31st EADV Congress
Late Breaking News Session
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TOP-LINE RESULTS FROM THRIVE-AA1: A PHASE 3 CLINICAL TRIAL OF CTP-543 (DEURUXOLITINIB), AN ORAL JAK INHIBITOR, IN ADULT PATIENTS WITH MODERATE TO SEVERE ALOPECIA AREATA

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Disclosures of Relationship with Industry

Brett King, MD, PhD

Disclosures:

- Dr. King has served on advisory boards and/or is a consultant and/or is a clinical trial investigator for Abbvie, AltruBio Inc, Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol-Meyers Squibb, Concert Pharmaceuticals Inc, Equillium, Horizon Therapeutics, Eli Lilly and Company, Incyte Corp, Janssen Pharmaceuticals, LEO Pharma, Otsuka/Visterra Inc, Pfizer Inc, Regeneron, Sanofi Genzyme, TWi Biotechnology Inc, and Viela Bio. He is on speaker bureaus for Abbvie, Incyte, Eli Lilly, Pfizer, Regeneron and Sanofi Genzyme.

Background and Objective

Background

- Alopecia areata (AA) is a common autoimmune disorder characterized by non-scarring hair loss
- The pathogenesis of AA involves interferon gamma and interleukin (IL)-15, which signal through the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway
- There is a single approved medicine, baricitinib (an oral Janus kinase (JAK) inhibitor), for treatment of AA

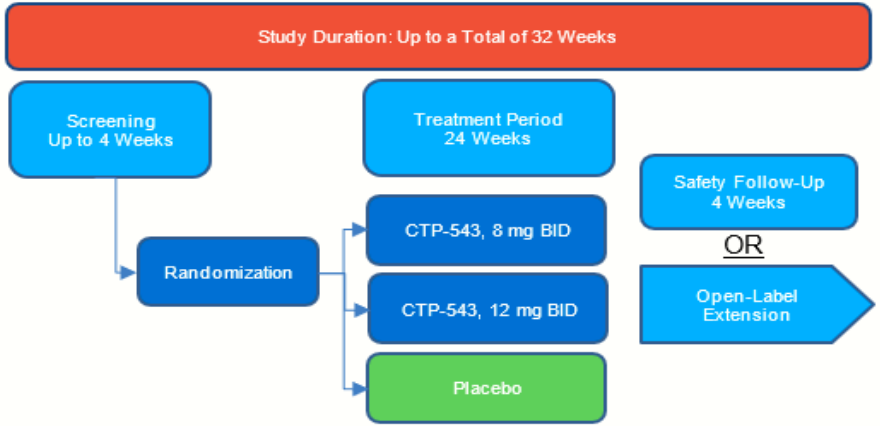
Objective

- To report 24-week results from a Phase 3 randomized, double-blind, placebo-controlled trial, THRIVE-AA1, evaluating CTP-543 (deuruxolitinib) for AA

** King B, et al. N Engl J Med 2022;386:1687-99*

Trial Design

THRIVE-AA1
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata



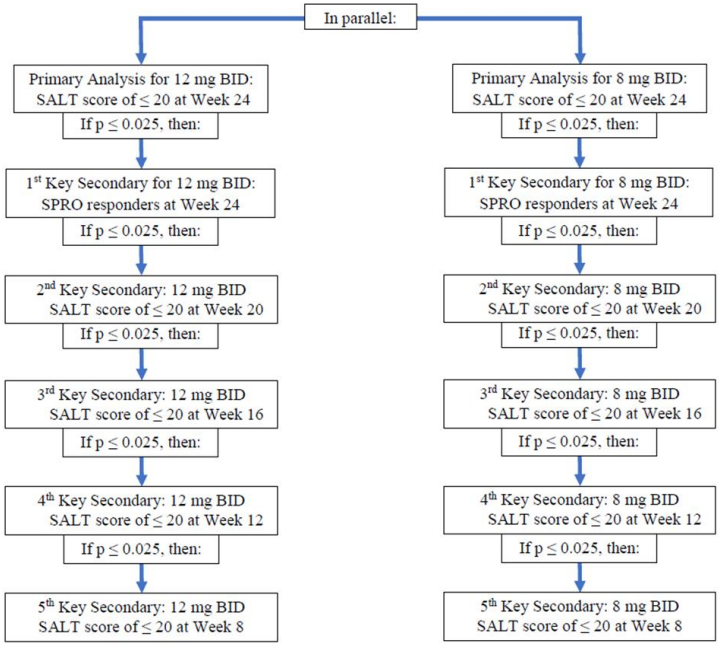
- Multinational trial in AA patients 18 to 65 years old
  - Trial sites in USA, Canada, France, Poland, Spain
- Entry criteria of at least 50% scalp hair loss as measured by Severity of Alopecia Tool (SALT)
  - Episode of hair loss >6 months and ≤10 years
- Randomization stratified by Baseline scalp hair loss:
  - Partial scalp hair loss (SALT score ≥50 and <95)
  - Complete or near-complete scalp hair loss (SALT score ≥95)

Key Trial Endpoints

THRIVE-AA1
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

- Primary Efficacy Endpoint
  - The percentage of patients achieving SALT score ≤20 at Week 24
- Key Secondary Efficacy Endpoints
  - The percentage of responders (defined as “satisfied” or “very satisfied”) on the Hair Satisfaction Patient Reported Outcome (SPRO) scale at Week 24
    - The SPRO is a single item questionnaire answered by the patient designed to measure satisfaction with their hair at the time of the assessment
  - The percentage of subjects achieving SALT score ≤20 at Weeks 20, 16, 12, and 8
- Additional secondary efficacy endpoints included:
  - Percentage of patients achieving SALT score ≤10 at Week 24
  - Relative change in SALT score from Baseline at Weeks 4, 8, 12, 16, 20, and 24
  - Change from Baseline on the Brigham Eyebrow Tool for Alopecia (BETA) score at Weeks 12 and 24
  - Change from Baseline on the Brigham Eyelash Tool for Alopecia (BELA) score at Weeks 12 and 24
- Hierarchical testing was used to control for multiple comparisons for primary and key secondary endpoints

Hierarchical Testing Scheme:
Primary and Key Secondary Efficacy Analyses



Demographics

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Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

	Placebo (n = 140)	CTP-543 8 mg BID (n = 351)	CTP-543 12 mg BID (n = 215)	Total (n = 706)
Age (years), Mean (SD)	38.7 (13.81)	38.9 (13.32)	38.2 (12.80)	38.6 (13.25)
Gender, n (%)				
Male	51 (36.4)	134 (38.2)	84 (39.1)	269 (38.1)
Female	89 (63.6)	217 (61.8)	131 (60.9)	437 (61.9)
Race: n (%)				
American Indian or Alaska Native	0	2 (0.6)	1 (0.5)	3 (0.4)
Asian	10 (7.1)	22 (6.3)	21 (9.8)	53 (7.5)
Black or African American	16 (11.4)	40 (11.4)	27 (12.6)	83 (11.8)
Native Hawaiian or Pac Islander	1 (0.7)	3 (0.9)	1 (0.5)	5 (0.7)
White	98 (70.0)	241 (68.7)	145 (67.4)	484 (68.6)
Other	15 (10.7)	43 (12.2)	20 (9.3)	78 (11.1)

Baseline Characteristics

THRIVE-AA1
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

	Placebo (n=140)	CTP-543 8 mg BID (n=351)	CTP-543 12 mg BID (n=215)	Total (n=706)
Baseline Total SALT score, Mean (SD)	88.1 (15.10)	85.5 (18.35)	85.2 (18.41)	85.9 (17.78)
Duration of Current Episode (years), Mean (SD)	3.9 (2.88)	3.6 (2.63)	3.6 (2.86)	3.7 (2.75)
Current **eyebrow** involvement, n (%)	97 (69.3)	245 (69.8)	151 (70.2)	493 (69.8)
Current **eyelash** involvement, n (%)	92 (65.7)	246 (70.1)	158 (73.5)	496 (70.3)
Alopecia Areata Classification, n (%)				
Partial scalp hair loss (SALT ≥50 and <95)	62 (44.3)	155 (44.2)	95 (44.2)	312 (44.2)
Complete or near-complete scalp loss (SALT ≥95)	78 (55.7)	196 (55.8)	120 (55.8)	394 (55.8)

Both Doses of CTP-543 Achieve Primary Efficacy Endpoint

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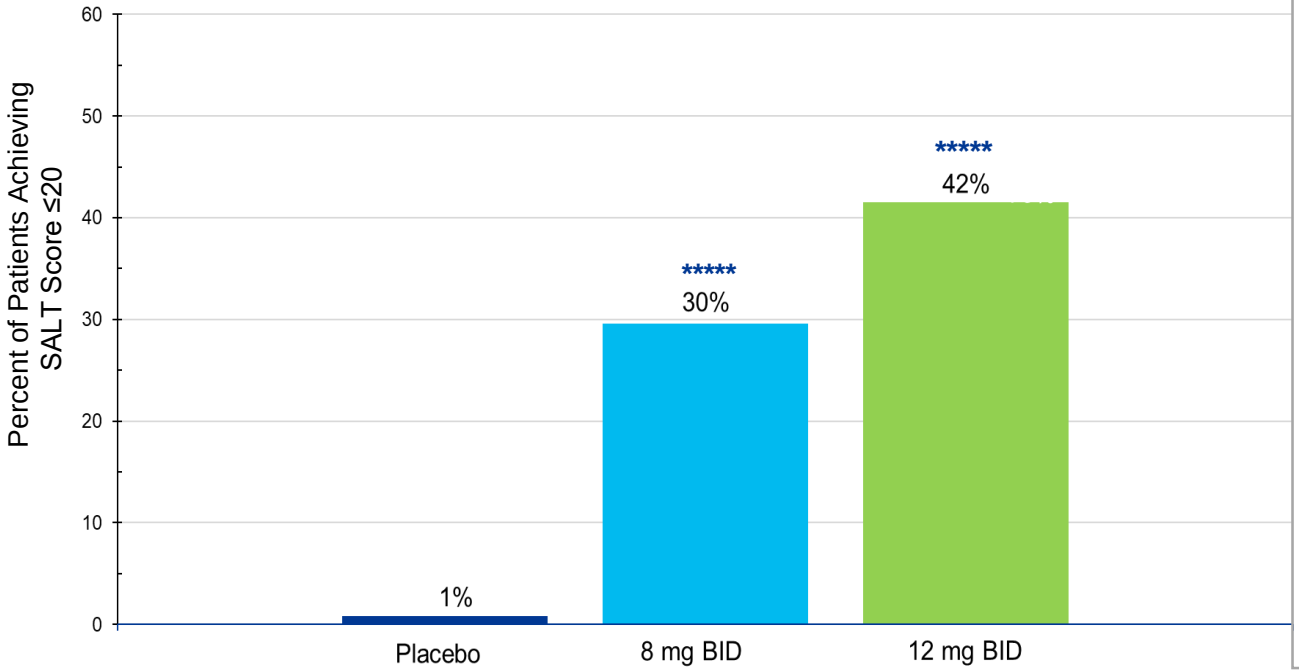
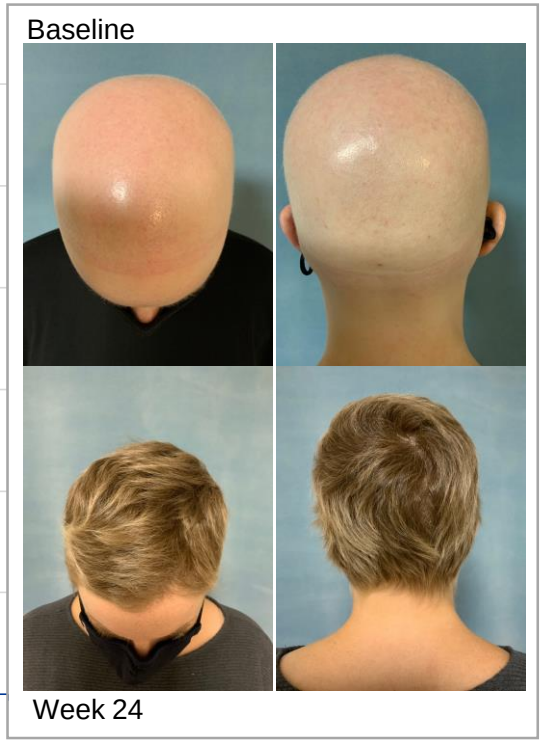
Primary Efficacy Endpoint: Proportion of patients achieving **SALT Score ≤20** at Week 24





***** P < 0.0001 vs PBO

Proportion of Patients Achieving SALT Score ≤20 Over 24 Weeks of Deuruxolitinib Treatment

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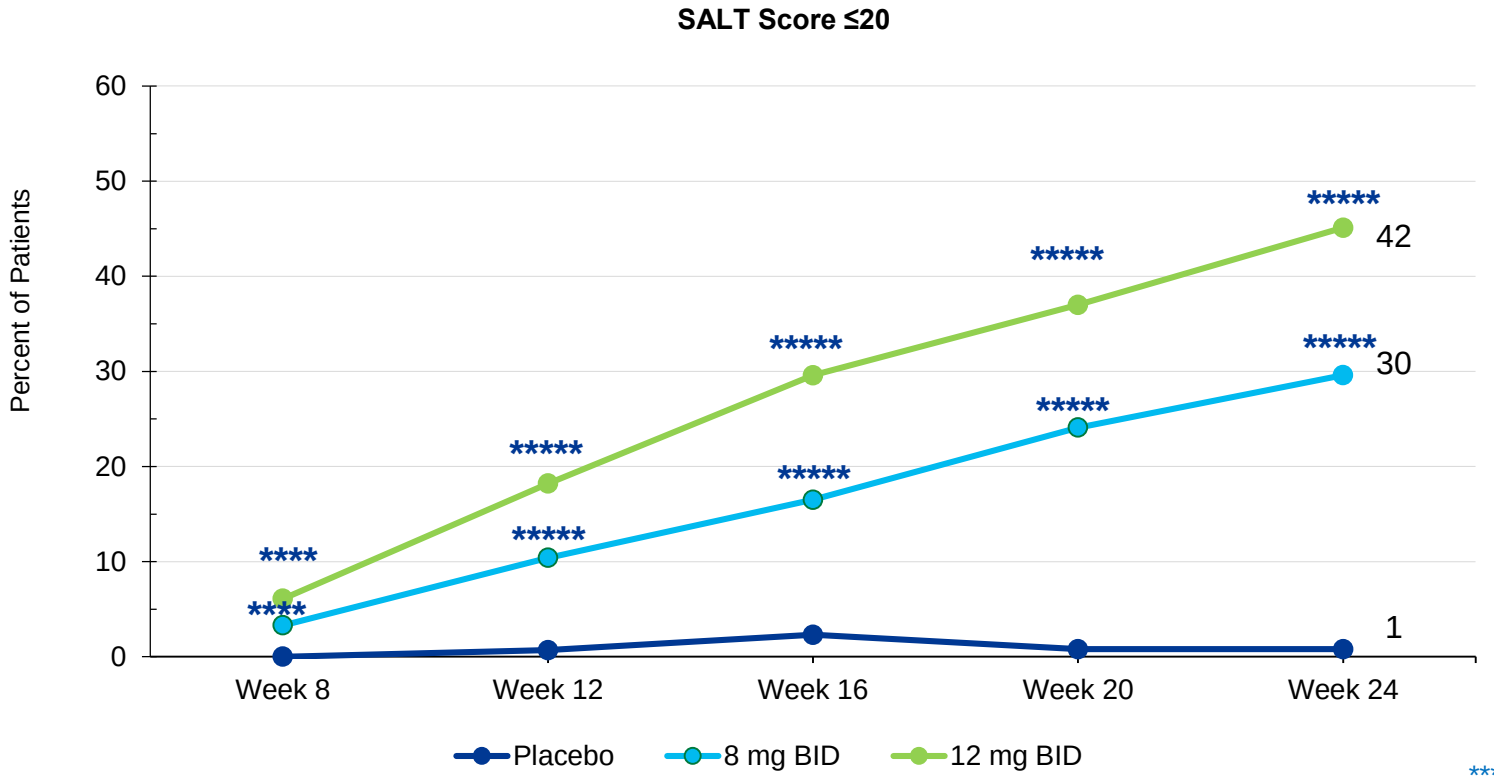
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata



***** P < 0.0001 vs PBO
**** P < 0.001 vs PBO

Significant Effects on SALT Score ≤10

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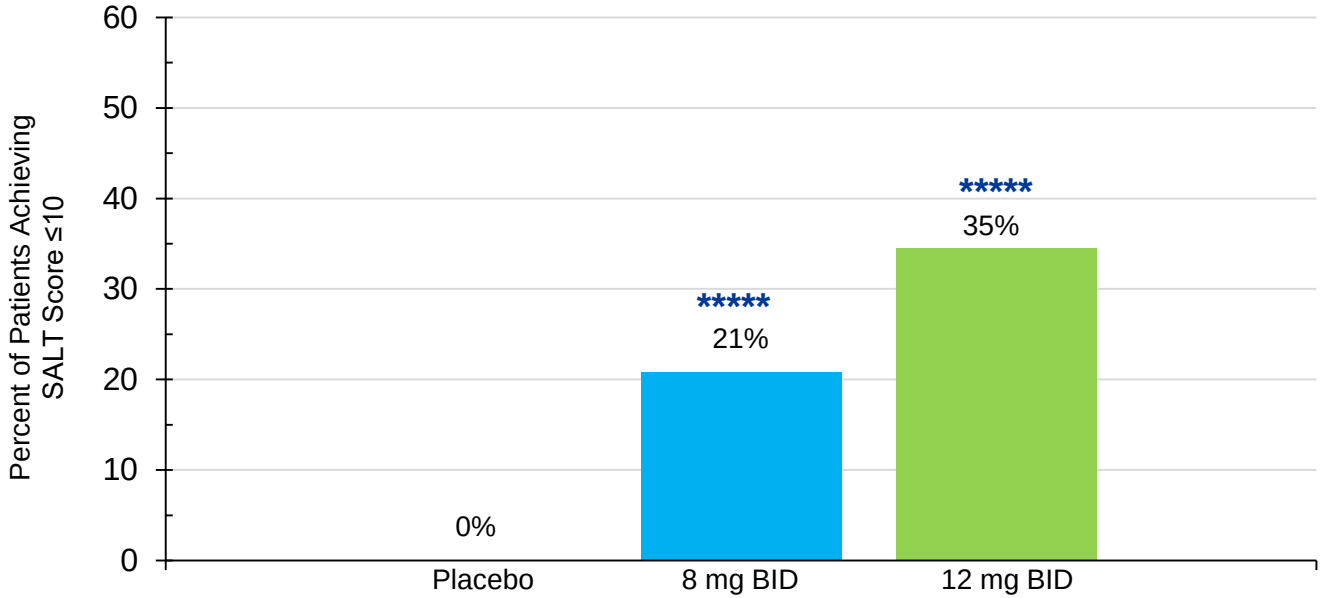
Secondary Endpoint: Proportion of patients achieving **SALT Score ≤10** at Week 24



***** P < 0.0001 vs PBO

Significant Changes in SALT Score as Early as Four Weeks

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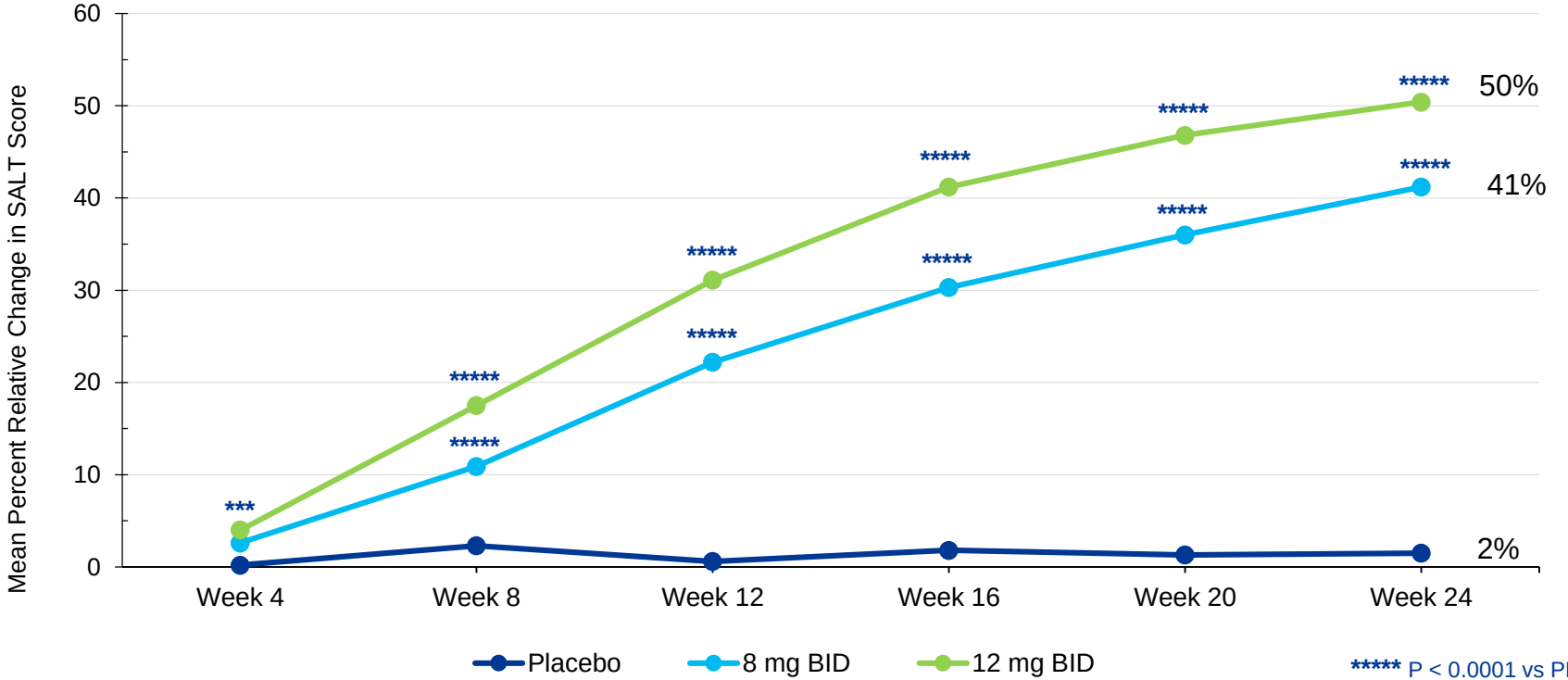
Secondary Endpoint: **Relative Change from Baseline SALT Score** over 24 weeks



***** P < 0.0001 vs PBO
*** P < 0.01 vs PBO

Significant Improvement in Eyebrow Regrowth

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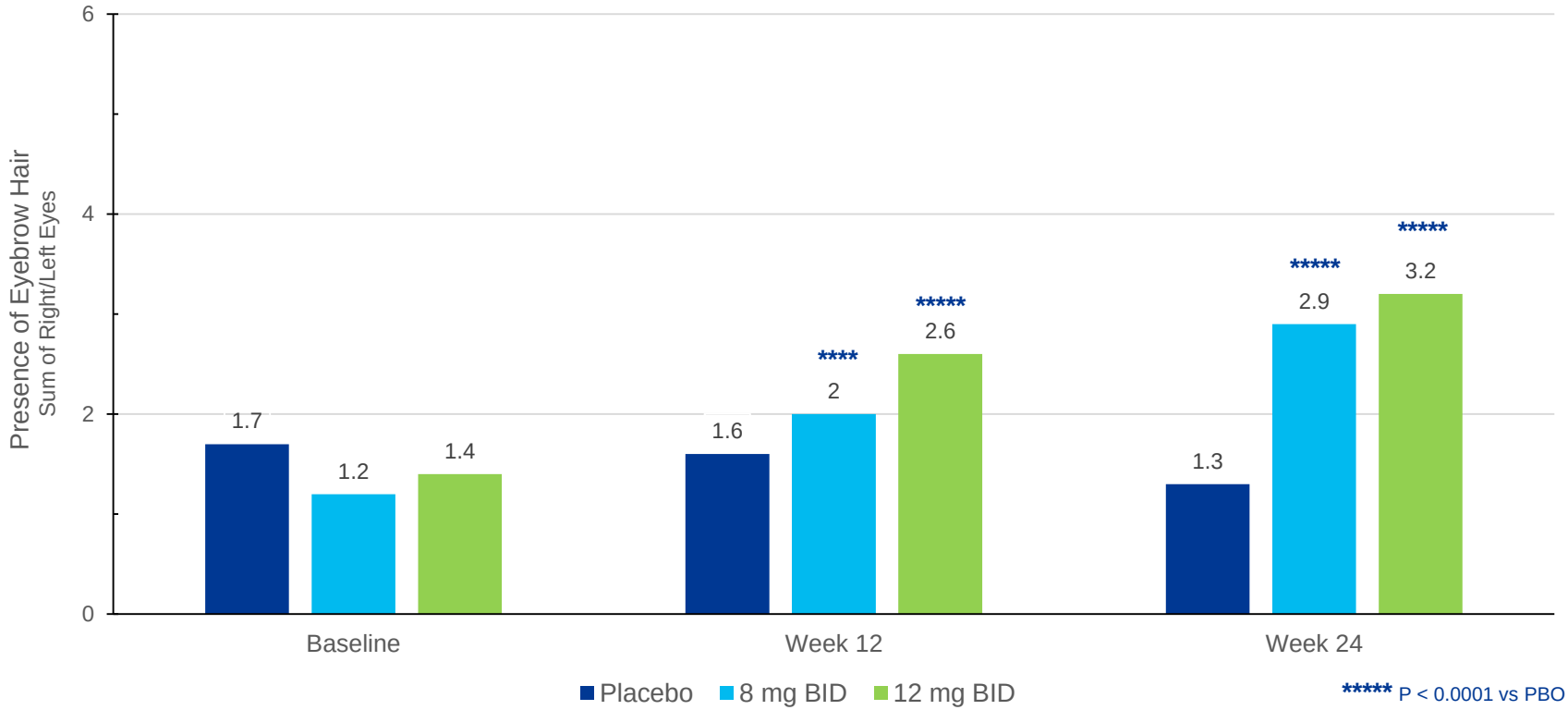
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

Secondary Endpoint: Brigham Eyebrow Tool for Alopecia (BETA) Score for Patients with Eyebrow Involvement at Baseline only*



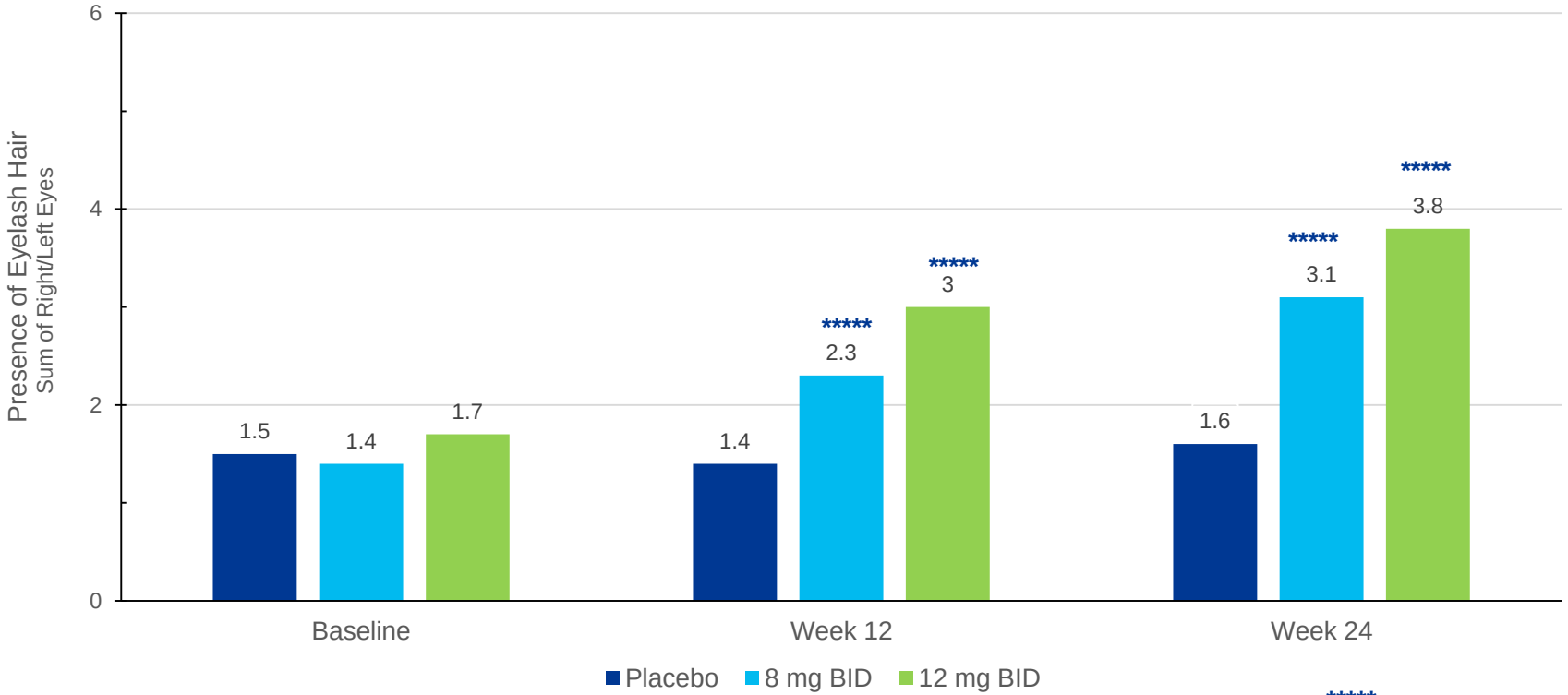
***** P < 0.0001 vs PBO
**** P < 0.001 vs PBO

* Approximately 40-60% of each group had eyebrow involvement at Baseline

Significant Improvement in Eyelash Regrowth

THRIVE-AA1
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

Secondary Endpoint: Brigham Eyelash Tool for Alopecia (BELA) Score for Patients with Eyebrow Involvement at Baseline only*



* Approximately 40-60% of each group had eyebrow involvement at Baseline

***** P < 0.0001 vs PBO

High Degree of Patient Satisfaction with Scalp Hair

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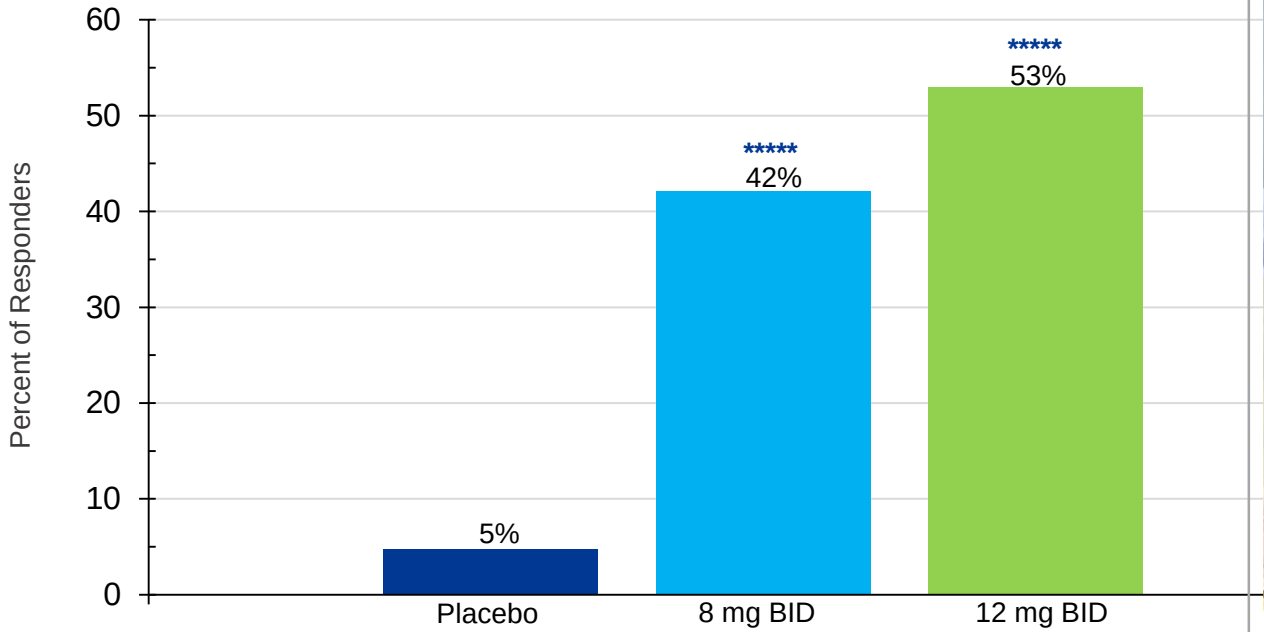
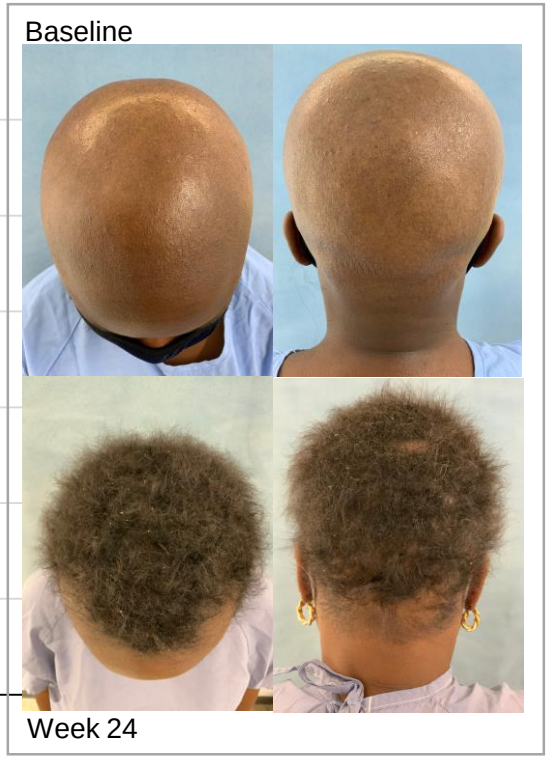
Key Secondary Endpoint: Patient response of **'very satisfied' or 'satisfied'** on Satisfaction of Hair Patient Reported Outcome (SPRO) at Week 24



***** P < 0.0001 vs PBO



Responders: Patient responding as 'very satisfied' or 'satisfied' on SPRO

Patient Disposition

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Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

	Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID	Total
Randomized, n (%)	**140**	**351**	**215**	**706**
Study Status, n (%)				
Completed	**129 (92.1)**	**318 (90.6)**	**199 (92.6)**	**646 (91.5)**
Entered OLE	127 (90.7)	312 (88.9)	194 (90.2)	633 (89.7)
Discontinued	**11 (7.9)**	**33 (9.4)**	**16 (7.4)**	**60 (8.5)**
Reason for Discontinuation, n				
TEAE	*2*	*8*	*4*	*14*
Lack of Efficacy	*2*	*1*	*0*	*3*
Noncompliance	*0*	*3*	*2*	*5*
Pregnancy	*0*	*0*	*1*	*1*
Protocol Violation	*2*	*0*	*1*	*3*
Other	*4*	*11*	*2*	*17*
Lost to Follow-up	*1*	*10*	*6*	*17*

THRIVE-AA1
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

Treatment Emergent Adverse Events

	Placebo (N=140)	CTP-543 8 mg BID (N=350)	CTP-543 12 mg BID (N=215)	Total (N=705)
Total number of TEAEs	186	551	376	1113
Number of patients with at least one TEAE, n (%)				
TEAE	78 (55.7)	228 (65.1)	137 (63.7)	443 (62.8)
Serious TEAE	4 (2.9)	4 (1.1)	1 (0.5)	9 (1.3)
TEAE Leading to study drug interruption	9 (6.4)	30 (8.6)	23 (10.7)	62 (8.8)
TEAE Leading to study drug discontinuation	2 (1.4)	9 (2.6)	6 (2.8)	17 (2.4)

Common Treatment Emergent Adverse Events (≥ 5%)

TEAE, n (%)	Placebo (n = 140)	CTP-543 8 mg BID (n = 350)	CTP-543 12 mg BID (n = 215)	Total (n = 705)
COVID-19	8 (5.7)	19 (5.4)	15 (7.0)	42 (6.0)
Nasopharyngitis	5 (3.6)	18 (5.1)	8 (3.7)	31 (4.4)
URI	9 (6.4)	9 (2.6)	8 (3.7)	26 (3.7)
Blood CPK increase	2 (1.4)	21 (6.0)	11 (5.1)	34 (4.8)
Headache	8 (5.7)	41 (11.7)	24 (11.2)	73 (10.4)
Acne	7 (5.0)	31 (8.9)	26 (12.1)	64 (9.1)

Serious Adverse Events

THRIVE-AA1
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

	Placebo (n=140)	CTP-543 8 mg BID (n=351)	CTP-543 12 mg BID (n=215)	Total (n=706)
Total SAEs, n	4	6	2	12
Number of patients with any SAE, n %	4 (2.9)	4 (1.1)	1 (0.5)	9 (1.3)
# patients with *related* SAE, n %	0	1 (0.3)	0	1 (0.1)
# patients with *not related* SAE, n %	4 (2.9)	3 (0.9)	1 (0.5)	8 (1.1)

Summary of *Related* SAEs

Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
	Pyrexia/Meningitis*	

* Considered possibly related by PI and Medical Monitor

Summary of Not Related SAEs by Preferred Term and Dose

Placebo	CTP-543 8 mg BID	CTP-543 12 mg BID
Appendicitis	Appendicitis	Appendicitis
Epilepsy	COVID-19	Ileus
Abortion spontaneous	Dyspnoea	
Adjustment disorder	Chest pain	

- There were no deaths, deep vein thromboses, or pulmonary embolisms reported in THRIVE-AA1

Conclusions

THRIVE-AA1
Phase 3 study of CTP-543 in adults with moderate to severe alopecia areata

- 42% and 30% of patients achieved SALT score ≤20 with deuruxolitinib (CTP-543) 12 mg BID and 8 mg BID, respectively, over 24 weeks of treatment
- Significant differences in SALT score ≤20 for both doses compared to placebo were seen as early as Week 8 and were maintained throughout study
- Patient satisfaction was significantly higher for both doses at Week 24 vs placebo
- CTP-543 treatment was generally well-tolerated
  - No DVT's or PEs observed in the 24-week trial
- >97% of eligible patients elected to roll into open label, long-term extension study
- The overall safety profile of CTP-543 and its potential to treat moderate to severe alopecia areata are promising