A Randomized, Multicenter, Double-blind, Vehicle-controlled, Phase 2a Study to Assess the Safety, Pharmacokinetics, and Preliminary Efficacy of PP405 in Adults with Androgenetic Alopecia

Protocol Number PP405-2001

[redacted]

Study Sponsor	Pelage Pharmaceuticals, Inc. 907 Westwood Blvd. # 384 Los Angeles, California 90024
Study Director	[redacted]
Medical Monitor	
Development Phase	2a
Clinical Trial Compliance	This clinical trial will be conducted in accordance with standards of Good Clinical Practice, as defined by the International Council for Harmonisation (ICH) and all applicable federal and local regulations.
Version (Amendment No)	5.0 (Amendment 4)
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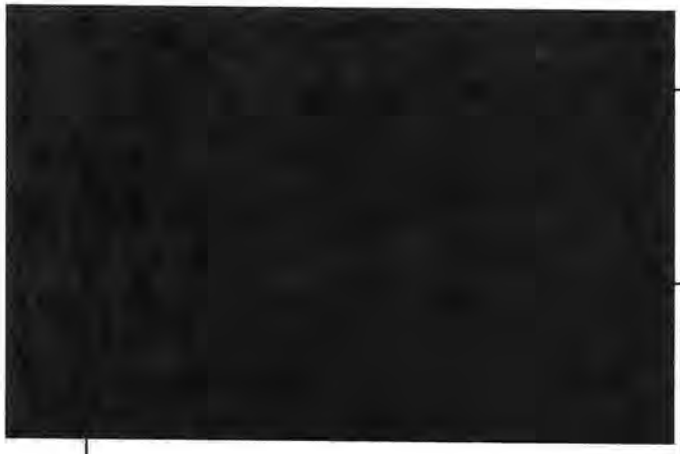

Date

30-Jun-2025

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1. INVESTIGATOR AGREEMENT

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2. LIST OF ABBREVIATIONS AND KEY TERMS

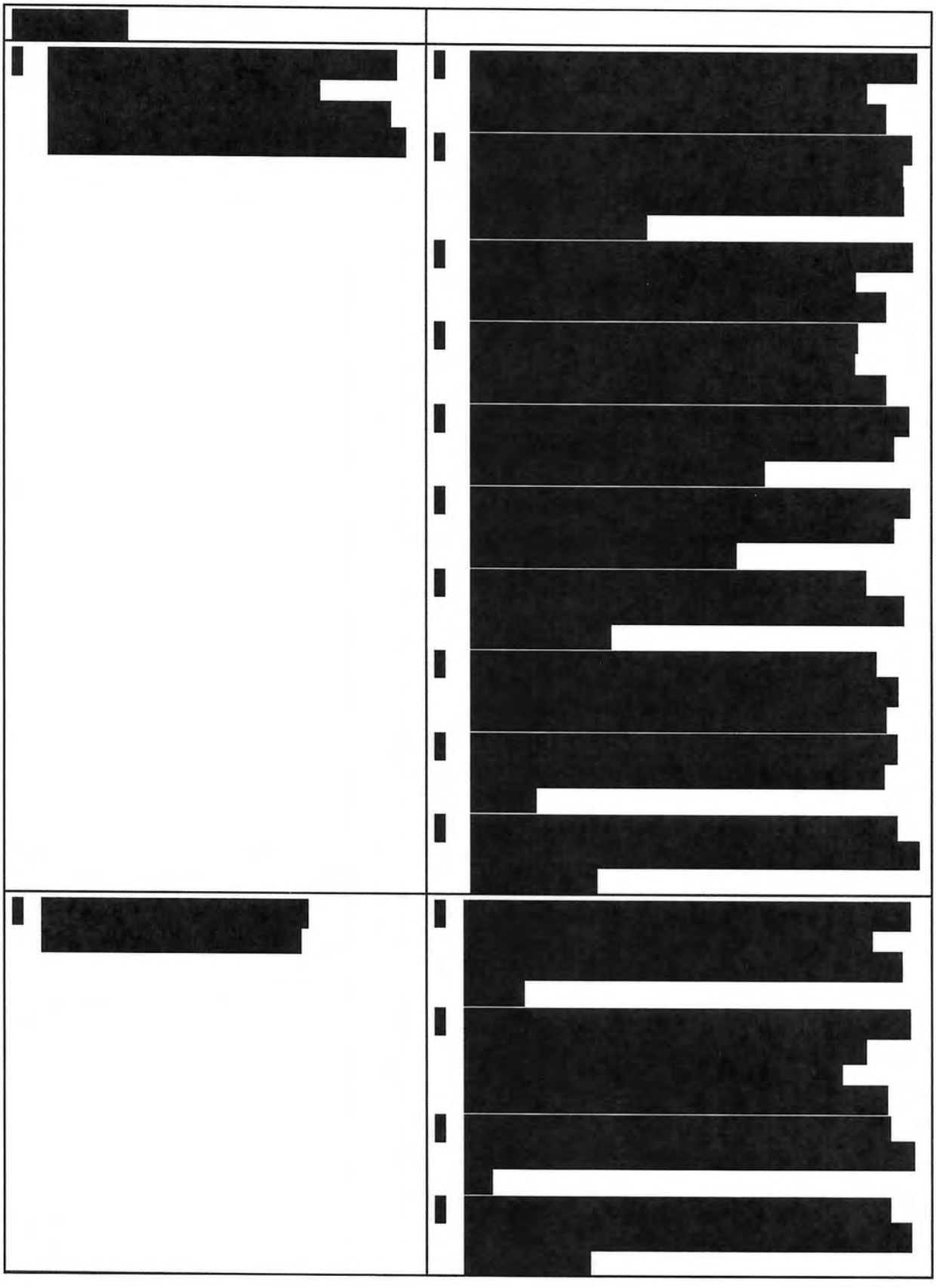
Abbreviations	Description of abbreviations
AE	Adverse event
AGA	Androgenetic alopecia
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
AUC	Area under the concentration-time curve
BID	Bis in die (twice a day)
BL	Baseline
BUN	Blood urea nitrogen
CFR	Code of Federal Regulations
C_{max}	Maximum plasma concentration
COVID-19	Corona virus disease of-2019
ClinRO	Clinician Reported Outcome
DHT	Dihydrotestosterone
DPCP	Diphenylcyclopropenone
ECG	Electrocardiogram
eCRF	Electronic case report form
EDC	Electronic data capture
eGFR	Estimated glomerular filtration rate
EOS	End of study
EOT	End of treatment
ET	Early Termination
FDA	Food and Drug Administration
FIH	First-in-human
GCP	Good clinical practice
GGT	Gamma-glutamyl transpeptidase
HFSCs	Hair follicle stem cells
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human immunodeficiency virus
ICF	Informed consent form
ICH	International Council for Harmonisation
INR	International normalized ratio
IRB	Institutional review board
ISF	Investigator site file
IWRS	Interactive web response system
LDH	Lactate dehydrogenase
LSR	Local skin reaction
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration

Abbreviations	Description of abbreviations
MCV	Mean corpuscular volume
MedDRA	Medical dictionary for regulatory activities
MPC	Mitochondrial pyruvate carrier
MPC 1	Mitochondrial pyruvate carrier 1
NOAEL	No-observed-adverse-effect level
OTC	Over-the-counter
PD	Pharmacodynamics
PHI	Protected health information
PK	Pharmacokinetics
PRO	Patient Reported Outcome
QD	Quaque die (once daily)
QTc	Corrected QT interval
RBC	Red blood cell
SAE	Serious adverse event
SD	Standard deviation
SI	Subject identifier
SN	Subject number
SoA	Schedule of assessments
[redacted]	
TE	Telogen effluvium
TEAE	Treatment emergent adverse event
TMF	Trial master file
T_{max}	Time to maximum observed concentration
US	United States

3. STUDY SUMMARY

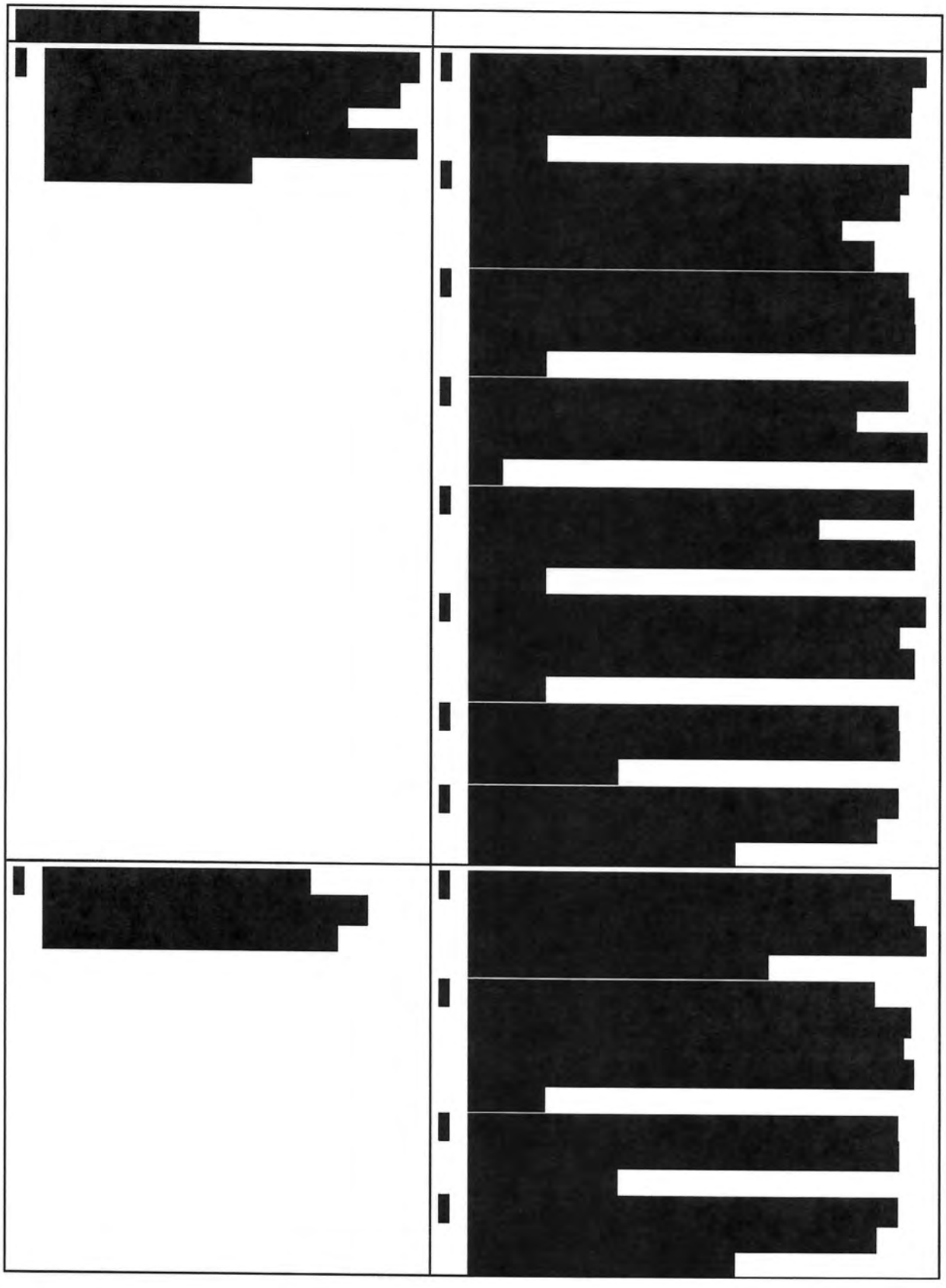
3.1. Synopsis

Title of Study: A Randomized, Multicenter, Double-blind, Vehicle-controlled, Phase 2a Study to Assess Safety, Pharmacokinetics, and Preliminary Efficacy of PP405 in Adults with Androgenetic Alopecia	
Sponsor: Pelage Pharmaceuticals, Inc.	
Phase of Study: Phase 2a	
Indication: Androgenetic alopecia	
Objectives (Randomized portion)	**Endpoints**
Primary	
• To evaluate the safety and tolerability of PP405 in subjects with androgenetic alopecia	• Incidence and magnitude of treatment-emergent laboratory abnormalities, local skin reactions (LSR), adverse events (AE), treatment emergent adverse events (TEAE) and serious adverse events (SAE) • Change from baseline in vital signs • Change from baseline in electrocardiogram (ECG)
Secondary	
• To assess the concentration of PP405 in plasma in subjects with androgenetic alopecia	• Plasma concentrations of PP405 on Days 1, 14, and 28



• [redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Objectives (Open-label Extension [OLE])	Endpoints
Primary (OLE)	
• To evaluate the safety and tolerability of 3 months of open-label treatment with daily PP405 in subjects with androgenetic alopecia	• Incidence and magnitude of treatment-emergent laboratory abnormalities, LSRs, AEs, TEAEs, and SAEs • Change from OLE baseline in vital signs. • Change from OLE baseline in ECGs
Secondary (OLE)	
• To assess the concentration of PP405 in plasma during 3 months of open-label treatment in subjects with androgenetic alopecia	• Plasma concentrations of PP405 on Days 1, 28 and 84



• [redacted]	[redacted]
[redacted]	[redacted]

Study Design: This is a multicenter, double-blind, vehicle-controlled study of the safety, tolerability and preliminary efficacy of PP405 in subjects with androgenetic alopecia. Approximately 60 subjects will be randomized 2:1 in the randomized portion to receive PP405 0.05% or vehicle, as once daily topical gels for 28 days (see Schema in Section 3.4). Subjects will have a final follow-up visit to evaluate endpoints on Day 84. Randomization will be stratified by sex at birth and by the hair loss type based on the Norwood Hamilton Scale (men) or the Savin Scale (women). Enrollment of women will be capped at no more than 15 subjects (or 25% of the planned study population).

At selected study sites, [redacted] Safety will be assessed through physical examination, vital signs, serum chemistry, hematology, urinalysis, 12-lead-electrocardiogram, incidence and severity of local skin reactions, adverse events, treatment emergent adverse events, and serious adverse events before and after the treatment. [redacted] The PK of PP405 will be evaluated in plasma. Assessment of these endpoints will occur at the timepoints specified in the Schedule of Assessments (SOA; Section 3.2).

Subjects randomized to the vehicle arm in the randomized portion of this study who complete the treatment period and the follow-up period may be eligible to participate in the OLE portion of the study. Subjects will be re-screened based on the OLE entry criteria (see below) and will then receive open-label treatment with once-daily PP405 topical gel for 12 weeks at the same dose (0.5%) administered in the randomized portion of the study (see schema in Section 3.5). Subjects will be evaluated with a subset of the assessments used during the randomized portion, as shown in the SOA for the OLE portion (Section 3.3).

Planned Sample Size: Approximately 60 subjects will be included in the randomized portion of the study, including approximately 40 randomized to PP405 and 20 randomized to vehicle control; the subjects randomized to vehicle during the randomized portion may subsequently enter the OLE.

Inclusion Criteria (Randomized Portion):

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Male or pre-menopausal female subjects aged ≥ 18 to 55 years at the time of consent.
2. Able and willing to provide written informed consent after the nature of the study is fully explained. Note: Consent must be obtained prior to initiating any study-related procedures.
3. Clinical onset of AGA for at least 6 months prior to screening (information obtained from medical chart or subject's physician, or directly from the subject)
4. Males must have an AGA modified Norwood-Hamilton Classification score of Type III vertex, Type IV, or Type V (Gupta 2016; Appendix B); females must have a Savin classification score of I-2, I-3, or I-4 (See Appendix C).

5. Willing to use a non-medicated shampoo/conditioner as outlined in Section 8.1 for the duration of the study (use of conditioner is optional for subjects who do not use conditioner).
6. Willing to keep the same hair style for the duration of the trial. Note: subjects may cut or dye their hair, but the style and color should not change during the study. Subjects should not shave their heads at any time during the study (hair should have a minimum length of approximately 3 mm).
7. Female subjects must agree to use an approved highly effective birth control method (< 1% failure rate per year) for at least 28 days prior to randomization, and for 56 days after the last dose of study drug, unless documented to have a reproductive status of non-childbearing potential as defined in Section 8.3.
8. Males with female partners must agree to, and attest that, female partners of childbearing potential are using one of the allowed highly effective methods of contraception as described in Section 8.3 for at least 28 days prior to randomization and for 56 days after the last dose of study drug. Vasectomy is acceptable as a highly effective method of contraception if the subject has received medical assessment of surgical success. Male subjects may not donate sperm for at least 56 days after the last dose of study drug.
9. Willing and able to complete all study protocol-required assessments (e.g., [redacted] eDiary [redacted] where applicable).

Exclusion Criteria (Randomized Portion):

A subject who meets any of the following criteria at the screening and/or baseline visits, as applicable, will be excluded from participation in this study:

1. Clinical diagnosis of alopecia areata, scarring alopecia, or other non-AGA forms of alopecia, excluding telogen effluvium (TE) diagnosed greater than 6 months prior to screening. Subjects with TE diagnosed greater than 6 months prior to screening that has since resolved are allowed.
2. Hair loss in the treatment area, due to disease (excluding AGA being studied under this protocol), scarring, injury, or medical therapy.
3. History of surgical correction of hair loss including hair transplant on the scalp at any time.
4. Treatment with platelet-rich plasma within 12 months of baseline.
5. Use of medical devices/procedures for the purpose of hair regrowth/preservation (e.g., low-level light/laser or cold therapy) within 6 months of baseline.
6. Use of permanent or semi-permanent hair products (e.g., texturizers, perms, or relaxers) within 30 days prior to baseline.
7. Use of medicated shampoo or conditioner (over the counter or prescription) within 14 days prior to baseline.
8. Use of tanning booth within 6 months of baseline.
9. Use of systemic finasteride, dutasteride, flutamide, cyproterone acetate, spironolactone, dihydrotestosterone (DHT) blockers, or any prescription products with hormonal effects (with the exclusion of birth control) within 12 months of baseline, use of systemic or topical minoxidil within 6 months of baseline, or use of other systemic therapies for treatment of hair loss (e.g., antihistamines including cimetidine) within 12 weeks prior to baseline. Note: There is no washout period for Over-the-counter (OTC) supplements, such as biotin, multivitamins,

Nutrafol/Viviscal and Saw Palmetto, etc. that are intended to treat AGA. However, if the subject is using any of these products for the purpose of AGA, they must stop using the products at the time of informed consent and for the duration of the trial.

10. Treatment with topical/local drugs including intralesional steroids, anthralin, squaric acid, diphenylcyclopropenone (DPCP), topical tacrolimus, topical finasteride, or other medication which in the opinion of the investigator may affect hair regrowth within 6 months of baseline.
11. Treatment with systemic steroids within 12 weeks of baseline. Note: Intranasal corticosteroids and inhaled corticosteroids are allowed; eye and ear drops containing corticosteroids are also allowed.
12. Treatment with MPC inhibitors such as thiazolidinediones, or CYP2C9 substrates with a narrow therapeutic index (i.e., warfarin, acenocoumarol, sulfonylureas, and phenytoin), 30 days prior to baseline.
13. History of hair loss at the vertex for greater than 10 years prior to screening.
14. Subjects on an intermittent fasting dietary regimen that would affect hair growth, in the opinion of the investigator.
15. Subjects who have experienced significant weight loss due to GLP1 inhibitors in the past 12 months prior to baseline that in the opinion of the investigator would contribute to hair loss.
16. Use of biologics for conditions such as psoriasis or rheumatoid arthritis within 6 months of baseline.
17. Use of beta-blockers for conditions such as hypertension within 12 weeks of baseline.
18. Concurrent use of an occlusive wig, hair extensions, or hair weaves.
19. Active skin diseases involving the scalp (e.g., psoriasis, atopic dermatitis, seborrheic dermatitis) or cuts and/or abrasions on the scalp (e.g., tattoos) that, in the opinion of the investigator, would put the subject at risk or interfere with the study conduct or study evaluations.
20. Known hypersensitivity or previous allergic reaction to any of the active or inactive ingredients in the study drug; subjects with known sensitivity to thiazolidinediones.
21. Women who are pregnant, breastfeeding, or planning to become pregnant during the study.
22. Diagnosis of COVID within $\leq$ 6 months of baseline. Note: COVID vaccination at any time is allowed.
23. Ongoing substance or alcohol abuse that would, in the investigator's opinion, interfere with hair growth/loss or interfere with the subject's participation in the trial.
24. Active medical conditions that in the opinion of the investigator would increase the risks associated with study participation.
25. Clinically significant abnormal laboratory results at screening, including estimated glomerular filtration rate (eGFR) level below 90 as assessed by the investigator.
26. Known history of chronic infectious disease (e.g., hepatitis B, hepatitis C, or human immunodeficiency virus [HIV]).
27. History of cancer in the last 5 years prior to baseline, other than non-melanoma skin cell cancers cured by local resection, or localized carcinoma in situ of the cervix.

28. Participation in any other investigational drug or medical device study which included administration of a study drug or medical device, within 30 days or 5 half-lives of the investigational agent, whichever is longer, prior to baseline. Subjects will also be excluded if the interventional clinical trial includes a biological drug within 12 weeks or 5 half-lives, whichever is longer, prior to baseline.
29. Presence of other diseases that can have an impact on hair loss or temporary hair loss condition within 6 months of baseline such as: thyroid problems, hepatic disease, and malnutrition.
30. Medical risk because of other systemic diseases or active uncontrolled infections, or any other condition which, in the judgment of the investigator, would put the subject at an unacceptable risk for participation in the study.
31. For subjects at sites [redacted]

Inclusion Criteria (Open-label Extension):

In order to be eligible to participate in the OLE portion of this study, a subject must meet all of the following criteria:

1. Randomized to the vehicle arm in the randomized portion of this study and completed the treatment period and the follow-up period through Day 84.
2. Able and willing to provide written informed consent after the nature of the study is fully explained. Note: Consent must be obtained prior to initiating any study-related procedures.
3. Males must have an AGA modified Norwood-Hamilton Classification score of Type III vertex, Type IV, or Type V (Gupta 2016; Appendix B); females must have a Savin classification score of I-2, I-3, or I-4 (See Appendix C). Any subjects who experienced a change (improvement or worsening) of AGA classification score by $\geq$ 2from baseline of the randomized portion to screening for the OLE portion will be excluded from the OLE.
4. Had no TEAEs or AEs that required them to stop the study drug during the randomized portion of the study.
5. Willing to use a non-medicated shampoo/conditioner as outlined in Section 8.1 for the duration of the study (use of conditioner is optional for subjects who do not use conditioner).
6. Willing to keep the same hair style from time of informed consent through Day 168. Note: subjects may cut or dye their hair, but the style and color should not change during the OLE. Subjects should not shave their heads at any time during the OLE (hair should have a minimum length of approximately 3 mm). Occlusive wigs, hair extensions, hair weaves, and tight hairstyles that create traction on the hair (e.g., tight braids, tight ponytails) are not allowed.
7. Female subjects must agree to use an approved highly effective birth control method (< 1% failure rate per year) for at least 28 days prior to OLE Day 1, and for 84 days after the last

dose of study drug, unless documented to have a reproductive status of non-childbearing potential as defined in Section 8.3.

8. Males with female partners must agree to, and attest that, female partners of childbearing potential are using one of the allowed highly effective methods of contraception as described in Section 8.3 for at least 28 days prior to OLE Day 1 and for 56 days after the last dose of study drug. Vasectomy is acceptable as a highly effective method of contraception if the subject has received medical assessment of surgical success. Male subjects may not donate sperm for at least 56 days after the last dose of study drug.
9. Willing and able to complete all study protocol-required assessments (e.g., [redacted], and eDiary). [redacted]

Exclusion Criteria (Open-label Extension):

A subject who meets any of the following criteria at the OLE screening and/or baseline visits, as applicable, will be excluded from participation in the OLE portion of the study:

1. Clinical diagnosis of alopecia areata, scarring alopecia, or other non-AGA forms of alopecia, excluding telogen effluvium (TE) diagnosed greater than 6 months prior to screening. Subjects with TE diagnosed greater than 6 months prior to screening that has since resolved are allowed.
2. Hair loss in the treatment area, due to disease (excluding AGA being studied under this protocol), scarring, injury, or medical therapy.
3. Treatment with platelet-rich plasma within 12 months of OLE baseline.
4. History of surgical correction of hair loss including hair transplant on the scalp at any time
5. Use of medical devices/procedures for the purpose of hair regrowth/preservation (e.g., low-level light/laser or cold therapy) within 6 months of OLE baseline.
6. Use of permanent or semi-permanent hair products (e.g., texturizers, perms, or relaxers) within 30 days prior to OLE baseline.
7. Use of medicated shampoo or conditioner (over the counter or prescription) within 14 days prior to OLE baseline.
8. Use of tanning booth within 6 months of OLE baseline.
9. Use of systemic finasteride, dutasteride, flutamide, cyproterone acetate, spironolactone, DHT blockers, or any prescription products with hormonal effects (with the exclusion of birth control) within 12 months of OLE baseline, use of systemic or topical minoxidil within 6 months of OLE baseline, or use of other systemic therapies for treatment of hair loss (e.g., antihistamines including cimetidine) within 12 weeks prior to OLE baseline. Note: There is no washout period for OTC supplements, such as biotin, multivitamins, Nutrafol/Viviscal and Saw Palmetto, etc. that are intended to treat AGA. However, if the subject is using any of these products for the purpose of AGA, they must stop using the products at the time of informed consent and for the duration of the trial.
10. Treatment with topical/local drugs including intralesional steroids, anthralin, squaric acid, DPCP, topical tacrolimus, topical finasteride, or other medication which in the opinion of the investigator may affect hair regrowth within 6 months of OLE baseline.

11. Treatment with systemic steroids within 12 weeks of OLE baseline. Note: intranasal corticosteroids and inhaled corticosteroids are allowed; eye and ear drops containing corticosteroids are also allowed.
12. Treatment with MPC inhibitors such as thiazolidinediones, or CYP2C9 substrates with a narrow therapeutic index (i.e., warfarin, acenocoumarol, sulfonylureas, and phenytoin), 30 days prior to OLE baseline.
13. Subjects on an intermittent fasting dietary regimen that would affect hair growth, in the opinion of the investigator.
14. Subjects who have experienced significant weight loss due to GLP1 inhibitors in the past 12 months prior to OLE baseline that in the opinion of the investigator would contribute to hair loss.
15. Use of biologics for conditions such as psoriasis or rheumatoid arthritis within 6 months of OLE baseline.
16. Use of beta-blockers for conditions such as hypertension within 12 weeks of OLE baseline.
17. Concurrent use of an occlusive wig, hair extensions, or hair weaves.
18. Active skin diseases involving the scalp (e.g., psoriasis, atopic dermatitis, seborrheic dermatitis) or cuts and/or abrasions on the scalp (e.g., tattoos) that, in the opinion of the investigator, would put the subject at risk or interfere with the study conduct or study evaluations.
19. Known hypersensitivity or previous allergic reaction to any of the active or inactive ingredients in the study drug; subjects with known sensitivity to thiazolidinediones.
20. Women who are pregnant, breastfeeding, or planning to become pregnant during the study.
21. Diagnosis of COVID within $\leq$ 6 months of OLE baseline. Note: COVID vaccination at any time is allowed.
22. Ongoing substance or alcohol abuse that would, in the investigator's opinion, interfere with hair growth/loss or interfere with the subject's participation in the trial.
23. Active medical conditions that in the opinion of the investigator would increase the risks associated with study participation.
24. Presence of other diseases that can have an impact on hair loss or temporary hair loss condition within 6 months of OLE baseline such as: thyroid problems, hepatic disease, and malnutrition.
25. Medical risk because of other systemic diseases or active uncontrolled infections, or any other condition which, in the judgment of the investigator, would put the subject at an unacceptable risk for participation in the study.
26. Clinically significant abnormal laboratory results at screening, including estimated glomerular filtration rate (eGFR) level below 90, any eGFR below 90 should be discussed with medical monitor prior to inclusion in the trial.
27. Known history of chronic infectious disease (e.g., hepatitis B, hepatitis C, or human immunodeficiency virus [HIV]).

28. History of cancer in the last 5 years prior to OLE baseline, other than non-melanoma skin cell cancers cured by local resection, or localized carcinoma in situ of the cervix.
29. Participation in any other investigational drug or medical device study which included administration of a study drug or medical device, within 30 days or 5 half-lives of the investigational agent, whichever is longer, prior to OLE baseline. Subjects will also be excluded if the interventional clinical trial includes a biological drug within 12 weeks or 5 half-lives, whichever is longer, prior to baseline (with the exception of participation in the randomized portion of this trial).

Duration of Study: Randomized Portion: Total duration of the study is up to approximately 114 days, including up to 30 days of screening, 28 days of treatment, and 56 days of post-treatment follow up
Open-label Extension: Total duration of the study is up to approximately 198 days, including up to 30 days of screening, 84 days of treatment, and 84 days of post-treatment follow up

Study Treatments and Administration:
Randomized Portion:

- PP405 Topical Gel, 0.05% (approximately 1 mL per application) applied once daily to the affected area on the scalp for 28 days. Male Subjects treating the frontal/temporal areas will apply an additional 1 mL to the frontal/temporal scalp in addition to the 1 mL for the vertex (crown).
- PP405 Vehicle Topical Gel (approximately 1 mL per application) applied once daily to the affected area on the scalp for 28 days. Male subjects treating the frontal/temporal areas will apply an additional 1 mL to the frontal/temporal scalp in addition to the 1 mL for the vertex (crown).

OLE Portion:

- PP405 Topical Gel, 0.05% (approximately 1 mL per application) applied once daily to the affected area on the scalp for 84 days. Male Subjects treating the frontal/temporal areas will apply an additional 1 mL to the frontal/temporal scalp in addition to the 1 mL for the vertex (crown).

Statistical Considerations:
Randomized Portion:
The sample size of 60 male and female subjects will be randomized 2:1 to receive PP405 0.05% or vehicle. The planned sample size is considered sufficient to meet all the objectives.

All continuous variables, including the changes from baseline, will be summarized by treatment with mean, standard deviation (SD), median, and range. All the categorical variables will be summarized by treatment with number and percentage of the subjects.

[redacted] Additional details will be provided in the Statistical Analysis Plan (SAP).

Open-label Extension:

[redacted]

3.2. Schedule of Assessments – Randomized Portion

Procedures	Screening [a]	Double-blinded Treatment Period				Follow Up Period [a]	
	-30 days	Day 1[a] (Baseline)	Day 2 [b] (Phone)	Day 14 [a]	Day 28 [a] (EOT/ET)	Day 56	Day 84 (EOS)
Visit Window (days)			+1	± 2	± 3	± 3	± 3
Informed Consent	X						
Demographics	X						
Medical History	X	X					
Inclusion/Exclusion Criteria	X	X					
Height and Weight [c]	X	X		X	X	X	X
Vital Signs (Blood pressure [sitting], heart rate, respiration rate, and body temperature)	X	X		X	X	X	X
Physical Examination [d]	X	X		X	X	X	X
12-lead ECG	X	X			X		
Treatment Area Identification		X					
Modified Norwood Hamilton Scale or Savin Scale	X	X					
[redacted]							
[redacted]							
[redacted]							
[redacted]							
[redacted]							
Randomization		X					
Local Skin Reactions [g]		X		X	X		
AE/TEAE/SAE collection [h]	X	X	X	X	X	X	X
Concomitant Medication	X	X	X	X	X	X	X
Serum Chemistry/Hematology/Urinalysis [i]	X	X		X	X		
COVID-19 Rapid Test	X	X					
Serum Pregnancy test for WOCBP	X						

Procedures	Screening [a]	Double-blinded Treatment Period				Follow Up Period [a]	
	-30 days	Day 1 [a] (Baseline)	Day 2 [b] (Phone)	Day 14 [a]	Day 28 [a] (EOT/ET)	Day 56	Day 84 (EOS)
Visit Window (days)			+1	± 2	± 3	± 3	± 3
Urine pregnancy test β hCG for WOCBP only [j]		X		X	X		X
Blood Sample for PK [k]		X		X	X		
[redacted]		[redacted]			[redacted]		
Dispense Study Drug		X		X			
Confirm subject using approved Shampoo/Conditioner [m]	X	X	X	X	X	X	X
Study Drug accountability & Return [n]				X	X		
Dispense Dosing Diary		X					
Review Dosing Diary [o]			X	X	X		
Drug Application at the clinic [p]		X		X	X		

AE = adverse event; ClinRO = clinician-reported outcome; eCRF = electronic case report form; EDC = electronic data capture system; PK = pharmacokinetics; PRO = patient reported outcome; TEAE = treatment-emergent AE

[a] Subjects will be evaluated in the clinic. Investigators should make every effort to adhere to the schedule as outlined above. In the event a subject misses a clinic visit, the subject should be instructed to complete dosing at home and return to the clinic as soon as possible to complete all study assessments required for the missed clinic visit.

[b] During the Day 2 phone call visit, the site should confirm that the subject is able to properly apply study drug.

[c] Height is only required at screening. Weight should be collected at screening and all other clinic visits.

[d] At screening and Days 1 and 28, a complete physical examination is required. On Days 14, 56, and 84, a symptom-related brief physical examination will occur if the subject is experiencing symptoms or AEs. If a symptom-related brief physical exam is required, it should include a review of all body systems that relate to the symptoms and/or AE the subject is experiencing.

[redacted]

[g] LSR assessment will be repeated pre and post application of study drug. See Section 10.10.5 for detailed instructions.

[h] SAEs will be collected at the time of informed consent and through the Day 84 follow-up visit. AEs and TEAEs will be collected from the first dose of study drug and through the Day 84 follow-up visit.

[i] If serum chemistry, hematology and urinalysis are completed ≤ 7 days prior to baseline, they will not need to be drawn on Day 1 and will be considered both screening and baseline labs. If serum chemistry, hematology, and urinalysis were completed > 7 days prior to baseline, then they will need to be drawn again on Day 1.

[j] A negative urine pregnancy test result must be obtained prior to application of the study drug. A positive urine pregnancy test at any time during the study requires immediate interruption of the study drug until a serum pregnancy test is performed and found to be negative. The subject must be discontinued from the study and followed if pregnancy is confirmed by a positive serum pregnancy test.

[k] Pk will be collected 2 hours (+/-10 minutes) post dose at each clinic visit.

[redacted]

[redacted]

[m] At each clinic visit the investigator should confirm that the subject has not changed the shampoo/conditioner since the last visit. If the subject has changed their shampoo/conditioner, the new product should be added to the concomitant medication page in the eCRF.

[n] Subjects should be instructed to bring their study drug bottles with them for each clinic visit on Days 14 and 28. The investigator or designee will weigh the pump bottles prior to dispensing (after priming) on Days 1 and 14 (as applicable) and then after dosing on Days 14 and 28. The weight should be documented in the subject's drug accountability log. Refer to Section 7.7 for instructions for final disposition and return of used bottles. On Day 14 and extra bottle of study drug will be dispensed to male subjects who are dosing both the frontal/temporal and vertex (crown) areas.

[o] Site staff should review the dosing diary with the subject at each clinic visit. During the Day 2 phone call visit site staff should confirm that subjects are completing their diaries. See Section 7.8 for dosing diary instructions and compliance.

[p] See Appendix A for guidance on the proper way to apply study drug. Subjects will apply study drug once per day every day for 28 days. It is recommended that subjects apply study drug in the evening at least 2 hours prior to bedtime. On Day 1 the subject should apply study drug themselves in the clinic under the supervision of trained study staff to ensure a complete understanding of how to apply the study drug. On Days 14 and 28 subjects should be instructed to apply study drug in the clinic rather than their normal dosing time at home.

3.3. Schedule of Assessments – Open-label Extension

Procedures	Screening [a]	Open-label Treatment Period				Follow-up Period [a]	
	-30 days	Day 1 [a] (Baseline)	Day 28 [a]	Day 56 [a]	Day 84 [a] (EOT/ET)	Day 124	Day 168 (EOS)
Visit Window (days)			± 5	± 5	± 5	± 7	± 7
Informed Consent	X						
Medical History	X	X					
Inclusion/Exclusion Criteria	X	X					
Weight	X	X	X	X	X	X	X
Vital Signs (Blood pressure [sitting], heart rate, respiration rate, and body temperature)	X	X	X	X	X	X	X
Physical Examination [b]	X	X	X	X	X	X	X
12-lead ECG	X	X			X		
Treatment Area Identification		X					
Modified Norwood Hamilton Scale or Savin Scale	X	X					
[redacted]							
[redacted]							
[redacted]							
[redacted]							
[redacted]							
[redacted]							
Local Skin Reactions [d]		X	X	X	X		
AE/TEAE/SAE collection [e]	X	X	X	X	X	X	X
Concomitant Medication	X	X	X	X	X	X	X
Serum Chemistry/Hematology/Urinalysis [f]	X	X	X	X	X		
COVID-19 Rapid Test	X	X					
Serum Pregnancy test for WOCBP	X						
Urine pregnancy test β hCG for WOCBP only [g]		X	X	X	X		X
Blood Sample for PK [h]		X	X	X	X		
Dispense Study Drug [i]		X	X	X			
Confirm subject using approved Shampoo/Conditioner [j]	X	X	X	X	X	X	X

Procedures	Screening [a]	Open-label Treatment Period				Follow-up Period [a]	
	-30 days	Day 1 [a] (Baseline)	Day 28 [a]	Day 56 [a]	Day 84 [a] (EOT/ET)	Day 124	Day 168 (EOS)
Visit Window (days)			± 5	± 5	± 5	± 7	± 7
Study Drug accountability & Return [k]			X	X	X		
Dispense Dosing Diary		X					
Review Dosing Diary [l]			X	X	X		
Drug Application at the clinic [m]		X	X	X	X		

AE = adverse event; ClinRO = clinician-reported outcome; eCRF = electronic case report form; PK = pharmacokinetics; PRO = patient reported outcome; TEAE = treatment-emergent AE.

[a] Subjects will be evaluated and dosed in the clinic. Investigators should make every effort to adhere to the schedule as outlined above. In the event a subject misses a clinic visit, the subject should be instructed to complete dosing at home and return to the clinic as soon as possible to complete all study assessments required for the missed clinic visit.

[b] At screening and Days 1 and 84, a complete physical examination is required. On Days 28, 56, 84 and 124, and 168, a symptom-related brief physical examination will occur if the subject is experiencing symptoms or AEs. If a symptom-related brief physical exam is required, it should include a review of all body systems that relate to the symptoms and/or AE the subject is experiencing.

[c] [redacted]

[d] LSR assessment will be repeated pre and post application of study drug. See Section 10.10.5 for detailed instructions.

[e] SAEs will be collected at the time of informed consent for the OLE and through the Day 168 follow-up visit. AEs and TEAEs will be collected from the first dose of OLE study drug and through the Day 168 follow-up visit.

[f] If serum chemistry, hematology and urinalysis are completed ≤ 7 days prior to baseline, they will not need to be drawn on Day 1 and will be considered both screening and baseline labs. If serum chemistry, hematology, and urinalysis were completed > 7 days prior to baseline, then they will need to be drawn again on Day 1.

[g] A negative urine pregnancy test result must be obtained prior to application of the study drug. A positive urine pregnancy test at any time during the study requires immediate interruption of the study drug until a serum pregnancy test is performed and found to be negative. The subject must be discontinued from the study and followed if pregnancy is confirmed by a positive serum pregnancy test.

[h] PK will be collected 2 hours (+/-10 minutes) post dose on Days 1, 28 and 56. For the Day 84 visit samples will be collected at 1, 2, and 4 hours post dose (+/-10 minutes).

[i] At every visit, 2 bottles will be dispensed for those subjects treating 1 area and 3 bottles for those treating 2 areas.

[j] At each clinic visit the investigator should confirm that the subject has not changed the shampoo/conditioner since the last visit. If the subject has changed their shampoo/conditioner, the new product should be added to the concomitant medication page in the eCRF.

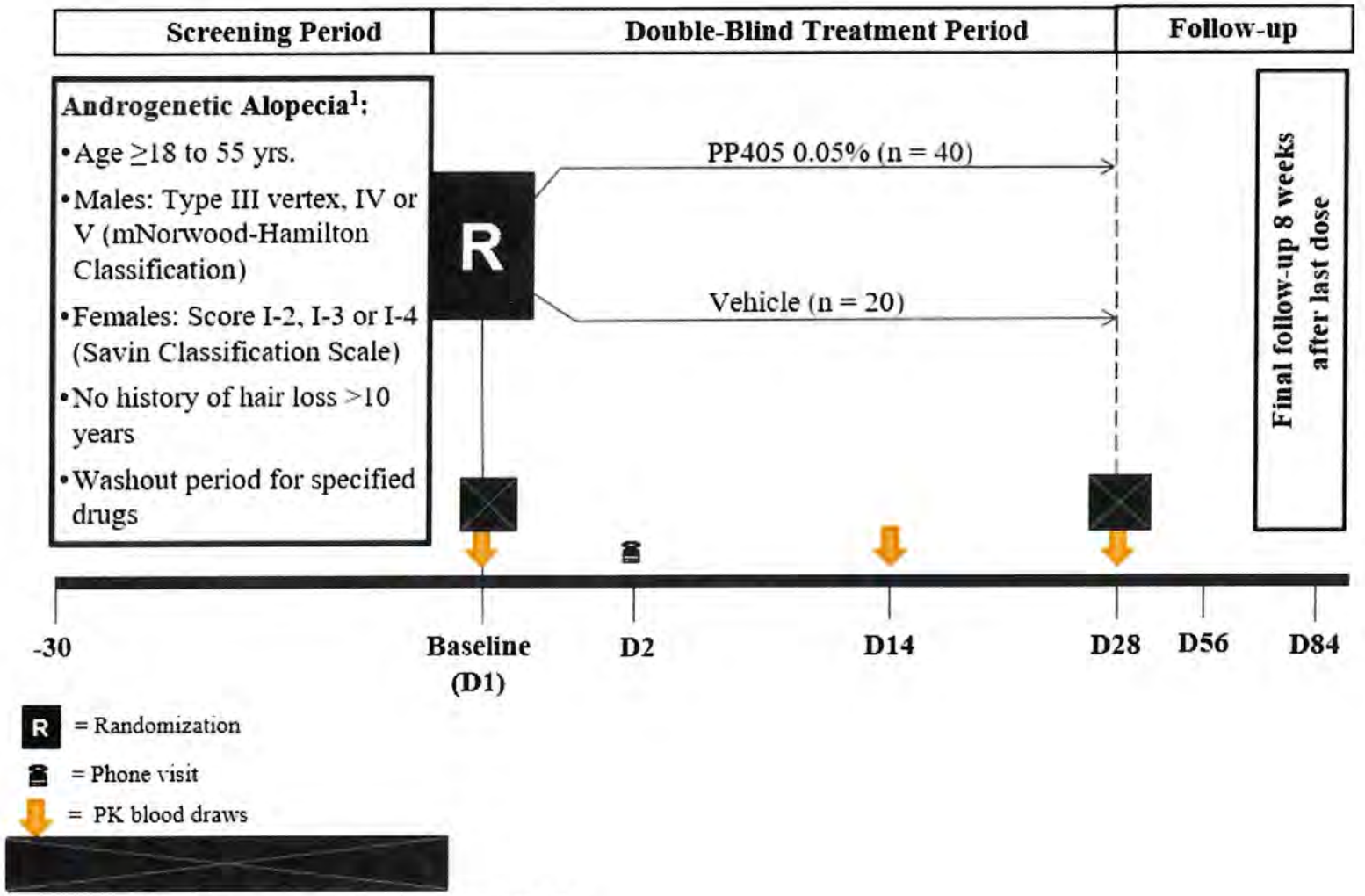
[k] Subjects should be instructed to bring their study drug bottles with them for each clinic visit on Days 28, 56, and 84. The investigator or designee will weigh the pump bottles prior to dispensing (after priming) on Days 1, 28, and 56 and then again after dosing. On Days 28 and 56 subjects should return the used study drug and new bottles should be dispensed. Subjects will be dosed in the clinic with the new bottles on Days 28 and 56. On Day 84 subjects will receive a final dose in the clinic and final weight of the bottle should be documented after dosing. The weight should be documented in the subject's drug accountability log. Refer to Section 7.7 for instructions for final disposition and return of used bottles.

[l] Site staff should review the dosing diary with the subject at each clinic visit and confirm completeness. See Section 7.8 for dosing diary instructions and compliance.

[m] See Appendix A for guidance on the proper way to apply study drug. Subjects will apply study drug once per day every day for 84 days. It is recommended that subjects apply study drug in the evening at least 2 hours prior to bedtime. On Day 1 the subject should apply study drug themselves in the clinic under the supervision of trained study staff to ensure a complete understanding of how to apply the study drug. On Days 28, 56, and 84 subjects should be instructed to apply study drug in the clinic rather than their normal dosing time at home.

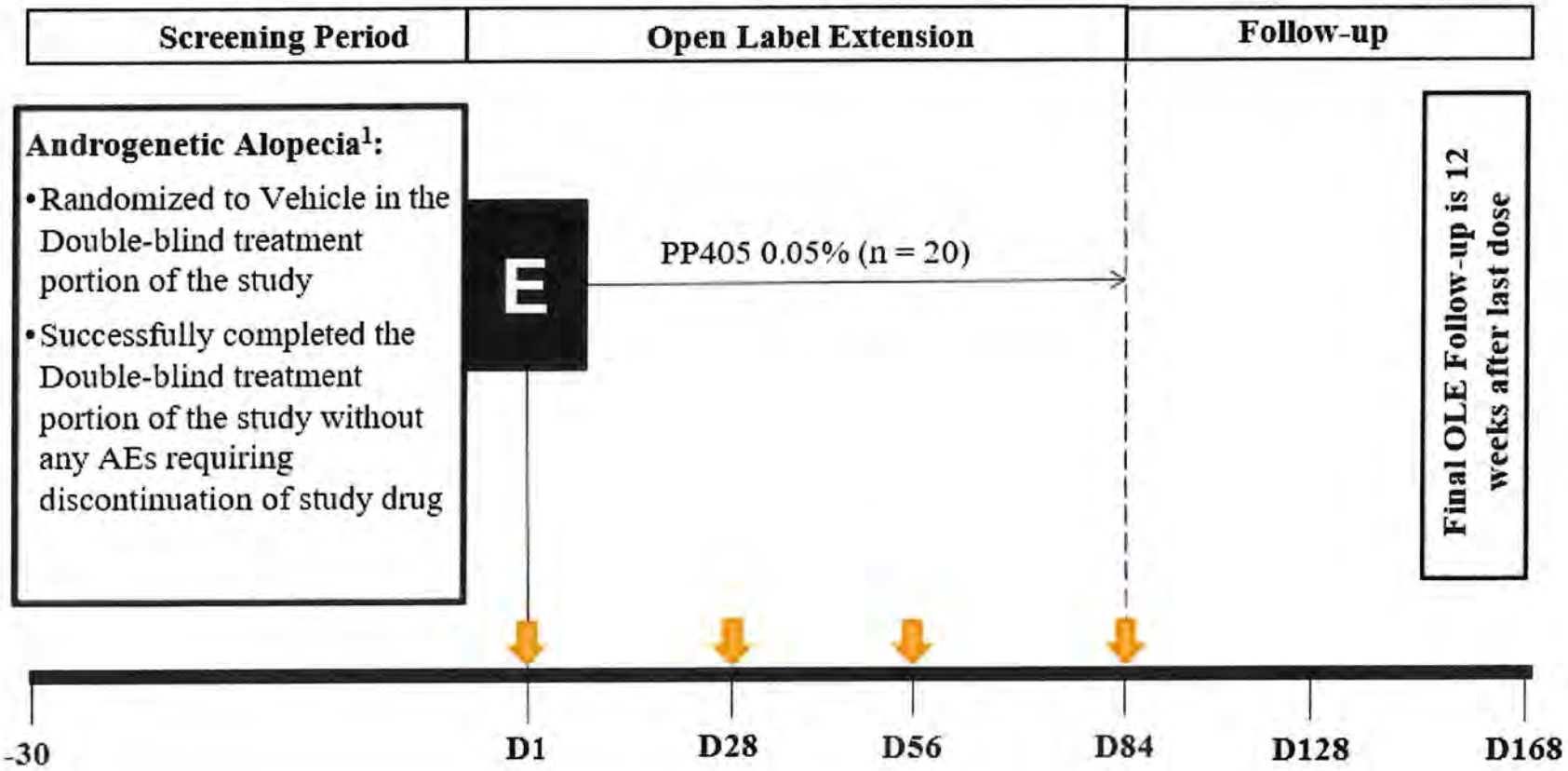
[n] [redacted]

3.4. Study Schema – Randomized Portion



[1] Refer to inclusion/exclusion criteria for a complete list.

3.5. Study Schema – Open-label Extension



E = Enroll

= PK blood draws

[1] Refer to inclusion/exclusion criteria for a complete list.

4. INTRODUCTION

4.1. Background and Rationale

4.1.1. PP405

PP405 is a specific inhibitor of mitochondrial pyruvate carrier (MPC). The MPC protein is located on mitochondrial membranes and is responsible for the transport of pyruvate from the cell cytoplasm into mitochondria. In the mitochondria, pyruvate acts as a main substrate in the Krebs cycle that drives aerobic metabolism. Inhibition of MPC shifts cellular metabolism from aerobic metabolism to anaerobic glycolytic metabolism, in which cytosolic pyruvate is converted to lactate by the key glycolytic enzyme, lactate dehydrogenase (LDH) (Schell 2014).

Activated hair follicle stem cells (HFSCs) utilize high levels of anaerobic metabolism. This was demonstrated by employing molecular genetics to block or induce the activity of LDH, specifically in HFSCs. Deletion of LDH activity in HFSCs led to a complete abrogation of HFSC activation. Conversely, genetically stimulating LDH activity by deleting MPC in HFSCs accelerated HFSC activation. This led to the hypothesis that blocking pyruvate oxidation by MPC inhibition should accelerate the natural activation of HFSCs (Dinh, Quan & Sinclair, Rodney. (2007). Female pattern hair loss: Current treatment concepts. Clinical interventions in aging. 2. 189-99.

Flores 2017).

[redacted]

4.1.2. Androgenetic Alopecia (AGA)

Alopecia is a broad term used for all types of hair loss; however, the clinical diagnosis of alopecia generally falls into 2 classifications: scarring alopecia or nonscarring alopecia. In scarring alopecia, the hair follicle is destroyed as a result of injury, infection, or inflammatory processes, and the hair follicle is replaced with scar tissue. Scarring alopecia is usually an irreversible condition.

Non-scarring alopecia is more common than scarring alopecia and includes androgenetic alopecia (AGA), alopecia areata, telogen effluvium, chemotherapy-induced alopecia, as well as other less common conditions.

The most common cause of nonscarring alopecia is AGA, also referred to as male pattern or female pattern hair loss, which is associated with the effects of dihydrotestosterone on the hair follicles. A variety of factors contribute to this condition including hormones, age, nutrition,

emotional stress, physical stress, drug effects, and genetics. In general, nonscarring hair loss including AGA can be improved or reversed with treatment (Garza 2011).

The exact prevalence of AGA is not well-established; however, most published data estimate that approximately 50% of Caucasian males will be affected by AGA by age of 50 (Severi 2003, Norwood 2001). Androgenetic alopecia can have an onset following puberty, and its prevalence increases with age.

In AGA, thick terminal hairs are gradually replaced with miniaturized, vellus hairs in well-established patterns. In males, the pattern of hair loss is well defined and involves loss of the frontal hairline with or without hair loss at the vertex and may progress to partial or complete baldness over time. The most commonly used classification in males with AGA is the Norwood–Hamilton scale, grading the extent of the hair loss from Type I (prepubertal scalp with terminal hair growth on the forehead and all over the scalp) to Type VIII (confluence of the balding areas with hair remaining only around the back and sides of the head) (Gupta 2016). Types IIIa, Iva, and Va are distinguished by prominent gradual receding of the middle portion of the frontal hairline and Type III vertex is characterized by hair loss, mainly on the scalp vertex, with frontotemporal recession that does not exceed Type III. In females, the pattern of hair loss is more variable but thinning hair is usually observed over the part line and crown, and typically does not involve frontal hairline recession or hair loss at the back of the head. Androgenetic alopecia in women typically does not lead to complete baldness. The Savin scale is the most common classification scale used to grade the severity of female pattern hair loss and ranges from I-1 to Advanced (Gupta 2016).

There are many treatment options for AGA including minoxidil, anti-androgen therapies, platelet rich plasma (PRP) therapy, low level light therapy (LLLT), and hair transplantation. The majority of these treatment modalities are not Food and Drug Administration (FDA) approved and can be associated with unwanted side effects in some cases, limiting their use. Additionally, they may not be effective in all patients or are not widely accessible due to cost (Rogers 2008). To date, the only approved medications for AGA are topical minoxidil and oral finasteride. First line therapy is typically minoxidil (2% or 5%). This product has demonstrated improvements in hair thickening and hair growth in both men and women and is generally well tolerated; however, it can be associated with local irritation, pruritus, and hypertrichosis on the face or other areas (Rogers 2008). Finasteride has demonstrated efficacy in hair growth in males with AGA but is contraindicated in women and despite its efficacy in men, is associated with side effects including decreased libido, erectile dysfunction, and mood dysregulation. (Organon, Propecia USPI June 2021).

While AGA is not life-threatening or painful, this condition has significant psychologic effects in men and women, is associated with depression and anxiety, and negatively impacts quality of life (Cash TF, Schmidt 2001, Stough 2005). Given the high prevalence of this condition, better treatment options are needed.

[redacted]

4.4. Rationale

This Phase 2a study will be randomized to ensure random allocation of subjects to treatment arms and reduce bias. [redacted], the randomized portion of the study will be double-blinded. The highest degree of subject and assessor blinding should be sought to achieve credible inferences. It is important to have a vehicle control in a Phase 2a study to control confounding factors, such as potential investigator bias, and to ensure that the statistical procedures can be appropriately applied.

A topical gel of 0.05% strength, applied once daily, has been selected as the dose regimen for this study because [redacted]

Study PP405-2001 is designed to validate safety results [redacted] while also characterizing longer term safety and PK following 28 days of administration. Additionally,

[redacted]

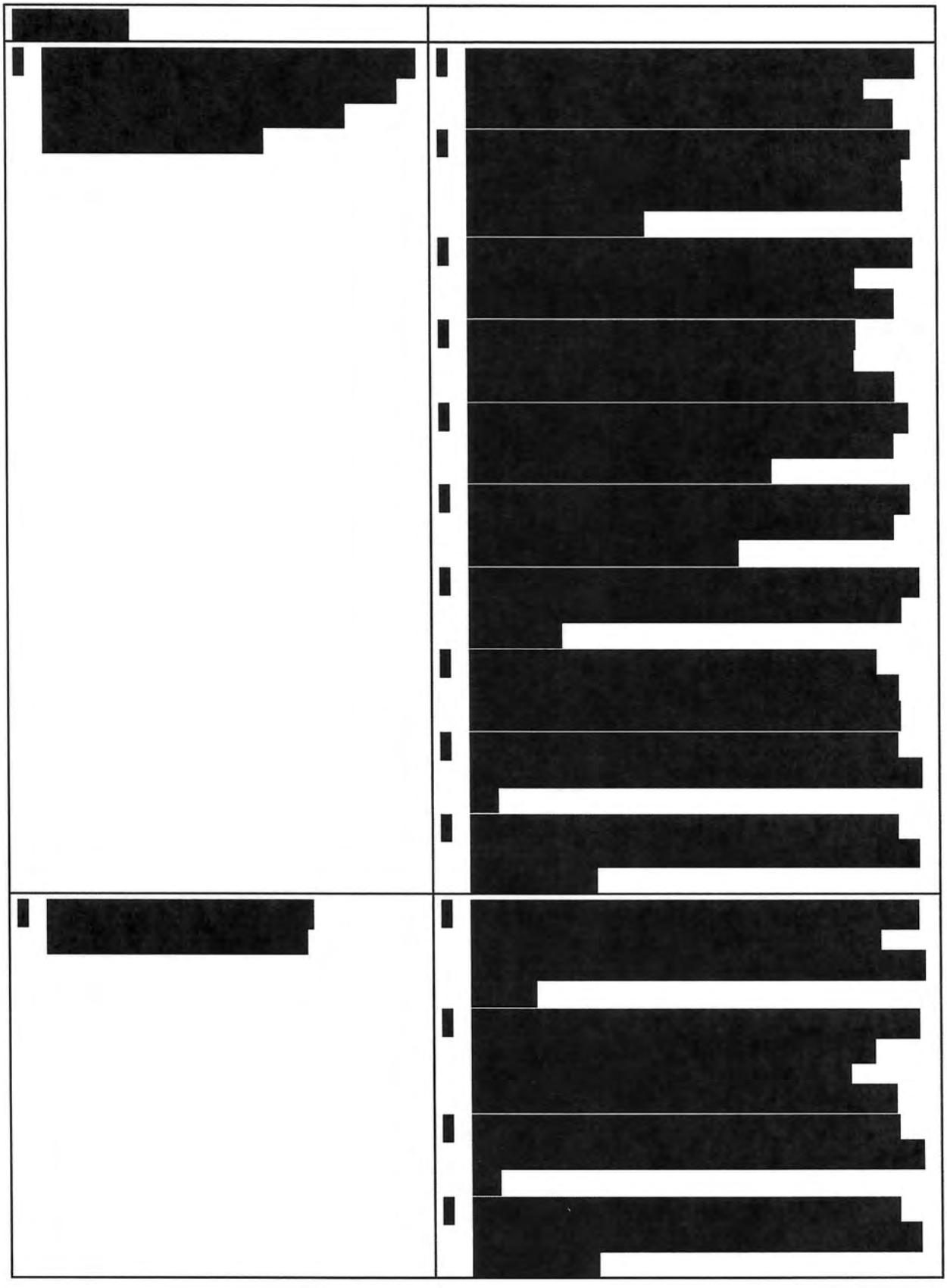
the study seeks to evaluate [redacted] of the PP405 0.05% topical gel drug product to inform further clinical development consideration.

The OLE portion of this study is intended to provide additional safety, PK, [redacted] with an extended duration of daily use 3 times longer than during the randomized portion of the study. In addition, subjects in the OLE will be able to serve as their own control after receiving vehicle in the randomized portion of the study.

5. STUDY OBJECTIVES, OUTCOMES, DESIGN AND DOSE RATIONALE

5.1. Study Objectives and Endpoints (Randomized Portion)

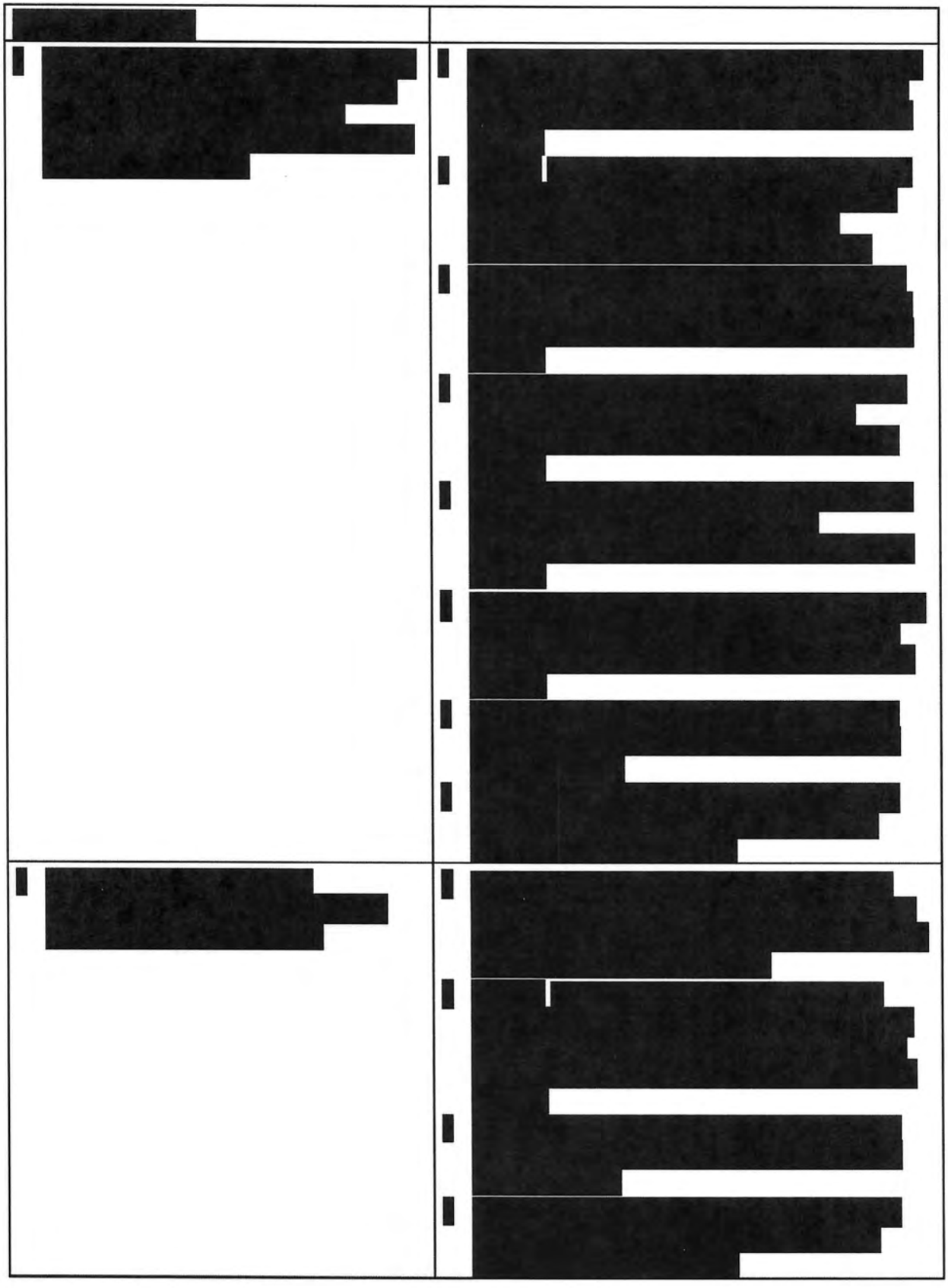
Objectives	Endpoints
Primary	
• To evaluate the safety and tolerability of PP405 in subjects with androgenetic alopecia	• Incidence and magnitude of treatment-emergent laboratory abnormalities, local skin reactions (LSR), adverse events (AE), treatment emergent adverse events (TEAE) and serious adverse events (SAE). • Change from baseline in vital signs. • Change from baseline in electrocardiogram (ECG).
Secondary	
• To assess the concentration of PP405 in plasma in subjects with androgenetic alopecia	• Plasma concentrations of PP405 on Days 1, 14, and 28.

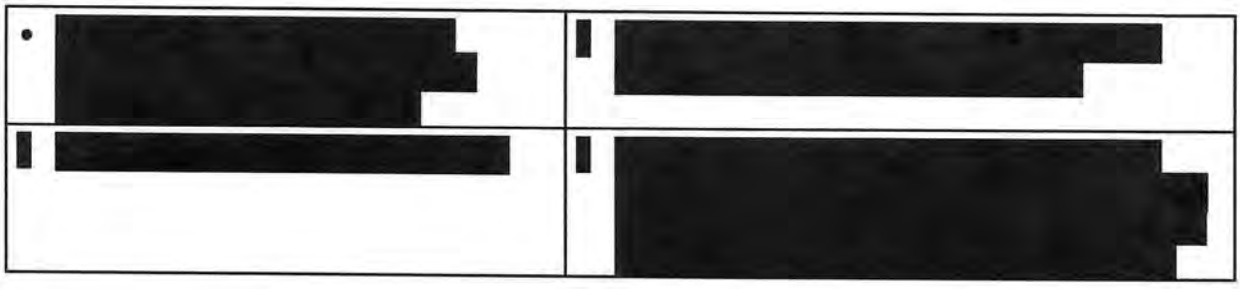


• [redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

5.2. Study Objectives and Endpoints (Open-label Extension)

Objectives (Open-label Extension [OLE])	Endpoints
Primary (OLE)	
• To evaluate the safety and tolerability of 3 months of open-label treatment with daily PP405 in subjects with androgenetic alopecia	• Incidence and magnitude of treatment-emergent laboratory abnormalities, LSRs, AEs, TEAEs, and SAEs • Change from OLE baseline in vital signs. • Change from OLE baseline in ECGs
Secondary (OLE)	
• To assess the concentration of PP405 in plasma during 3 months of open-label treatment in subjects with androgenetic alopecia	• Plasma concentrations of PP405 on Days 1, 28 and 84





5.3. Investigational Plan

5.3.1. Study Design

This is a multicenter, double-blind, vehicle-controlled study of the safety, tolerability, [redacted] of PP405 in subjects with androgenetic alopecia. Approximately 60 subjects will be randomized 2:1 in the randomized portion to receive PP405 0.05% or vehicle as once daily topical gels for 28 days (see Schema in Section 3.4). Subjects will have a final follow-up visit to evaluate the endpoints on Day 84. Randomization will be stratified by sex at birth and by the hair loss type based on the Norwood Hamilton Scale (men) or the Savin Scale (women). Enrollment of women will be capped at no more than 15 subjects (or 25% of the planned study population).

At selected study sites, a subgroup of approximately 15 male subjects will be identified by the sponsor to participate in the [redacted] on Days 1 and 28. Safety will be assessed through physical examination, vital signs, serum chemistry, hematology, urinalysis, 12-lead-electrocardiogram, incidence and severity of local skin reactions, adverse events, treatment emergent adverse events, and serious adverse events before and after the treatment. [redacted] he PK of PP405 will be evaluated in plasma. Assessment of these endpoints will occur at the timepoints specified in the Schedule of Assessments (SOA; Section 3.2).

Subjects randomized to the vehicle arm in the randomized portion of this study who complete the treatment period and the follow-up period may be eligible to participate in the OLE portion of the study. Subjects will be re-screened based on the OLE entry criteria (see Section 6.3) and will then receive open-label treatment with once-daily PP405 topical gel for 12 weeks at the same dose (0.5%) administered in the randomized portion of the study and followed for an additional 12 weeks (see schema in Section 3.5). Subjects will be evaluated with a subset of the assessments used during the randomized portion, as shown in the SOA for the OLE portion (Section 3.3).

5.3.2. Number of Centers

This study will be conducted at approximately 8 sites within the US.

5.3.3. Number of Subjects

A total of approximately 60 subjects will be enrolled in the study, including approximately 40 randomized to receive PP405 and 20 to receive vehicle during the randomized portion of the study. Of the 60 subjects, no more than 15 will be female.

In the OLE portion of the study, the subjects who received vehicle initially during the randomized portion of the study and who consent to participate and are eligible to participate, will enter the OLE to receive active treatment.

6. STUDY POPULATION

6.1. Inclusion Criteria (Randomized portion)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Male or pre-menopausal female subjects aged ≥ 18 to 55 years at the time of consent.
2. Able and willing to provide written informed consent after the nature of the study is fully explained. Note: Consent must be obtained prior to initiating any study-related procedures.
3. Clinical onset of AGA for at least 6 months prior to screening (information obtained from medical chart or subject's physician, or directly from the subject)
4. Males must have an AGA modified Norwood-Hamilton Classification score of Type III vertex, Type IV, or Type V (Gupta 2016; Appendix B); females must have a Savin classification score of I-2, I-3, or I-4 (See Appendix C).
5. Willing to use a non-medicated shampoo/conditioner as outlined in Section 8.1 for the duration of the study (use of conditioner is optional for subjects who do not use conditioner).
6. Willing to keep the same hair style for the duration of the trial. Note: subjects may cut or dye their hair, but the style and color should not change during the study. Subjects should not shave their heads at any time during the study (hair should have a minimum length of approximately 3 mm).
7. Female subjects must agree to use an approved highly effective birth control method (< 1% failure rate per year) for at least 28 days prior to randomization, and for 56 days after the last dose of study drug, unless documented to have a reproductive status of non-childbearing potential as defined in Section 8.3.
8. Males with female partners must agree to, and attest that, female partners of childbearing potential are using one of the allowed highly effective methods of contraception as described in Section 8.3 for at least 28 days prior to randomization and for 56 days after the last dose of study drug. Vasectomy is acceptable as a highly effective method of

contraception if the subject has received medical assessment of surgical success. Male subjects may not donate sperm for at least 56 days after the last dose of study drug.

9. Willing and able to complete all study protocol-required assessments (e.g., [redacted], eDiary [redacted] where applicable).

6.2. Exclusion Criteria (Randomized portion)

A subject who meets any of the following criteria at the screening and/or baseline visits, as applicable, will be excluded from participation in this study:

1. Clinical diagnosis of alopecia areata, scarring alopecia, or other non-AGA forms of alopecia, excluding telogen effluvium (TE) diagnosed greater than 6 months prior to screening. Subjects with TE diagnosed greater than 6 months prior to screening that has since resolved are allowed.
2. Hair loss in the treatment area, due to disease (excluding AGA being studied under this protocol), scarring, injury, or medical therapy.
3. History of surgical correction of hair loss including hair transplant on the scalp at any time.
4. Treatment with platelet-rich plasma within 12 months of baseline.
5. Use of medical devices/procedures for the purpose of hair regrowth/preservation (e.g., low-level light/laser or cold therapy) within 6 months of baseline.
6. Use of permanent or semi-permanent hair products (e.g., texturizers, perms, or relaxers) within 30 days prior to baseline.
7. Use of medicated shampoo or conditioner (over the counter or prescription) within 14 days prior to baseline.
8. Use of tanning booth within 6 months of baseline.
9. Use of systemic finasteride, dutasteride, flutamide, cyproterone acetate, spironolactone, dihydrotestosterone (DHT) blockers, or any prescription products with hormonal effects (with the exclusion of birth control) within 12 months of baseline, use of systemic or topical minoxidil within 6 months of baseline, or use of other systemic therapies for treatment of hair loss (e.g., antihistamines including cimetidine) within 12 weeks prior to baseline. Note: There is no washout period for over-the-counter (OTC) supplements, such as biotin, multivitamins, Nutrafol/Viviscal and Saw Palmetto, etc. that are intended to treat AGA. However, if the subject is using any of these products for the purpose of AGA, they must stop using the products at the time of informed consent and for the duration of the trial.
10. Treatment with topical/local drugs including intralesional steroids, anthralin, squaric acid, diphenylcyclopropenone (DPCP), topical tacrolimus, topical finasteride, or other

medication which in the opinion of the investigator may affect hair regrowth within 6 months of baseline.

11. Treatment with systemic steroids within 12 weeks of baseline. Note: Intranasal corticosteroids and inhaled corticosteroids are allowed; eye and ear drops containing corticosteroids are also allowed.
12. Treatment with MPC inhibitors such as thiazolidinediones, or CYP2C9 substrates with a narrow therapeutic index (i.e., warfarin, acenocoumarol, sulfonylureas, and phenytoin), 30 days prior to baseline.
13. History of hair loss at the vertex for greater than 10 years prior to screening.
14. Subjects on an intermittent fasting dietary regimen that would affect hair growth, in the opinion of the investigator.
15. Subjects who have experienced significant weight loss due to GLP1 inhibitors in the past 12 months prior to baseline that in the opinion of the investigator would contribute to hair loss.
16. Use of biologics for conditions such as psoriasis or rheumatoid arthritis within 6 months of baseline.
17. Use of beta-blockers for conditions such as hypertension within 12 weeks of baseline.
18. Concurrent use of an occlusive wig, hair extensions, or hair weaves.
19. Active skin diseases involving the scalp (e.g., psoriasis, atopic dermatitis, seborrheic dermatitis) or cuts and/or abrasions on the scalp (e.g., tattoos) that, in the opinion of the investigator, would put the subject at risk or interfere with the study conduct or study evaluations.
20. Known hypersensitivity or previous allergic reaction to any of the active or inactive ingredients in the study drug; subjects with known sensitivity to thiazolidinediones.
21. Women who are pregnant, breastfeeding, or planning to become pregnant during the study.
22. Diagnosis of COVID within $\leq$ 6 months of baseline. Note: COVID vaccination at any time is allowed.
23. Ongoing substance or alcohol abuse that would, in the investigator's opinion, interfere with hair growth/loss or interfere with the subject's participation in the trial.
24. Active medical conditions that in the opinion of the investigator would increase the risks associated with study participation.
25. Clinically significant abnormal laboratory results at screening, including estimated glomerular filtration rate (eGFR) level below 90 as assessed by the investigator.

26. Known history of chronic infectious disease (e.g., hepatitis B, hepatitis C, or human immunodeficiency virus [HIV]).
27. History of cancer in the last 5 years prior to baseline, other than non-melanoma skin cell cancers cured by local resection, or localized carcinoma in situ of the cervix.
28. Participation in any other investigational drug or medical device study which included administration of a study drug or medical device, within 30 days or 5 half-lives of the investigational agent, whichever is longer, prior to baseline. Subjects will also be excluded if the interventional clinical trial includes a biological drug within 12 weeks or 5 half-lives, whichever is longer, prior to baseline.
29. Presence of other diseases that can have an impact on hair loss or temporary hair loss condition within 6 months of baseline such as: thyroid problems, hepatic disease, and malnutrition.
30. Medical risk because of other systemic diseases or active uncontrolled infections, or any other condition which, in the judgment of the investigator, would put the subject at an unacceptable risk for participation in the study.
31. For subjects at sites [redacted]

6.3. Inclusion Criteria (Open-label Extension)

In order to be eligible to participate in the OLE portion of this study, a subject must meet all of the following criteria:

1. Randomized to the vehicle arm in the randomized portion of this study and completed the treatment period and the follow-up period through Day 84.
2. Able and willing to provide written informed consent after the nature of the study is fully explained. Note: Consent must be obtained prior to initiating any study-related procedures.
3. Males must have an AGA modified Norwood-Hamilton Classification score of Type III vertex, Type IV, or Type V (Gupta 2016; Appendix B); females must have a Savin classification score of I-2, I-3, or I-4 (See Appendix C). Any subjects who experienced a change (improvement or worsening) of AGA classification score by ≥ 2 from baseline of the randomized portion to screening for the OLE portion will be excluded from the OLE.
4. Had no TEAEs or AEs that required them to stop the study drug during the randomized portion of the study.

5. Willing to use a non-medicated shampoo/conditioner as outlined in Section 8.1 for the duration of the study (use of conditioner is optional for subjects who do not use conditioner).
6. Willing to keep the same hair style from the time of informed consent through Day 168. Note: subjects may cut or dye their hair, but the style and color should not change during the OLE. Subjects should not shave their heads at any time during the OLE (hair should have a minimum length of approximately 3 mm). Occlusive wigs, hair extensions, hair weaves, and tight hairstyles that create traction on the hair (e.g., tight braids, tight ponytails) are not allowed.
7. Female subjects must agree to use an approved highly effective birth control method (< 1% failure rate per year) for at least 28 days prior to OLE Day 1, and for 84 days after the last dose of study drug, unless documented to have a reproductive status of non-childbearing potential as defined in Section 8.3.
8. Males with female partners must agree to, and attest that, female partners of childbearing potential are using one of the allowed highly effective methods of contraception as described in Section 8.3 for at least 28 days prior to OLE Day 1 and for 56 days after the last dose of study drug. Vasectomy is acceptable as a highly effective method of contraception if the subject has received medical assessment of surgical success. Male subjects may not donate sperm for at least 56 days after the last dose of study drug.
9. Willing and able to complete all study protocol-required assessments (e.g., [redacted] and eDiary). [redacted]

6.4. Exclusion Criteria (Open-label Extension)

A subject who meets any of the following criteria at the OLE screening and/or baseline visits, as applicable, will be excluded from participation in the OLE portion of the study:

1. Clinical diagnosis of alopecia areata, scarring alopecia, or other non-AGA forms of alopecia, excluding telogen effluvium (TE) diagnosed greater than 6 months prior to screening. Subjects with TE diagnosed greater than 6 months prior to screening that has since resolved are allowed.
2. Hair loss in the treatment area, due to disease (excluding AGA being studied under this protocol), scarring, injury, or medical therapy.
3. Treatment with platelet-rich plasma within 12 months of OLE baseline.
4. History of surgical correction of hair loss including hair transplant on the scalp at any time
5. Use of medical devices/procedures for the purpose of hair regrowth/preservation (e.g., low-level light/laser or cold therapy) within 6 months of OLE baseline.
6. Use of permanent or semi-permanent hair products (e.g., texturizers, perms, or relaxers) within 30 days prior to OLE baseline.

7. Use of medicated shampoo or conditioner (over the counter or prescription) within 14 days prior to OLE baseline.
8. Use of tanning booth within 6 months of OLE baseline.
9. Use of systemic finasteride, dutasteride, flutamide, cyproterone acetate, spironolactone, DHT blockers, or any prescription products with hormonal effects (with the exclusion of birth control) within 12 months of OLE baseline, use of systemic or topical minoxidil within 6 months of OLE baseline, or use of other systemic therapies for treatment of hair loss (e.g., antihistamines including cimetidine) within 12 weeks prior to OLE baseline. Note: There is no washout period for OTC supplements, such as biotin, multivitamins, Nutrafol/Viviscal and Saw Palmetto, etc. that are intended to treat AGA. However, if the subject is using any of these products for the purpose of AGA, they must stop using the products at the time of informed consent and for the duration of the trial.
10. Treatment with topical/local drugs including intralesional steroids, anthralin, squaric acid, DPCP, topical tacrolimus, topical finasteride, or other medication which in the opinion of the investigator may affect hair regrowth within 6 months of OLE baseline.
11. Treatment with systemic steroids within 12 weeks of OLE baseline. Note: intranasal corticosteroids and inhaled corticosteroids are allowed; eye and ear drops containing corticosteroids are also allowed.
12. Treatment with MPC inhibitors such as thiazolidinediones, or CYP2C9 substrates with a narrow therapeutic index (i.e., warfarin, acenocoumarol, sulfonylureas, and phenytoin), 30 days prior to OLE baseline.
13. Subjects on an intermittent fasting dietary regimen that would affect hair growth, in the opinion of the investigator.
14. Subjects who have experienced significant weight loss due to GLP1 inhibitors in the past 12 months prior to OLE baseline that in the opinion of the investigator would contribute to hair loss.
15. Use of biologics for conditions such as psoriasis or rheumatoid arthritis within 6 months of OLE baseline.
16. Use of beta-blockers for conditions such as hypertension within 12 weeks of OLE baseline.
17. Concurrent use of an occlusive wig, hair extensions, or hair weaves.
18. Active skin diseases involving the scalp (e.g., psoriasis, atopic dermatitis, seborrheic dermatitis) or cuts and/or abrasions on the scalp (e.g., tattoos) that, in the opinion of the investigator, would put the subject at risk or interfere with the study conduct or study evaluations.
19. Known hypersensitivity or previous allergic reaction to any of the active or inactive ingredients in the study drug; subjects with known sensitivity to thiazolidinediones.
20. Women who are pregnant, breastfeeding, or planning to become pregnant during the study.

21. Diagnosis of COVID within ≤ 6 months of OLE baseline. Note: COVID vaccination at any time is allowed.
22. Ongoing substance or alcohol abuse that would, in the investigator's opinion, interfere with hair growth/loss or interfere with the subject's participation in the trial.
23. Active medical conditions that in the opinion of the investigator would increase the risks associated with study participation.
24. Presence of other diseases that can have an impact on hair loss or temporary hair loss condition within 6 months of OLE baseline such as: thyroid problems, hepatic disease, and malnutrition.
25. Medical risk because of other systemic diseases or active uncontrolled infections, or any other condition which, in the judgment of the investigator, would put the subject at an unacceptable risk for participation in the study.
26. Clinically significant abnormal laboratory results at screening, including estimated glomerular filtration rate (eGFR) level below 90, any eGFR below 90 should be discussed with medical monitor prior to inclusion in the trial.
27. Known history of chronic infectious disease (e.g., hepatitis B, hepatitis C, or human immunodeficiency virus [HIV]).
28. History of cancer in the last 5 years prior to OLE baseline, other than non-melanoma skin cell cancers cured by local resection, or localized carcinoma in situ of the cervix.
29. Participation in any other investigational drug or medical device study which included administration of a study drug or medical device, within 30 days or 5 half-lives of the investigational agent, whichever is longer, prior to OLE baseline. Subjects will also be excluded if the interventional clinical trial includes a biological drug within 12 weeks or 5 half-lives, whichever is longer, prior to OLE baseline (with the exception of participation in the randomized portion of this trial).

7. STUDY DRUG

7.1. Drug Product

PP405 Topical Gel, 0.05% [redacted]

The PP405 vehicle topical gel appearance and odor match the PP405 Topical Gel, 0.05% appearance.

7.2. Packaging and Labeling

Randomized portion: Study drug will be packaged in a non-sterile [redacted] ach bottle contains [redacted] of study drug or vehicle. The bottles will be labeled according to regulations.

Two pump bottles will be dispensed on Day 1 for all subjects. An additional bottle will be dispensed on the Day 14 visit for male subjects who are treating the vertex and frontal/temporal areas.

Open-label Extension: Active study drug will be the same as that used for the randomized portion of the study. On Days 1, 28, and 56, 2 bottles will be dispensed for those subjects treating 1 area and 3 bottles for those treating 2 areas, as described in the SOA.

7.3. Storage

Study drug must be stored at controlled room temperature, between 20° to 25°C (68° to 77°F); in a secure area and dispensed only to the subject entering the clinical study. Study drug must be protected from light and stored away from heat and moisture. Temperature excursions between 15°C and 30°C (59°F to 86°F) are allowed. Sites will monitor the temperature of the storage area and report any temperature excursions as described in the Investigational Product (IP) Manual.

7.4. Blinding and Unblinding of Study Drug

Randomized Portion:

In this blinded portion of the study, the designated group and treatment assigned to each subject will not be revealed to the investigator, the subject, or the Sponsor or designee, until the decision is made to unblind the study. Data from individual subjects may be unblinded if deemed medically necessary by the investigator or as required by local regulation in the case of an unexpected SAE. The IWRS will be used to perform emergency unblinding by authorized individuals.

The master randomization schedule will be maintained within the IWRS system and will be kept secured until the study blind is broken at the end of the randomized portion. The Sponsor or designee will specify the names of the individuals who will be unblinded prior to the database lock within a separate unblinding plan.

During the study, the blind is to be broken only when the safety of a subject is at risk and the treatment plan is dependent on the study drug received. If the unblinding occurs without the knowledge of the Sponsor and/or designee, the investigator must notify the Sponsor and/or designee as soon as possible and no later than the next business morning. All circumstances surrounding a premature unblinding must be clearly documented in the source records. The subject for whom the blind has been broken will be discontinued from the study and the investigator should make every effort to complete all procedures for the ET visit.

The sponsor or designee will not release the randomization schedule to any party except upon formal written request by the Sponsor. The request must be approved by the appropriate Sponsor personnel. Details of any disclosure of the randomization schedule will be recorded in the site's study files and the Trial Master File (TMF). A copy will also be sent to the Sponsor and/or designee. The blinding of the study will be broken after the database has been locked for the randomized portion of the study.

Open-label Extension:

After database lock for the randomized portion of the study, all subjects who were on vehicle and are eligible to participate in the OLE will receive active study medication without blinding.

7.5. Treatment Assignment

Randomized Portion:

The study subjects will be randomized in a 2:1 ratio stratified by sex at birth and severity of AGA after confirmation of eligibility using the IWRS. Further guidance and information on randomization via IWRS can be obtained in a separate manual. Subjects will be randomized to one of the following treatment groups:

Treatment Group	N
PP405 Topical Gel, 0.05% Once Daily (QD)	40
Vehicle Topical Gel (QD)	20

Open-label Extension:

All eligible subjects will receive PP405 Topical Gel, 0.05%, QD during the OLE period. Enrollment to the OLE and study drug dispensation will be managed as per the IWRS manual. Eligible subjects are those that were randomized to the vehicle arm in the randomized portion of this study and completed the treatment period and the follow-up period.

7.6. Study Drug Application

On Day 1 of the randomized portion of the study, the investigator will identify the areas of the scalp to be treated, and application of study drug will occur in the clinic under the supervision of the study site staff. Study drug should be applied to clean and dry scalp at the same time every day, preferably in the evening at least 2 hours before bed. Male subjects treating the frontal/temporal areas will apply an additional 1 mL to the frontal/temporal scalp in addition to the 1 mL for the vertex (crown). Subjects and site staff should wash their hands prior to and following study drug application and avoid contact with the eyes and mouth.

Subjects may engage in activities that require excessive sweating, shower, bathe, swim, shampoo, apply sunscreen or other approved products as long as their scalp and hair has been cleaned and dried prior to applying the study drug or it has been at least 2 hours after study drug application. after. Detailed instructions can be found in Appendix A.

Missed doses should be applied if there are at least 4 hours until the next scheduled application. The study drug must be used by the study subjects only. The treatment area(s) identified on Day 1 are the only areas the subject should apply the study drug for the duration of the treatment period.

During the OLE, the study drug application procedures will be the same as those used during the randomized portion of the study. The treatment area(s) for each subject participating in the OLE will also remain the same as the randomized portion of the study.

7.7. Dispensing and Return

The study drug will be dispensed by the investigator or designee to the subject on the days specified in the SOAs (Sections 3.2 and 3.3). The investigator or designee will prime the pump bottles and then weigh the pump bottles after priming and prior to dispensing, and then again after dispensing per the OLE SOA. Subjects will be instructed to bring their study drug with them to each clinic visit. The investigator or designee will document the weight of the pump bottles after dosing on subsequent visit days on the subject's drug accountability log. The investigator is responsible for appropriate documentation of study drug receipt, use, loss, return, disposition in the study drug dispensing and accountability log. The study drug identity, quantity, weight, and date dispensed or returned will be properly recorded in that log. The study drug dispensing and accountability will be recorded and filed appropriately in the investigator site file (ISF) and trial master file (TMF).

At the completion of the study, all used and unused study drugs will be returned to the sponsor (or designee) for disposal per the sponsor (or designee) written instructions.

7.8. Compliance

Subjects will be asked to record study drug applications during study participation using a dosing diary. The investigator or designee should review the dosing diary regularly for completeness and document the findings of the review in the subjects' source documents. If the subject has been significantly non-compliant in completing the diary the investigator should counsel the subject on the importance of properly completing the diary daily and document this discussion in the source. A subject will also be considered significantly noncompliant if he or she intentionally or repeatedly uses more than the prescribed amount of study drug as judged by the investigator.

7.9. Study Drug Accountability and Disposal

Study drug inventory and accountability records must be kept current and should be available for review by the clinical monitor.

Authorized study personnel with the monitor's guidance are responsible to reconcile any discrepancies. Following study drug reconciliation at the site, the monitor will arrange to have the study drug returned for destruction.

The investigator or designee is responsible for ensuring accountability for the study drug, including reconciliation of study drug and maintenance of study drug records. Upon receipt of study drug, the clinical site will check for accurate delivery and acknowledge receipt by signing (or initialing) and dating the documentation provided. One copy of this document will be returned to the sponsor (or designee) and the original will be maintained in the study file. In addition, an accurate study drug disposition record will be kept up to date, specifying the amount dispensed for each subject and the date of dispensing. This inventory record will be available for inspection at any time upon request. The study drug disposal documentation will be filed appropriately in the ISF and TMF. All used and unused bottles of study drug at the clinic visits will be returned to the sponsor.

8. CONCOMITANT MEDICATIONS AND PROCEDURES

All medications taken by the subject within 30 days prior to screening of the randomized portion and through the end of study participation for the randomized portion, including OTC drugs, vitamins, antacids, herbal supplements, exercise supplements (such as creatine), skin care products applied to the scalp and use of shampoo/conditioner during screening and throughout the study will be recorded in the eCRF. Note: COVID-19 vaccination should also be included on the concomitant medications log if received at any time within 6 months from screening and until the end of study participation.

OLE portion:

All medications taken by the subject from completion of the follow-up period of the randomized portion and through the end of study participation for the OLE, including OTC drugs, vitamins, antacids, herbal supplements, exercise supplements (such as creatine), skin care products applied to the scalp and use of shampoo/conditioner during screening and throughout the study will be recorded in the eCRF. Note: COVID-19 vaccination should also be included on the concomitant medications log if received at any time within 6 months from screening and until the end of study participation.

Medication entries should be specific to the generic name (if a combination drug, then marketed product name) and will include the dose, unit, and frequency of administration and/or treatment, route of administration, start date, discontinuation date, and indication.

The investigator should examine the acceptability of all concomitant procedures, medications, topical preparations, and dietary supplements not explicitly prohibited in this study.

In order to ensure that appropriate concomitant therapy is administered, subjects will be instructed to consult with the investigator prior to taking any medication (either self-administered non-prescription drugs or prescription therapy prescribed by another physician).

8.1. Permitted Treatments

Any treatment that the investigator considers necessary for a subject's welfare may be administered at the discretion of the investigator in keeping with community standards of medical care.

Subjects can use a shampoo/conditioner of their choice as long as it does not contain any of the following ingredients, ciclopirox, clindamycin, or ketoconazole or minoxidil. For both the randomized portion and the OLE portion of the study subjects should be instructed to bring their choice of shampoo/conditioner with them to the clinic or provide a picture of the bottles showing the ingredients, at screening and on Day 1. The investigator should review the ingredients listed on the subject's shampoo/conditioner and confirm it meets protocol requirements. Subjects will be instructed to use their approved shampoo beginning at least 14 days prior to dosing, throughout the treatment period and through EOS. If a subject uses a prohibited shampoo after the Day 84 visit for the randomized portion and they are participating in the OLE a wash out period of 14 days prior to Day 1 of OLE enrollment will be required. Shampoo and conditioner

product information will be documented in the source notes and eCRF. Subjects should maintain the same hair style while in the study. In addition, subjects are allowed to use sunscreen on their scalp as long as their scalp is clean and dry just prior to study drug application, or it is applied at least 2 hours after study drug application.

Subjects may continue lifestyle daily habits, such as scalp massage.

8.2. Prohibited Treatments and Procedures

Certain medications should not be administered to subjects participating in either portion of this study due to the propensity of that medication to confound the results of the study.

If the investigator determines that any of the following medications/procedures are deemed necessary to provide adequate medical support to the subject, the subject must be withdrawn from further administration of study drug:

- Any prescription or OTC product that is intended to treat AGA.
- Use of tanning booth
- Surgical correction of hair loss or hair transplant on the scalp
- Medical devices/procedures for the purpose of hair regrowth/preservation (e.g., low-level light/laser or cold therapy)
- Permanent or semi-permanent hair products; including texturizers, perms or relaxers.
- Occlusive wig, hair extensions, hair weaves, or tight hairstyles that create traction on the hair (e.g., tight braids, tight ponytails).
- Medicated shampoo or conditioner containing ciclopirox, clindamycin, ketoconazole or minoxidil (over the counter or prescription)
- Platelet-rich plasma
- Topical or systemic anti-androgenetic therapies (e.g., spironolactone, flutamide, cyproterone acetate, dutasteride and antihistamines; including cimetidine)
- Topical or intralesional steroids, systemic steroids, anthralin, squaric acid, DPCP, topical tacrolimus, minoxidil (systemic or topical), finasteride (systemic or topical) or other medications affecting hair regrowth.
- Biologics for conditions such as psoriasis or rheumatoid arthritis
- MPC inhibitors including thiazolidinediones
- Beta-blockers
- CYP2C9 substrates with narrow index (i.e., warfarin, acenocoumarol, sulfonylureas and phenytoin)
- Use of other any other investigational therapy or medical device.

8.3. Contraception

Female subjects of childbearing potential involved in any sexual intercourse that could lead to pregnancy, and male subjects with female partners of childbearing potential who participate in this study must agree to, and attest to the use (either by themselves or on behalf of their female partner) of a highly effective contraceptive method for at least 28 days prior to randomization and for 56 Days after the last dose of study drug for the randomization portion of the study. During the OLE portion of the study, contraceptive use must extend for 28 days before enrollment and for 56 days (males) or 84 days (females) after the last dose of study drug. For this study, females of childbearing potential are defined as, following menarche and until becoming post-menopausal unless permanently sterile. Permanent sterilization methods include total hysterectomy, bilateral oophorectomy, bilateral salpingectomy, or bilateral hysteroscopic sterilization at least 3 months prior to screening. For this study the following methods of contraception are acceptable highly effective contraception measures (based on a failure rate of < 1% when used consistently and correctly):

- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
    - Oral
    - Intravaginal
    - Transdermal
- Progestogen-only hormonal contraception associated with inhibition of ovulation
    - Oral
    - Injectable
    - Implantable
- Intrauterine device
- Intrauterine hormone-releasing system
- Bilateral tubal occlusion
- Vasectomy
- Sexual abstinence: **Note:** Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire study period of risk associated with the study drugs; for this study that includes from the time the subject has been randomized and for 56 days after the last dose of study drug during the randomization portion of the study (or, during the OLE, from time of enrollment to 56 days [for males] or 84 days [for females] after the last dose of study drug). The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial. The investigator must confirm that the subject is still practicing sexual abstinence and document the discussion in the subject's source documents.

9. STUDY PROCEDURES BY VISIT

The schedule of visits and procedures is provided for randomized treatment in Section 3.2 and for the open-label extension in Section 3.3. Details of the examinations and procedures are provided in a Procedure Manual and details for sample collection and processing for the clinical laboratory evaluations (hematology and clinical chemistry) and PK assessments are provided in a Laboratory/PK Manual.

Any delays in visits or assessments that are related to COVID-19 should be documented as such.

For both the Randomization and OLE portions of the study all subjects must sign the study ICF before beginning any screening procedures, and a copy of the ICF must be given to the subject. The investigator or designee must record the date when the ICF was signed in the subject's medical records.

The procedures should occur as presented in Sections 3.2 or 3.3 as applicable.

9.1. Screening

In both the randomized portion and the OLE, all subjects will have a screening period of up to 30 days. Assessments for determining eligibility will be conducted per the SOAs, see Sections 3.2 or 3.3. Written informed consent will be obtained from all subjects prior to beginning any study-related screening procedures. The collection of SAEs will begin after the subject has signed the informed consent form (ICF). Following the screening period of up to 30 days, eligible subjects will be enrolled and begin the treatment period.

An assessment by the sponsor and sponsor designee of the global photography at Screening for both the randomized portion and the OLE portion of the study will be required to confirm severity of Norwood Hamilton or Savin Scale. The investigator must receive an approval in writing by the Sponsor or designee that the subject meets the criteria as outlined in the inclusion criteria, (Section 6.1).

9.2. Treatment Period

Randomized Treatment:

After confirmation of eligibility, subjects will be randomized into one of the 2 treatment groups (active or vehicle) and begin the 28-day treatment period. Some visits in the treatment period will be required to be conducted in the clinic and some will be completed via phone.

Open-label Extension:

After confirmation of eligibility, subjects will begin the 84-day treatment period with open-label study drug. All visits in the treatment period will be required to be conducted in the clinic.

Both Periods:

The investigator should make every effort to adhere to the schedule as outlined in the respective SOAs. In the event a subject misses a clinic visit, the subject should be instructed to continue

dosing at home and return to the clinic as soon as possible to complete all study assessments required for the missed clinic visit.

If a subject needs to discontinue study drug or terminate study participation before completion of the treatment period, please refer to Section 12.3 for detailed instructions regarding recommended follow-up.

9.3. Follow Up Visit

For both the randomized and the OLE portions of the study, all subjects, regardless of when they complete their last dose of study drug, will complete 2 follow up visits as per the SOAs.

During follow-up visits, the investigator or designee will obtain information on safety laboratories, concomitant medication use, SAEs, and any AEs that were ongoing at the time of the EOT visit. In addition, subjects will be asked to [redacted]

9.4. Unscheduled Visits

Additional visits may be scheduled as necessary for [redacted] or to ensure the safety and well-being of subjects who experience AEs. Physical examination and laboratory evaluations, if necessary, should be conducted. Laboratory evaluations should be collected and analyzed using the laboratory for this study. All data for an unscheduled visit will be recorded in the eCRF.

10. STUDY PROCEDURES

10.1. Informed Consent

Subject must voluntarily sign and date the institutional review board (IRB)-approved ICF at screening before any study-related procedures are performed. A subject is considered enrolled when the investigator decides that the subject has met all the eligibility criteria and has been randomized/enrolled using the IWRS on Day 1. The investigator should document this decision and date in the eCRF.

If a subject has not met all eligibility criteria at the end of the screening period, the subject will be registered as a screen failure. All subjects who are considered screen failures will need to be entered into the EDC system along with minimal data such as demographics, screen failure details, eligibility criteria, and any SAEs, further details can be found in the eCRF completion guidelines. Screen failure subjects may be re-screened at the discretion of the investigator and in consultation with the sponsor. Rescreened subjects should be assigned a different subject number than the initial screening. All procedures planned at the screening visit, including signature of a new consent form will be performed. Subjects can only be re-screened once, if the subject screen fails during the re-screen, the subject is no longer eligible to participate in the study.

A screening and enrollment log of all potential study candidates will be maintained. The screening and enrollment log will contain limited information about the potential subject including date of signed informed consent and outcome of screening process (e.g., enrolled, reason for ineligibility, or refused to participate).

10.2. Subject Number Assignment

At the study site, each screened subject will be assigned a unique subject identifier number during the screening that will be used on all subject documentation. [redacted] Subjects entering the OLE will continue to use the same subject identifier that was assigned during the randomization portion of the study.

10.3. Treatment Area Identification

The investigator will identify the treatment area on the scalp of each subject on Day 1 of the randomization portion of the study, at the clinic. For male subjects who have hair loss in multiple areas of the scalp, both the frontal/temporal and the vertex (crown) may be treated and imaged. The margins around areas of thinning should be included in the treatment area. The treatment area for subjects who participate in the OLE will be the same areas treated during the randomized portion of the study.

10.4. Demographics

The investigator or designee will collect demographic data including sex at birth, gender, age, race, and ethnicity at screening. Demographics will not need to be recollected during the OLE.

10.5. Medical History

The investigator or designee will collect relevant medical history. Medical history will include information on the subject's concurrent medical conditions including the onset of AGA. Medical history will also include prior medical procedures and surgeries. Additionally, COVID-19 infection history and COVID-19 vaccination, within 6 months from screening, will be collected. All findings should be recorded in the eCRF. For subjects participating in the OLE, any new medications, procedures, or illness that occurs after the subject has completed the randomized portion of the study through Day 1 of the OLE will be recorded in the subject's medical history.

10.6. Prior AGA Treatment

Subjects who have used or are using AGA treatments within windows of exclusion as previously outlined are excluded from the trial. All prior AGA treatments used by the subjects will be recorded in the subject's medical history and the eCRF, and should include the dose, unit, and frequency of administration and/or treatment, route of administration, start date, discontinuation date, if known.

10.7. Modified Norwood-Hamilton Scale

For both the randomized portion and the OLE, the investigator will assess male subjects AGA using the modified Norwood-Hamilton Classification. (See Appendix B).

10.8. Savin Scale

For both the randomized portion and the OLE, the investigator will assess female subjects AGA using the Savin scale. The Savin scale measures overall thinning of the crown scalp and consists of 8 vertex density images reflecting a range from no hair loss to severe hair loss (Stages I-1, I-2, I-3, I-4, II-1, II-2, III, advanced; Dinh 2007). In this study women with hair loss stages of I-2, I-3, or I-4 will be eligible. See Appendix C.

10.10. Safety Assessments

Safety will be assessed throughout the study by the investigator or a designated and appropriately trained staff member as outlined in Sections 3.2 and 3.3. All the safety assessment findings should be recorded in the eCRF. Any safety measure that is, in the opinion of the investigator, abnormal and clinically significant must be recorded as history if found prior to the first dose of study drug, or as an AE if found after the first dose of study drug.

Open Label Extension:

Any safety measure that is, in the opinion of the investigator, abnormal and clinically significant must be recorded as history if found after the subject has completed the randomized portion of the study and prior to the first dose of study drug during the OLE. If found after the first dose of study drug during the OLE, it should be recorded as a treatment-emergent AE.

10.10.1. Vital Signs

The investigator or designee will perform vital signs assessment. Subject must be sitting in a rested and calm state for at least 5 minutes before assessment of vital signs. The following items will be measured: body temperature, pulse rate, respiration rate, and blood pressure (systolic and diastolic).

10.10.2. Physical Examination

A complete physical examination will be conducted at the timepoints noted in the SOAs and cover general appearance, dermatological, head, ears, eyes, nose, throat, respiratory,

cardiovascular, abdominal, neurological, musculoskeletal, and lymphatic body systems. A symptom-directed physical examination will occur at other visits noted in the SOAs if the subject is experiencing symptoms or AEs. If a symptom-related brief physical exam is required, it should include review of all body systems that relate to the symptoms and/or AE the subject is experiencing.

10.10.3. 12-lead Electrocardiogram (ECG)

Standard 12-lead ECG will be performed by a qualified staff member. To ensure a steady heart rate, the subject must rest quietly in the supine position for at least 5 minutes prior to performing the ECG. The ECG must include the following measurements: heart rate, QRS, QT, corrected QT interval (QTc), RR and PR intervals. ECG must be performed prior to any blood draws, study drug application and after vital signs.

ECG will be performed using equipment provided by a centralized vendor. All ECGs will be evaluated by a central ECG vendor. Details on processing will be provided to the sites in a separate ECG manual.

For both the randomized and the OLE portions, the investigator must obtain and review results of the subject's screening ECG from the central readers prior to Day 1 to determine eligibility.

In the event any abnormalities that warrant further clinical investigation or management are found, the ECG may be repeated once during the screening period to determine if the abnormality has resolved. If an abnormality still exists, the subject must be excluded from the study. In the event a clinically significant abnormality is found after the start of the first dose of study drug it must be reported as an AE.

10.10.4. Safety Laboratory Assessments

All subjects will have safety laboratory assessments as per the SOAs. All safety labs will be collected locally by a qualified staff member and sent to a central laboratory. Safety labs can be fasting or non-fasting based on the site's standard process. The safety laboratory assessments include the following:

Hematology: hematocrit, hemoglobin, red blood cell (RBC) count, white blood cell (WBC) count, mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean corpuscular volume (MCV), RBC morphology, platelet count, absolute neutrophils, absolute lymphocytes, absolute monocytes, absolute eosinophils, and absolute basophils.

Serum Chemistry: sodium, potassium, chloride, calcium, phosphorus, bicarbonate, uric acid, blood urea nitrogen (BUN), creatinine, estimated glomerular filtration rate (eGFR), total protein, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactic dehydrogenase (LDH), gamma-glutamyl transpeptidase (GGT), alkaline phosphatase, bilirubin (total and direct), international normalized ratio (INR), cortisol and random glucose.

Urinalysis: Specific gravity, color, clarity, pH, glucose, protein, blood, ketones, bilirubin, urobilinogen, nitrite, leukocyte esterase.

The results of the clinical laboratory tests will be reported by the central laboratory. The investigator must note non-clinically significant or clinically significant to define the clinical relevance of any result that is outside the normal range for the laboratory. The investigator must review, sign, and date every laboratory report. Screening labs may be repeated once at the discretion of the investigator as long as they are still within the screening window.

Pregnancy Testing: Women of childbearing potential must have a pregnancy test at study visits indicated on the SOAs (Sections 3.2 and 3.3). A negative serum pregnancy test at screening and verification of appropriate contraception as outlined in Section 8.3 is requited. At subsequent visits a urine pregnancy test is required as outlined in the SOAs. Additionally, if the site staff become aware of a subject having missed a menstrual cycle between visits, the subject should come to the site for a urine pregnancy test and entered into the EDC as an unscheduled visit. A positive urine pregnancy test at any time during the study requires immediate interruption of the study drug until a serum pregnancy test is performed and found to be negative. The subject must be discontinued from the study and followed if pregnancy is confirmed by a positive serum pregnancy test.

10.10.5. Local Skin Reactions

A static assessment of LSRs will be conducted in all subjects during the randomized and OLE portions of the study. LSRs include burning/stinging, pruritus, edema, erythema, dryness, and scaling. Each LSR will be scored as 0 (None), 1 (Mild), 2 (Moderate) or 3 (Severe).

Burning/stinging and pruritus will be assessed by the subject (Table 1) and edema/swelling, erythema, dryness, and scaling will be assessed by the investigator/designee (Table 2). Subjects will be read the definition of each subject assessed LSR and asked to select the appropriate definition. The corresponding grade will be assigned by the site and entered in the eCRF.

On the visits specified in the SOAs, LSRs will be collected prior to study drug application and approximately 15 to 45 minutes following application of study drug. All LSRs that occur after the first dose of study drug application or worsen at any time point during the study will be recorded as LSRs/AEs.

Table 1: Subject Assessed Local Skin Reactions

Score	Grade	Burning/Stinging	Pruritus
0	None	No stinging/burning	No pruritus
1	Mild	Slightly warm, tingling sensation; not really bothersome	Occasional, slight itching/scratching
2	Moderate	Definite warm; tingling/stinging sensation that is somewhat bothersome	Intermittent itching/scratching which does not disturb sleep
3	Severe	Hot, tingling/stinging sensation that has caused definite discomfort	Bothersome itching/scratching which disturbs sleep

Table 2: Investigator Assessed Local Skin Reactions

Score	Grade	Edema/swelling	Erythema	Dryness	Scaling
0	None	No edema	No erythema present	None	None
1	Mild	Slight, barely perceptible edema	Slight erythema: very light pink	Perceptible dryness with no flakes or fissure formation	Slight diffuse scaling
2	Moderate	Distinct presence of edema	Dull red, clearly distinguishable	Easily noted dryness and flakes but no fissure formation	Diffuse scaling
3	Severe	Marked, intense edema	Deep/dark red	Easily noted dryness with flakes and fissure formation	Prominent, dense scaling

10.10.6. Adverse Events

10.10.6.1. Definition

An adverse event (AE) is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related. This includes the following:

- Any clinically significant worsening of a pre-existing condition;

  Note: Emergence of a new pathogen associated with a clinical event during therapy at a site other than the initial site of infection will be considered an AE.
- Any recurrence of a pre-existing condition;
- An AE occurring from overdose of a Sponsor study drug whether accidental or intentional (i.e., a dose higher than that prescribed by a health care professional for clinical reasons);
- An AE occurring from abuse of a Sponsor study drug (i.e., use for non-clinical reasons);
- An AE that has been associated with the discontinuation of the use of a Sponsor study drug.

Note: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention. A procedure is not an AE, but the reason for a procedure may be an AE.

A pre-existing condition is a clinical condition (including a condition being treated) that is diagnosed before the subject signs the Informed Consent Form (ICF) and that is documented as part of the subject's medical history.

The questions concerning whether the condition existed before the start of the active phase of the study and whether it has increased in severity and/or frequency will be used to determine whether an event is a TEAE. An AE is considered to be treatment emergent if:

1. It is not present when the active phase of the study begins and is not a chronic condition that is part of the subject's medical history; or,

2. It is present at the start of the active phase of the study or as part of the subject's medical history, but the severity or frequency increases during the active phase.

For the randomized portion of the study, the active phase of the study begins at the time of the first dose of the study drug. The active phase of the study ends at the Day 84 Follow-up visit.

For the OLE portion of the study, the active phase of the study begins at the time of first dose of study drug during the OLE and ends at the Day 168 Follow-up visit.

10.10.6.2. Serious Adverse Events

A SAE is defined as any untoward medical occurrence that at any dose:

- results in death
- is life-threatening
- requires in-patient hospitalization or prolongation of an existing hospitalization
- results in persistent or significant disability/incapacity
- is a congenital anomaly/birth defect.

Reporting for SAEs must start when the subject signs the ICF and continue until the end of the subject's last visit for both the randomized portion of the study and the OLE portion of the study. SAEs that occur after completion of the randomization portion of the study and prior to signing the ICF for the OLE portion will be collected as medical history. A hospitalization meeting the regulatory requirement for the "serious" criteria is any in-patient hospital admission or prolongation of existing hospitalization as a result of the AE.

A life-threatening adverse drug experience is one that places the subject, in the view of the investigator, at immediate risk of death from the reaction as it occurred. It does not include a reaction that, had it occurred in more severe form, might have caused death.

Additionally, important medical events that may not be immediately life-threatening or result in death or hospitalization but that may jeopardize the subject, represent a significant hazard in the investigator's opinion, or require intervention to prevent one of the outcomes listed above, or result in urgent investigation, may be considered serious.

10.10.6.3. Reporting Procedures for All Adverse Events

All SAEs occurring after the subject signs the ICF and AEs occurring after the first dose of study drug observed by the investigator or reported by the subject (whether or not attributed to study drug), will be recorded in the source documents and on the eCRF. Serious adverse events and medically significant AEs considered related to the study drug by the investigator, or the sponsor will be followed until resolved or considered stable. If a treatment-related AE is not resolved but is considered stable at the end-of-study visit, this must be source documented.

The following attributes must be assigned by the investigator: clinical description of the event; dates of onset and resolution; severity; assessment of relatedness to study drug, serious (yes or no) and action taken.

It will be left to the investigator's clinical judgment whether or not an AE is of sufficient severity to require the subject's removal from treatment. A subject may also voluntarily withdraw from treatment due to what he perceives as an intolerable AE. If the subject was permanently withdrawn from the study or study drug due to an AE, this information must be documented in either the initial or follow-up SAE report (if the event was serious) and on the relevant eCRF.

Severity

The investigator is to define the severity of each AE using the following definitions as a guideline. The investigator will consider the range of the possible severity of the event and identify the severity that is the most appropriate according to her/his medical judgment.

- Mild – Awareness of signs or symptoms, but easily tolerated.
- Moderate – Discomfort, enough to cause interference with usual activity.
- Severe – Incapacitating with inability to perform usual activity.

The relationship of AEs to the study drug will be assessed as follows:

Relationship to Study Treatment:

The investigator will make a determination of the relationship of the AE/SAE to the study drug using a 3-category system according to the following guidelines:

Not Related: when the AE/SAE is definitely caused by the subject's clinical state, or the study procedure/conditions, or the subject did not receive the drug;

Possibly Related: when the AE follows a reasonable temporal sequence from the time of drug administration but could have been produced by the subject's clinical state or the study procedures/conditions.

Definitely Related: when the AE follows a reasonable temporal sequence from administration of the drug, abates upon discontinuation of the drug, follows a known or hypothesized cause-effect relationship, and (if appropriate) reappears when the drug is reintroduced.

10.10.6.4. Serious Adverse Event Reporting Procedures

All SAEs, including deaths occurring in the study (in both the randomized and OLE portions of the study), must be reported to the Sponsor or designee within 24 hours of discovery or notification of the event occurring after signing the ICF and until the end of study participation, regardless of study drug relationship. For subjects participating in the OLE potion of the study, if an SAE occurs after completion of the randomized portion of the study and prior to signing the ICF for the OLE, it should be reported as medical history. SAE reporting for the OLE will be required from the time the subject consents to participation in the OLE through the end of study participation regardless of AE relationship.

Initial SAE information and all amendments or additions must be recorded on a SAE report form and emailed or faxed to the following:

[redacted]

Fax number: [redacted]

Relevant medical records and other relevant information (e.g., concomitant medication eCRF, medical history eCRF, laboratory test results) should be emailed to the Sponsor or designee Safety Department as soon as they become available; autopsy reports should be provided for deaths, if available.

If a subject is permanently withdrawn from the study because of a SAE, this information must be included in the initial or follow-up SAE report form as well as the relevant eCRF.

The investigator shall notify the IRB of SAEs occurring at the site and other AE reports received from the Sponsor, in accordance with local procedures.

If the investigator becomes aware of an SAE any time after study completion of the randomized or OLE portion, and determines it is related to the study drug, the SAE must be reported to the Sponsor or designee within 24 hours of the investigator's knowledge of the SAE.

10.10.6.5. Pregnancy

Pregnancy in and of itself is not an AE, although pregnancies occurring in subjects or partners of male subjects are considered immediately reportable events. If a pregnancy occurs in a subject, study drug must be discontinued immediately, and the investigator should make every effort to complete the EOT/ET evaluations according to the SOAs (Sections 3.2 and 3.3). The pregnancy must be reported to the Sponsor or designee via email at [redacted] within 24 hours of the investigator's knowledge of the pregnancy using the Pregnancy Reporting Form.

The investigator will follow the pregnant woman until completion of the pregnancy, and must notify the Sponsor or designee, of the outcome within 24 hours of the investigator's knowledge of the pregnancy outcome. The investigator will provide this information on the Pregnancy Reporting Form. This notification includes pregnancies resulting in live, "normal" births.

If the pregnant subject experiences an SAE during pregnancy, or the outcome of the pregnancy meets the criteria for immediate classification as an SAE (i.e., spontaneous abortion [any congenital anomaly detected in an aborted fetus is to be documented], stillbirth, neonatal death, or congenital anomaly), the investigator should follow the procedures for reporting SAEs (ie, report the event to the Sponsor or designee via email at [redacted] within 24 hours of the investigator's knowledge of the event).

All neonatal deaths and congenital anomalies that occur within 30 days of birth (regardless of causality) should be reported as SAEs to the Sponsor or designee. In addition, any infant death or

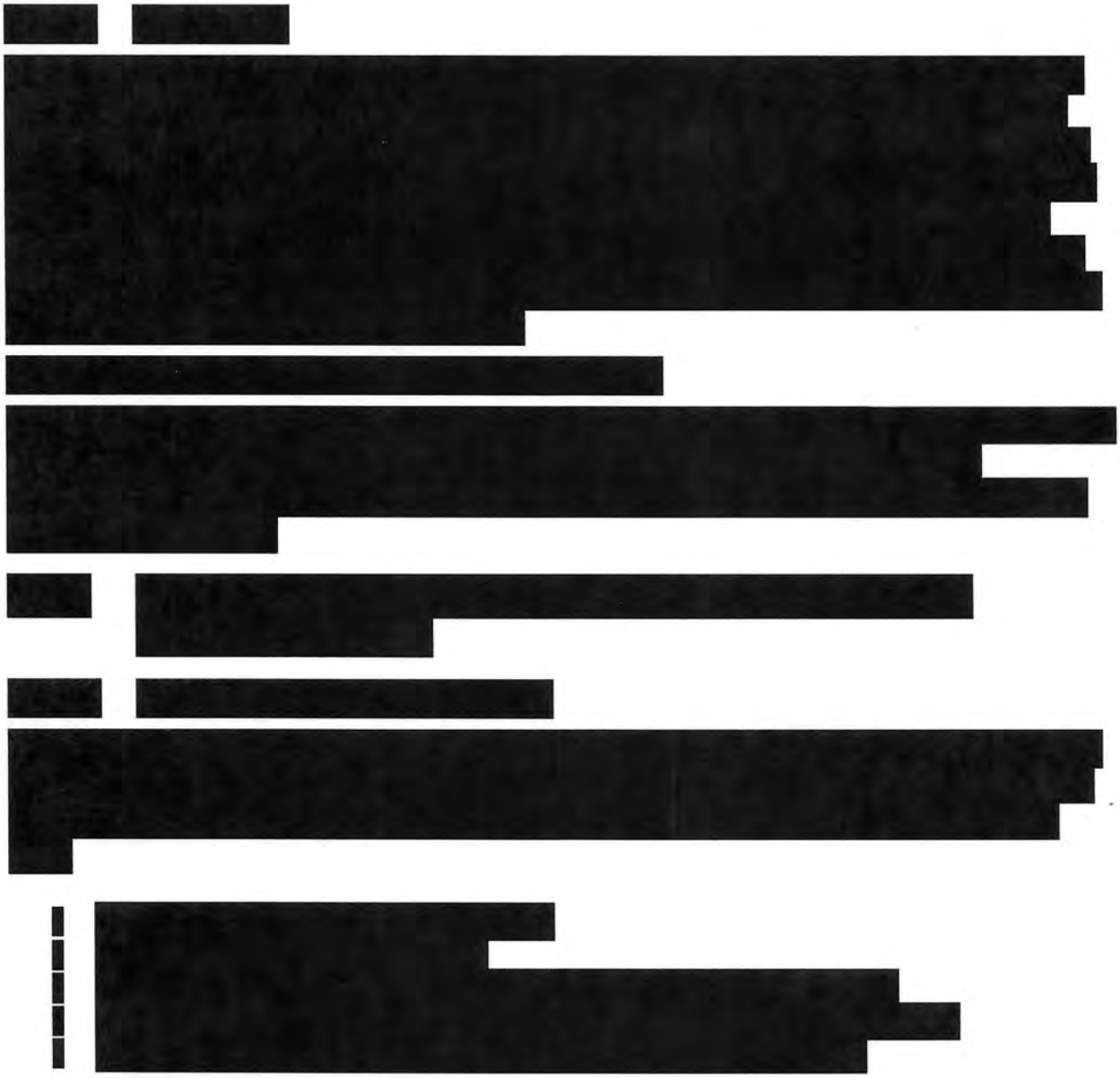
congenital anomaly occurring after study completion that the investigator suspects is related to the in-utero exposure to the study drug should also be reported to the Sponsor or designee.

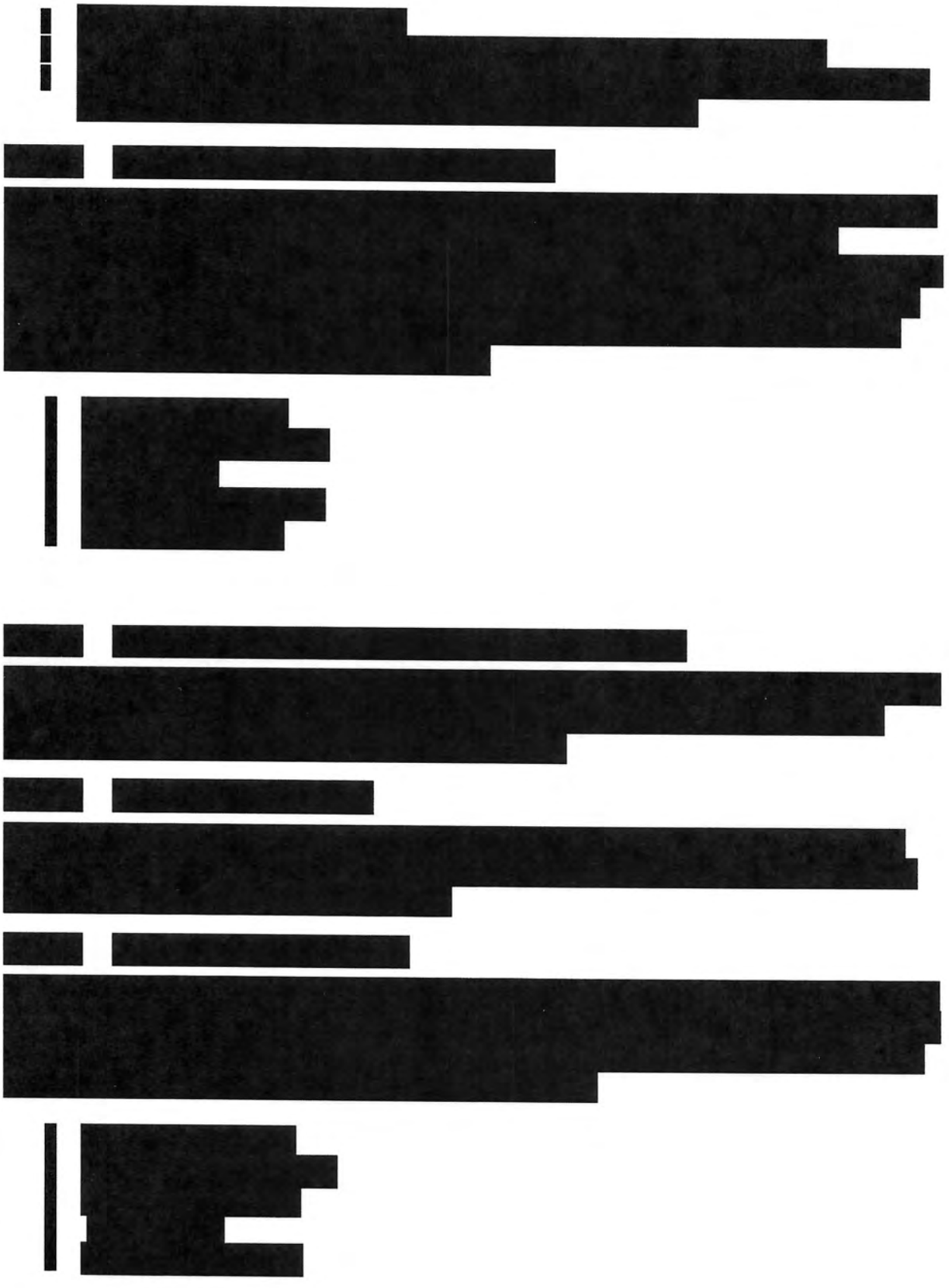
10.11. Pharmacokinetics and Pharmacodynamics

10.11.1. Blood Sample Collection

Blood samples for PK analysis of PP405 will be collected at the time points indicated on the SOAs (Sections 3.2 and 3.3).

All supplies will be provided to the study site for the collection of blood samples. Additional details regarding the collection and shipment of the PK samples can be found in the laboratory manual.





11. DOSE REDUCTION AND INTERRUPTION GUIDELINES

Subjects with a score of Grade 3 on the investigator-assessed LSR table should reduce dosing to every other day for a maximum of 5 days and then resume dosing to daily once the irritation has resolved to Grade 1 or 0. If the irritation has not resolved to Grade 1 or 0 after 5 days of every other day dosing, study drug should be discontinued.

12. REMOVAL AND REPLACEMENT OF SUBJECTS

12.1. Removal of Subjects

Subjects have the right to withdraw from the study at any time and for any reason without prejudice to his future medical care by the physician or at the institution.

Any subject who withdraws consent to participate in the study will be removed from treatment and/or study observation immediately upon the date of request. Subjects may also be removed from the study for following reasons:

- Decision by the sponsor
- Decision by study investigator
- Withdrawal of consent from study
- Death
- Lost to follow-up.

Reasons for removal from the study will be recorded on the eCRF.

12.2. Replacement of Subjects

Subject enrollment will continue until approximately 60 subjects have been randomized. Subjects who are randomized and do not complete the randomized portion or the OLE will not be replaced.

12.3. Discontinuation Criteria

Subjects have the right to withdraw from study drug, protocol procedures, or the study at any time and for any reason.

The investigator and/or sponsor can decide to withdraw a subject(s) from study drug, protocol procedures, or the study as a whole at any time prior to study completion if it is not in the best interest of the subject to continue the study.

12.3.1. Discontinuation of Study Drug

Subjects can decline to continue receiving study drug and/or protocol-required procedures at any time during the study. If this occurs, the investigator should discuss with the subject the appropriate processes for discontinuation from study drug or other protocol-required procedures and must discuss with the subject the possibilities of continuation of the SOA visits for collection of data, including outcomes, AEs, disease-related events, and must document this decision in the subject's medical records and eCRF. Subjects who have discontinued study drug and/or other protocol-required procedures should not be automatically removed from the study. Whenever safe and feasible, it is imperative that subjects should remain in the study to ensure safety surveillance and/or collection of outcome data.

Reasons for removal from protocol-required study drugs or procedural assessments include any of the following:

- Decision by the sponsor
- Decision by study investigator
- Lost to follow-up.
- Death
- Ineligibility per inclusion/exclusion criteria of the study
- Non-compliance
- Adverse Event
- Subject request

12.3.2. Withdrawal From the Study

Subjects can withdraw their consent any time during the study indicating that the subject does not wish to or is unable to continue further study participation. Subject data up to withdrawal of consent will be included in the analysis of the study, and where permitted, publicly available data can be included after withdrawal of consent. The investigator is to discuss with the subject appropriate procedures for withdrawal from the study and must document the subject's decision to withdraw in the subject's medical records and eCRF.

If a subject withdraws from the study, may request destruction of any samples taken and not tested, if this happens the investigator must make every effort get this information in writing from the subject and notify the sponsor.

In addition, once the investigator has confirmed the subject has withdrawn consent, every effort should be made to have the subject return to the clinic and complete the EOT/ET visit as described in the SOAs, see Sections 3.2 and 3.3.

12.3.3. Lost to Follow-up

A subject will be considered lost to follow-up if the subject repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a subject fails to return to the clinic for a required study visit:

- The study site must attempt to contact the subject and reschedule the missed visit as soon as possible and counsel the subject on the importance of maintaining the assigned visit schedule and ascertain whether or not the subject wishes to and/or is able to continue in the study.
- Prior to deeming the subject lost to follow-up, the investigator or designee must make every effort to regain contact with the subject (where possible, 3 telephone calls, and emails and, if necessary, a certified letter to the subject's last known mailing address or local equivalent methods). These contact attempts are to be documented in the subject's medical record and eCRF.
- If the subject continues to be unreachable, he will be considered to have withdrawn from the study with a primary reason of lost to follow-up.
- For subjects who are lost to follow-up, the investigator can search publicly available records (where permitted) to ascertain survival status. This ensures that the data set(s) produced as an outcome of the study is/are as comprehensive as possible.

13. STATISTICAL CONSIDERATIONS

13.1. Analysis Sets

The study analysis populations for the randomized portion of the study will consist of:

Population	Description
Intent-to-Treat (ITT)	All randomized/enrolled subjects.
[redacted]	[redacted]
Per-Protocol (PP)	All subjects in the ITT Population who have no major protocol violations. [redacted]

Population	Description
Safety Population (SP)	All randomized/enrolled subjects who receive any amount of study drug. The SP will be analyzed according to the treatment received. The SP will be used for safety analyses.
Pharmacokinetics (PK)	The Pharmacokinetic (PK) analysis population will include all randomized subjects who receive at least one dose of PP405 0.05% and have at least one post-baseline plasma concentration available. All subjects will be analyzed according to the actual treatment they received. This analysis population will be used to summarize PP405 plasma concentrations

The study analysis populations for the OLE portion of the study will consist of:

Population	Description
OLE Intent-to-Treat (OLE_ITT)	All enrolled subjects in the OLE portion of the study.
OLE Safety Population (OLE_SP)	All enrolled subjects in the OLE portion of the study who receive any amount of study drug. The OLE_SP will be used for safety analyses.
OLE Pharmacokinetics (OLE_PK)	The Pharmacokinetic (PK) analysis population will include all enrolled subjects in the OLE portion of the study who receive at least one dose of PP405 0.05% and have at least one post-baseline plasma concentration available. This analysis population will be used to summarize PP405 plasma concentrations

13.2. Statistical Methods for the Randomized Portion

A detailed statistical analysis plan will be signed before database lock for both the randomized portion and the OLE portion of the study.

13.2.1. Safety

All safety analyses will be summarized for all subjects in the safety population. Safety parameters include physical examinations, vital signs, 12-lead ECG, LSRs, clinical laboratory assessments, AEs, TEAEs, and SAEs. All results and changes in safety parameters will be presented by treatment and visit (where applicable).

Continuous variables will be presented using the following descriptive statistics: N, mean, standard deviation (SD), median, minimum, and maximum. Categorical variables will be presented using frequencies and percentages.

Adverse Events

AEs will be tabulated by medical dictionary for regulatory activities (MedDRA) system organ class and preferred term. The following summaries will be presented:

- Overall AEs
- TEAEs
- SAEs
- AEs by severity

Clinical Laboratory Assessments

Descriptive statistics will be presented for data related to chemistry, hematology and quantitative urinalysis. Change from baseline values will be presented for each post-baseline assessment. Frequencies and percentages for each result will be provided for qualitative urinalysis data. Separate listings of all data for chemistry, hematology, urinalysis, and pregnancy test will be provided.

Vital Signs

Descriptive statistics will be presented for data related to vital signs (systolic blood pressure diastolic blood pressure, pulse rate, respiratory rate, and body temperature). Change from baseline values will be presented for each post-baseline assessment. A listing of all vital sign assessments will be provided.

Physical Examination

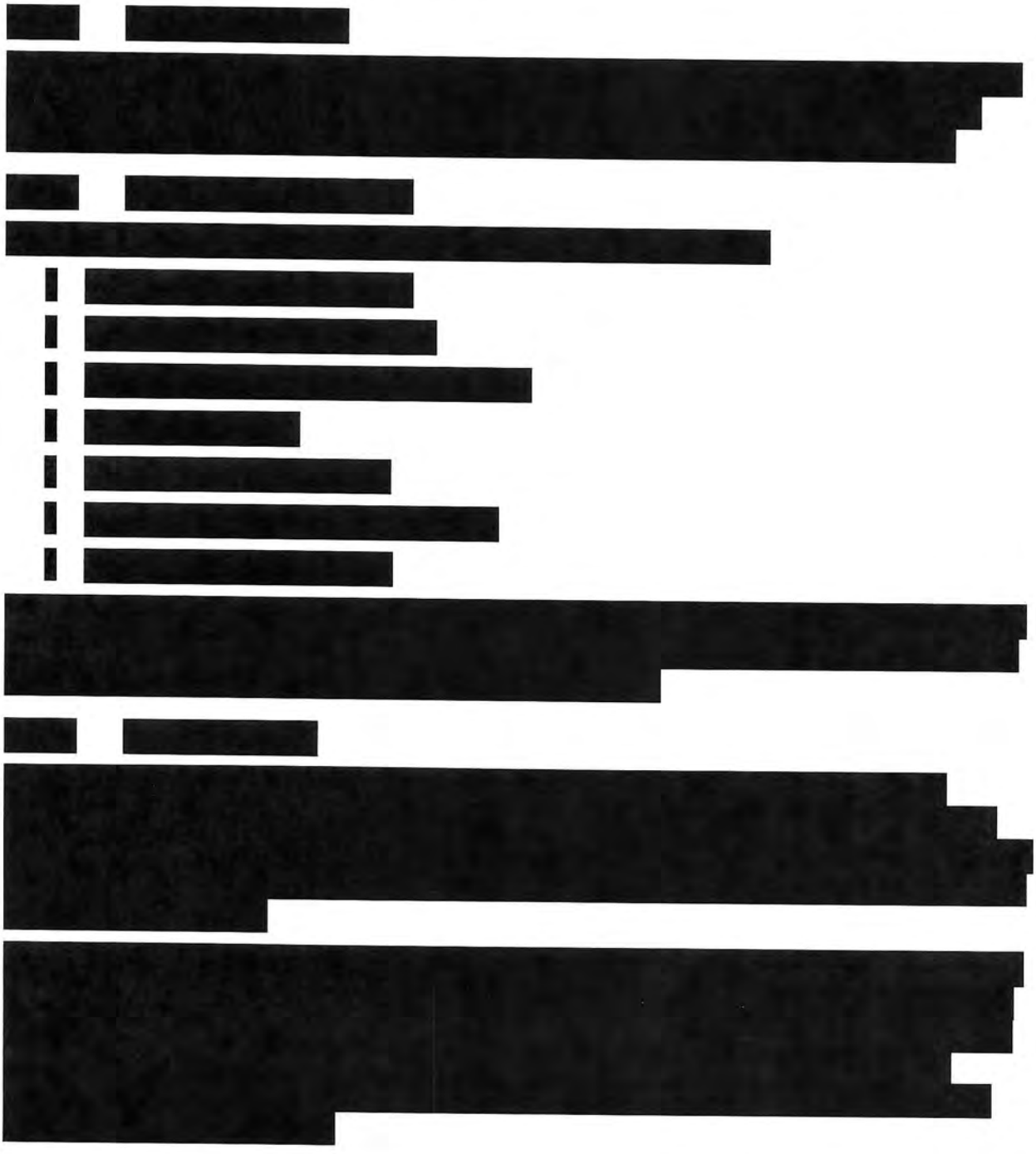
Listings of abnormal physical examinations and all physical examination assessments will be provided.

Electrocardiogram (ECG)

Descriptive statistics will be presented for data related to ECGs (heart rate, RR interval, PR interval, QRS duration, QT interval and QTcF interval). Change from baseline values will be presented for each post-baseline assessment. A listing of ECG assessments will be provided.

13.2.2. Pharmacokinetics

Plasma concentrations of PP405 on Days 1, 14, and 28 will be summarized by visit using descriptive statistics, using the ITT population: N, mean, SD, median, minimum, maximum, geometric mean, and coefficient of variation.



13.2.6. Sample Size Considerations

Sample size has been based on clinical considerations only. The sample size of 60 male and female subjects will be randomized 2:1 to receive PP405 0.05% or vehicle. The planned sample size is considered sufficient to meet all the objectives, [redacted] ith a 20% dropout rate, the sample size of 15 male subjects in the vehicle group and 30 male subjects in PP405 group will be enrolled.

Up to 15 female subjects will be included to evaluate gender affect. So, a total of 60 male and female subjects will be randomized 2:1 to receive PP405 0.05% or vehicle stratified by sex at birth (75% male and 25% female) and hair loss type based on the Norwood Hamilton Scale (male) or the Savin Scale (female).

Further details will be provided in the SAP.

13.2.7. Interim Analysis

There is no formal interim analysis planned for this study.

13.3. Statistical Methods for the Open-label Extension

13.3.1. Safety

All the planned analyses described in Section 13.2.1 will be performed using the OLE_SP population.

13.3.2. Pharmacokinetics of OLE Subjects

Plasma concentrations of PP405 on Days 1, 28, and 84 will be summarized by visit using descriptive statistics, using the OLE_PK population: N, mean, SD, median, minimum, maximum, geometric mean, and coefficient of variation.

[redacted]

[redacted]

13.3.5. Sample Size Considerations for OLE Portion

Enrollment into the OLE of at least 16 of the subjects who were randomized to the vehicle arm in the randomized portion of this study (who completed the Day 28 treatment period and the follow-up period) [redacted]

14. ETHICAL CONSIDERATIONS AND REGULATORY OBLIGATIONS

14.1. Informed Consent

Informed consent will be obtained in accordance with the Declaration of Helsinki, ICH Good Clinical Practice (GCP) (ICH GCP E6 [R2]), United States (US) Code of Federal Regulations (CFR) for Protection of Human Subjects (21 CFR 50.25[a,b], CFR 50.27, and CFR Part 56, Subpart A), the Health Insurance Portability and Accountability Act (HIPAA), and local regulations.

A study specific Informed Consent Form (ICF) will be provided to study sites by the Sponsor or designee. Updates to the template requested by the site or IRB must be approved by the sponsor and will be communicated by an email from the clinical study manager. The written informed consent document must be prepared in the language(s) of the potential subject population.

Before a subject's participation in each portion of the study, the investigator is responsible for obtaining written informed consent from the subject after adequate explanation of the aims, methods, anticipated benefits, and potential hazards of the study and before any protocol-specific screening procedures or study drugs are administered. The investigator is also responsible for asking the subject if the subject agrees to have his primary care physician informed of the subject's participation in the clinical study. If the subject agrees to such notification, the investigator shall inform the subject's primary care physician of the subject's participation in the clinical study.

The acquisition of informed consent and the subject's agreement or refusal of his notification of the primary care physician should be documented in the subject's medical records, and the ICF

should be signed and personally dated by the subject and by the person who conducted the informed consent discussion (not necessarily an investigator). The original signed and dated ICF should be retained in accordance with institutional policy, and a copy of the signed and dated ICF should be provided to the subject. Information should be given in both oral and written form and subjects must be given ample opportunity to inquire about details of the study.

14.2. Supply of New and Important Information Influencing the Subject's Consent and Revision of the Written Information

When any new and important information that may be relevant to the subject's consent is obtained, the investigator and the sponsor should consult with each other on how to deal with the information.

1. The investigator will immediately inform the subject verbally whenever new information becomes available that may be relevant to the subject's consent or may influence the subject's willingness to continue participation in the study (e.g., report of serious adverse drug reactions). The communication should be documented in the subject's medical records, and it should be confirmed whether the subject is willing to remain in the study or not.
2. If the investigator recognizes the necessity to revise the written information such as the ICF and other study materials given to the subject, the written information should be revised immediately based upon the newly available information and be reviewed and approved by the IRB.
3. The investigator must re-consent subjects to confirm their continued participation in the clinical study, even if subjects have already been informed of the relevant information verbally. The investigator or other responsible study personnel should document the re-consenting process in the subject's study chart and the subject should sign and date the updated ICF. The investigator or other responsible personnel should give a copy of the signed ICF to the subject and store the original ICF appropriately.

14.3. Institutional Review Board

A copy of the protocol proposed ICF, other written subject information, and any proposed advertising material must be submitted to the IRB for written approval. A copy of the written approval of the protocol and ICF must be received by the sponsor before recruitment of subjects into the study and shipment of study drug.

The investigator must submit and, where necessary, obtain written approval from the IRB for all subsequent protocol amendments and changes to the informed consent document. The investigator is required to notify the IRB of deviations from the protocol or SAEs occurring at the site and other AE reports received from the sponsor, in accordance with local requirements.

The investigator will be responsible for obtaining annual written approval/renewal throughout the duration of the study. Copies of the investigator's reports and the IRB continuance of approval must be sent to the sponsor.

14.4. Disclosure and Subject Confidentiality

The investigator must ensure that the subject's confidentiality is maintained at all times. On the eCRFs or other documents submitted to the sponsor, subjects should be identified by their SI number only. Documents that are not for submission to the sponsor (e.g., signed ICFs) should be kept strictly confidential by the investigator. The data collected as a part of the study will not be used for any purpose other than for reviewing or performing the study, without written consent of the sponsor.

In compliance with Declaration of Helsinki, Federal regulations/ICH GCP Guidelines, the investigator, and the institution are required to permit authorized representatives of the sponsor and co-sponsors, regulatory agency(s), and the IRB direct access to review the subject's original medical records for verification of study-related procedures and data. Direct access includes examining, analyzing, verifying, and reproducing any records and reports that are important to the evaluation of the study. The investigator is obligated to inform and obtain the subject's consent to permit named representatives to have access to study-related records without violating the subject's confidentiality.

For US sites, the HIPAA Privacy Rule provides federal protection for the privacy of protected health information (PHI) by implementing standards to protect and guard against the misuse of individually identifiable health information of subjects participating in sponsored clinical studies. Authorization is required from each research subject, i.e., specific permission granted by an individual to a covered entity for the use or disclosure of an individual's PHI. A valid authorization must meet the implementation specifications under the HIPAA Privacy Rule. This authorization may be combined into the Informed Consent document (approved by the IRB) or it may be a separate document (approved by the IRB) or provided by the investigator or sponsor (without the IRB). It is the responsibility of the investigator and institution to obtain such waiver/authorization in writing from the appropriate individual.

14.5. Ethical Conduct of the Study

The clinical study must be conducted with adherence to ICH GCP, Declaration of Helsinki and applicable FDA regulations/guidelines set forth in 21 CFR (Parts 11, 50, 54, 56, and 312) and the HIPAA. Consideration of the subject's rights, safety, and well-being is regarded as the most significant issue and has a higher priority than the scientific and social benefits of the study.

The investigator(s) and all parties involved in this study must conduct the study in adherence to ICH GCP, and all applicable laws and regulations.

14.6. Study Conduct

With the exception of eliminating an immediate hazard to a subject, the investigator should not deviate from the protocol or implement any changes without prior written approval from the sponsor representative or designee and prior review and documented approval from the IRB.

The investigator should document and explain any deviation or violation from the protocol. Prospective approval of protocol deviations, also known as waivers or exemptions, are not allowed. A protocol deviation is any noncompliance with the clinical study protocol, GCP, or manual of operations and procedures requirements. The noncompliance may be either on the part of the subject, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

A protocol violation is defined is defined as an accidental or unintentional change to, or non-compliance with the IRB approved protocol without prior sponsor approval. Protocol violations generally increased risk or decrease benefit, affecting the subject's rights, safety, or welfare, or the integrity of the data. All protocol violations must be reviewed by the Sponsor and/or the sponsor's designee and reported to the IRB by the investigator, as directed by the IRB-specific procedures.

14.7. Quality Control and Quality Assurance

This study will be organized, performed, and reported in compliance with the protocol, standard operating procedures, working practice documents, ICH GCP, Declaration of Helsinki, the HIPAA and applicable regulations and guidelines. Site audits will be made periodically by the sponsor's or the clinical research organization's qualified compliance auditing team, which is an independent function from the study team responsible for conduct of the study.

The investigator is to maintain a list of appropriately qualified persons to whom he/she has delegated study duties and maintain accurate documentation (source data) that supports the information entered in the eCRF.

Source documents are original documents, data, and records from which the subject's eCRF data are obtained. These include but are not limited to hospital records, clinical and office charts, laboratory and pharmacy records, diaries, microfiches, radiographs, and correspondence.

The data entered in eCRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

The investigator must permit study-related monitoring, audits, IRB review, and regulatory agency inspections and provide direct access to source data documents.

The sponsor or designee is responsible for the data management of this study including quality checking of the data.

Clinical monitors will perform ongoing source data verification to confirm that data entered into the eCRF by authorized study center personnel are accurate, complete, and verifiable from source documents; that the safety and rights of subjects are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements.

All software applications used in the collection of data will be properly validated following standard computer system validation that is compliant with all regulatory requirements.

15. DATA HANDLING AND RECORD KEEPING

15.1. Case Report Forms and Source Documents

An eCRF is required and should be completed for each included subject. Electronic case report forms (eCRFs) must be completed using a validated web-based application. Study site personnel will be trained in the use of the application and will enter the clinical data from source documentation. Unless explicitly allowed in the eCRF instructions, blank data fields are not acceptable.

In the event of an entry error, or if new information becomes available, the value will be corrected by deselecting the erroneous response and then selecting or entering the factual response. In compliance with Title 21 of the CFR Part 11, the system will require the personnel making the correction to enter a reason for changing the value. The documented audit trail will include the reason for the change, the original value, the new value, the time of the correction and the identity of the operator.

The completed original eCRFs are the sole property of sponsor and should not be made available in any form to third parties, except for authorized representatives of sponsor or appropriate regulatory authorities, without written permission from sponsor.

The investigator should maintain a list of appropriately qualified persons to whom he has delegated study duties. All persons authorized to make entries and/or corrections on eCRFs will be included on the sponsor Delegation of Authority Form.

Source documents are original documents, data, and records from which the subject's eCRF data are obtained. These include but are not limited to hospital records, clinical and office charts, laboratory and pharmacy records, diaries, microfiches, and correspondence, whether maintained electronically or in paper form.

The investigator and study staff are responsible for maintaining a comprehensive and centralized filing system of all study-related (essential) documentation, suitable for inspection at any time by representatives from the sponsor and/or applicable regulatory authorities. Elements should include:

- Subject files containing ICFs and supporting original copies of source documentation.
- Study files containing the protocol with all amendments, investigator's brochure, copies of pre-study documentation, and all correspondence to and from the IRB and the sponsor.
- Proof of receipt, Study drug Accountability Record, Documentation of Study drug for Destruction, Final Study drug Reconciliation Statement, and all study drug-related correspondence

In addition, all original source documents supporting entries in the eCRFs must be maintained and be readily available.

No study document should be destroyed without prior written agreement between the sponsor and the investigator. Should the investigator wish to assign the study records to another party or move them to another location, he must notify the sponsor in writing of the new responsible person and/or the new location.

15.2. Data Collection and Study Monitoring

The sponsor representative and regulatory authority inspectors are responsible for contacting and visiting the investigator for the purpose of inspecting the facilities and, upon request, inspecting the various records of the study (e.g., eCRFs and other pertinent data) provided that subject confidentiality is respected.

Centralized monitoring, which consists of remote review of accumulating data from all sites, will be performed as detailed in the Centralized Monitoring Plan.

The sponsor monitor is responsible for inspecting the eCRFs or electronic data at regular intervals, as documented in the study monitoring plan throughout the study to verify adherence to the protocol; completeness, accuracy, and consistency of the data; and adherence to local regulations on the conduct of clinical research. The monitor should have access to subject medical records and other study-related records needed to verify the entries on the eCRFs.

The investigator agrees to cooperate with the monitor to ensure that any problems detected in the course of these monitoring visits, including delays in completing eCRFs, are promptly resolved.

The investigator will complete eCRF using an EDC system provided by the sponsor. Investigative site staff will complete training on the system prior to being given unique user accounts and passwords. Only investigative staff can complete eCRFs and make changes to study data. Corrections to electronic forms will be automatically documented through the software's "audit trail".

- In addition to investigative site eCRF EDC completion a clinical data management review will be performed on subject data received at the sponsor. During this review, subject data will be checked for consistency, omissions, and any apparent discrepancies. In addition, the data will be reviewed for adherence to the protocol and GCP. To resolve any questions arising from the clinical data management review process, data queries and/or site notifications will be sent to the site for completion and return to the sponsor. These queries may be generated by Clinical Data Management, Clinical Monitors, or Clinical Safety.
- The principal investigator will sign and date the indicated places on the eCRF. These signatures will indicate that the principal investigator inspected or reviewed the data on the eCRF, the data queries, and the site notifications, and agrees with the content.

15.3. Audits and Inspections

In accordance with ICH GCP and the sponsor's audit plans, this study may be selected for audit by representatives from the sponsor (or designees). Inspection of site facilities (e.g., pharmacy, study drug storage areas, laboratories) and review of study-related records will occur to evaluate the study conduct and compliance with the protocol, ICH GCP, and applicable regulatory requirements.

These audits will require access to all study records, including source documents, for inspection and comparison with the eCRFs. Subject privacy must, however, be respected. The investigator agrees to allow the sponsor representative (or designee) to inspect the drug storage area, study drug stocks, drug accountability records, subject charts and study source documents, and other records relative to study conduct. The investigator and participating site personnel are responsible for being present and available for consultation during routinely scheduled site audit visits conducted by the sponsor or its designees.

15.4. Record Retention

To enable evaluations and/or audits from regulatory authorities or sponsor, the investigator should keep records, including the identity of all participating subjects (sufficient information to link records, e.g., eCRFs and hospital records), all original signed informed consent documents, copies of all CRFs, safety reporting forms, source documents, and detailed records of treatment disposition, and adequate documentation of relevant correspondence (e.g., letters, meeting minutes, telephone calls reports). Institution shall retain and preserve one (1) copy only of all data and records generated in the course of the study for the longer of

(i) two (2) years after the last marketing authorization for the Study Drug has been approved or the sponsor has discontinued its research with respect to such treatment.

or

(ii) Longer period as required by applicable regulatory requirements. At the end of such a period, the institution must obtain written approval from the sponsor before destruction of such data.

16. ADMINISTRATIVE AND LEGAL OBLIGATIONS

16.1. Protocol Amendments and Study Termination

When the sponsor is aware of information on matters concerning the quality, efficacy, and safety of the study drugs, as well as other important information that may affect proper conduct of the clinical study, the sponsor may discontinue the clinical study and send a written notice of the discontinuation along with the reasons to the investigator.

If an investigator intends to discontinue participation in the study, the investigator must immediately inform the sponsor.

Protocol amendments must be made only with the prior written approval of the sponsor. Agreement from the investigator must be obtained for all protocol amendments and amendments to the informed consent document. The IRB must be informed of all amendments and give approval for any amendments likely to affect the safety of the subjects or the conduct of the study. The investigator must send a copy of the approval letter from the IRB to the sponsor.

Both the sponsor, the Institution, and the investigator reserve the right to terminate the study, according to the Clinical Study Agreement. The sponsor may stop the study (and/or the study site) for any reason with appropriate notification. The investigator should notify the IRB in writing of the study's completion or early termination and send a copy of the notification to the sponsor.

16.2. Language

All written information and other material to be used by subjects and investigative staff must use vocabulary and language that are clearly understood.

16.3. Publications

The publication policy will be addressed in the Research and Financial Agreement and all details outlined in the agreement will apply to this protocol The Sponsor, or designee, will register the study and post study results regardless of outcome, on clinicaltrials.gov in accordance with the applicable local laws and regulations.

17. REFERENCES

Cash TF. The psychosocial consequences of androgenetic alopecia: a review of the research literature. *Br J Dermatol.* 1999 Sep;141(3):398-405. doi: 10.1046/j.1365-2133.1999.03030.x. PMID: 10583042.

Dinh, Quan & Sinclair, Rodney. (2007). Female pattern hair loss: Current treatment concepts. Clinical interventions in aging. 2. 189-99.

Flores A, Schell J, Krall AS, Jelinek D, Miranda M, Grigorian M, et al. Lactate dehydrogenase activity drives hair follicle stem cell activation. *Nat Cell Biol.* 2017 Sep;19(9):1017-1026. doi: 10.1038/ncb3575. Epub 2017 Aug 14. PMID: 28812580; PMCID: PMC5657543.

Garza LA, Yang CC, Zhao T, Blatt HB, Lee M, He H, et al. Bald scalp in men with androgenetic alopecia retains hair follicle stem cells but lacks CD200-rich and CD34-positive hair follicle progenitor cells. *J Clin Invest.* 2011;121(2):613-622. https://doi.org/10.1172/JCI44478.

Gupta M, Mysore V. Classifications of Patterned Hair Loss: A Review. *J Cutan Aesthet Surg.* 2016 Jan-Mar;9(1):3-12. doi: 10.4103/0974-2077.178536. PMID: 27081243; PMCID: PMC4812885.

ICH GCP E6 (R2) https://database.ich.org/sites/default/files/E6_R2_Addendum.pdf Accessed on 28 August 2023.

Norwood OT. Incidence of female androgenetic alopecia (female pattern alopecia). *Dermatol Surg*. 2001 Jan;27(1):53-54. PMID: 11231244.

Propecia (finasteride) tablets for oral use USPI: Organon Global Inc; June 2021. uspi-og0906-1t-2106r001.

Rogers NE, Avram MR. Medical treatments for male and female pattern hair loss. *J Am Acad Dermatol*. 2008 Oct;59(4):547-66; quiz 567-568.

Schell JC, Olson KA, Jiang L, Hawkins AJ, Van Vranken JG, Xie J, et al. A role for the mitochondrial pyruvate carrier as a repressor of the Warburg effect and colon cancer cell growth. *Mol Cell*. 2014 Nov 6;56(3):400-413.

Schmidt S, Fischer TW, Chren MM, Strauss BM, Elsner P. Strategies of coping and quality of life in women with alopecia. *Br J Dermatol*. 2001 May;144(5):1038-1043.

Severi G, Sinclair R, Hopper JL, English DR, McCredie MR, Boyle P, et al. Androgenetic alopecia in men aged 40-69 years: prevalence and risk factors. *Br J Dermatol*. 2003 Dec;149(6):1207-1213.

Stough D, Stenn K, Haber R, Parsley WM, Vogel JE, Whiting DA, et al. Psychological effect, pathophysiology, and management of androgenetic alopecia in men. *Mayo Clin Proc*. 2005 Oct;80(10):1316-1322.

18. APPENDICES

Appendix A. Subject Instructions for Study Drug Application to the Scalp

General Instructions:

- Your scalp should be clean, dry, and free of hair styling products and sunscreen before applying study drug.
- Only use non-medicated shampoo and conditioner, approved by your doctor to wash your hair during the screening period, the duration of the treatment period, and through final follow up visit.
- You must wait at least 2 hours after study drug application before you engage in activities that involve excessive sweating, swimming, shampooing, or applying sunscreen or other approved products.
- You should apply study drug at approximately the same time every day. **It is recommended that you apply study drug at least 2 hours prior to bedtime.** If engaging in the above activities, ensure your scalp and hair has been cleaned and dried prior to applying the study drug.
- You should maintain the same hairstyle while you are on the study. Do not use texturizers, perms, or relaxers on your hair from the time of informed consent through the final follow-up visit. Hair coloring is allowed as long as you do not change the color during study participation.
- Avoid contact of study drug with the eyes or mouth. If the study drug gets on any part of your body other than your scalp, rinse the area well with water for at least 15 minutes.
- Missed doses should be applied if there is at least 4 hours until the next scheduled application.
- Remember to bring your study drug bottle(s) back to the clinic at every visit.
- Store the study drug in a location protected from light and away from heat and moisture at room temperature, within a temperature range of 15°C to 30°C (59°F to 86°F).

Study Drug Application:

1. Gather the study drug bottle and your patient diary.
2. Wash and dry your hands.
3. **For male subjects treating the vertex (crown) only:**
   a) Depress the bottle dispenser completely, dispensing approximately 1 mL of the gel onto your fingertips.
   b) Gently rub the gel over the entire treatment area at the vertex (crown) on your scalp. This should include:
      i. the area of hair loss

ii. the thinning hair area that transitions between hair loss and fuller hair

[redacted]

Note: [redacted]

c) Thoroughly wash your hands to remove any residual study gel from your hands.

d) Store the study drug bottle at room temperature, in a dry and dark location such as a cabinet or drawer until the next application.

e) Record the application date and time in your study drug diary. The study drug should be applied at approximately the same time every day. We recommend applying in the evening, at least 2 hours before bed to allow for adequate absorption.

Male subjects treating the frontal/temporal area and the vertex (crown):

a) Depress the bottle dispenser completely, dispensing approximately 1 mL of the gel onto your fingertips.

b) Gently rub the gel over the entire treatment area at the vertex (crown) on your scalp. This should include:

i. the area of hair loss

ii. the thinning hair area that transitions between hair loss and fuller hair

[redacted]

Note: [redacted]

c) Depress the bottle dispenser completely, dispensing approximately 1 mL of the gel onto your fingertips. With your other hand scoop half of the gel and apply to one side of the frontal/temporal hairline and then apply the other half of the gel to the other side of the frontal/temporal hairline.

d) Gently rub the gel over the entire treatment area at the frontal-temporal hairline equally. This should include:

i. the area of hair loss

ii. the thinning hair area that transitions between hair loss and fuller hair

[redacted]

e) Thoroughly wash your hands to remove any residual study gel from your hands.

f) Store the study drug bottle at room temperature, in a dry and dark location such as a cabinet or drawer until the next application. Record the application date and time in your study drug diary. The study drug should be applied at

approximately the same time every day. We recommend applying in the evening, at least 2 hours before bed to allow for adequate absorption.

Female subjects:

a) Depress the bottle dispenser completely, dispensing approximately 1 mL of the gel onto your fingertips.

b) Gently rub the gel over the entire treatment area at the midline part on your scalp. This should include:

   i. the area of hair loss

   ii. the thinning hair area that transitions between hair loss and fuller hair

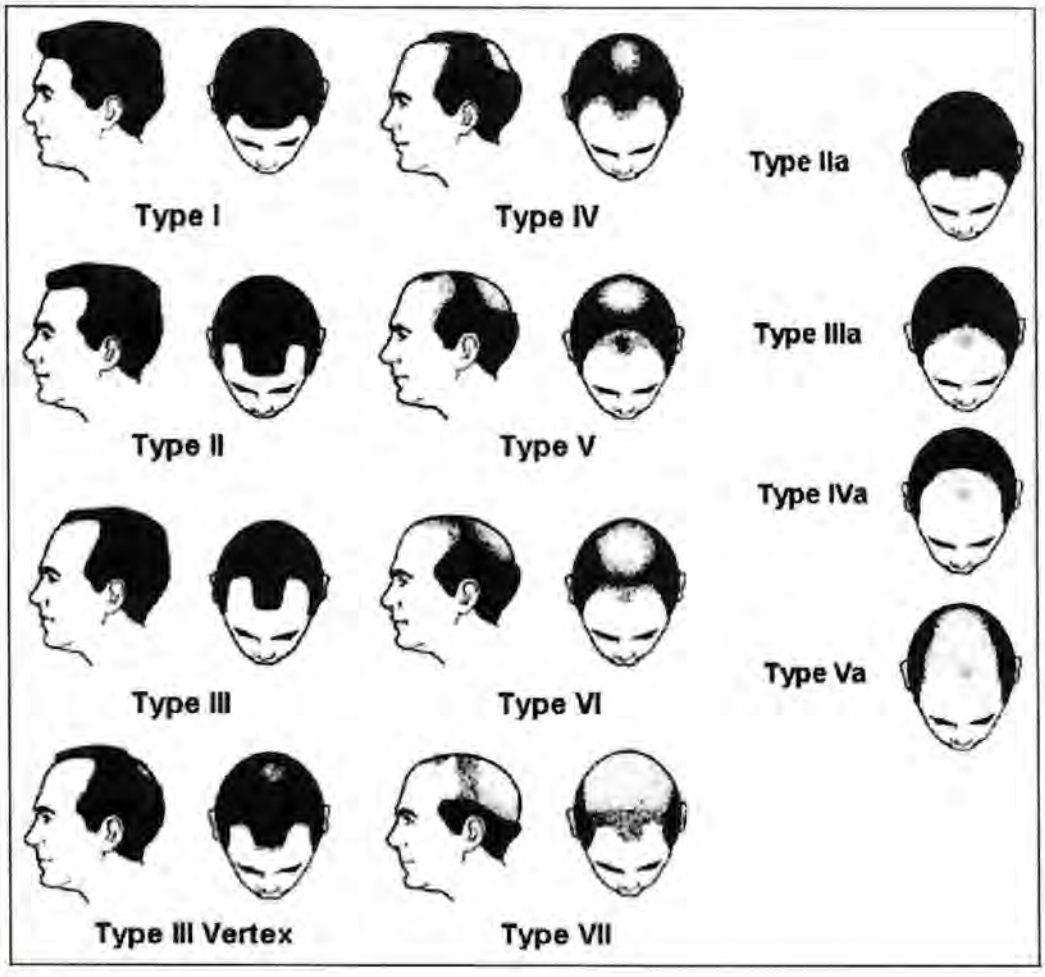
[redacted]

c) Thoroughly wash your hands to remove any residual study gel from your hands.

d) Store the study drug bottle at room temperature, in a dry and dark location such as a cabinet or drawer until the next application.

e) Record the application date and time in your study drug diary. The study drug should be applied at approximately the same time every day. We recommend applying in the evening, at least 2 hours before bed to allow for adequate absorption.

Appendix B. Modified Norwood Hamilton Scale



(Gupta 2016)

Type I: Minimal or no recession of the hairline

Type II: Triangular, usually symmetrical, areas of recession at the frontotemporal hairline

Type III: Deep symmetrical recession at the temples that are bare or only sparsely covered by hair. In Type III vertex, the hair loss is primarily from the vertex with limited recession of the frontotemporal hairline that does not exceed the degree of recession seen in Type III.

Type IV: Frontotemporal recession is more severe than in Type III and there is sparse hair or no hair on the vertex. The two areas of hair loss are separated by a band of moderately dense hair that extends across the top. The is band connects with the fully haired fringe on the sides of the scalp.

Type V: The vertex hair loss region is still separated from the frontotemporal region but it is less distinct. The band of hair across the crown is narrower and sparser and the vertex and frontotemporal regions of hair loss are bigger.

Type VI: The bridge of hair that crosses the crown is gone with only sparse hair remaining. The frontotemporal and vertex regions are joined together, and the extent of hair loss is greater.

Type VII: The most severe form of hair loss and only a narrow band of hair in a horseshoe shape remains on the sides and back of the scalp. This hair is usually not dense and may be quite fine.

Appendix C. Savin Scale

I-1

I-2

I-3

I-4

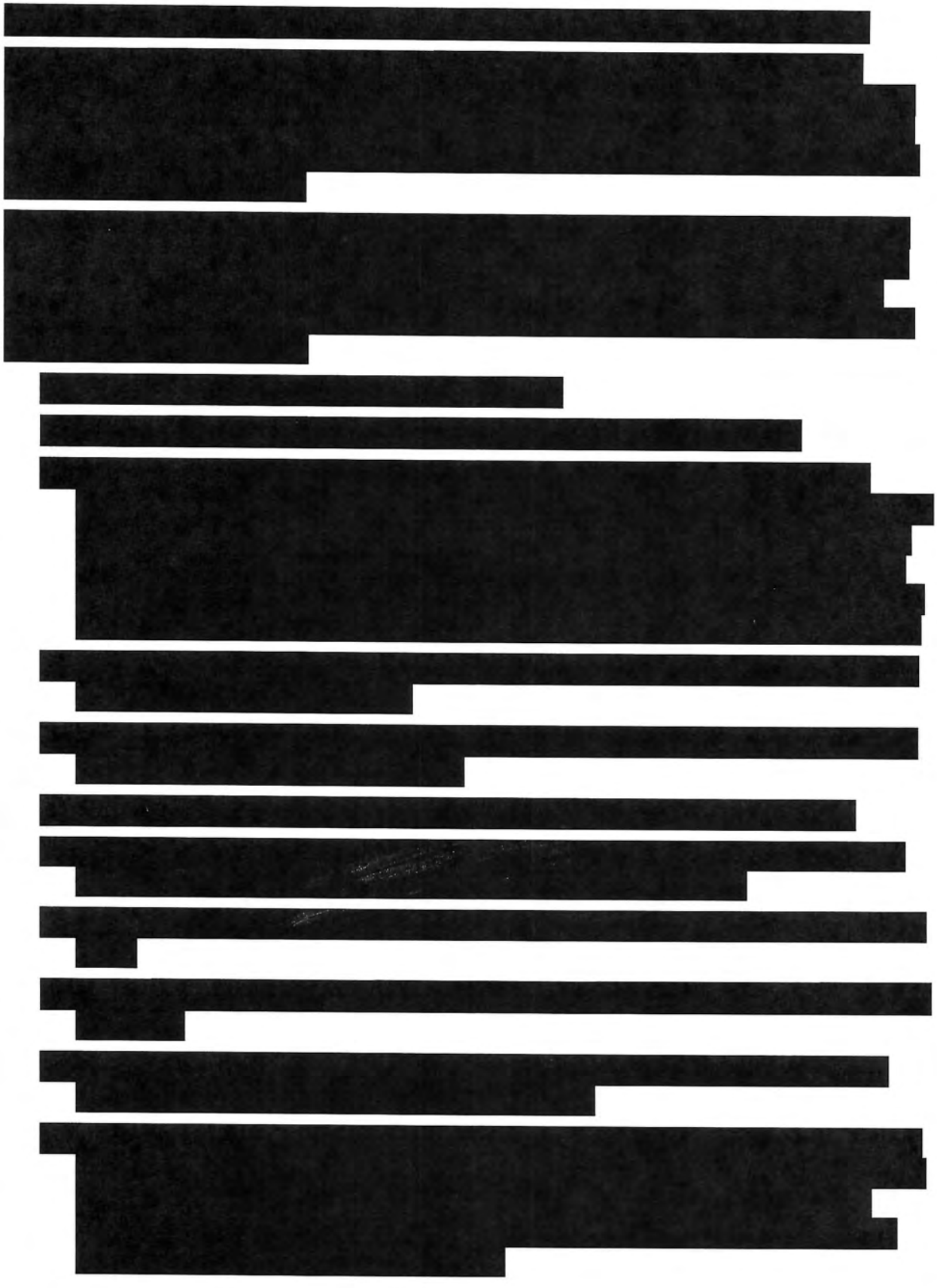
II-1

II-2

III

Advanced

Frontal



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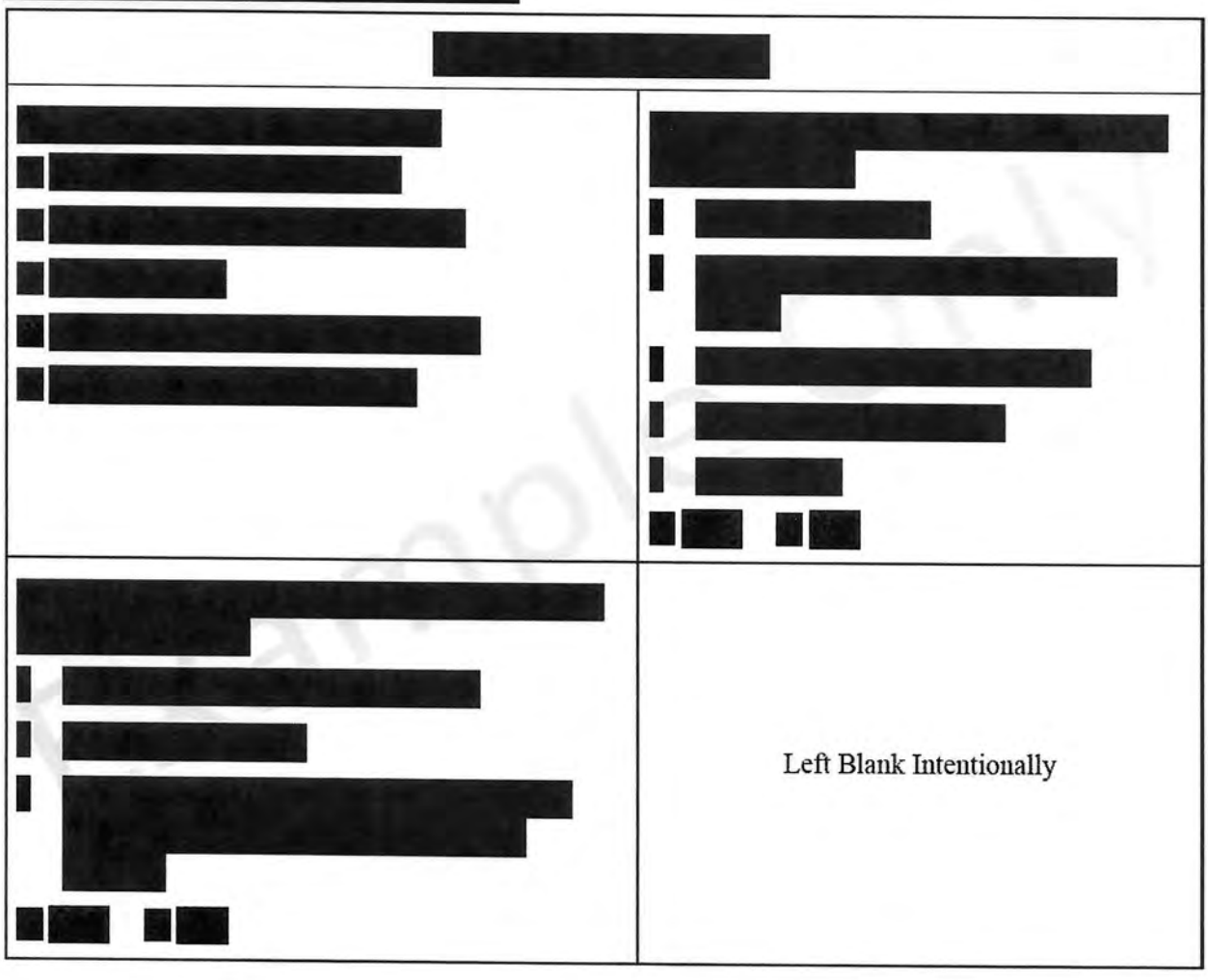
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