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CTP-543, an Oral JAK Inhibitor, Achieves Primary Endpoint in Phase 2 Randomized, Placebo-Controlled Dose-Ranging Trial in Patients with Moderate-to-Severe Alopecia Areata

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Disclosures of Relationship with Industry

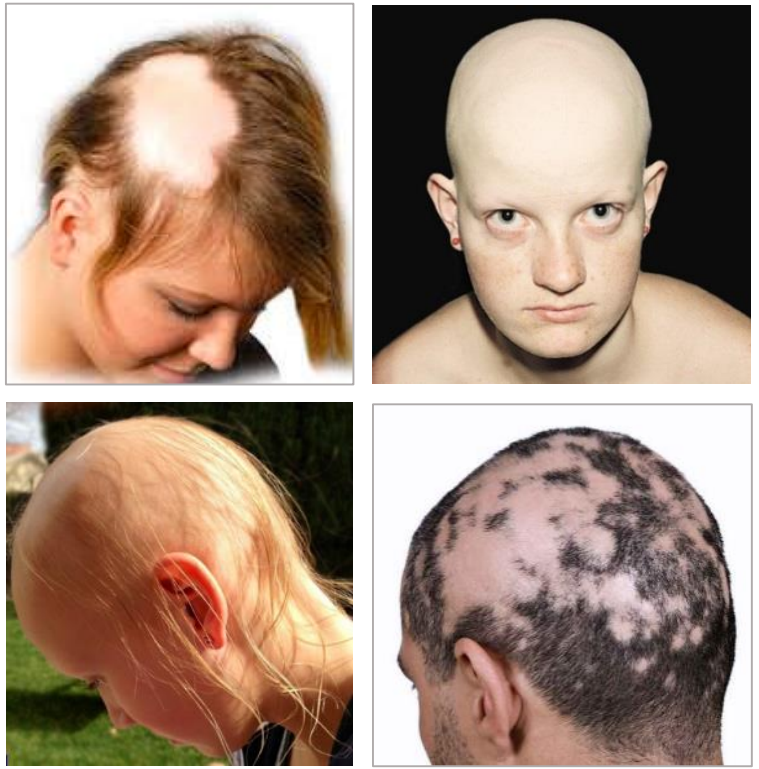
James V. Cassella, PhD

DISCLOSURES

- Concert Pharmaceuticals: Employee; Salary and Stock Received

Alopecia Areata: A Serious Medical Disease

- A devastating and poorly treated autoimmune disease
- Alopecia Areata occurs worldwide
  - Incidence of 0.1–0.2% of the population with a lifetime risk of 1.7% - 2%*
- Chronic condition affecting women, men and children of all ages
- Disease profoundly impacts patients; associated with anxiety, depression and other autoimmune conditions
- In the US, no FDA-approved treatment options

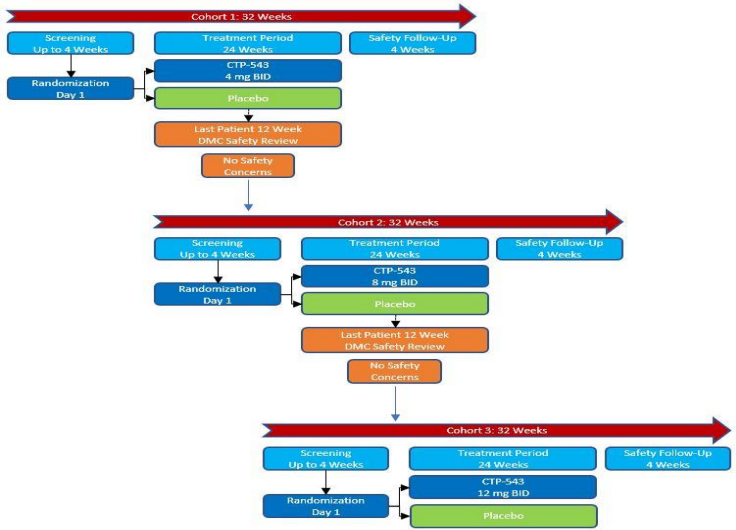


*Safavi et al., 1995; Fricke M., 2015

CTP-543: Phase 2 Dose-Ranging Trial

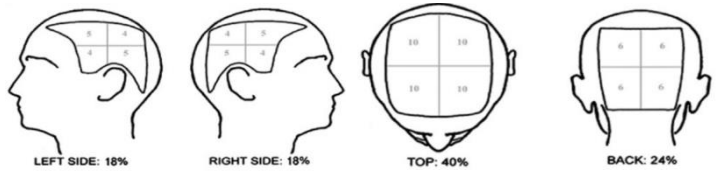
- Double-blind, randomized, placebo-controlled trial in adult patients with moderate-to-severe alopecia areata
- Entry criteria of at least 50% hair loss as measured by Severity of Alopecia Tool (SALT)
- Patients sequentially randomized to receive either 4, 8, or 12 mg BID CTP-543 or placebo BID for 24 weeks
- Primary endpoint: Percent of patients achieving a 50% relative reduction in SALT at Week 24 from baseline
- Additional clinical endpoints include:
  - Percent of patients achieving 75% and 90% relative change in SALT at Week 24 from baseline
  - Patient Global Impression of Improvement

Trial Design



Cohort 3: Eligible to enroll in open label extension study

SALT Scoring



Study Demographics

	Placebo	CTP-543 4 mg	CTP-543 8 mg	CTP-543 12 mg
Randomized Population	44	30	38	37
Efficacy Population	43	28	38	36
Age: Mean (SD)	38 (14%)	36 (11%)	37 (14%)	36 (12%)
Males, n (%)	15 (34%)	8 (27%)	12 (32%)	9 (24%)
Females, n (%)	29 (66%)	22 (73%)	26 (68%)	28 (76%)
Race: n (%)				
White	33 (75%)	25 (83%)	26 (68%)	30 (81%)
Black or African American	7 (16%)	2 (7%)	7 (18%)	3 (8%)
Asian	2 (4.5%)	2 (7%)	2 (5%)	4 (11%)
Other	2 (4.5%)	1 (3%)	3 (8%)	0 (0%)

Baseline Characteristics: Alopecia Areata

	Placebo	CTP-543 4 mg	CTP-543 8 mg	CTP-543 12 mg
Episode Duration: Yr, Mean	4.1	6	3.8	3.5
SALT score, Mean (SD)	86.8 (18.4)	88.8 (16.2)	89.1 (16.4)	87.3 (18.7)
AA Patchy, n (%)	21 (47.7%)	16 (53.3%)	16 (42.1%)	16 (43.2%)
AA Totalis, n (%)	6 (13.6%)	2 (6.7%)	6 (15.8%)	8 (21.6%)
AA Universalis, n (%)	17 (38.6%)	12 (40.0%)	14 (36.8%)	10 (27.0%)
AA Ophiasis, n (%)	0 (0%)	0 (0%)	2 (5.3%)	3 (8.1%)

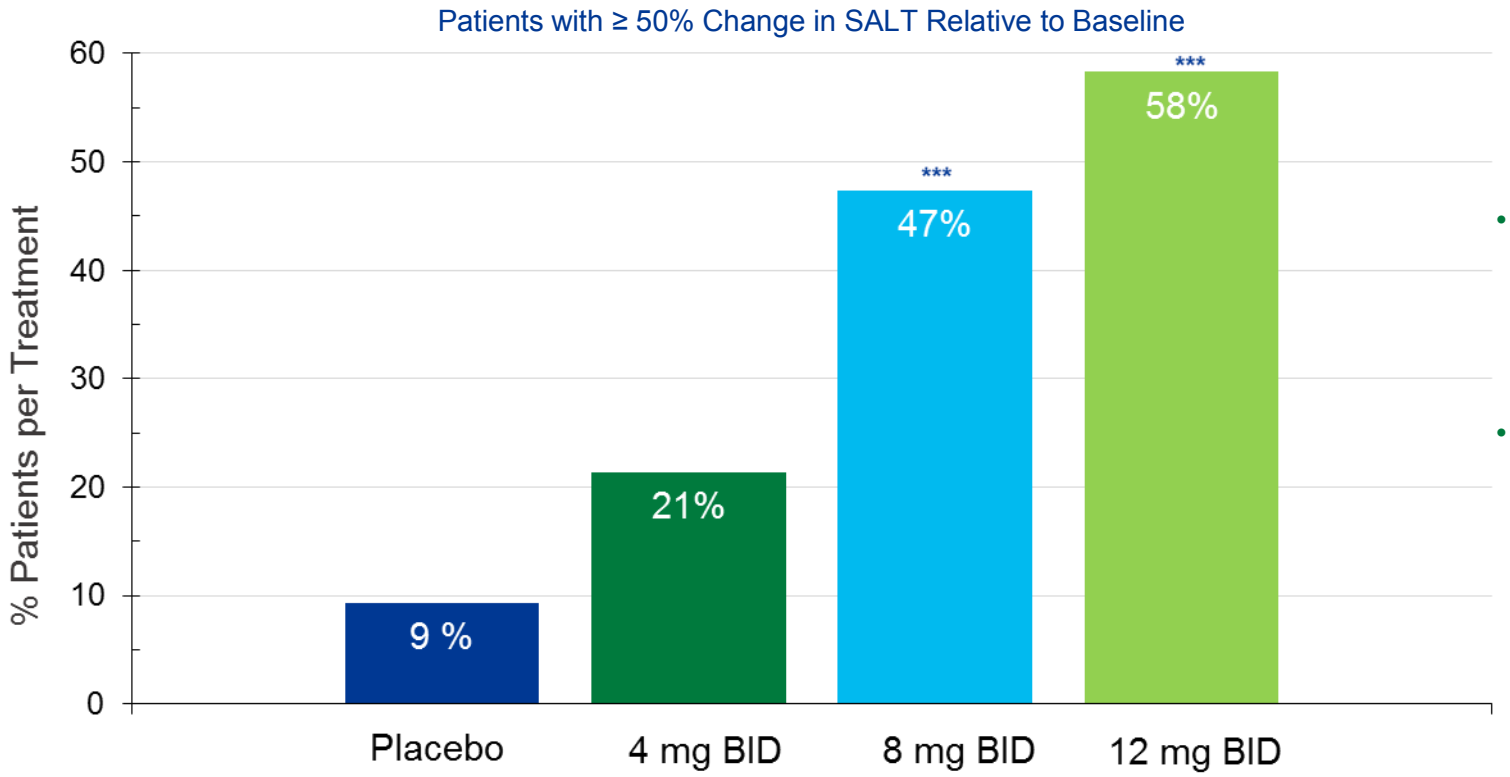
Adverse Events and Hematology

	Placebo (n = 44)	CTP-543 4 mg (n = 29)	CTP-543 8 mg (n = 38)	CTP-543 12 mg (n = 36)
Total # TEAEs	100	95	137	115
# Patients with TEAEs, n (%)	31 (70.5%)	25 (86.2%)	31 (81.6%)	30 (83.3%)
# Patients with Moderate or Severe TEAEs, n (%)	14 (31.8%)	9 (31.0%)	15 (39.5%)	7 (19.4%)
# Patients Discontinued, (n) %	9 (20.5%)	7 (23.3%)	8 (21.1%)	1 (2.7%)
Discontinued Due to AE, (n) %	3/9 (33.3%)	0/7 (0%)	2/8 (25%)	0/1 (0%)
Grade 3 or 4 Hematology: Neutropenia, (n) %	1 (2.3%) *(Pt discontinued)*	1 (3.6%)	1 (2.6%) *(Pt dose interrupted)*	0 (0%)
SAE, n (%)	0	0	0	1 (2.8%) *Cellulitis; Brief dose interruption; Pt completed trial*

Common (≥ 10%) Treatment Emergent Adverse Events (# Patients)

Preferred Term	Placebo	CTP-543 4 mg	CTP-543 8 mg	CTP-543 12 mg
Headache	4 (9.1%)	5 (17.2%)	10 (26.3%)	7 (19.4%)
Nasopharyngitis	1 (2.3%)	3 (10.3%)	3 (7.9%)	9 (25.0%)
URI	7 (15.9%)	2 (6.9%)	2 (5.3%)	7 (19.4%)
Acne	2 (4.5%)	4 (13.8%)	4 (10.5%)	6 (16.7%)
Nausea	4 (9.1%)	4 (13.8%)	4 (10.5%)	1 (2.8%)
Cough	0	4 (13.8%)	1 (2.6%)	2 (5.6%)
LDL increase	0	0	4 (10.5%)	0
Diarrhea	3 (6.8%)	3 (10.3%)	1 (2.6%)	0
Folliculitis	0	3 (10.3%)	2 (5.3%)	1 (2.8%)
Blood CPK (increase)	1 (2.3%)	3 (10.3%)	2 (5.3%)	1 (2.8%)
Oropharyngeal pain	1 (2.3%)	3 (10.3%)	1 (2.6%)	0

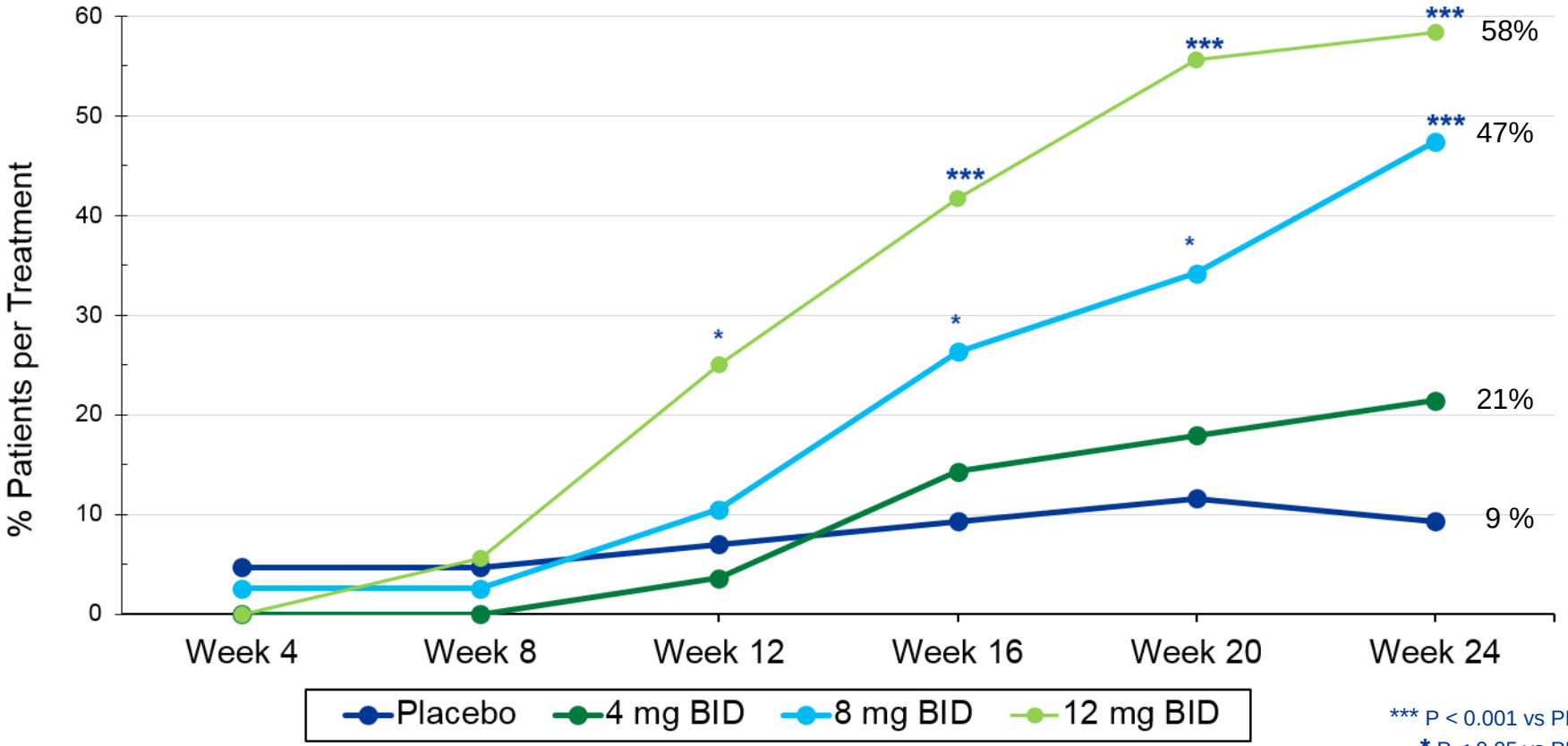
Primary Analysis: Responders at Week 24



- 12 mg BID responders average 86% SALT improvement
- 8 mg BID responders average 78% SALT improvement

*** P < 0.001 vs PBO

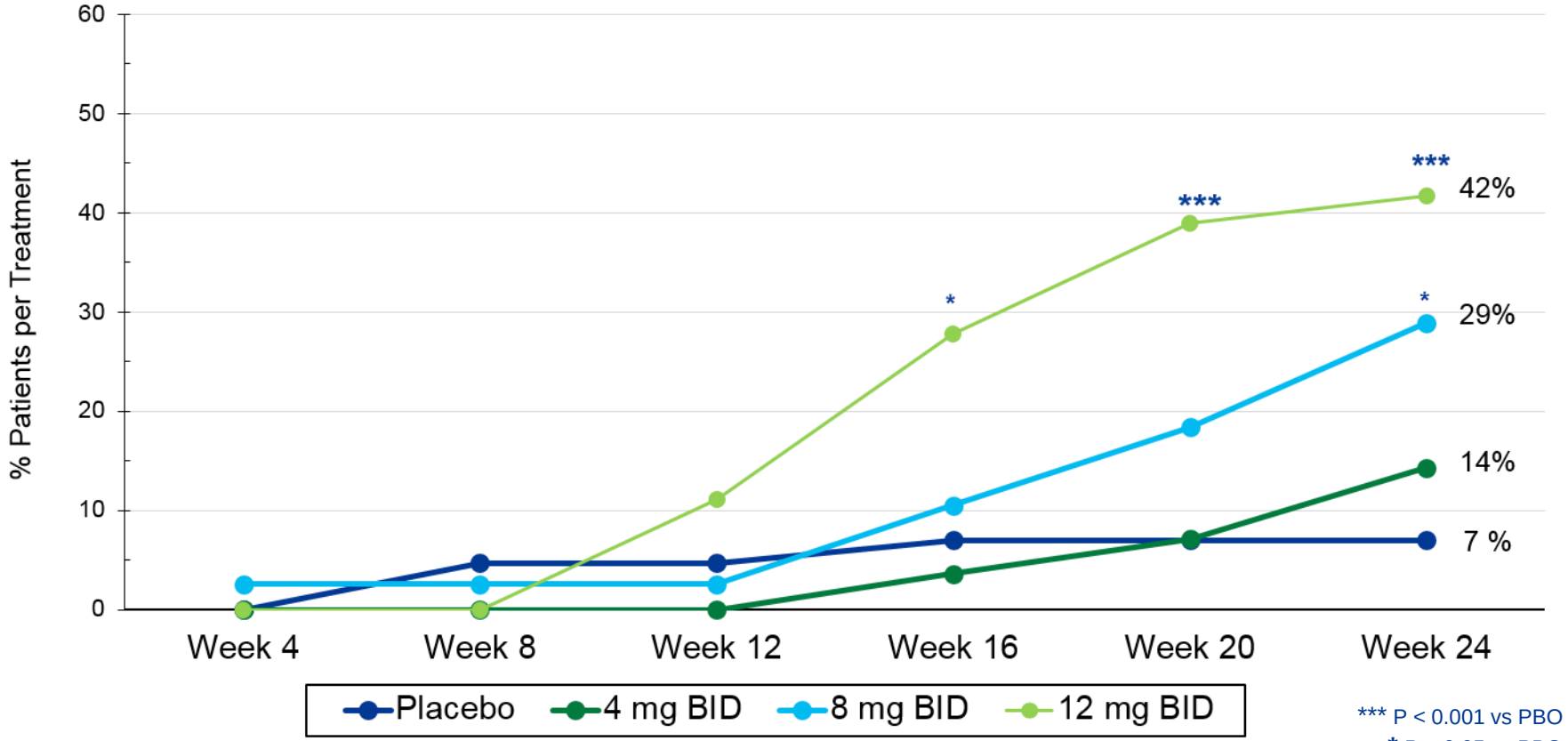
Responders: ≥ 50% Change in SALT Relative to Baseline



*** P < 0.001 vs PBO

* P < 0.05 vs PBO

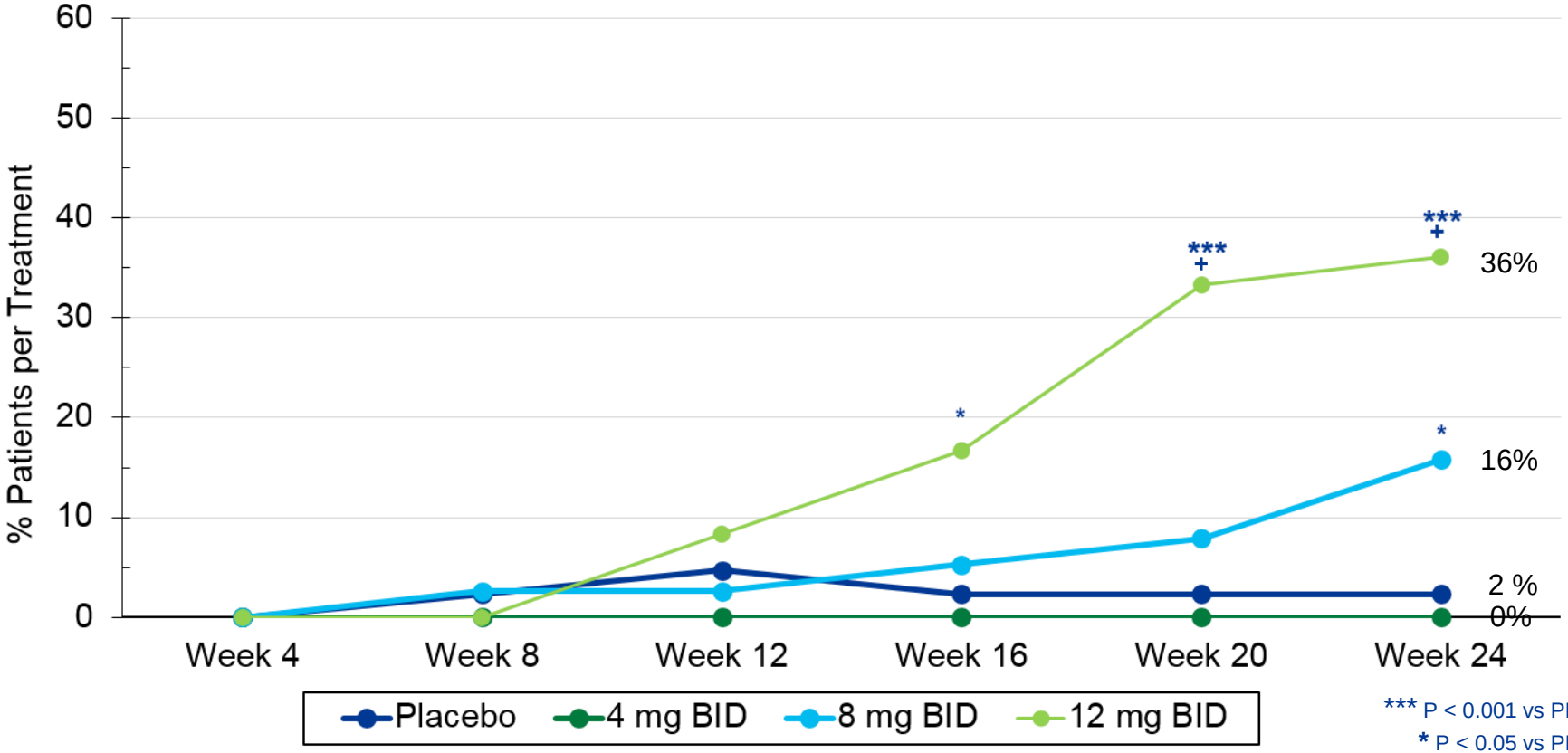
Responders: ≥ 75% Change in SALT Relative to Baseline



*** P < 0.001 vs PBO

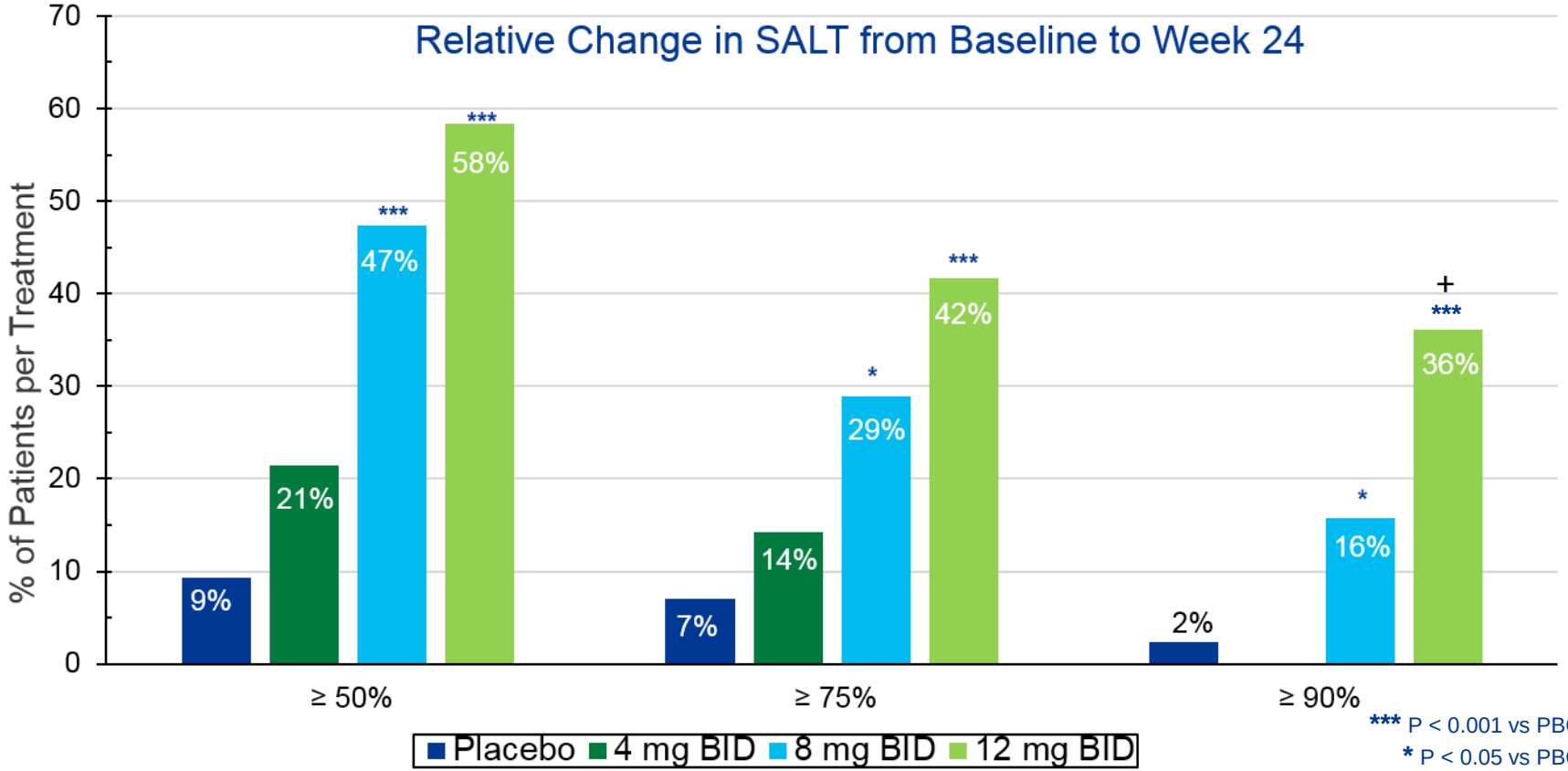
* P < 0.05 vs PBO

Responders: ≥ 90% Change in SALT Relative to Baseline

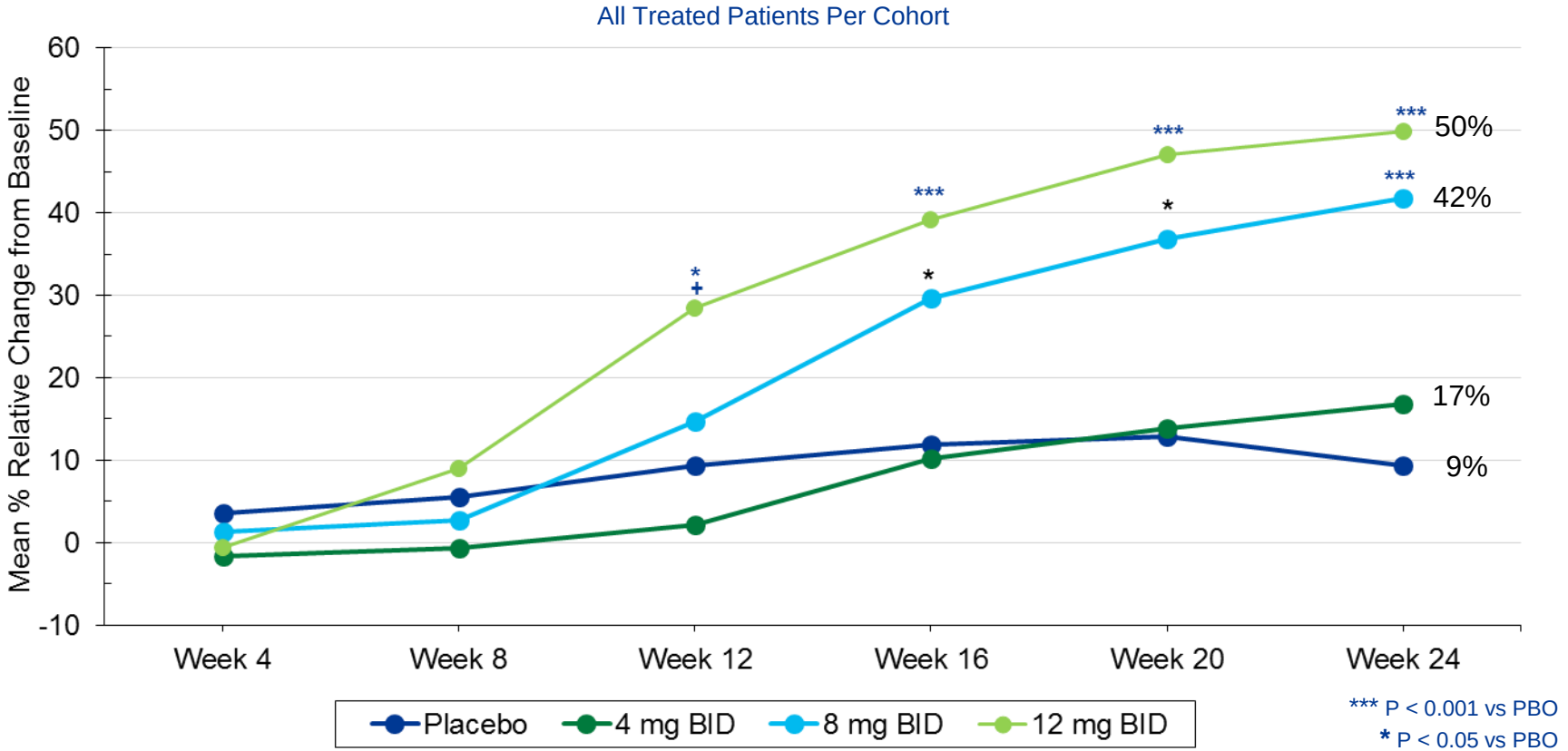


*** P < 0.001 vs PBO
* P < 0.05 vs PBO
+ P < 0.05 vs 8 mg

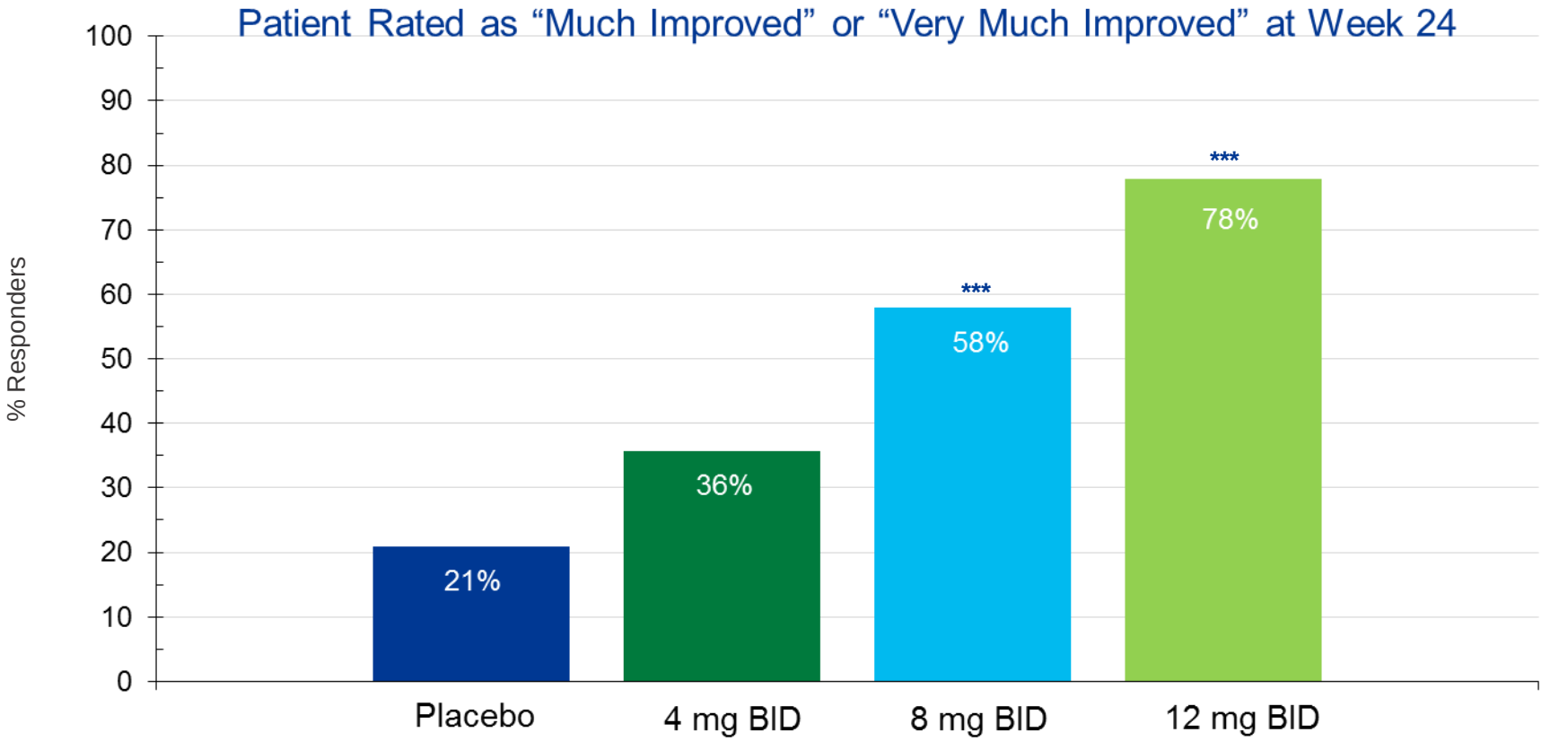
Patient SALT Improvement Thresholds



Relative Change in SALT



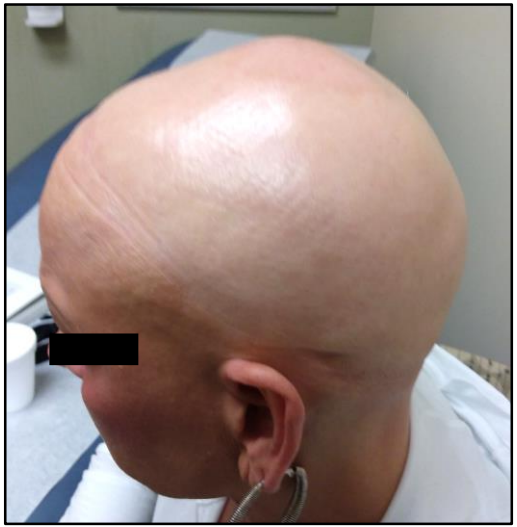
Patient Global Impression of Improvement: Responders



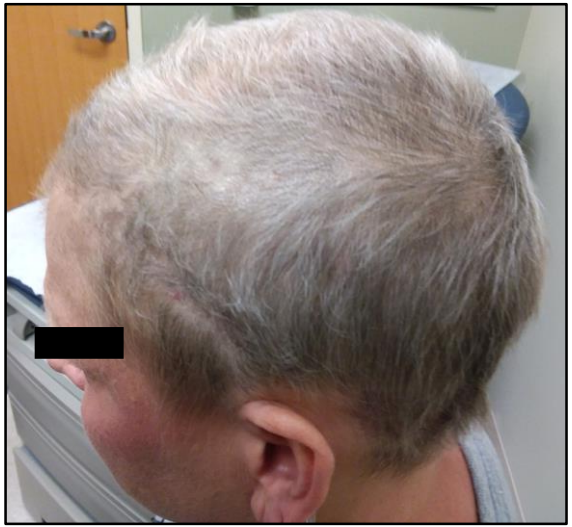
*** P < 0.001 vs PBO

CTP-543 Response: 12 mg BID

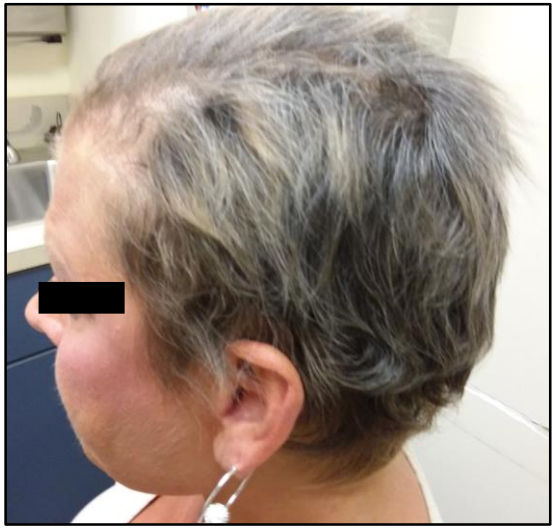
Baseline



Week 12

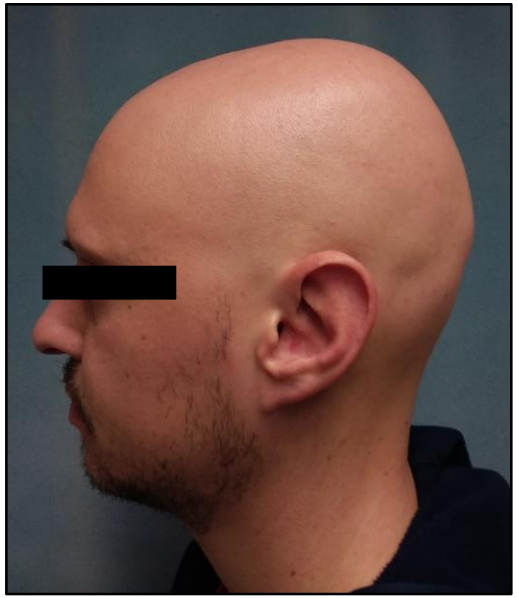


Week 24

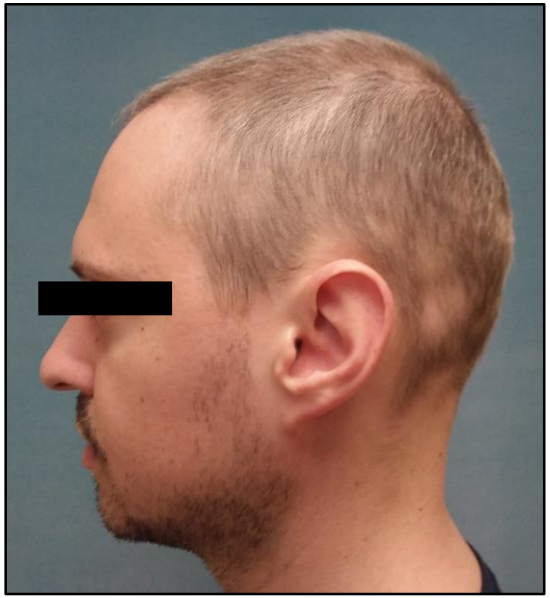


CTP-543 Response: 12 mg BID

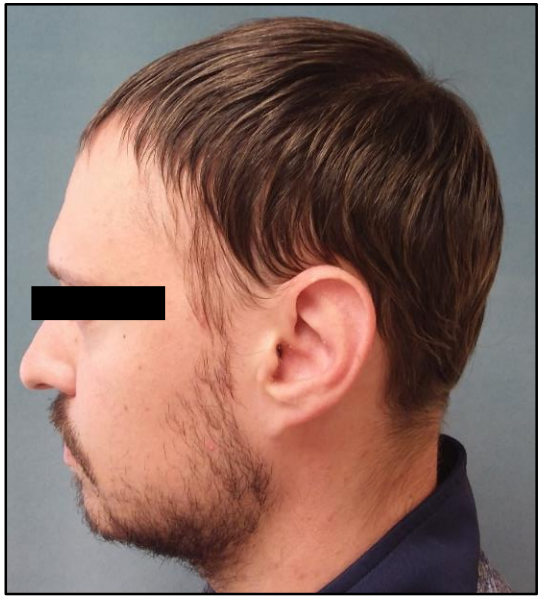
Baseline



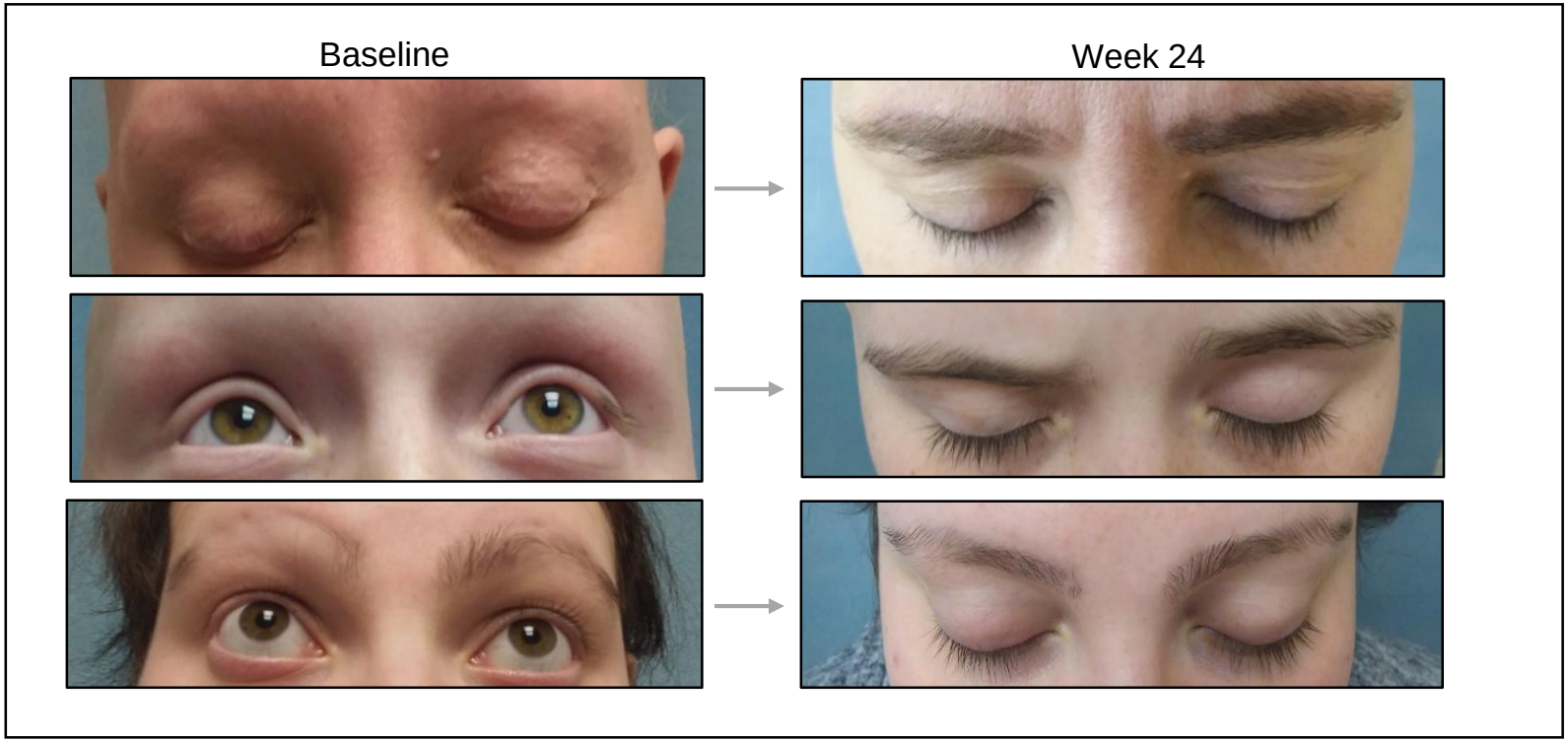
Week 12



Week 24



CTP-543 Eyebrow/Eyelash Response: 12 mg BID



Conclusion

- The primary efficacy endpoint was met for 8 mg BID and 12 mg BID
- Dose-related improvements for 8 mg BID and 12 mg BID across all efficacy assessments
  - 8 mg BID and 12 mg BID significantly different from placebo on all SALT measures and Patient Global Impression of Improvement (PGI-I)
    - PGI-I: 78% of patients in the 12 mg BID cohort reported “Much Improved” or “Very Much Improved” at Week 24
  - 12 mg BID numerically superior and generally produced faster onset and greater magnitude of effect compared to 8 mg BID
- CTP-543 treatment generally well-tolerated
  - Majority of patients from 12 mg BID cohort rolled into long-term open label extension study
- Results support advancement of CTP-543 into Phase 3 Trials

Thank You

- To the Alopecia Areata Patients who volunteer to participate in clinical studies
- To the CTP-543 Investigators and clinical study teams:
  - **Wilma Bergfeld**
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