil and one or more active agents wherein the minoxidil and the one or more active agents are each in subtherapeutic amounts.

[00146] In some embodiments of the kit described herein, the daily dose of minoxidil is about 25% to about 500% of the amount of the immediate-release oral minoxidil used to treat hypertension. In some embodiments, the daily dose of minoxidil is about 10% to about 90% of the amount of the immediate-release oral minoxidil used to treat hypertension. In some embodiments, the daily dose of minoxidil is about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 100%, about 125%, about 150%, about 175%, about 200%, about 225%, about 250%, about 275%, about 300%, about 325%, about 350%, about 375%, about 400%, about 425%, about 450%, about 475%, about 500% of the amount of the immediate-release oral minoxidil used to treat hypertension, or any range within these values.

[00147] In some embodiments of the kit described herein, the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.5 mg to about 2.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.625 mg to about 7.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg. In some embodiments, the daily dose of minoxidil is about 0.25 mg to about 20 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.125 mg to about 100 mg. In some embodiments, the daily dose of minoxidil is about 2.5 mg. In some embodiments, the daily dose of minoxidil is in an amount of about 0.125 mg, about 0.25 mg, about 5 mg, about 0.625 mg, about 0.75 mg, about 1 mg, about 1.25 mg, about 1.5 mg, about 2 mg, about 2.5 mg, about 3 mg, about 3.5 mg, about 4 mg, about 4.5 mg, about 5 mg, about 5.5 mg, about 6 mg, about 6.5 mg, about 7 mg, about 7.5 mg, about 8 mg, about 9 mg, about 10 mg, about 12 mg, about 15mg, about 18 mg, about 20 mg, about 25 mg, about 30 mg, about 35 mg, about 40 mg, about 45 mg, about 50 mg, about 55 mg, about 60 mg, about 65 mg, about 70 mg, about 75 mg, about 80 mg, about 85 mg, about 90 mg, about 95 mg, about 100 mg, or any range within these values.

[00148] In some embodiments of the kit described herein, the daily dose of minoxidil is administered to a subject in an amount of about 0.00625 mg/kg/day to about 0.375 mg/kg/day. In some embodiments, the daily dose of the minoxidil is about 0.00625 mg/kg/day to about 0.5 mg/kg/day. In some embodiments, the daily dose of the minoxidil is about 0.00625 mg/kg/day, about 0.0125 mg/kg/day, about 0.025 mg/kg/day, about 0.0375 mg/kg/day, about 0.05 mg/kg/day, about 0.0625 mg/kg/day, about 0.075 mg/kg/day, about 0.0875 mg/kg/day, about 0.1 mg/kg/day, about 0.125 mg/kg/day, about 0.25 mg/kg/day, about 0.5 mg/kg/day, or any range within these values.

[00149] In some embodiments of the method described herein, the daily dose of minoxidil is in an amount of about 0.625 mg four times per day.

[00150] In some embodiments of the kit described herein, the oral administration of the daily dose minoxidil results in a C_{max} of about 0.25 ng/ml to about 20 ng/ml. In some embodiments, the oral administration of the daily dose minoxidil results in a C_{max} that is devoid of cardiac effects.

[00151] In some embodiments of the kit described herein, the oral administration results in a half-life of the daily dose of minoxidil of about 4 hours to about 24 hours. In some embodiments, the oral administration results in a half-life of the daily dose of minoxidil of about 4 hours, about 5 hours, about 6 hours, about 7 hours, about 8 hours, about 9 hours, about 10 hours, about 12 hours, about 14 hours, about 16 hours, about 18 hours, about 20 hours, about 22 hours, about 24 hours, or any range within these values.

[00152] In some embodiments of the kit described herein, the oral administration of the daily dose of minoxidil results in a T_{max} of about 30 to about 360 minutes. In some embodiments, the oral administration of the daily dose of minoxidil results in a delayed release that results in a T_{max} between both 30 to 360 minutes and between 390 minutes and 1080 minutes.

[00153] In some embodiments of the kit described herein, the oral administration of the daily dose of modified release minoxidil results in an AUC that is greater than an equivalent dose of an immediate release formulation.

[00154] In some embodiments of the kit described herein, the slow modified release vehicle is an inert solid vehicle, or matrix, in which a drug is uniformly suspended, including in the form of tablets or small beads. In some embodiments, the matrix is a gelling material

including gelatin, methylcellulose, gum tragacanth, Veegum, and alginic acid. In some embodiments, the matrix is a polymer including polylactic acid copolymer, polyacrylate, methacrylate, polyester, ethylene—vinyl acetate copolymer (EVA), polyglycolide, polylactide, and silicone. In some embodiments, the slow modified release vehicle is a slow-release pellet, bead, or granule. In some embodiments, the modified release formulation is an extended release tablet where the solubility of a drug is modified for extended release. In some embodiments, the extended release tablet is formed by using the nonionized base or acid form of the drug. In some embodiments, the extended release tabled is formed by granulating the drug with excipients (including stearic acid, castor wax, high-molecular-weight polyethylene glycol (Carbowax), glyceryl monostearate, white wax, spermaceti oil, magnesium stearate and hydrogenated vegetable oil (Sterotex)) to decrease the aqueous solubility of the drug. In some embodiments, the slow modified release vehicle is an ion-exchange preparation whereby an anionic or cationic drug is complexed with an oppositely charged ionic resin to form an insoluble nonabsorbable resin—drug complex.

[00155] In some embodiments of the kit described herein, the slow modified release vehicle further comprises one or more pharmaceutically acceptable excipients. Examples of pharmaceutically acceptable excipients that may be present in the composition include but are not limited to fillers/vehicles, solvents/co-solvents, preservatives, antioxidants, suspending agents, surfactants, antifoaming agents, buffering agents, chelating agents, sweeteners, flavoring agents, binders, extenders, disintegrants, diluents, lubricants, fillers, wetting agents, glidants, and combinations thereof.

[00156] In some embodiments of the kit described herein, the slow modified release vehicle can further comprise one or more exemplary fillers. Examples of exemplary fillers

include cellulose and cellulose derivatives such as microcrystalline cellulose; starches such as dry starch, hydrolyzed starch, and starch derivatives such as corn starch; cyclodextrin; sugars such as powdered sugar and sugar alcohols such as lactose, mannitol, sucrose and sorbitol; inorganic fillers such as aluminum hydroxide gel, precipitated calcium carbonate, carbonate, magnesium aluminometasilicate, dibasic calcium phosphate; and sodium chloride, silicon dioxide, titanium dioxide, titanium oxide, dicalcium phosphate dihydrate, calcium sulfate, alumina, kaolin, talc, or combinations thereof. Fillers may be present in the composition from about 20 wt% to about 65 wt%, about 20 wt% to about 50 wt%, about 20 wt% to about 40 wt%, about 45 wt% to about 65 wt%, about 50 wt% to about 65 wt%, or about 55 wt% to about 65 wt% of the total weight of the composition, or any value between these ranges.

[00157] In some embodiments of the kit described herein, the slow modified release vehicle further comprises one or more disintegrants. Examples of disintegrants include starches, alginic acid, crosslinked polymers such as crosslinked polyvinylpyrrolidone, croscarmellose sodium, potassium starch glycolate, sodium starch glycolate, clays, celluloses, starches, gums, or combinations thereof. Disintegrants may be present in the composition from about 1 wt% to about 10 wt%, about 1 wt% to about 9 wt%, about 1 wt% to about 8 wt%, about 1 wt% to about 7 wt%, about 1 wt% to about 6 wt%, or about 1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[00158] In some embodiments of the kit described herein, the slow modified release vehicle further comprises one or more binders, including but not limited to celluloses such as hydroxypropylcellulose, methyl cellulose, and hydroxypropylmethylcellulose; starches such as corn starch, pregelatinized starch, and hydroxypropyl starch; waxes and natural and synthetic gums such as acacia, tragacanth, sodium alginate; synthetic polymers such as polymethacrylates

and polyvinylpyrrolidone; and povidone, dextrin, pullulane, agar, gelatin, tragacanth, macrogol, or combinations thereof. Binders may be present in the composition from about 0.5 wt% to about 5 wt%, about 0.5 wt% to about 4 wt%, about 0.5 wt% to about 3 wt%, about 0.5 wt% to about 2 wt%, or about 0.5 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[00159] In some embodiments of the kit described herein, slow modified release vehicle further comprises one or more wetting agents, including but not limited to oleic acid, glyceryl monostearate, sorbitan mono-oleate, sorbitan monolaurate, triethanolamine oleate, polyoxyethylene sorbitan mono-oleate, polyoxyethylene sorbitan monolaurate, sodium oleate, sodium lauryl sulfate, poloxamers, poloxamer 188, polyoxyethylene ethers, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene fatty acid esters, polyethylene glycol fatty acid esters, polyoxyethylene hardened castor oil, polyoxyethylene alkyl ethers, polysorbates, cetyl alcohol, glycerol fatty acid esters (for example, triacetin, glycerol monostearate, etc.), polyoxymethylene stearate, sodium lauryl sulfate, sorbitan fatty acid esters, sucrose fatty acid esters, benzalkonium chloride, polyethoxylated castor oil, and combinations thereof. Wetting agents may be present in the composition from about 0.1 wt% to about 1 wt%, about 0.1 wt% to about 2 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 4 wt%, or about 0.1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[00160] In some embodiments of the kit described herein, the slow modified release vehicle further comprises one or more lubricants, including but not limited to stearic acid, magnesium stearate, calcium hydroxide, talc, corn starch, sodium stearyl fumarate, alkali-metal and alkaline earth metal salts, waxes, boric acid, sodium benzoate, sodium acetate, sodium chloride, leucine, polyethylene glycol (PEG), a methoxypolyethylene glycol, propylene glycol,

sodium oleate, glyceryl behenate, glyceryl palmitostearate, glyceryl benzoate, magnesium lauryl sulfate, sodium lauryl sulfate, and combinations thereof. Lubricants may be present in the composition from about 0.1 wt% to about 5 wt%, about 0.1 wt% to about 4 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 2 wt%, or about 0.1 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[00161] In some embodiments of the kit described herein, slow modified release vehicle further comprises one or more glidants, including but not limited to colloidal silicon dioxide, talc, sodium lauryl sulfate, native starch, and combinations thereof. Glidants may be present in the composition from about 0.05 wt% to about 1 wt%, about 0.05 wt% to about 0.9 wt%, about 0.05 wt% to about 0.8 wt%, about 0.05 wt% to about 0.5 wt%, or about 0.05 wt% to about 0.1 wt% of the total weight of the composition, or any value between these ranges.

[00162] In some embodiments of the kit described herein, the slow modified release vehicle is a tablet and further comprises a top coat, such as hydroxypropyl-methylcellulose coating or polyvinyl alcohol coating, and are available under the trade name Opadry, such as Opadry White, Opadry II (Opadry is a registered trademark of BPSI Holdings LLC, Wilmington, DE, USA). Top coats may be present in the composition from about 1 wt% to about 10 wt%, about 1 wt% to about 9 wt%, about 1 wt% to about 8 wt%, about 1 wt% to about 7 wt%, about 1 wt% to about 6 wt%, or about 1 wt% to about 5 wt% of the total weight of the composition, or any value between these ranges.

[00163] In some embodiments of the kit described herein, the slow modified release vehicle can further comprise one or more preservative agents. Examples of preservative agents include sodium benzoate, paraoxybenzoic acid esters, methyl, ethyl, butyl, and propyl parabens, chlorobutanol, benzyl alcohol, phenylethylalcohol, dehydroacetic acid, sorbic acid,

benzalkonium chloride (BKC), benzethonium chloride, phenol, phenylmercuric nitrate, thimerosal, or combinations thereof. Preservative agents can be included in the liquid dosage form. The preservative agents can be in an amount sufficient to extend the shelf-life or storage stability, or both, of the liquid dosage form. Preservatives may be present in the composition from about 0.05 wt% to about 1 wt%, about 0.05 wt% to about 0.9 wt%, about 0.05 wt% to about 0.8 wt%, about 0.05 wt% to about 0.5 wt%, or about 0.05 wt% to about 0.1 wt% of the total weight of the composition, or any value between these ranges.

[00164] In some embodiments of the kit described herein, the slow modified release vehicle can further comprise one or more flavoring agents. Examples of flavoring agents include synthetic flavor oils and flavoring aromatics and/or natural oils, extracts from plants leaves, flowers, fruits, and so forth and the like or any combinations thereof. Additional examples include cinnamon oil, oil of wintergreen, peppermint oils, clove oil, bay oil, anise oil, eucalyptus, thyme oil, cedar leaf oil, oil of nutmeg, oil of sage, oil of bitter almonds, and cassia oil and the like or any combinations thereof. Also useful as flavors are vanilla, citrus oil, including lemon, orange, grape, lime and grapefruit, and fruit essences, including apple, banana, pear, peach, strawberry, raspberry, cherry, plum, pineapple, apricot, strawberry flavor, tutti-fruity flavor, mint flavor, or any combinations thereof. Flavoring agents may be present in the composition from about 0.1 wt% to about 5 wt%, about 0.1 wt% to about 4 wt%, about 0.1 wt% to about 3 wt%, about 0.1 wt% to about 2 wt%, or about 0.1 wt% to about 1 wt% of the total weight of the composition, or any value between these ranges.

[00165] In some embodiments of the kit described herein, the slow modified release vehicle can generally be in any physical form suitable for use in treating a subject. These forms can be referred to as a unit dosage form, such as an individual pill or tablet. In some examples,

the pharmaceutical compositions can be formulated as tablets, capsules, granules, powders, liquids, suspensions, gels, syrups, slurries, suppositories, patches, nasal sprays, aerosols, injectables, implantable sustained-release formulations, or mucoadherent films. In some examples, the pharmaceutical formulation may be formed as a tablet, a bi-layer tablet, a capsule, a multiparticulate, a drug coated sphere, a matrix tablet, or a multicore tablet. A physical form can be selected according to the desired method of treatment.

[00166] In some embodiments of the kit described herein, the slow modified release vehicle can be manufactured by various conventional methods such as conventional mixing, dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping, or lyophilizing processes. Slow modified release vehicles can be formulated in a conventional manner using one or more physiologically acceptable carriers, diluents, excipients or auxiliaries that facilitate processing of the active agent into preparations that can be used pharmaceutically. Proper formulation can be selected upon the oral route of administration chosen.

[00167] In some embodiments, the slow modified release vehicle is a core tablet, or a tablet within a tablet, whereby the inner core is used for the slow-drug-release component, and the outside shell contains a rapid-release dose of drug. In some embodiments, the slow modified release vehicle is achieved via microencapsulation whereby microscopic drug particles are encapsulated with a special coating material, such as ethylcellulose. In some embodiments, the slow modified release vehicle is an osmotic drug delivery system in the form of a tablet which contains an outside semipermeable membrane and an inner core filled with a mixture of drug and osmotic agent (salt solution). In some embodiments, the slow modified release vehicle is a gastroretentive system that can remain in the gastric region for several hours and prolong the

gastric residence time of a drug. In some embodiments, the slow modified release vehicle is a combination of any of the above-described embodiments.

[00168] In some embodiments of the kit described herein, for oral administration, the slow modified release vehicle can combine minoxidil with another pharmaceutical agent with one or more pharmaceutically acceptable carriers well known in the art. Such carriers facilitate formulation as tablets, pills, dragees, capsules, liquids, gels, syrups, slurries, suspensions and the like, for oral ingestion by a patient to be treated. For oral solid formulations such as, for example, powders, capsules and tablets, suitable excipients include fillers such as sugars, such as lactose, sucrose, mannitol and sorbitol; cellulose preparations such as maize starch, wheat starch, rice starch, potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP); granulating agents; and binding agents. If desired, disintegrating agents may be added, such as the cross-linked polyvinylpyrrolidone, agar, or alginic acid or a salt thereof such as sodium alginate. If desired, solid dosage forms may be sugar-coated or enteric-coated using standard techniques.

[00169] For oral liquid preparations such as, for example, suspensions, elixirs and solutions, suitable carriers, excipients or diluents include water, glycols, oils, alcohols, etc. Additionally, flavoring agents, preservatives, coloring agents and the like can be added. For buccal administration, the compositions may take the form of tablets, lozenges, etc. formulated in conventional manner.

[00170] In some embodiments of the kit described herein, the slow modified release vehicles may comprise a matrix selected from microcrystalline cellulose, sodium carboxymethylcellulose, hydroxyalkylcelluloses such as hydroxy propyl methylcellulose and hydroxypropylcellulose, polyethylene oxide, alkylcelluloses such as methylcellulose and

ethylcellulose, polyethylene glycol, polyvinylpyrrolidone, cellulose acetate, cellulose acetate butyrate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl acetate phthalate, polyalkylmethacrylates, polyvinyl acetate and mixtures thereof.

Further Embodiments

[00171] Provided herein is embodiment A, a pharmaceutical formulation for oral administration, comprising a daily dose of minoxidil, wherein the pharmaceutical formulation is a modified release formulation.

[00172] In an embodiment B, pharmaceutical formulation of embodiment A, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00173] In an embodiment C, the pharmaceutical formulation of embodiment A, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00174] In an embodiment D, the pharmaceutical formulation of embodiment B, wherein the non-steroid anti-androgen is selected from flutamide, clascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof.

[00175] In an embodiment E, the pharmaceutical formulation of embodiment B, wherein the 17 α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof.

[00176] In an embodiment F, the pharmaceutical formulation of embodiment B, wherein the 19-norprogesterone derivative is nomegestrol acetate.

[00177] In an embodiment G, the pharmaceutical formulation of embodiment B, wherein the 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof.

[00178] In an embodiment H, the pharmaceutical formulation of embodiment B, wherein the 17 α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof.

[00179] In an embodiment I, the pharmaceutical formulation of embodiment B, wherein the 5- α reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof.

[00180] In an embodiment J, the pharmaceutical formulation of embodiment B, wherein the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof.

[00181] In an embodiment K, the pharmaceutical formulation of embodiment B, wherein the GnRH analog is a GnRH agonist.

[00182] In an embodiment L, the pharmaceutical formulation of embodiment K, wherein the GnRH agonist is selected from goserelin, buserelin, leuprorelin, and combinations thereof.

[00183] In an embodiment M, the pharmaceutical formulation of embodiment B, wherein the GnRH analog is a GnRH antagonist.

[00184] In an embodiment N, the pharmaceutical formulation of embodiment M, wherein the GnRH antagonist is cetrorelix.

[00185] In an embodiment O, the pharmaceutical formulation of embodiment B, wherein the prostaglandin F2 α analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof.

[00186] In an embodiment P, the pharmaceutical formulation of embodiment B, wherein the prostamide is bimatoprost.

[00187] In an embodiment Q, the pharmaceutical formulation of embodiment B, wherein the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof.

[00188] In an embodiment R, the pharmaceutical formulation of embodiment B, wherein the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof.

[00189] In an embodiment S, the pharmaceutical formulation of embodiment B, wherein the prostaglandin E2 analog is sulprostone.

[00190] In an embodiment T, the pharmaceutical formulation of embodiment B, wherein the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof.

[00191] In an embodiment U, the pharmaceutical formulation of embodiment B, wherein the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof.

[00192] In an embodiment V, the pharmaceutical formulation of embodiment B, wherein the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof.

[00193] In an embodiment W, the pharmaceutical formulation of embodiment B, wherein the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.

[00194] In an embodiment X, the pharmaceutical formulation of embodiment A, wherein the modified release formulation is selected from an extended release formulation, a sustained release formulation, a controlled release formulation, or a delayed release formulation.

[00195] In an embodiment Y, the pharmaceutical formulation of embodiment A, wherein the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg.

[00196] In an embodiment Z, the pharmaceutical formulation of embodiment A, wherein the oral administration of the daily dose of minoxidil results in a steady state blood level of the minoxidil of about 1 ng/ml to about 20 ng/ml.

[00197] In an embodiment AA, the pharmaceutical formulation of embodiment Z, wherein the steady state blood level of the daily dose of minoxidil is maintained for at least about 12 hours.

[00198] In an embodiment AB, the pharmaceutical formulation of embodiment A, wherein the oral administration of the daily dose of minoxidil results in a C_{max} of about 0.25 ng/ml to about 20 ng/ml.

[00199] In an embodiment AC, the pharmaceutical formulation of embodiment A, wherein the oral administration of the daily dose of minoxidil results in a T_{max} of about 30 to about 360 minutes.

[00200] In an embodiment AD, the pharmaceutical formulation of embodiment A, wherein the daily dose of minoxidil is administered to a subject in an amount of about 0.00625 mg/kg/day to about 0.375 mg/kg/day.

[00201] In an embodiment AE, the pharmaceutical formulation of embodiment A, wherein oral administration results in a half-life of the daily dose of minoxidil of about 4 hours to about 24 hours.

[00202] In an embodiment AF, the pharmaceutical formulation of embodiment X, wherein the extended release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration.

[00203] In an embodiment AG, the pharmaceutical formulation of embodiment A, wherein the pharmaceutical formulation is administered only once daily.

[00204] In an embodiment AH, the pharmaceutical formulation of embodiment A, wherein the pharmaceutical formulation is administered at least once daily.

[00205] In an embodiment AI, the pharmaceutical formulation of embodiment A, wherein the pharmaceutical formulation is administered four times per day.

[00206] In an embodiment AJ, the pharmaceutical formulation of embodiment A, wherein the pharmaceutical formulation is administered three times per day.

[00207] In an embodiment AK, the pharmaceutical formulation of embodiment A, wherein the pharmaceutical formulation is administered two times per day.

[00208] Provided herein is embodiment AL, a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

[00209] In an embodiment AM, the pharmaceutical formulation of embodiment AL, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiolactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00210] In an embodiment AN, the pharmaceutical formulation of embodiment AL, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00211] Provided herein is embodiment AO, a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a Tmax of about 30 to about 360 minutes.

[00212] In an embodiment AP, the pharmaceutical formulation of embodiment AO, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiolactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00213] In an embodiment AQ, the pharmaceutical formulation of embodiment AO, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00214] Provided herein is embodiment AR, a pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a C_{max} of about 0.25 ng/ml to about 20 ng/ml.

[00215] In an embodiment AS, the pharmaceutical formulation of embodiment AR, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5- α reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F₂ α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D₂ receptor antagonist, a prostglandin E₂ analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00216] In an embodiment AT, the pharmaceutical formulation of embodiment AR, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00217] Provided herein is embodiment AU, a method of treating hair loss, comprising administering to a subject in need thereof a daily dose of a composition comprising a modified release formulation of minoxidil.

[00218] In an embodiment AV, the method of embodiment AU, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a

19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00219] In an embodiment AW, the method of embodiment AU, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00220] In an embodiment AX, the method of embodiment AV, wherein the non-steroid anti-androgen is selected from flutamide, clascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof.

[00221] In an embodiment AY, the method of embodiment AV, wherein the 17 α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof.

[00222] In an embodiment AZ, the method of embodiment AV, wherein the 19-norprogesterone derivative is nomegestrol acetate.

[00223] In an embodiment BA, the method of embodiment AV, wherein the 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof.

[00224] In an embodiment BB, the method of embodiment AV, wherein the 17 α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof.

[00225] In an embodiment BC, the method of embodiment AV, wherein the 5-alpha reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof.

[00226] In an embodiment BD, the method of embodiment AV, wherein the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof.

[00227] In an embodiment BE, the method of embodiment AV, wherein the GnRH analog is a GnRH agonist.

[00228] In an embodiment BF, the method of embodiment BE, wherein the GnRH agonist is selected from goserelin, buserelin, leuprorelin, and combinations thereof.

[00229] In an embodiment BG, the method of embodiment AV, wherein the GnRH analog is a GnRH antagonist.

[00230] In an embodiment BH, the method of embodiment BG, wherein the GnRH antagonist is cetrorelix.

[00231] In an embodiment BI, the method of embodiment AV, wherein the prostaglandin F2 α analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof.

[00232] In an embodiment BJ, the method of embodiment AV, wherein the prostamide is bimatoprost.

[00233] In an embodiment BK, the method of embodiment AV, wherein the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof.

[00234] In an embodiment BL, the method of embodiment AV, wherein the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof.

[00235] In an embodiment BM, the method of embodiment AV, wherein the prostaglandin E2 analog is sulprostone.

[00236] In an embodiment BN, the method of embodiment AV, wherein the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof.

[00237] In an embodiment BO, the method of embodiment AV, wherein the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof.

[00238] In an embodiment BP, the method of embodiment AV, wherein the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof.

[00239] In an embodiment BQ, the method of embodiment AV, wherein the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.

[00240] In an embodiment BR, the method of embodiment AU, wherein the composition is administered orally.

[00241] In an embodiment BS, the method of embodiment BR, wherein the modified release formulation is an extended release formulation, a sustained release formulation, a controlled release formulation, or a delayed release formulation.

[00242] In an embodiment BT, the method of embodiment BR, wherein the subject in need thereof is diagnosed with hair loss.

[00243] In an embodiment BU, the method of embodiment BT, wherein the subject is diagnosed with at least one cardiac condition selected from heart disease, chronic congestive

heart failure, cardiomyopathy, tachyarrhythmia, renal disease, preexisting pulmonary hypertension, and chronic congestive heart failure not secondary to hypertension.

[00244] In an embodiment BV, the method of embodiment BT, wherein the hair loss is selected from male pattern hair loss, female pattern hair loss, hereditary hair loss, telogen effluvium, alopecia areata, central centrifugal cicatricial alopecia, lichen planopilaris, or traction alopecia.

[00245] In an embodiment BW, the method of embodiment BU, wherein the subject is taking at least one of the following for treatment of the at least one cardiac condition, an anti-hypertensive, an ace-inhibitor, an angiotensin receptor blocker, a direct renin inhibitor, a loop diuretic, a thiazide diuretic, a calcium channel blocker, a beta blocker, an anti-arrhythmic, and a diuretic.

[00246] In an embodiment BX, the method of embodiment BT, wherein administering results in hair regrowth.

[00247] In an embodiment BY, the method of embodiment BT, wherein administering results in hair regrowth within about 6 months.

[00248] In an embodiment BZ, the method of embodiment BT, wherein administering results in an increased improvement in hair growth as compared to administration of an immediate-release dosage form of minoxidil.

[00249] In an embodiment CA, the method of embodiment BT, wherein the composition is administered only once daily.

[00250] In an embodiment CB, the method of embodiment BT, wherein the composition is administered at least once daily.

[00251] In an embodiment CC, the method of embodiment BT, wherein the composition is administered four times per day.

[00252] In an embodiment CD, the method of embodiment BT, wherein the composition is administered three times per day.

[00253] In an embodiment CE, the method of embodiment BT, wherein the composition is administered two times per day.

[00254] In an embodiment CF, the method of embodiment BT, wherein the composition is administered daily for at least about 3 months with substantially no adverse effects and substantially no cardiac effects.

[00255] In an embodiment CG, the method of embodiment BT, wherein the composition is administered daily for at least about 4 months with substantially no adverse effects and substantially no cardiac effects.

[00256] In an embodiment CH, the method of embodiment BT, wherein the composition is administered daily for at least about 6 months with substantially no adverse effects and substantially no cardiac effects.

[00257] In an embodiment CI, the method of embodiment BT, wherein the composition is administered daily for at least about 1 year with substantially no adverse effects and substantially no cardiac effects.

[00258] In an embodiment CJ, the method of embodiment BT, wherein the composition is administered daily indefinitely with substantially no adverse effects and substantially no cardiac effects.

[00259] In an embodiment CK, the method of embodiment BT, wherein administering results in hair regrowth with substantially no clinically significant hemodynamic changes in blood pressure.

[00260] In an embodiment CL, the method of embodiment BT, wherein administering results in substantially no cardiac effects.

[00261] In an embodiment CM, the method of embodiment CL, wherein the cardiac effects are selected from tachycardia, hypotension, premature ventricular contractions, and other tachyarrhythmias.

[00262] In an embodiment CN, the method of embodiment BT, wherein administering results in hair regrowth with substantially no cardiac effects.

[00263] In an embodiment CO, the method of embodiment BT, wherein the daily dose of minoxidil results in fewer cardiac effects or hemodynamic effects as compared to administration of an amount of an immediate-release oral minoxidil used to treat hypertension.

[00264] In an embodiment CP, the method of embodiment CO, wherein the cardiac effects are selected from tachycardia, hypotension, premature ventricular contractions, and other tachyarrhythmias.

[00265] In an embodiment CQ, the method of embodiment CO, wherein the daily dose of minoxidil results in substantially no cardiac effects or hemodynamic effects as compared to administration of an immediate-release oral minoxidil used to treat hypertension.

[00266] In an embodiment CR, the method of embodiment CO, wherein the daily dose of minoxidil is about 25% to about 500% of the amount of the immediate-release oral minoxidil used to treat hypertension.

[00267] In an embodiment CS, the method of embodiment CO, wherein the daily dose of minoxidil is about 10% to about 90% of the amount of the immediate-release oral minoxidil used to treat hypertension.

[00268] In an embodiment CT, the method of embodiment BT, wherein the daily dose of the minoxidil is about 0.625 mg to about 20 mg.

[00269] In an embodiment CU, the method of embodiment BT, wherein the daily dose of the minoxidil is selected from an amount of about 0.625mg, about 1mg, about 1.25 mg, about 1.5mg, about 2.5mg, about 3mg, about 3.5mg, about 4mg, about 4.5mg, about 5mg, about 5.5mg, about 6mg, about 6.5mg, about 7.0 mg, about 7.5mg, about 8 mg, about 8.5 mg, about 9mg, about 9.5 mg, or about 10 mg.

[00270] In an embodiment CV, the method of embodiment BT, wherein the daily dose of the minoxidil is about 0.25 mg to about 20 mg per day.

[00271] In an embodiment CW, the method of embodiment BT, wherein the daily dose of the minoxidil is about 2.5 mg per day.

[00272] In an embodiment CX, the method of embodiment BT, wherein the daily dose of the minoxidil is about 0.00625 mg/kg/day to about 0.5 mg/kg/day.

[00273] In an embodiment CY, the method of embodiment BT, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration.

[00274] In an embodiment CZ, the method of embodiment BT, wherein the subject has a minoxidil plasma concentration versus time curve with a Tmax of about 30 to about 360 minutes.

[00275] In an embodiment DA, the method of embodiment BT, wherein the subject has a minoxidil plasma concentration versus time curve with a C_{max} of about 2.5 ng/ml to about 20 ng/ml.

[00276] In an embodiment DB, the method of embodiment BT, wherein the minoxidil in the subject has a half-life of about 4 to about 24 hours.

[00277] In an embodiment DC, the method of embodiment BT, wherein the minoxidil is in an amount of about 0.625 mg four times per day.

[00278] In an embodiment DD, the method of embodiment BT, wherein the minoxidil is in an orally dissolving tablet.

[00279] Provided herein is embodiment DE, a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

[00280] In an embodiment DF, the method of embodiment DE, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F₂ α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D₂ receptor antagonist, a prostglandin E₂ analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00281] In an embodiment DG, the method of embodiment DE, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipiprant, valproic acid, and combinations thereof.

[00282] Provided herein is embodiment DH, a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a Tmax of about 30 to about 360 minutes.

[00283] In an embodiment DI, the method of embodiment DH, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiolactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00284] In an embodiment DJ, the method of embodiment DH, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00285] Provided herein is embodiment DK, a method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a Cmax of about 0.25 ng/ml to about 20 ng/ml.

[00286] In an embodiment DL, the method of embodiment DK, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiolactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00287] In an embodiment DM, the method of embodiment DK, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00288] Provided herein is embodiment DN, a kit comprising, a slow modified release vehicle comprising oral minoxidil.

[00289] In an embodiment DO, the kit of embodiment DN, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

[00290] In an embodiment DP, the kit of embodiment DN, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

[00291] In an embodiment DQ, the kit of embodiment DO, wherein the non-steroid anti-androgen is selected from flutamide, clascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof.

[00292] In an embodiment DR, the kit of embodiment DO, wherein the 17α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof.

[00293] In an embodiment DS, the kit of embodiment DO, wherein the 19-norprogesterone derivative is nomegestrol acetate.

[00294] In an embodiment DT, the kit of embodiment DO, wherein the 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof.

[00295] In an embodiment DU, the kit of embodiment DO, wherein the 17 α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof.

[00296] In an embodiment DV, the kit of embodiment DO, wherein the 5-alpha reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof.

[00297] In an embodiment DW, the kit of embodiment DO, wherein the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof.

[00298] In an embodiment DX, the kit of embodiment DO, wherein the GnRH analog is a GnRH agonist.

[00299] In an embodiment DY, the kit of embodiment DX, wherein the GnRH agonist is selected from goserelin, buserelin, leuprorelin, and combinations thereof.

[00300] In an embodiment DZ, the kit of embodiment DO, wherein the GnRH analog is a GnRH antagonist.

[00301] In an embodiment EA, the kit of embodiment DZ, wherein the GnRH antagonist is cetrorelix.

[00302] In an embodiment EB, the kit of embodiment DO, wherein the prostaglandin F2 α analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof.

[00303] In an embodiment EC, the kit of embodiment DO, wherein the prostamide is bimatoprost.

[00304] In an embodiment ED, the kit of embodiment DO, wherein the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof.

[00305] In an embodiment EE, the kit of embodiment DO, wherein the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof.

[00306] In an embodiment EF, the kit of embodiment DO, wherein the prostaglandin E2 analog is sulprostone.

[00307] In an embodiment EG, the kit of embodiment DO, wherein the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof.

[00308] In an embodiment EH, the kit of embodiment DO, wherein the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof.

[00309] In an embodiment EI, the kit of embodiment DO, wherein the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof.

[00310] In an embodiment EJ, the kit of embodiment DO, wherein the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.

[00311] In an embodiment EK, the kit of embodiment DN, wherein the kit comprises an information sheet.

[00312] In an embodiment EL, the kit of embodiment EK, wherein the information sheet comprises instructions for selecting an oral dosage form based on a body weight of a patient.

[00313] In an embodiment EM, the kit of embodiment EK, wherein the information sheet comprises a warning of adverse effects.

[00314] In an embodiment EN, the kit of embodiment EM, wherein the adverse effects are selected from peripheral edema and hirsutism.

EXAMPLES:

[00315] The following are provided for exemplification purposes only and are not intended to limit the scope of the embodiments described in broad terms above.

Example 1: Case Study- 28-Year Old Male with Androgenetic Alopecia

[00316] A 28-year old male with androgenetic alopecia was treated with minoxidil 1.25 mg QID. At baseline, the patient's blood pressure was 118/82. His resting heart rate was 64. The patient rechecked his blood pressure and heart rate 30 minutes after administration of each dose of minoxidil for 1 week and did not observe any change in heart rate, systolic blood pressure, or diastolic blood pressure > 10% from baseline. The patient reported improvement in his androgenetic alopecia with subjective improvement in hair thickness and hair density at the frontal scalp and crown of the scalp. No unwanted hair growth or other adverse events, including any cardiac effects, were noticed.

Example 2: Case Study- 51-Year Old Male with Androgenetic Alopecia and Hypertension

[00317] A 51-year-old male with androgenetic alopecia was treated with minoxidil 2.5 mg tablet PO BID and experienced reductions in blood pressure after each administration. The patient administered the minoxidil by mouth each morning between 6am-9am and each evening

between 6pm-9pm. The patient rechecked his blood pressure 30 minutes after administration of each administration of minoxidil for 1 week. The patient noted a consistent decrease of systolic blood pressure by approximately 10mmHg. Even after decreasing the dose to 2.5mg per day, the patient continued to note a decrease in blood pressure by approximately 10mmHg within thirty minutes after dosing. The patient was instructed to take 0.625mg minoxidil four times a day and surprisingly did not experience significant reductions in blood pressure. The patient also reported improvement in his androgenetic alopecia with the subjective improvement in hair thickness and hair density at the frontal scalp and crown of the scalp. No unwanted hair growth or other adverse events were noticed. The patient reported that despite the same total daily dose of 2.5mg, minoxidil at 0.625mg four times a day did not significantly lower blood pressure and was associated with improved hair growth.

Example 3: Case Study– 81-Year-Old Male with Androgenetic Alopecia and Atrial Fibrillation

[00318] An 81-year-old male with androgenetic alopecia presented for evaluation for treatment of his hair loss. The patient specifically requested a prescription of minoxidil immediate release. The patient disclosed a personal history of chronic atrial fibrillation requiring amiodarone therapy. On consultation with the patient's other physician, the decision was made to not proceed with minoxidil therapy due to risk of worsening his atrial fibrillation.

Example 4: Case Study – 70-Year-Old Male with Androgenetic Alopecia and Premature Ventricular Contractures

[00319] A 70-year-old male with androgenetic alopecia presented for evaluation for treatment of his hair loss. The patient specifically requested a prescription of minoxidil

immediate release. The patient disclosed a personal history of chronic premature ventricular contractions requiring flecainide therapy. On consultation with the patient's other physician, the decision was made to not proceed with minoxidil therapy due to risk of worsening his premature ventricular contractions.

CLAIMS

What Is Claimed Is:

1. A pharmaceutical formulation for oral administration, comprising a daily dose of minoxidil, wherein the pharmaceutical formulation is a modified release formulation.
2. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F 2α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D 2 receptor antagonist, a prostglandin E 2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.
3. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.
4. The pharmaceutical formulation of claim 2, wherein the non-steroid anti-androgen is selected from flutamide, clascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof.
5. The pharmaceutical formulation of claim 2, wherein the 17α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof.
6. The pharmaceutical formulation of claim 2, wherein the 19-norprogesterone derivative is nomegestrol acetate.
7. The pharmaceutical formulation of claim 2, wherein the 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof.
8. The pharmaceutical formulation of claim 2, wherein the 17α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof.

9. The pharmaceutical formulation of claim 2, wherein the 5-alpha reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof.
10. The pharmaceutical formulation of claim 2, wherein the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof.
11. The pharmaceutical formulation of claim 2, wherein the GnRH analog is a GnRH agonist.
12. The pharmaceutical formulation of claim 11, wherein the GnRH agonist is selected from goserelin, buserelin, leuprorelin, and combinations thereof.
13. The pharmaceutical formulation of claim 2, wherein the GnRH analog is a GnRH antagonist.
14. The pharmaceutical formulation of claim 13, wherein the GnRH antagonist is cetrorelix.
15. The pharmaceutical formulation of claim 2, wherein the prostaglandin F2 α analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof.
16. The pharmaceutical formulation of claim 2, wherein the prostamide is bimatoprost.
17. The pharmaceutical formulation of claim 2, wherein the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof.
18. The pharmaceutical formulation of claim 2, wherein the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof.
19. The pharmaceutical formulation of claim 2, wherein the prostaglandin E2 analog is sulprostone.
20. The pharmaceutical formulation of claim 2, wherein the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof.

21. The pharmaceutical formulation of claim 2, wherein the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof.
22. The pharmaceutical formulation of claim 2, wherein the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof.
23. The pharmaceutical formulation of claim 2, wherein the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.
24. The pharmaceutical formulation of claim 1, wherein the modified release formulation is selected from an extended release formulation, a sustained release formulation, a controlled release formulation, or a delayed release formulation.
25. The pharmaceutical formulation of claim 1, wherein the daily dose of minoxidil is in an amount of about 0.5 mg to about 10 mg.
26. The pharmaceutical formulation of claim 1, wherein the oral administration of the daily dose of minoxidil results in a steady state blood level of the minoxidil of about 1 ng/ml to about 20 ng/ml.
27. The pharmaceutical formulation of claim 26, wherein the steady state blood level of the daily dose of minoxidil is maintained for at least about 12 hours.
28. The pharmaceutical formulation of claim 1, wherein the oral administration of the daily dose of minoxidil results in a C_{max} of about 0.25 ng/ml to about 20 ng/ml.
29. The pharmaceutical formulation of claim 1, wherein the oral administration of the daily dose of minoxidil results in a T_{max} of about 30 to about 360 minutes.
30. The pharmaceutical formulation of claim 1, wherein the daily dose of minoxidil is administered to a subject in an amount of about 0.00625 mg/kg/day to about 0.375 mg/kg/day.

31. The pharmaceutical formulation of claim 1, wherein oral administration results in a half-life of the daily dose of minoxidil of about 4 hours to about 24 hours.

32. The pharmaceutical formulation of claim 24, wherein the extended release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration.

33. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is administered only once daily.

34. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is administered at least once daily.

35. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is administered four times per day.

36. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is administered three times per day.

37. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is administered two times per day.

38. A pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

39. The pharmaceutical formulation of claim 38, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F 2α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D 2 receptor antagonist, a prostglandin E 2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

40. The pharmaceutical formulation of claim 38, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

41. A pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a T_{max} of about 30 to about 360 minutes.

42. The pharmaceutical formulation of claim 41, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

43. The pharmaceutical formulation of claim 41, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

44. A pharmaceutical formulation comprising a modified release formulation of minoxidil, wherein the modified release formulation has a C_{max} of about 0.25 ng/ml to about 20 ng/ml.

45. The pharmaceutical formulation of claim 44, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

46. The pharmaceutical formulation of claim 44, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

47. A method of treating hair loss, comprising administering to a subject in need thereof a daily dose of a composition comprising a modified release formulation of minoxidil.

48. The method of claim 47, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

49. The method of claim 47, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

50. The method of claim 48, wherein the non-steroid anti-androgen is selected from flutamide, elascoterone, bicalutamide, pyrilutamide, enzualutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof.

51. The method of claim 48, wherein the 17 α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof.

52. The method of claim 48, wherein the 19-norprogesterone derivative is nomegestrol acetate.

53. The method of claim 48, wherein the 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof.

54. The method of claim 48, wherein the 17 α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof.

55. The method of claim 48, wherein the 5-alpha reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof.

56. The method of claim 48, wherein the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof.

57. The method of claim 48, wherein the GnRH analog is a GnRH agonist.

58. The method of claim 57, wherein the GnRH agonist is selected from goserelin, buserelin, leuporelin, and combinations thereof.
59. The method of claim 48, wherein the GnRH analog is a GnRH antagonist.
60. The method of claim 59, wherein the GnRH antagonist is cetrorelix.
61. The method of claim 48, wherein the prostaglandin F_{2α} analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof.
62. The method of claim 48, wherein the prostamide is bimatoprost.
63. The method of claim 48, wherein the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof.
64. The method of claim 48, wherein the prostaglandin D₂ receptor antagonist is laropiprant, AM211, and combinations thereof.
65. The method of claim 48, wherein the prostaglandin E₂ analog is sulprostone.
66. The method of claim 48, wherein the EP₂ receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof.
67. The method of claim 48, wherein the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, jacktinib, and combinations thereof.
68. The method of claim 49, wherein the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof.
69. The method of claim 48, wherein the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.
70. The method of claim 47, wherein the composition is administered orally.

71. The method of claim 70, wherein the modified release formulation is an extended release formulation, a sustained release formulation, a controlled release formulation, or a delayed release formulation.

72. The method of claim 70, wherein the subject in need thereof is diagnosed with hair loss.

73. The method of claim 72, wherein the subject is diagnosed with at least one cardiac condition selected from heart disease, chronic congestive heart failure, cardiomyopathy, tachyarrhythmia, renal disease, preexisting pulmonary hypertension, and chronic congestive heart failure not secondary to hypertension.

74. The method of claim 72, wherein the hair loss is selected from male pattern hair loss, female pattern hair loss, hereditary hair loss, telogen effluvium, alopecia areata, central centrifugal cicatricial alopecia, lichen planopilaris, or traction alopecia.

75. The method of claim 73, wherein the subject is taking at least one of the following for treatment of the at least one cardiac condition, an anti-hypertensive, an ace-inhibitor, an angiotensin receptor blocker, a direct renin inhibitor, a loop diuretic, a thiazide diuretic, a calcium channel blocker, a beta blocker, an anti-arrhythmic, and a diuretic.

76. The method of claim 70, wherein administering results in hair regrowth.

77. The method of claim 70, wherein administering results in hair regrowth within about 6 months.

78. The method of claim 70, wherein administering results in an increased improvement in hair growth as compared to administration of an immediate-release dosage form of minoxidil.

79. The method of claim 70, wherein the composition is administered only once daily.

80. The method of claim 70, wherein the composition is administered at least once daily.

81. The method of claim 70, wherein the composition is administered four times per day.

82. The method of claim 70, wherein the composition is administered three times per day.

83. The method of claim 70, wherein the composition is administered two times per day.
84. The method of claim 70, wherein the composition is administered daily for at least about 3 months with substantially no adverse effects and substantially no cardiac effects.
85. The method of claim 70, wherein the composition is administered daily for at least about 4 months with substantially no adverse effects and substantially no cardiac effects.
86. The method of claim 70, wherein the composition is administered daily for at least about 6 months with substantially no adverse effects and substantially no cardiac effects.
87. The method of claim 70, wherein the composition is administered daily for at least about 1 year with substantially no adverse effects and substantially no cardiac effects.
88. The method of claim 70, wherein the composition is administered daily indefinitely with substantially no adverse effects and substantially no cardiac effects.
89. The method of claim 70, wherein administering results in hair regrowth with substantially no clinically significant hemodynamic changes in blood pressure.
90. The method of claim 70, wherein administering results in substantially no cardiac effects.
91. The method of claim 90, wherein the cardiac effects are selected from tachycardia, hypotension, premature ventricular contractions, and other tachyarrhythmias.
92. The method of claim 70, wherein administering results in hair regrowth with substantially no cardiac effects.
93. The method of claim 70, wherein the daily dose of minoxidil results in fewer cardiac effects or hemodynamic effects as compared to administration of an amount of an immediate-release oral minoxidil used to treat hypertension.
94. The method of claim 93, wherein the cardiac effects are selected from tachycardia, hypotension, premature ventricular contractions, and other tachyarrhythmias.

95. The method of claim 93, wherein the daily dose of minoxidil results in substantially no cardiac effects or hemodynamic effects as compared to administration of an immediate-release oral minoxidil used to treat hypertension.

96. The method of claim 93, wherein the daily dose of minoxidil is about 25% to about 500% of the amount of the immediate-release oral minoxidil used to treat hypertension.

97. The method of claim 93, wherein the daily dose of minoxidil is about 10% to about 90% of the amount of the immediate-release oral minoxidil used to treat hypertension.

98. The method of claim 70, wherein the daily dose of the minoxidil is about 0.625 mg to about 20 mg.

99. The method of claim 70, wherein the daily dose of the minoxidil is selected from an amount of about 0.625mg, about 1mg, about 1.25 mg, about 1.5mg, about 2.5mg, about 3mg, about 3.5mg, about 4mg, about 4.5mg, about 5mg, about 5.5mg, about 6mg, about 6.5mg, about 7.0 mg, about 7.5mg, about 8 mg, about 8.5 mg, about 9mg, about 9.5 mg, or about 10 mg.

100. The method of claim 70, wherein the daily dose of the minoxidil is about 0.25 mg to about 20 mg per day.

101. The method of claim 70, wherein the daily dose of the minoxidil is about 2.5 mg per day.

102. The method of claim 70, wherein the daily dose of the minoxidil is about 0.00625 mg/kg/day to about 0.5 mg/kg/day.

103. The method of claim 70, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after the oral administration.

104. The method of claim 70, wherein the subject has a minoxidil plasma concentration versus time curve with a Tmax of about 30 to about 360 minutes.

105. The method of claim 70, wherein the subject has a minoxidil plasma concentration versus time curve with a Cmax of about 2.5 ng/ml to about 20 ng/ml.

106. The method of claim 70, wherein the minoxidil in the subject has a half-life of about 4 to about 24 hours.

107. The method of claim 70, wherein the minoxidil is in an amount of about 0.625 mg four times per day.

108. The method of claim 70, wherein the minoxidil is in an orally dissolving tablet.

109. A method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation releases about 50% to about 98% of the daily dose of minoxidil within about 12 hours after oral administration.

110. The method of claim 109, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F 2α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D 2 receptor antagonist, a prostglandin E 2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

111. The method of claim 109, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

112. A method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a T $_{max}$ of about 30 to about 360 minutes.

113. The method of claim 112, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F 2α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D 2 receptor antagonist, a

prostaglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

114. The method of claim 112, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

115. A method of treating hair loss, comprising administering to a subject in need thereof a modified release formulation of minoxidil, wherein the modified release formulation has a C_{max} of about 0.25 ng/ml to about 20 ng/ml.

116. The method of claim 115, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

117. The method of claim 115, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

118. A kit comprising, a slow modified release vehicle comprising oral minoxidil.

119. The kit of claim 118, wherein the pharmaceutical formulation further comprises one or more active agents selected from a non-steroid anti-androgen, a 17 α -hydroxyprogesterone derivative, a 19-norprogesterone derivative, a 19-nortestosterone derivative, a 17 α -spiro lactone derivative, a 5-alpha reductase inhibitor, an estrogen, a GnRH analog, a prostaglandin F2 α analog, a prostamide, a prostanoid receptor agonist, a prostaglandin D2 receptor antagonist, a prostglandin E2 analog, an EP 2 receptor agonist, a JAK inhibitor, an alopecia areata medication, a supplement, and combinations thereof.

120. The kit of claim 118, wherein the pharmaceutical formulation further comprises medrogestone, cetirizine, setipirant, valproic acid, and combinations thereof.

121. The kit of claim 119, wherein the non-steroid anti-androgen is selected from flutamide, enclatorone, bicalutamide, pyrilutamide, enzalutamide, nilutamide, apalutamide, proxilutamide, cimetidine, topalutamide, and combinations thereof.

122. The kit of claim 119, wherein the 17α -hydroxyprogesterone derivative is selected from chlormadinone acetate, cyproterone acetate, megestrol acetate, osaterone acetate, and combinations thereof.

123. The kit of claim 119, wherein the 19-norprogesterone derivative is nomegestrol acetate.

124. The kit of claim 119, wherein the 19-nortestosterone derivative is selected from dienogest, oxendolone, and combinations thereof.

125. The kit of claim 119, wherein the 17α -spiro lactone derivative is selected from drospirenone, spironolactone, and combinations thereof.

126. The kit of claim 119, wherein the 5- α reductase inhibitor is selected from alfatradiol, dutasteride, epristeride, finasteride, saw palmetto extract, bexlosteride, izonsteride, epigallocatechin, fluridil, and combinations thereof.

127. The kit of claim 119, wherein the estrogen is selected from estradiol, estradiol esters, ethinylestradiol, conjugated estrogens, diethylstilbestrol, and combinations thereof.

128. The kit of claim 119, wherein the GnRH analog is a GnRH agonist.

129. The kit of claim 128, wherein the GnRH agonist is selected from goserelin, buserelin, leuprorelin, and combinations thereof.

130. The kit of claim 119, wherein the GnRH analog is a GnRH antagonist.

131. The kit of claim 130, wherein the GnRH antagonist is cetrorelix.

132. The kit of claim 119, wherein the prostaglandin $F2\alpha$ analog is latanoprost, travoprost, tafluprost, unoprostone, dinoprost, AS604872, BOL303259X, PF3187207, carboprost, and combinations thereof.

133. The kit of claim 119, wherein the prostamide is bimatoprost.
134. The kit of claim 119, wherein the prostanoid receptor agonist is fluprostenol, cicaprost, and combinations thereof.
135. The kit of claim 119, wherein the prostaglandin D2 receptor antagonist is laropiprant, AM211, and combinations thereof.
136. The kit of claim 119, wherein the prostaglandin E2 analog is sulprostone.
137. The kit of claim 119, wherein the EP2 receptor agonist is butaprost, diazoxide, kopexil, pinacidil, ET-02, and combinations thereof.
138. The kit of claim 119, wherein the JAK inhibitor is abrocitinib, baricitinib, brepocitinib, decernotinib, delgocitinib, deuruxolitinib, deucravacitinib, fedratinib, filgotinib, gusacitinib, itacitinib, oclacitinib, pacritinib, peficitinib, ritlecitnib, ruxolitinib, tofacitinib, upadacitinib, SHR0302, ATI-2138, Jacktinib, and combinations thereof.
139. The kit of claim 119, wherein the alopecia areata medication is selected from etrasimod, fingolimod, ozanimod, siponimod, ponesimod, and combinations thereof.
140. The kit of claim 119, wherein the supplement is selected from biotin, zinc, selenium, caffeine, sodium chloride, marine collagen, and combinations thereof.
141. The kit of claim 118, wherein the kit comprises an information sheet.
142. The kit of claim 141, wherein the information sheet comprises instructions for selecting an oral dosage form based on a body weight of a patient.
143. The kit of claim 141, wherein the information sheet comprises a warning of adverse effects.
144. The kit of claim 143, wherein the adverse effects are selected from peripheral edema and hirsutism.

ABSTRACT

The compositions and methods provided herein include a pharmaceutical formulation for oral administration comprising a daily dose of a modified release formulation of minoxidil. Also provided herein are pharmaceutical formulations for oral administration comprising a daily dose of a modified release formulation of minoxidil and one or more additional active agents. Also provided herein are methods of treating hair loss by administering to a subject in need thereof a daily dose of a modified release formulation of minoxidil. Further provided herein is a kit including a slow modified release vehicle comprising oral minoxidil.

Electronic Acknowledgement Receipt	
EFS ID:	47224743
Application Number:	63433203
International Application Number:	
Confirmation Number:	5249
Title of Invention:	COMPOSITIONS AND METHODS OF USE FOR MODIFIED RELEASE MINOXIDIL
First Named Inventor/Applicant Name:	Reid WALDMAN
Customer Number:	185628
Filer:	Marissa Stearns Kuzirian/Charles Vrscek
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1	Application Data Sheet	Appln_Data_Sheet.pdf	2410067	no	8
			3524bcf0d7524cef986395e837d758c6935ced55		
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Warnings:					
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3	Fee Worksheet (SB06)	fee-info.pdf	37529	no	2
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