

# A multicenter, open-label, Phase 1 study of the safety, tolerability, systemic exposure, pharmacodynamics, and treatment effect of calcipotriene foam, 0.005% in pediatric subjects (ages 2 to 11 years) with plaque psoriasis.

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## SYNOPSIS

According to the National Psoriasis Foundation approximately 150,000 new psoriasis patients are diagnosed in the United States each year.<sup>1</sup> Almost 20,000 (13%) of newly diagnosed patients are children under the age of 10 with most manifesting with plaque psoriasis (68.6%) with lesions localized to the scalp, post auricular region, elbows, and knees.<sup>2</sup> Although the relative frequency of plaque psoriasis differs between adults and children, the etiology is thought to be the same as evidenced by similar response rates to therapies.<sup>3,4</sup> There are few therapeutic options for the pediatric population that have proven safety and efficacy and that have FDA approval in the pediatric population. Calcipotriene is a synthetic vitamin D3 derivative that has been used effectively for many years for the treatment of plaque-type psoriasis.<sup>5</sup> The efficacy and safety of calcipotriene foam, 0.005%, was established in Phase III clinical trials for the treatment of adults and recently the FDA adjusted the indication to include treatment in patients 12 years and older due to proven safety in a Phase I study in adolescents.<sup>6,7</sup> The data presented here highlight the results of an additional Phase I clinical study in pediatric subjects aged 2 to 11 years.

## OBJECTIVES

### Primary Objective:

- To evaluate the safety and tolerability of calcipotriene foam, 0.005%, in pediatric subjects, ages 2 to 11 years, with mild to moderate plaque psoriasis.

### Secondary Objectives:

- To evaluate the pharmacodynamic effect on calcium metabolism of calcipotriene foam 0.005%, in pediatric subjects, ages 2 to 11 years, with mild to moderate plaque psoriasis.
- To describe the plasma concentrations of calcipotriene following administration of calcipotriene foam, 0.005% in pediatric subjects, ages 2 to 11 years, with moderate plaque psoriasis.
- To describe the treatment effect of calcipotriene foam, 0.005%, in pediatric subjects, ages 2 to 11 years, with mild to moderate plaque psoriasis.

## METHODS

- Phase 1 multicenter, open-label, repeat-dose study with 36 subjects ages 2 to 11 years from 16 sites.
- Two cohorts:
  - Maximum use cohort defined as ISGA score of 3 or higher at screening and at least 3% Body Surface Index (BSA) with some scalp involvement.
  - General use cohort defined as ISGA score of 2 or 3 at screening with no BSA minimum
- Subjects or their caregivers applied a thin layer of study product twice a day to the treatment areas (excluding the face) for 8 weeks:
  - In the event that the lesions cleared prior to the end of the study, subjects or their primary caregivers were to continue to apply study product to treatment areas originally affected by psoriasis.
  - Any new psoriatic lesions which appeared in treatment areas during the treatment period were also treated with the study product.
- Safety assessments (adverse event and serious adverse event query) occurred at all study visits.
- Treatment effect, urine calcium metabolism, and application site tolerability assessments were performed for all subjects at all in-clinic visits.
- Blood samples were taken from all subjects at Screening for evaluation of pharmacodynamic (PD) assessments and 25-OH vitamin D levels at baseline, and an additional blood draw for PD parameters was taken at Week 2 for the maximum-use cohort only.
- The % of subjects who were ISGA responders was compared to the Phase III adult clinical trial results using Bayesian analysis.

DEMOGRAPHICS	Calcipotriene Foam, 0.005% n=32	Vehicle Foam n=4	DEMOGRAPHICS	Calcipotriene Foam, 0.005% n=32	Vehicle Foam n=4
<b>Age (yrs)</b>			<b>Baseline BSA: (%)</b>		
Mean (SD)	8.6 (2.06)	8.5 (2.65)	Mean (SD)	12.2 (9.94)	16.5 (8.26)
Median	9	9	Median	7.8	19.1
Min, Max	4,11	5,11	Min,Max	0.5,36.5	5,23
<b>Race: n (%)</b>			<b>Baseline ISGA Body</b>		
Caucasian	25 (78)	3 (75)	Mean SD	2.5 (0.92)	3 (0)
African American	4 (13)	0	Median	3	3
Asian	0	1 (25)	Min,Max	0,4	3,3
Native American/Alaskan	1 (3)	0	<b>Baseline ISGA Scalp</b>		
Other	2 (6)	0	Mean SD	1.9 (1.34)	2.8 (0.50)
			Median	2	3
			Min,Max	0,4	2,3
<b>Gender: n (%)</b>			<b>Height (cm)</b>		
Male	15 (47)	2 (50)	Mean SD	136.2 (13.91)	129.2 (11.59)
Female	17 (53.)	2 (50)	Median	137.2	124.2
			Min,Max	104,159	122,147
<b>Ethnicity: n (%)</b>			<b>Weight (kg)</b>		
Hispanic/Latino	13 (42)	1 (25)	Mean SD	42.1 (15.56)	36.2 (12.23)
Not Hispanic/Latino	18 (58)	3 (75)	Median	41.6	35.3
			Min,Max	17.8,77.1	22.7,51.3

## RESULTS

- PD markers showed a general lack of change over time and there were no quantifiable systemic concentrations of calcipotriene observed. The average values of corrected calcium, magnesium and phosphorus were consistent over time. The iPTH and alkaline phosphatase showed some variability across time, but no consistent trends and similar values at screening and day 15. The variability in these values could likely be attributed to small sample size, especially in the subgroups. There was no relationship seen between urinary calcium/creatinine ratio and %BSA treated or age.
- No serious adverse events were reported. Of the 29 adverse events that were reported; 7 were considered related to the treatment. These adverse events presented themselves as mostly topical in nature. Local tolerability results remained 0 from baseline to study end in 22 subjects (61.11%).
- No evidence of a drug effect was noted for body weight, height, or vital signs.
- ISGA scores improved with treatment, but differences between treatments could not be assessed because of the small number of subjects receiving vehicle and the study was not designed to show efficacy. However, response rates (% of subjects with an ISGA score of 0 or 1 for body or scalp at week 8) were consistent with that observed in the double-blind, vehicle controlled Phase III studies in adults.

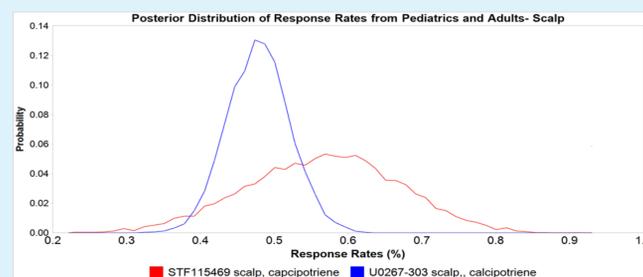
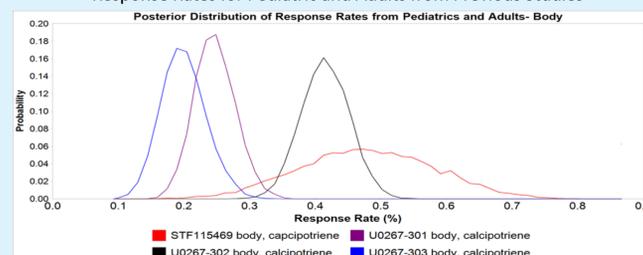
PD Marker at Screening, Day 1, Day 13-16 and Day 56-59

PD Marker	Visit	Calcipotriene (CAL)			Vehicle		
		n	Mean (SD)	Min - Max	n	Mean (SD)	Min - Max
Corrected Calcium (mmol/l)	Screening	21	9.3 (0.22)	8.8 - 9.7	2	9.4 (0.14)	9.3 - 9.5
	Day 1	3	9.1 (0.17)	9.0 - 9.3	2	9.1 (0.07)	9.0 - 9.1
	Day 13 - 16	7	9.2 (0.24)	8.9 - 9.6	2	9.4 (0.35)	9.1 - 9.6
	Day 56 - 59	3	9.3 (0.35)	9.0 - 9.7	2	9.4 (0.14)	9.3 - 9.5
iPTH (pmol/l)	Screening	19	29.0 (10.54)	12.0 - 46.0	2	54.0 (53.74)	16.0 - 92.0
	Day 1	3	45.0 (23.00)	22.0 - 68.0	2	49.0 (26.87)	30.0 - 68.0
	Day 13 - 16	7	32.1 (23.58)	16.0 - 84.0	2	25.0 (9.90)	18.0 - 32.0
	Day 56 - 59	3	49.7 (49.10)	16.0 - 106.0	2	26.5 (0.71)	26.0 - 27.0
Alkaline Phosphatase (u/l)	Screening	21	274.4 (69.43)	160.0 - 415.0	2	267.0 (69.30)	218.0 - 316.0
	Day 1	3	357.7 (121.18)	221.0 - 452.0	2	272.0 (77.78)	217.0 - 327.0
	Day 13 - 16	6	292.3 (99.83)	184.0 - 446.0	2	296.0 (106.07)	221.0 - 371.0
	Day 56 - 59	3	316.7 (110.59)	190.0 - 394.0	2	279.0 (28.28)	259.0 - 299.0
Magnesium (mmol/l)	Screening	21	1.8 (0.10)	1.6 - 1.9	2	1.6 (0.00)	1.6 - 1.6
	Day 1	3	1.7 (0.21)	1.5 - 1.9	2	1.7 (0.21)	1.5 - 1.8
	Day 13 - 16	6	1.7 (0.15)	1.5 - 1.9	2	1.7 (0.14)	1.6 - 1.8
	Day 56 - 59	3	1.8 (0.15)	1.6 - 1.9	2	1.6 (0.00)	1.6 - 1.6
Phosphorus (mmol/l)	Screening	21	5.0 (0.47)	3.5 - 5.8	2	4.6 (0.42)	4.3 - 4.9
	Day 1	3	5.1 (0.06)	5.0 - 5.1	2	4.3 (0.42)	4.0 - 4.6
	Day 13 - 16	6	4.8 (0.56)	4.1 - 5.6	2	4.4 (0.49)	4.0 - 4.7
	Day 56 - 59	3	5.3 (0.46)	5.0 - 5.8	2	4.8 (0.21)	4.6 - 4.9
Calcium/Creatinine (mg/g creat)	Screening	18	77.0 (43.57)	11.0 - 172.0	2	101.5 (64.35)	56.0 - 147.0
	Day 1	21	66.9 (76.84)	7.0 - 286.0	2	101.5 (64.35)	56.0 - 147.0
	Day 13 - 16	18	72.5 (56.57)	7.0 - 220.0	2	67.0 (29.70)	46.0 - 88.0
	Day 56 - 59	19	90.2 (80.83)	5.0 - 285.0	2	61.0 (36.77)	35.0 - 87.0

Relative Change from Day 1 to Day 15 and Day 22 for PD Markers

PD Marker	Treatment	n	Geometric Mean	95% CI	90% CI
Corrected Calcium (mmol/l)	CAL	7	0.997	0.976 - 1.018	0.971 - 1.024
	Vehicle	2	0.994	0.898 - 1.101	0.810 - 1.220
iPTH (pmol/l)	CAL	7	1.069	0.697 - 1.639	0.624 - 1.831
	Vehicle	2	0.626	0.015 - 25.445	0.000 - 1083.9
Alkaline Phosphatase (u/l)	CAL	6	0.955	0.872 - 1.045	0.851 - 1.071
	Vehicle	2	1.091	0.686 - 1.734	0.429 - 2.772
Magnesium (mmol/l)	CAL	6	0.971	0.923 - 1.021	0.910 - 1.035
	Vehicle	2	1.061	0.731 - 1.538	0.502 - 2.242
Phosphorus (mmol/l)	CAL	6	0.991	0.907 - 1.082	0.885 - 1.109
	Vehicle	2	0.945	0.857 - 1.041	0.777 - 1.148

Response Rates for Pediatric and Adults from Previous Studies



Summary of Treatment emergent Adverse Events\*

TEAE Type	n (%)	# of Events
<b>OVERALL</b>	<b>6 (16%)</b>	<b>7</b>
Application site pain	2 (6.3%)	2
Contact Dermatitis	2 (6.3%)	2
Psoriasis	3 (9.4%)	3

\*No AEs reported in Vehicle control group

% Subjects with ISGA Score 0 or 1 at Week 8

	Body n (%)	Scalp n (%)
Calcipotriene Foam, 0.005%	14 (45.16)	19 (61.29)
Vehicle Foam	1 (33.3)	1 (33.3)

## CONCLUSIONS

Calcipotriene foam, 0.005%, was well tolerated with a low incidence of adverse events in the pediatric population. There were no quantifiable systemic concentrations of calcipotriene nor effect seen on calcium metabolism with repeated application. While this study was not designed as an efficacy study, the % of subjects who were ISGA responders was found to be consistent with the efficacy in the treatment of body and scalp in adults. Overall, the results in this pediatric population are consistent with previously reported clinical findings for adolescents and adults indicating that calcipotriene foam, 0.005% is safe, well tolerated, and effective treatment option for pediatric psoriasis patients.

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## AFFILIATIONS AND DISCLAIMERS

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