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RESULTS FROM A PHASE 3 TRIAL, THRIVE-AA1, OF THE ORAL JAK INHIBITOR CTP-543 (DEURUXOLITINIB) IN ADULT PATIENTS WITH MODERATE TO SEVERE ALOPECIA AREATA

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Disclosures of Relationship with Industry

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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

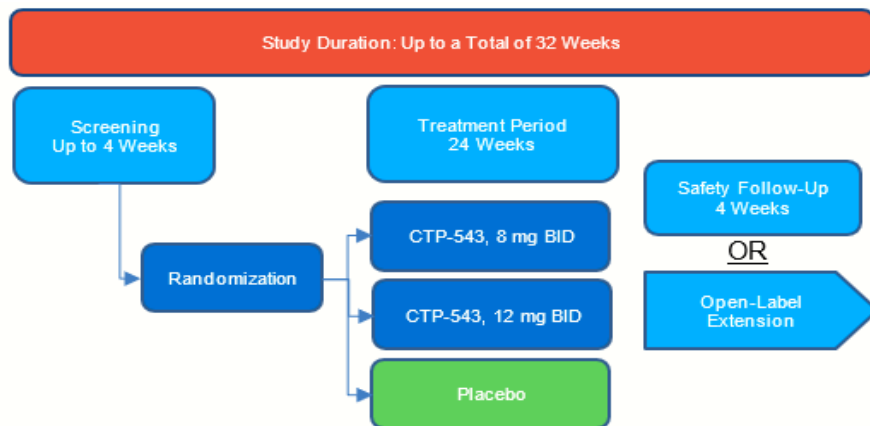
Background

- 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

Trial Design



- 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

- 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

Demographics

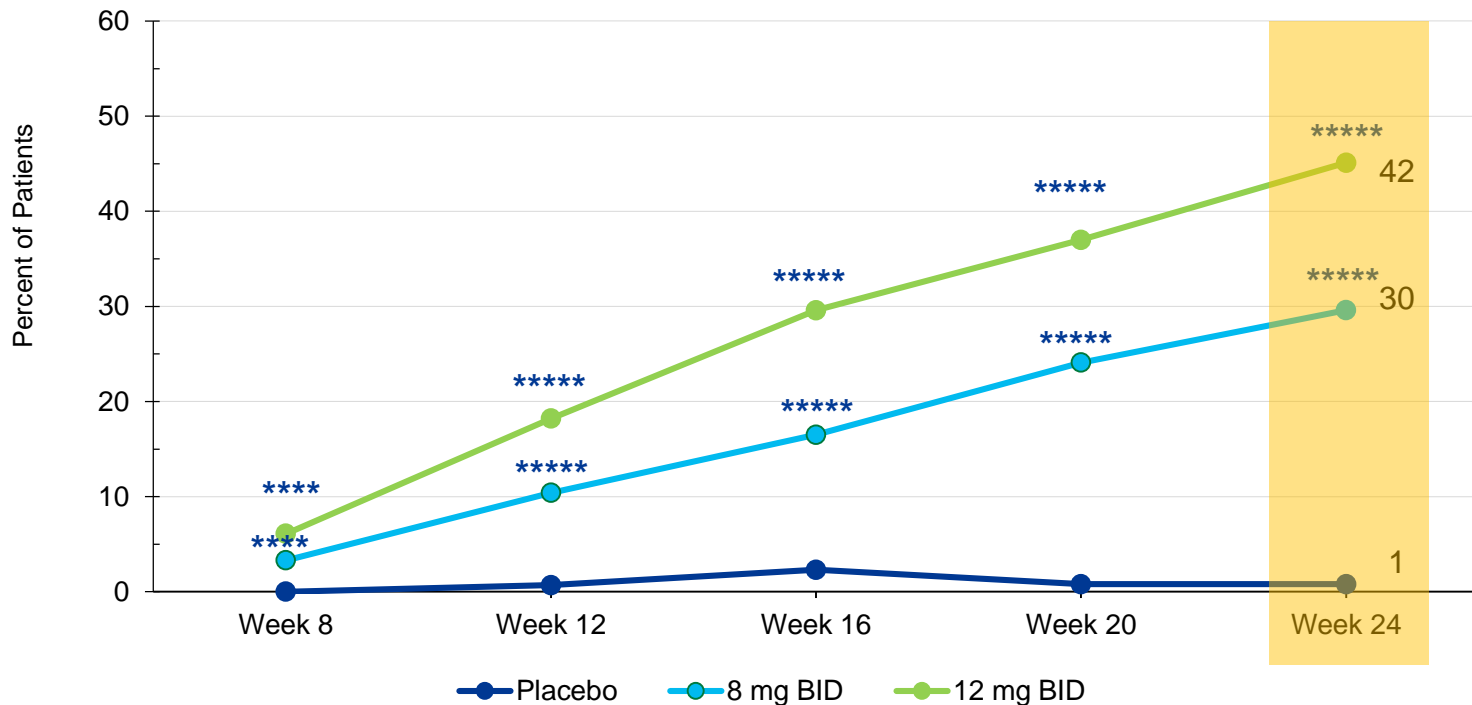
| | Placebo (n = 140) | CTP-543 8 mg BID (n = 351) | CTP-543 12 mg BID (n = 215) | Total (n = 706) |
|----------------------------------|----------------------|----------------------------------|-----------------------------------|--------------------|
| Age (years), Mean (SD) | 38.7 (13.81) | 38.9 (13.32) | 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

| | 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 \geq 50 and $<$ 95) | 62 (44.3) | 155 (44.2) | 95 (44.2) | 312 (44.2) |
| Complete or near-complete scalp loss (SALT \geq 95) | 78 (55.7) | 196 (55.8) | 120 (55.8) | 394 (55.8) |

Both Doses of CTP-543 Achieve Primary Efficacy Endpoint

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



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

Meaningful Regrowth of Scalp Hair: 8 mg BID

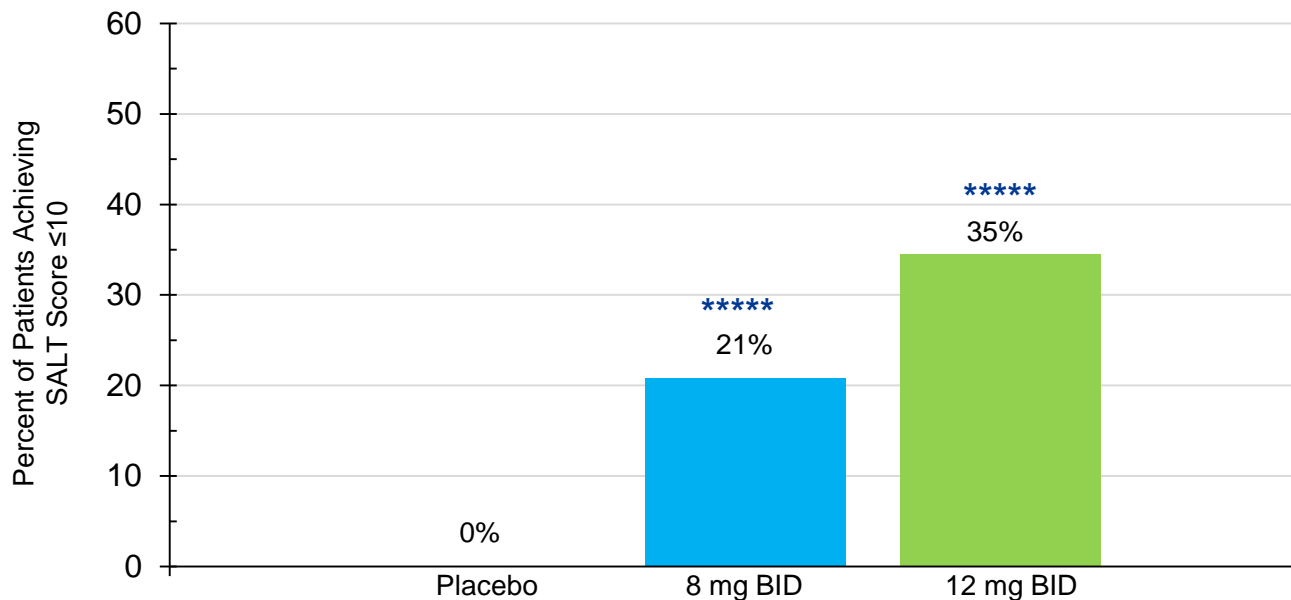


Baseline

Week 24

Significant Effects on SALT Score ≤ 10

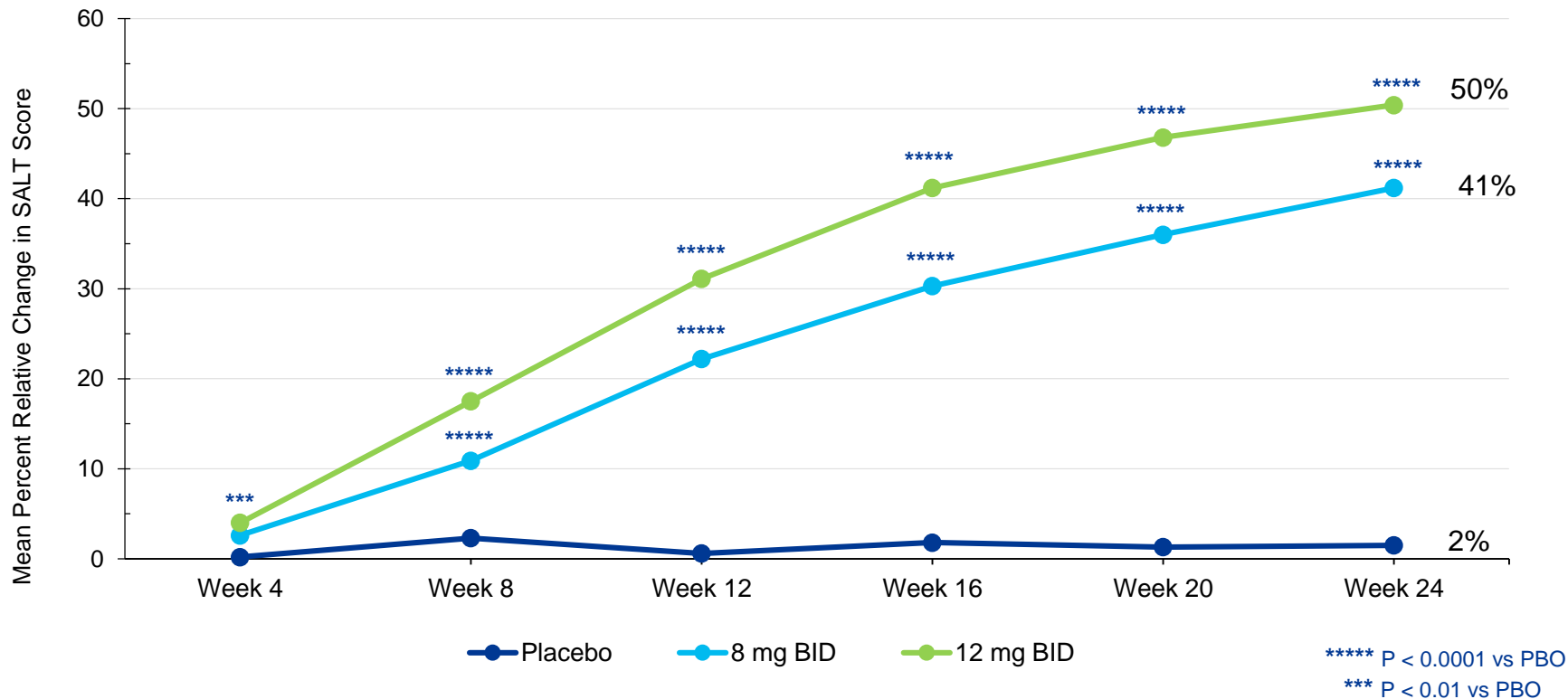
Secondary Endpoint: Proportion of patients achieving **SALT Score ≤ 10** at Week 24



***** P < 0.0001 vs PBO

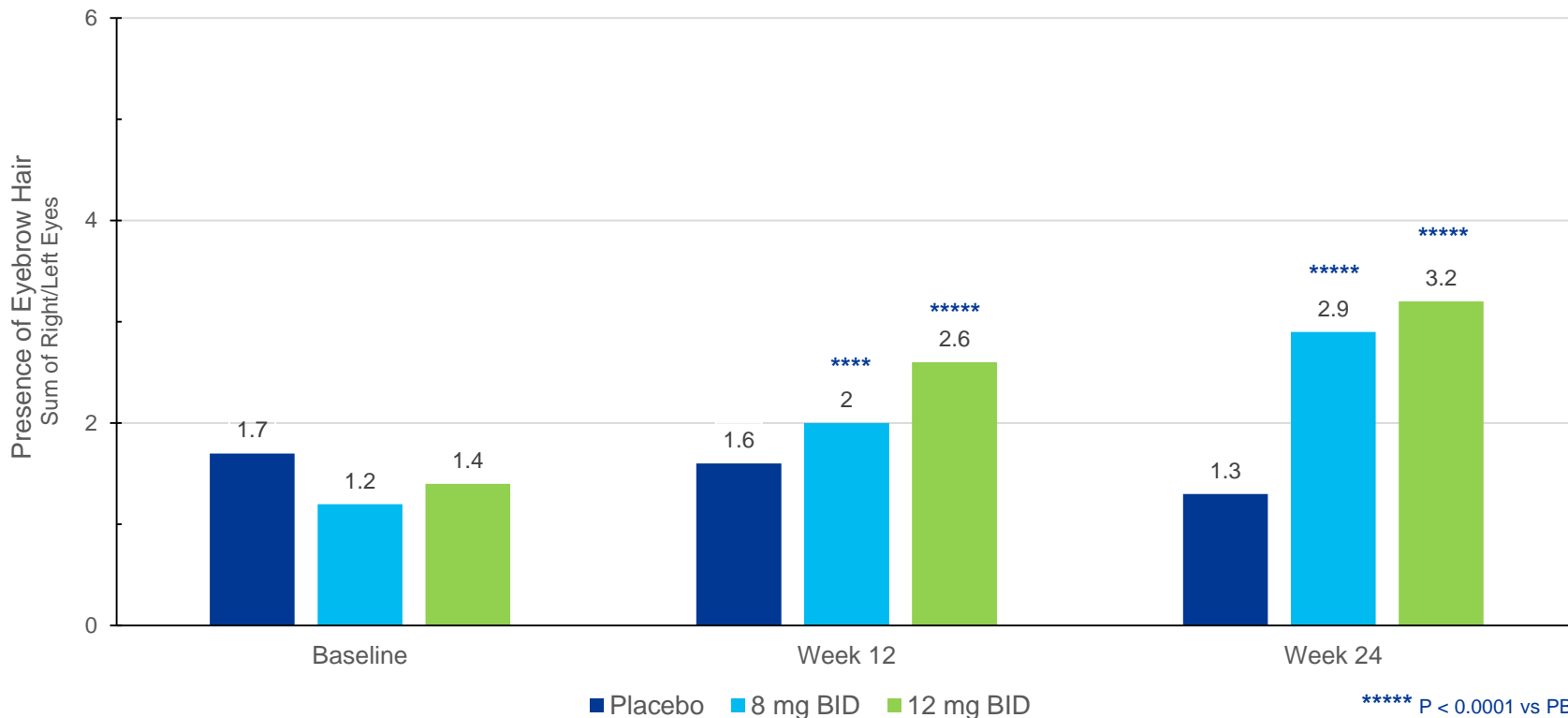
Significant Changes in SALT Score as Early as Four Weeks

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



Significant Improvement in Eyebrow Regrowth

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

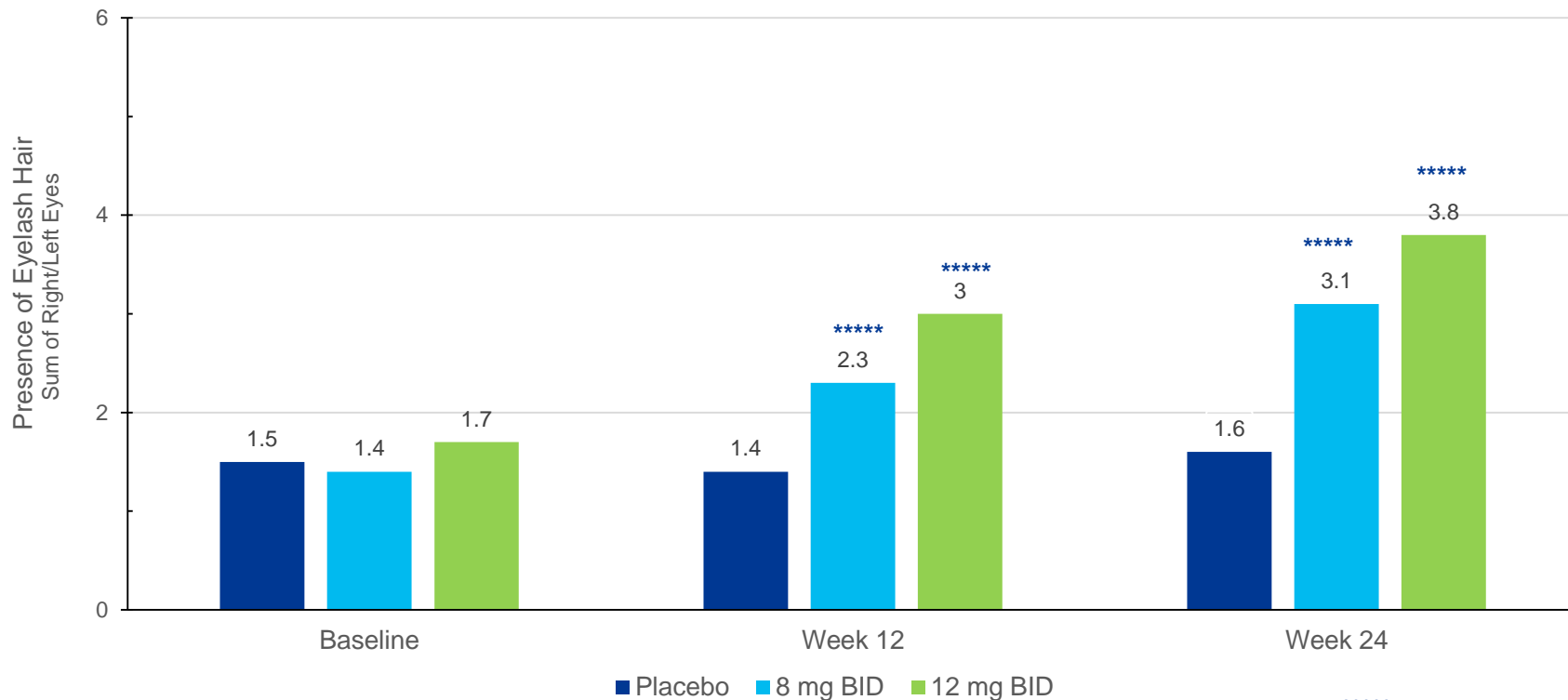


* Approximately 40-60% of each group had eyebrow involvement at Baseline

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

Significant Improvement in Eyelash Regrowth

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



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

**** P < 0.0001 vs PBO

Improvement in Eyebrows and Eyelashes

12 mg BID Deuruxolitinib



Baseline

8 mg BID Deuruxolitinib

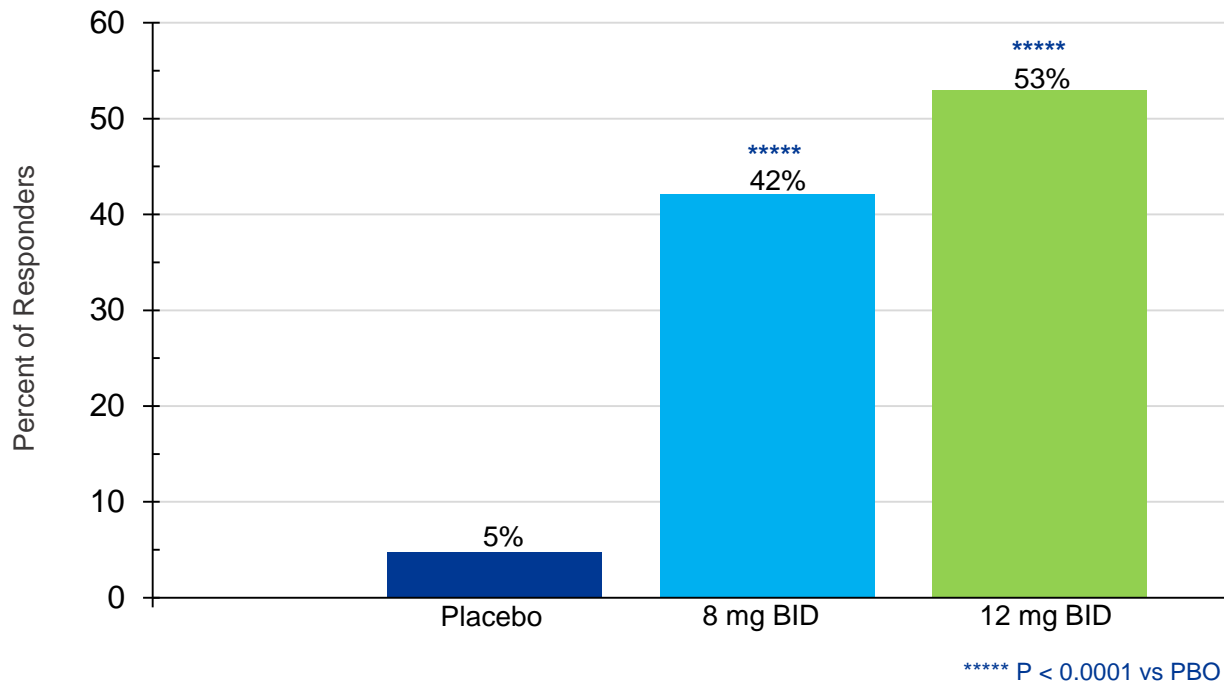


Week 24



High Degree of Patient Satisfaction with Scalp Hair

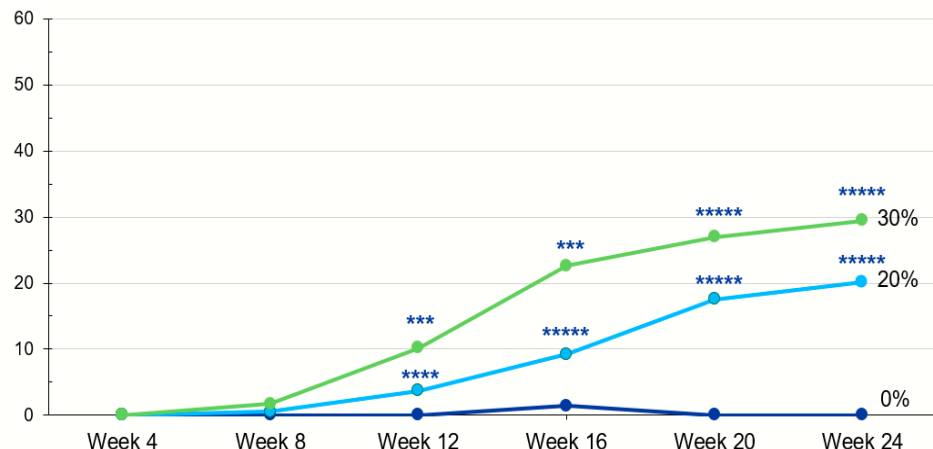
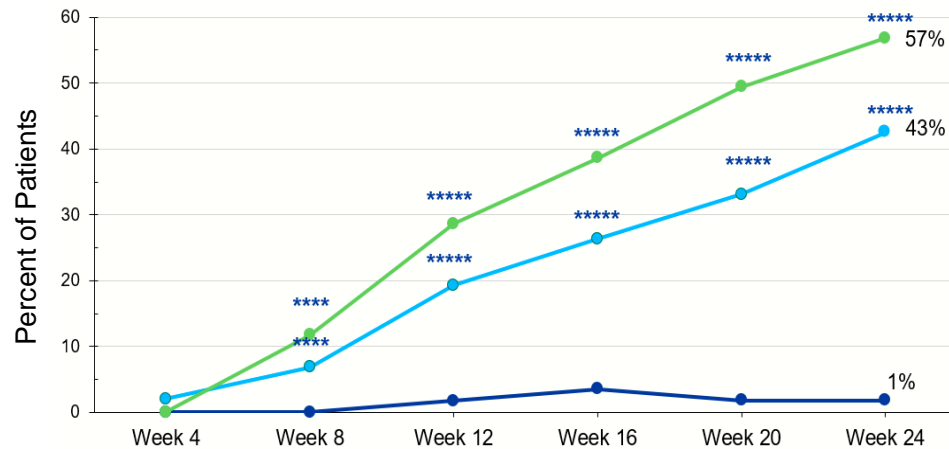
Key Secondary Endpoint: Patient response of **'very satisfied'** or **'satisfied'** on Satisfaction of Hair Patient Reported Outcome (SPRO) at Week 24



Proportion of Patients Achieving SALT Score ≤ 20 Analyzed By Extent of Baseline Scalp Hair Loss

Patients With **Partial Scalp Hair Loss** (**SALT Score <95**) at Baseline

Patients With **Complete/Near Complete Scalp Hair Loss** (**SALT Score ≥ 95**) at Baseline



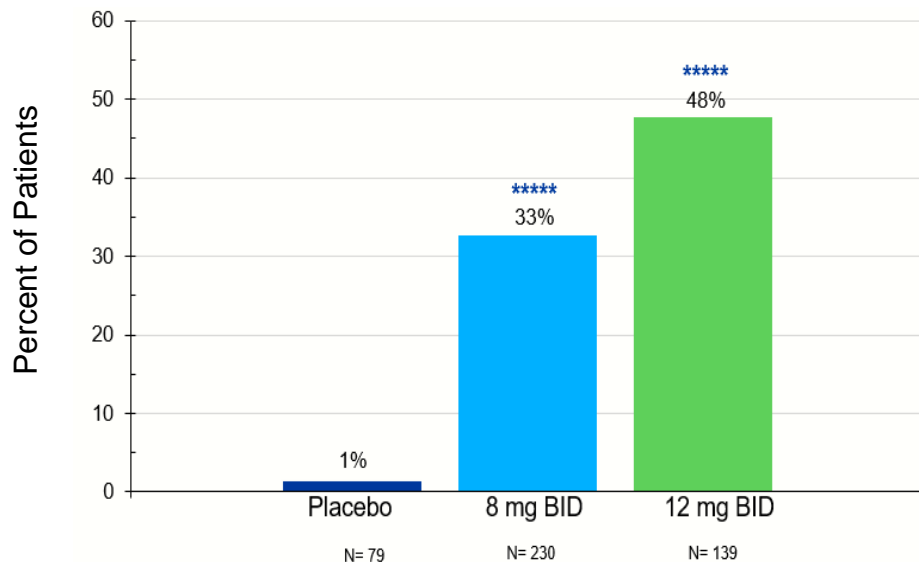
**** P < 0.0001 vs PBO

**** P < 0.001 vs PBO

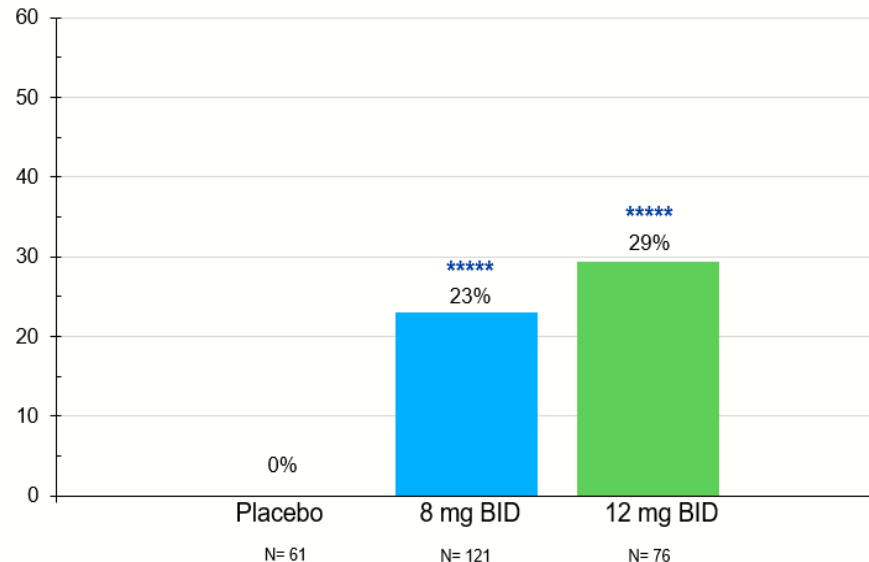
*** P < 0.005 vs PBO

Proportion of Patients Achieving SALT Score ≤ 20 by Week 24 Analyzed by Duration of Current Episode

Current Episode of Hair Loss ≤ 4 years



Current Episode of Hair Loss > 4 years



**** P < 0.0001 vs PBO

Patient Disposition

| | 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) |
| <i>Reason for Discontinuation, n</i> | | | | |
| <i>TEAE</i> | 2 | 8 | 4 | 14 |
| <i>Lack of Efficacy</i> | 2 | 1 | 0 | 3 |
| <i>Noncompliance</i> | 0 | 3 | 2 | 5 |
| <i>Pregnancy</i> | 0 | 0 | 1 | 1 |
| <i>Protocol Violation</i> | 2 | 0 | 1 | 3 |
| <i>Other</i> | 4 | 11 | 2 | 17 |
| <i>Lost to Follow-up</i> | 1 | 10 | 6 | 17 |

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

| | 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 <i>related</i> SAE, n % | 0 | 1 (0.3) | 0 | 1 (0.1) |
| # patients with <i>not related</i> 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

- 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
- Response to treatment is increased for current AA episode duration ≤ 4 years (vs. > 4 years) and for baseline SALT Score 50-94 (vs. 95-100)
- 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