



## Clinical trial results:

### A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY AND SAFETY OF CTP-543 IN ADULT PATIENTS WITH MODERATE TO SEVERE ALOPECIA AREATA

#### Summary

EudraCT number	2021-000387-30
Trial protocol	FR HU ES
Global end of trial date	29 June 2022

#### Results information

Result version number	v1 (current)
This version publication date	21 June 2023
First version publication date	21 June 2023

#### Trial information

##### Trial identification

Sponsor protocol code	CP543.3002
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04797650
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Concert Pharmaceuticals, Inc.
Sponsor organisation address	65 Hayden Avenue, Lexington, MA, United States, 02421
Public contact	Medical Manager, Linical France SARL, +40 256207271, diana.chera@linical.com
Scientific contact	Medical Manager, Linical France SARL, +40 256207271, diana.chera@linical.com

Notes:

#### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 June 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 June 2022
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

This study evaluates the safety and effectiveness of an investigational study drug (called CTP-543) in adults (18 years and older) who have 50% or greater scalp hair loss.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 June 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 66
Country: Number of subjects enrolled	United States: 135
Country: Number of subjects enrolled	Poland: 61
Country: Number of subjects enrolled	Spain: 56
Country: Number of subjects enrolled	France: 48
Country: Number of subjects enrolled	Germany: 135
Country: Number of subjects enrolled	Hungary: 16
Worldwide total number of subjects	517
EEA total number of subjects	316

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	515
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled at study centers in Canada, France, Germany, Hungary, Poland, Spain and the United States from 10 June 2021 to 29 June 2022.

### Pre-assignment

Screening details:

671 subjects were screened, out of which 517 subjects who experienced moderate to severe hair loss due to alopecia areata were enrolled to receive CTP-543 or placebo.

### Period 1

Period 1 title	Overall Study (Overall Period) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Placebo

Arm description:

Subjects received CTP-543 matched placebo tablets, orally, twice daily (BID) for up to 24 weeks.

Arm type	Placebo
Investigational medicinal product name	CTP-543 matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CTP-543 matched placebo administered BID for up to 24 weeks.

<b>Arm title</b>	CTP-543 8 mg BID
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Arm description:

Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.

Arm type	Experimental
Investigational medicinal product name	CTP-543
Investigational medicinal product code	
Other name	Deuruxolitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CTP-543 administered BID for up to 24 weeks.

<b>Arm title</b>	CTP-543 12 mg BID
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Arm description:

Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.

Arm type	Experimental
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Investigational medicinal product name	CTP-543
Investigational medicinal product code	
Other name	Deuruxolitinib
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

CTP-543 administered BID for up to 24 weeks.

<b>Number of subjects in period 1</b>	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Started	130	258	129
Completed	119	233	120
Not completed	11	25	9
Non-compliance with Study Drug	-	-	2
Lost to follow-up	-	-	1
Lost to follow-up	4	6	-
Reason not specified	5	12	5
Treatment Emergent or Worsening Adverse Event	1	7	-
Lack of efficacy	1	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received CTP-543 matched placebo tablets, orally, twice daily (BID) for up to 24 weeks.	
Reporting group title	CTP-543 8 mg BID
Reporting group description:	
Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.	
Reporting group title	CTP-543 12 mg BID
Reporting group description:	
Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.	

Reporting group values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Number of subjects	130	258	129
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	39.7	38.4	39.7
standard deviation	± 12.49	± 12.30	± 12.90
Gender categorical			
Units: Subjects			
Female	88	177	84
Male	42	81	45
Ethnicity			
Units: Subjects			
Hispanic or Latino	11	23	9
Not Hispanic or Latino	108	205	111
Unknown	11	30	9
Race			
Units: Subjects			
American Indian or Alaska Native	1	5	0
Asian	7	4	4
Black or African American	10	17	7
White	100	203	109
Other	1	1	0
Not reported	11	28	9

Reporting group values	Total		
Number of subjects	517		
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean			

standard deviation	-		
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Gender categorical			
Units: Subjects			
Female	349		
Male	168		
Ethnicity			
Units: Subjects			
Hispanic or Latino	43		
Not Hispanic or Latino	424		
Unknown	50		
Race			
Units: Subjects			
American Indian or Alaska Native	6		
Asian	15		
Black or African American	34		
White	412		
Other	2		
Not reported	48		

## End points

### End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received CTP-543 matched placebo tablets, orally, twice daily (BID) for up to 24 weeks.	
Reporting group title	CTP-543 8 mg BID
Reporting group description:	
Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.	
Reporting group title	CTP-543 12 mg BID
Reporting group description:	
Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.	

### Primary: Percentage of Subjects Achieving an Absolute Severity of Alopecia Tool (SALT) Score $\leq 20$ at Week 24

End point title	Percentage of Subjects Achieving an Absolute Severity of Alopecia Tool (SALT) Score $\leq 20$ at Week 24
End point description:	
SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.	
End point type	Primary
End point timeframe:	
Week 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of subjects				
number (not applicable)	0.8	33.0	38.3	

### Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[1]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.31



Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.37
Variability estimate	Standard error of the mean
Dispersion value	0.031

Notes:

[1] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.044

Notes:

[2] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### **Secondary: Percentage of Responders on the Hair Satisfaction Patient Reported Outcome (SPRO) Scale at Weeks 12, 16, 20, and 24**

End point title	Percentage of Responders on the Hair Satisfaction Patient Reported Outcome (SPRO) Scale at Weeks 12, 16, 20, and 24
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End point description:

SPRO is a questionnaire answered by the subject and designed to measure how satisfied alopecia areata subjects are with their hair at the time of the assessment. The responses range from 1 to 5: 1= very satisfied, 2= satisfied, 3= neither satisfied nor dissatisfied, 4= dissatisfied, and 5= very dissatisfied. Responders were defined as subjects with responses of "satisfied" or "very satisfied". Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of responders				
number (not applicable)				
Week 12	4.9	43.2	41.0	
Week 16	4.9	41.0	45.1	
Week 20	1.7	40.1	52.5	
Week 24	1.7	46.5	51.7	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[3]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	0.46
Variability estimate	Standard error of the mean
Dispersion value	0.038

Notes:

[3] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[4]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.36

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.049

Notes:

[4] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[5]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.037

Notes:

[5] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[6]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.049

Notes:

[6] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[7]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	0.46
Variability estimate	Standard error of the mean
Dispersion value	0.034

Notes:

[7] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[8]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.59
Variability estimate	Standard error of the mean
Dispersion value	0.047

Notes:

[8] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[9]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.52
Variability estimate	Standard error of the mean
Dispersion value	0.035

Notes:

[9] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[10]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	0.58
Variability estimate	Standard error of the mean
Dispersion value	0.047

Notes:

[10] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### **Secondary: Percentage of Subjects Achieving an Absolute SALT Score of ≤20 at Weeks 4, 8, 12, 16, and 20**

End point title	Percentage of Subjects Achieving an Absolute SALT Score of ≤20 at Weeks 4, 8, 12, 16, and 20
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End point description:

SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 4, 8, 12, 16, and 20

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of subjects				
number (not applicable)				
Week 4	0	0.4	0	
Week 8	0.8	2.9	2.4	
Week 12	0.8	10.5	12.3	
Week 16	0.8	20.2	21.1	
Week 20	0.8	24.8	28.8	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 4	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3175 <sup>[11]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.004

Notes:

[11] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.102 <sup>[12]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.013

Notes:

[12] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3103 <sup>[13]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.05
Variability estimate	Standard error of the mean
Dispersion value	0.016

Notes:

[13] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	CTP-543 8 mg BID v Placebo
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[14]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.14
Variability estimate	Standard error of the mean
Dispersion value	0.021

Notes:

[14] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[15]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[15] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[16]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	0.24
Variability estimate	Standard error of the mean
Dispersion value	0.026



Notes:

[16] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[17]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.037

Notes:

[17] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[18]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	0.29
Variability estimate	Standard error of the mean
Dispersion value	0.028

Notes:

[18] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[19]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.35
Variability estimate	Standard error of the mean
Dispersion value	0.041

Notes:

[19] - P-value was calculated by Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### Secondary: Relative Change in SALT Scores From Baseline at Weeks 4, 8, 12, 16, 20, and 24

End point title	Relative Change in SALT Scores From Baseline at Weeks 4, 8, 12, 16, 20, and 24
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End point description:

SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Relative change (percent change) from baseline (CFB) is calculated as:  $100 \times ([\text{post-baseline SALT score} - \text{baseline SALT score}] / \text{baseline SALT score})$ . Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 4, 8, 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	125	242	125	
Units: percent change				
arithmetic mean (standard deviation)				
Relative CFB at Week 4 (n=124, 242, 124)	0.4 (± 5.40)	-2.6 (± 10.10)	-3.2 (± 9.45)	
Relative CFB at Week 8 (n= 125, 239, 125)	-2.0 (± 13.41)	-11.5 (± 20.63)	-16.4 (± 23.92)	
Relative CFB at Week 12 (n= 123, 237, 122)	-0.7 (± 14.72)	-23.9 (± 29.06)	-30.3 (± 31.85)	
Relative CFB at Week 16 (n= 124, 238, 123)	0.9 (± 13.19)	-34.3 (± 34.93)	-39.9 (± 35.43)	
Relative CFB at Week 20 (n= 120, 234, 118)	0.4 (± 15.49)	-38.9 (± 37.64)	-47.7 (± 37.62)	
Relative CFB at Week 24 (n= 119, 233, 120)	1.6 (± 16.54)	-44.6 (± 39.58)	-52.7 (± 38.44)	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 4	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0039 <sup>[20]</sup>
Method	MMRM
Parameter estimate	Least Square (LS) Mean Difference
Point estimate	-2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.97

Notes:

[20] - P-value was calculated by mixed model repeated measures (MMRM) analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 4	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0027 <sup>[21]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.6
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	1.12

Notes:

[21] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[22]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-9.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.6
upper limit	-5.1
Variability estimate	Standard error of the mean
Dispersion value	2.15

Notes:

[22] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 8	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[23]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-14.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19
upper limit	-9.3
Variability estimate	Standard error of the mean
Dispersion value	2.47

Notes:

[23] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[24]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.8
upper limit	-17.3
Variability estimate	Standard error of the mean
Dispersion value	2.92

Notes:

[24] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[25]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-29.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-35.9
upper limit	-22.7
Variability estimate	Standard error of the mean
Dispersion value	3.36

Notes:

[25] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[26]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-34.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-41.4
upper limit	-28.2
Variability estimate	Standard error of the mean
Dispersion value	3.37

Notes:

[26] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [27]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-40.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-47.8
upper limit	-32.6
Variability estimate	Standard error of the mean
Dispersion value	3.86

Notes:

[27] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [28]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-38.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.9
upper limit	-31.6
Variability estimate	Standard error of the mean
Dispersion value	3.63

Notes:

[28] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [29]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-46.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.8
upper limit	-38.4
Variability estimate	Standard error of the mean
Dispersion value	4.17

Notes:

[29] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [30]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-45.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.4
upper limit	-38.5
Variability estimate	Standard error of the mean
Dispersion value	3.8

Notes:

[30] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[31]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-52.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61.4
upper limit	-44.2
Variability estimate	Standard error of the mean
Dispersion value	4.36

Notes:

[31] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

### Secondary: Percentage of Responders Assessed Using the Clinician Global Impression of Improvement (CGI-I) at Weeks 12, 16, 20, and 24

End point title	Percentage of Responders Assessed Using the Clinician Global Impression of Improvement (CGI-I) at Weeks 12, 16, 20, and 24
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End point description:

The CGI-I is a questionnaire that asks the clinician to evaluate the improvement or worsening of the subject's alopecia areata as compared to the start of the study on a 7-point scale. Responses range from 1 (very much worse) to 7 (very much improved). Responders were defined as subjects with responses of 6 (much improved) or 7 (very much improved). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of responders				
number (not applicable)				
Week 12	3.3	38.0	44.3	
Week 16	3.2	45.0	52.0	
Week 20	1.7	50.0	59.0	
Week 24	2.5	54.1	61.7	

### Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 12



Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[32]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[32] - P-value was calculated by cochrane mantel haenszel (CMH) test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 12

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[33]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[33] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 16

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[34]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[34] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 16

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[35]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[35] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 20

Comparison groups	Placebo v CTP-543 8 mg BID
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Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[36]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[36] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 20

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[37]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[37] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[38]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[38] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[39]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[39] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

## Secondary: Percentage of Responders Assessed Using the Patient Global Impression of Improvement (PGI-I) at Weeks 12, 16, 20, and 24

End point title	Percentage of Responders Assessed Using the Patient Global Impression of Improvement (PGI-I) at Weeks 12, 16, 20, and 24
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**End point description:**

The PGI-I is a self-administered questionnaire that asks the subject to evaluate the improvement or worsening of their alopecia areata as compared to the start of the study on a 7-point scale. Responses range from 1 (very much worse) to 7 (very much improved). Responders were defined as subjects with responses of 6 (much improved) or 7 (very much improved). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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**End point timeframe:**

Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of responders				
number (not applicable)				
Week 12	3.3	43.3	49.2	
Week 16	4.0	46.2	59.8	
Week 20	5.8	48.7	64.4	
Week 24	1.7	50.9	68.3	

**Statistical analyses**

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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**Statistical analysis description:**

Week 12

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[40]</sup>
Method	Cochran-Mantel-Haenszel

**Notes:**

[40] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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**Statistical analysis description:**

Week 12

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[41]</sup>
Method	Cochran-Mantel-Haenszel

**Notes:**

[41] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[42]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[42] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[43]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[43] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[44]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[44] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[45]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[45] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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## Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[46]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[46] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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## Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[47]</sup>
Method	Cochran-Mantel-Haenszel

Notes:

[47] - P-value was calculated by CMH test stratified by baseline scalp hair loss (partial vs complete/near-complete) for responders in each treatment group compared to placebo.

## Secondary: Change in the Clinician Global Impression of Severity (CGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24

End point title	Change in the Clinician Global Impression of Severity (CGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24
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End point description:

The CGI-S is a questionnaire that asks the clinician to evaluate the symptom severity of the subject's alopecia areata at the time of assessment. The symptom severity was rated on a scale ranging from 1 to 7, where 1=normal, no hair loss; 2=borderline hair loss; 3=mild hair loss; 4=moderate hair loss; 5=marked hair loss; 6=severe hair loss; 7=among the most extreme hair loss. Higher scores indicate more hair loss. A negative CFB less hair loss. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed (n) indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	123	236	124	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	6.4 (± 0.82)	6.5 (± 0.83)	6.4 (± 0.76)	
CFB at Week 12 (n= 121, 232, 122)	0.0 (± 0.75)	-1.3 (± 1.45)	-1.5 (± 1.52)	
CFB at Week 16 (n= 122, 234, 123)	0.1 (± 0.67)	-1.6 (± 1.61)	-1.8 (± 1.69)	
CFB at Week 20 (n= 118, 231, 118)	-0.0 (± 0.96)	-1.8 (± 1.80)	-2.2 (± 1.83)	

CFB at Week 24 (n= 117, 229, 120)	0.1 ( $\pm$ 0.79)	-2.1 ( $\pm$ 1.97)	-2.4 ( $\pm$ 1.96)	
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## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[48]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[48] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[49]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[49] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[50]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[50] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[51]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-1.5
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[51] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[52]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.18

Notes:

[52] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[53]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.7
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[53] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	359
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[54]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-2.2



Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.8
Variability estimate	Standard error of the mean
Dispersion value	0.19

Notes:

[54] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	247
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [55]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-2
Variability estimate	Standard error of the mean
Dispersion value	0.22

Notes:

[55] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

### **Secondary: Change in the Patient Global Impression of Severity (PGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24**

End point title	Change in the Patient Global Impression of Severity (PGI-S) Scores From Baseline at Weeks 12, 16, 20, and 24
End point description:	
<p>The PGI-S is a self-administered questionnaire that asks the subject to evaluate the symptom severity of their alopecia areata at the time of assessment. Symptom severity was rated on a scale ranging from 1 to 7, where 1= normal, no hair loss; 2= borderline hair loss; 3= mild hair loss; 4= moderate hair loss; 5= marked hair loss; 6= severe hair loss; 7= among the most extreme hair loss. Higher scores indicate more hair loss. A negative CFB indicates less hair loss. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.</p>	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, 16, 20, and 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	124	236	124	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	6.7 (± 0.64)	6.6 (± 0.79)	6.5 (± 0.78)	
CFB at Week 12 (n= 122, 234, 122)	-0.2 (± 0.97)	-1.6 (± 2.05)	-1.8 (± 1.88)	
CFB at Week 16 (n= 123, 234, 122)	-0.2 (± 1.06)	-1.8 (± 2.10)	-2.0 (± 1.90)	
CFB at Week 20 (n= 119, 232, 118)	-0.3 (± 1.26)	-2.0 (± 2.20)	-2.2 (± 1.91)	
CFB at Week 24 (n= 118, 228, 120)	-0.2 (± 1.04)	-2.3 (± 2.26)	-2.5 (± 1.98)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[56]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[56] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[57]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[57] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[58]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[58] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[59]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	-1.4
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[59] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[60]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.21

Notes:

[60] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[61]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	-1.5
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[61] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[62]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	-1.7
Variability estimate	Standard error of the mean
Dispersion value	0.21

Notes:

[62] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[63]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	-1.8
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[63] - P-value was calculated by MMRM with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

### **Secondary: Percentage of Subjects Achieving at Least a 75% and 90% Relative Reduction in SALT Score From Baseline at Weeks 12 and 24**

End point title	Percentage of Subjects Achieving at Least a 75% and 90% Relative Reduction in SALT Score From Baseline at Weeks 12 and 24
End point description:	
SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Percentage of subjects achieving at least a 75% and 90% relative reduction in SALT score from baseline at Weeks 12 and 24 are reported. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.	
End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, and 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of subjects				
number (not applicable)				
75% Relative Reduction: Week 12	0	8.9	11.5	
75% Relative Reduction: Week 24	0	33.5	38.3	
90% Relative Reduction: Week 12	0	1.7	4.9	
90% Relative Reduction: Week 24	0	21.9	25.0	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description: 75% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[64]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.018

Notes:

[64] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description: 75% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[65]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.06
upper limit	0.17
Variability estimate	Standard error of the mean
Dispersion value	0.029

Notes:

[65] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: 75% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[66]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.38
Variability estimate	Standard error of the mean
Dispersion value	0.03

Notes:

[66] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: 75% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[67]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.45
Variability estimate	Standard error of the mean
Dispersion value	0.043

Notes:

[67] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0409 <sup>[68]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.03
Variability estimate	Standard error of the mean
Dispersion value	0.009

Notes:

[68] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012 <sup>[69]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.09
Variability estimate	Standard error of the mean
Dispersion value	0.019

Notes:

[69] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID



Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[70]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.26
Variability estimate	Standard error of the mean
Dispersion value	0.026

Notes:

[70] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
90% Relative Reduction: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[71]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	0.31
Variability estimate	Standard error of the mean
Dispersion value	0.038

Notes:

[71] - P-value was calculated by mantel-haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

## Secondary: Change in the Brigham Eyebrow Tool for Alopecia (BETA) Scores From Baseline at Weeks 12 and 24

End point title	Change in the Brigham Eyebrow Tool for Alopecia (BETA) Scores From Baseline at Weeks 12 and 24
End point description:	
<p>BETA is a clinician-rated scale that assesses the total eyebrow hair present. The BETA score is calculated based on hair density and surface area of each individual eyebrow of the subject, ranging from 0 to 3, where 0= no eyebrow, 1= minimal eyebrow, 2= moderate eyebrow, and 3= normal eyebrow. The BETA score is the sum of the right and left eyebrow scores, ranging from 0 to 6. Higher scores indicate less hair loss of eyebrows. A positive CFB indicates less hair loss of eyebrows. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed (n) indicates the number of subjects with data available for analysis at the specified timepoint.</p>	
End point type	Secondary

End point timeframe:

Baseline, Weeks 12, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	173	90	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	0.9 (± 1.64)	0.7 (± 1.44)	1.1 (± 1.65)	
CFB at Week 12 (n= 88, 157, 80)	-0.3 (± 0.93)	0.8 (± 1.53)	0.7 (± 1.66)	
CFB at Week 24 (n= 86, 156, 83)	-0.3 (± 1.10)	1.2 (± 1.76)	1.2 (± 1.81)	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[72]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.4
Variability estimate	Standard error of the mean
Dispersion value	0.17

Notes:

[72] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[73]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[73] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	268
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[74]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.8
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[74] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	185
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[75]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.3
upper limit	2.2
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[75] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

## Secondary: Change in the Brigham Eyelash Tool for Alopecia (BELA) Scores From Baseline at Weeks 12 and 24

End point title	Change in the Brigham Eyelash Tool for Alopecia (BELA) Scores From Baseline at Weeks 12 and 24
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End point description:

BELA is a clinician-rated scale that assesses the total eyelash hair present. The BELA is calculated based on distribution and grade values, ranging from 0 (no eyelashes) to 3 (full eyelashes). The BELA score is the sum of the individual scores for the left and right eyes, ranging from 0 to 6. Higher scores indicate less hair loss of eyelashes. A positive CFB indicates less hair loss of eyelashes. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed (n) indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	85	165	82	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	0.7 (± 1.38)	0.9 (± 1.68)	1.1 (± 1.83)	
CFB at Week 12 (n= 84, 156, 81)	-0.1 (± 0.91)	0.9 (± 1.60)	1.0 (± 1.76)	
CFB at Week 24 (n= 78, 153, 69)	-0.0 (± 0.93)	1.4 (± 2.09)	1.3 (± 1.97)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 12

Comparison groups	Placebo v CTP-543 8 mg BID
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Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[76]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.5
Variability estimate	Standard error of the mean
Dispersion value	0.2

Notes:

[76] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[77]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.6
Variability estimate	Standard error of the mean
Dispersion value	0.23

Notes:

[77] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	250
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[78]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	2
Variability estimate	Standard error of the mean
Dispersion value	0.24

Notes:

[78] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [79]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	1.5

Confidence interval

level	95 %
sides	2-sided
lower limit	1
upper limit	2.1
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[79] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

## Secondary: Change in the SPRO Scale From Baseline at Weeks 12, 16, 20, and 24

End point title	Change in the SPRO Scale From Baseline at Weeks 12, 16, 20, and 24
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End point description:

SPRO is a questionnaire answered by the subject and designed to measure how satisfied alopecia areata subjects are with their hair at the time of the assessment. The responses range from 1 to 5: 1= very satisfied, 2= satisfied, 3= neither satisfied nor dissatisfied, 4= dissatisfied, and 5= very dissatisfied. Higher scores indicate the greater hair dissatisfaction. A negative CFB indicate the greater hair satisfaction. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed (n) indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 12, 16, 20, and 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	124	236	124	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Baseline	4.5 (± 0.85)	4.6 (± 0.71)	4.6 (± 0.80)	
CFB at Week 12 (n=122, 234, 122)	-0.4 (± 1.14)	-1.6 (± 1.39)	-1.7 (± 1.33)	
CFB at Week 16 (n= 123, 234, 122)	-0.1 (± 1.10)	-1.6 (± 1.31)	-1.7 (± 1.36)	
CFB at Week 20 (n= 119, 232, 118)	-0.1 (± 0.97)	-1.5 (± 1.40)	-1.9 (± 1.38)	
CFB at Week 24 (n= 118, 228, 120)	-0.1 (± 0.93)	-1.6 (± 1.47)	-1.9 (± 1.41)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[80]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[80] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[81]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[81] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[82]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[82] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[83]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.15



Notes:

[83] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [84]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[84] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [85]
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	-1.4
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[85] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[86]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[86] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[87]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.1
upper limit	-1.4
Variability estimate	Standard error of the mean
Dispersion value	0.16

Notes:

[87] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, and baseline value.

### **Secondary: Percentage of Subjects Achieving a $\geq 2$ -point Change From Baseline in the SPRO Scale at Weeks 12, 16, 20, and 24**

End point title	Percentage of Subjects Achieving a $\geq 2$ -point Change From Baseline in the SPRO Scale at Weeks 12, 16, 20, and 24
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End point description:

SPRO is a questionnaire answered by the subject and designed to measure how satisfied alopecia areata subjects are with their hair at the time of the assessment. The responses range from 1 to 5: 1= very satisfied, 2= satisfied, 3= neither satisfied nor dissatisfied, 4= dissatisfied, and 5= very dissatisfied. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Weeks 12, 16, 20, and 24

<b>End point values</b>	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of subjects				
number (not applicable)				
Week 12	15.6	50.4	59.0	
Week 16	9.8	52.6	57.4	
Week 20	9.2	50.4	63.6	
Week 24	8.5	52.6	61.7	

## Statistical analyses

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[88]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.43
Variability estimate	Standard error of the mean
Dispersion value	0.046

Notes:

[88] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[89]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.54
Variability estimate	Standard error of the mean
Dispersion value	0.055

Notes:

[89] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
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Statistical analysis description:

Week 16

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[90]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.43

Confidence interval

level	95 %
sides	2-sided
lower limit	0.35
upper limit	0.51
Variability estimate	Standard error of the mean
Dispersion value	0.042

Notes:

[90] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 16

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[91]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.47

Confidence interval

level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.57
Variability estimate	Standard error of the mean
Dispersion value	0.052

Notes:

[91] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [92]
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.5
Variability estimate	Standard error of the mean
Dispersion value	0.041

Notes:

[92] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [93]
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	0.63
Variability estimate	Standard error of the mean
Dispersion value	0.05

Notes:

[93] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[94]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.52
Variability estimate	Standard error of the mean
Dispersion value	0.041

Notes:

[94] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
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Statistical analysis description:

Week 24

Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[95]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	0.62
Variability estimate	Standard error of the mean
Dispersion value	0.051

Notes:

[95] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

### **Secondary: Change in the Individual Items of the Hair Quality Patient Reported Outcome (QPRO) Scale From Baseline at Weeks 12, 16, 20, and 24**

End point title	Change in the Individual Items of the Hair Quality Patient Reported Outcome (QPRO) Scale From Baseline at Weeks 12, 16, 20, and 24
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End point description:

The QPRO questionnaire provides additional details on key attributes of hair and helps provide context to the SPRO response. The individual items of QPRO are: Satisfied thickness hair coverage (STHC); Satisfied evenness hair coverage (SEHC); How satisfied with your eyebrows (HSWYE); How satisfied with your eyelashes (HSWYEI), scored on a scale ranging from 1 to 5 where 1=very satisfied, 2=satisfied, 3=neither satisfied nor dissatisfied, 4=dissatisfied, 5=very dissatisfied. Higher scores indicate the greater dissatisfaction on hair quality. A negative CFB indicate the greater satisfaction on hair quality. Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed indicates the number of subjects with data available for analysis of this end point. Number of subjects analysed indicates the number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
End point timeframe:	
Baseline, Weeks 12, 16, 20, and 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	124	236	124	
Units: Score on a scale				
arithmetic mean (standard deviation)				
STHC: Baseline	4.6 (± 0.76)	4.6 (± 0.66)	4.6 (± 0.83)	
STHC: CFB at Week 12 (n=122, 234, 122)	-0.3 (± 0.95)	-1.3 (± 1.20)	-1.4 (± 1.35)	
STHC: CFB at Week 16 (n= 123, 234, 122)	-0.1 (± 0.91)	-1.3 (± 1.23)	-1.5 (± 1.30)	
STHC: CFB at Week 20 (n= 119, 232, 118)	-0.1 (± 0.85)	-1.3 (± 1.35)	-1.7 (± 1.36)	
SHTC: CFB at Week 24 (n=118, 228, 120)	-0.1 (± 0.89)	-1.4 (± 1.46)	-1.6 (± 1.41)	
SEHC: Baseline	4.7 (± 0.61)	4.7 (± 0.58)	4.7 (± 0.74)	
SEHC: CFB at Week 12 (n= 122, 234, 122)	-0.3 (± 0.78)	-1.2 (± 1.10)	-1.3 (± 1.26)	
SEHC: CFB at Week 16 (n= 123, 234, 122)	-0.2 (± 0.82)	-1.1 (± 1.12)	-1.3 (± 1.20)	
SEHC: CFB at Week 20 (n= 119, 232, 118)	-0.1 (± 0.76)	-1.3 (± 1.27)	-1.5 (± 1.29)	
SEHC: CFB at Week 24 (n= 118, 228, 120)	-0.1 (± 0.71)	-1.4 (± 1.36)	-1.6 (± 1.37)	
HSWYE: Baseline	4.3 (± 1.07)	4.3 (± 1.16)	4.1 (± 1.32)	
HSWYE: CFB at Week 12 (n= 122, 234, 122)	-0.2 (± 0.84)	-1.3 (± 1.31)	-1.3 (± 1.42)	
HSWYE: CFB at Week 16 (n= 123, 234, 122)	-0.2 (± 0.78)	-1.2 (± 1.28)	-1.4 (± 1.54)	
HSWYE: CFB at Week 20 (n= 119, 232, 118)	-0.1 (± 0.78)	-1.4 (± 1.40)	-1.4 (± 1.47)	
HSWYE: CFB at Week 24 (n= 118, 228, 120)	-0.1 (± 0.81)	-1.4 (± 1.43)	-1.6 (± 1.50)	
HSWYEI: Baseline	4.1 (± 1.23)	4.1 (± 1.32)	3.8 (± 1.42)	
HSWYEI: CFB at Week 12 (n= 122, 234, 122)	-0.2 (± 0.72)	-1.1 (± 1.34)	-1.0 (± 1.29)	
HSWYEI: CFB at Week 16 (n= 123, 234, 122)	-0.2 (± 0.82)	-1.1 (± 1.29)	-1.1 (± 1.41)	
HSWYEI: CFB at Week 20 (n= 119, 232, 118)	-0.1 (± 0.83)	-1.2 (± 1.39)	-1.2 (± 1.31)	
HSWYEI: CFB at Week 24 (n= 118, 228, 120)	-0.1 (± 0.73)	-1.3 (± 1.41)	-1.3 (± 1.45)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 12	

Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[96]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[96] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[97]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[97] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[98]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1



Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[98] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[99]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[99] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[100]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[100] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[101]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	-1.3
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[101] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
STHC: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[102]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[102] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
STHC: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID

Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[103]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[103] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[104]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[104] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[105]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[105] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[106]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.11

Notes:

[106] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[107]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[107] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[108]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[108] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[109]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[109] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
SEHC: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[110]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[110] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
SEHC: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[111]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[111] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[112]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[112] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[113]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[113] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[114]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[114] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[115]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[115] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[116]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[116] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID



Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[117]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[117] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYE: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[118]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.13

Notes:

[118] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYE: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[119]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.8
upper limit	-1.2
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[119] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWYEL: Week 12	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[120]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[120] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWYEL: Week 12	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[121]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[121] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWEI: Week 16	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[122]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	-0.7
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[122] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWEI: Week 16	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[123]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[123] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWEI: Week 20	
Comparison groups	Placebo v CTP-543 8 mg BID

Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[124]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	-0.8
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[124] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWEI: Week 20	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[125]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	-1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[125] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
HSWEI: Week 24	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[126]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	-0.9
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[126] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
HSWEI: Week 24	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	248
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[127]</sup>
Method	MMRM
Parameter estimate	LS Mean Difference
Point estimate	-1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	-1.1
Variability estimate	Standard error of the mean
Dispersion value	0.14

Notes:

[127] - P-value was calculated by MMRM analysis with effects for treatment, visit, treatment-by-visit interaction, baseline value, and baseline SALT score.

## **Secondary: Change in the Anxiety and Depression Scale Scores of the Hospital Anxiety and Depression Scale (HADS) From Baseline at Week 24**

End point title	Change in the Anxiety and Depression Scale Scores of the Hospital Anxiety and Depression Scale (HADS) From Baseline at Week 24
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End point description:

HADS is questionnaire designed to assess anxiety and depression symptoms which is completed by subjects. The questionnaire is comprised of two separate scales with a total of 14 items: A 7-item scale related to anxiety and 7-item scale related to depression. Each item within both scales is scored using a 4-point scale, ranging from 0 to 3 and the total scores in each scale can range from 0 to 21. Separate scores were created for anxiety and depression. A score between 0-7 is considered normal, 8-10 is mild, 11-14 is moderate, and >14 is severe anxiety or depression. Higher scores indicate greater severity. A negative CFB indicates less severity. Efficacy population= all subjects who were randomised in the study and dispensed study drug during the treatment period. Overall number of subjects analysed=number of subjects with data available for analysis of this end point. Number of subjects analysed (n) = number of subjects with data available for analysis at the specified timepoint.

End point type	Secondary
End point timeframe:	
Baseline and Week 24	

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	118	228	120	
Units: Score on a scale				
arithmetic mean (standard deviation)				
Anxiety: Baseline	6.2 (± 3.99)	6.4 (± 4.21)	6.2 (± 3.79)	
Anxiety: CFB at Week 24	-0.6 (± 2.74)	-1.1 (± 3.00)	-0.8 (± 2.85)	
Depression: Baseline	4.7 (± 3.96)	4.2 (± 3.66)	4.3 (± 3.56)	
Depression: CFB at Week 24	-0.6 (± 2.97)	-1.2 (± 3.16)	-1.5 (± 2.60)	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Anxiety	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1206 <sup>[128]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	1
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[128] - P-value was calculated by analysis of covariance (ANCOVA) analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Anxiety	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5367 <sup>[129]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.9
Variability estimate	Standard error of the mean
Dispersion value	0.34

Notes:

[129] - P-value was calculated by ANCOVA analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 8 mg BID
Statistical analysis description:	
Depression	
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0064 <sup>[130]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.3
Variability estimate	Standard error of the mean
Dispersion value	0.29

Notes:

[130] - P-value was calculated by ANCOVA analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

<b>Statistical analysis title</b>	Placebo vs CTP-543 12 mg BID
Statistical analysis description:	
Depression	
Comparison groups	Placebo v CTP-543 12 mg BID
Number of subjects included in analysis	238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0011 <sup>[131]</sup>
Method	ANCOVA
Parameter estimate	LS Mean Difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.7
Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[131] - P-value was calculated by ANCOVA analysis with effects for treatment, visit, baseline SALT score, and baseline HADS value.

## Secondary: Percentage of Subjects Achieving an Absolute SALT Score of $\leq 10$ at Week 24

End point title	Percentage of Subjects Achieving an Absolute SALT Score of $\leq 10$ at Week 24
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End point description:

SALT is a quantitative assessment of scalp hair loss with scores ranging in severity from 0 (no scalp hair loss) to a maximum of 100 (complete scalp hair loss). Efficacy population included all subjects who were randomised in the study and dispensed study drug during the treatment period.

End point type	Secondary
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End point timeframe:

Week 24

End point values	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	127	249	127	
Units: Percentage of subjects				
number (not applicable)	0	24.9	26.7	

## Statistical analyses

Statistical analysis title	Placebo vs CTP-543 8 mg BID
Comparison groups	Placebo v CTP-543 8 mg BID
Number of subjects included in analysis	376
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[132]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.3
Variability estimate	Standard error of the mean
Dispersion value	0.027

Notes:

[132] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

Statistical analysis title	Placebo vs CTP-543 12 mg BID
Comparison groups	Placebo v CTP-543 12 mg BID



Number of subjects included in analysis	254
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 <sup>[133]</sup>
Method	Mantel-Haenszel
Parameter estimate	Risk difference (RD)
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.18
upper limit	0.33
Variability estimate	Standard error of the mean
Dispersion value	0.039

Notes:

[133] - P-value was calculated by the Mantel-Haenszel estimate stratified by baseline scalp hair loss (partial vs complete/near-complete) for each treatment group compared to placebo.

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: Randomisation up to Week 28; Adverse events: From first dose of study drug up to last follow up visit (Week 28)

Adverse event reporting additional description:

All-cause mortality: All randomised subjects included all subjects who were randomised in the study (N= 130, 258, 129). Adverse events: Safety Population included all subjects who received study drug during the treatment period.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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### Reporting groups

Reporting group title	Placebo
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Reporting group description:

Subjects received CTP-543 matched placebo tablets, orally, BID for up to 24 weeks.

Reporting group title	CTP-543 8 mg BID
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Reporting group description:

Subjects received CTP-543 8 mg tablets, orally, BID for up to 24 weeks.

Reporting group title	CTP-543 12 mg BID
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Reporting group description:

Subjects received CTP-543 12 mg tablets, orally, BID for up to 24 weeks.

Serious adverse events	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 130 (0.00%)	3 / 256 (1.17%)	2 / 129 (1.55%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	0 / 130 (0.00%)	0 / 256 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Migraine with aura			
subjects affected / exposed	0 / 130 (0.00%)	1 / 256 (0.39%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Osteoarthritis			
subjects affected / exposed	0 / 130 (0.00%)	0 / 256 (0.00%)	1 / 129 (0.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 130 (0.00%)	1 / 256 (0.39%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	0 / 130 (0.00%)	1 / 256 (0.39%)	0 / 129 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

<b>Non-serious adverse events</b>	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 130 (46.15%)	137 / 256 (53.52%)	67 / 129 (51.94%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	4 / 130 (3.08%)	13 / 256 (5.08%)	15 / 129 (11.63%)
occurrences (all)	4	13	15
Nervous system disorders			
Headache			
subjects affected / exposed	19 / 130 (14.62%)	32 / 256 (12.50%)	13 / 129 (10.08%)
occurrences (all)	19	32	13
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	3 / 130 (2.31%)	23 / 256 (8.98%)	13 / 129 (10.08%)
occurrences (all)	3	23	13
Infections and infestations			
COVID-19			
subjects affected / exposed	22 / 130 (16.92%)	60 / 256 (23.44%)	24 / 129 (18.60%)
occurrences (all)	22	60	24
Asymptomatic COVID-19			

subjects affected / exposed	22 / 130 (16.92%)	33 / 256 (12.89%)	21 / 129 (16.28%)
occurrences (all)	22	33	21
Nasopharyngitis			
subjects affected / exposed	16 / 130 (12.31%)	33 / 256 (12.89%)	16 / 129 (12.40%)
occurrences (all)	16	33	16

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported