Cassiopea Announces Very Positive Phase II Twelve Months Results for Breezula® (Clascoterone) in Treating Androgenetic Alopecia

Lainate, Italy – April 16, 2019 - Cassiopea SpA (SIX: SKIN), a clinical-stage pharmaceutical company developing and commercializing innovative medical dermatology products, today announced very positive results of the twelve months phase II dose ranging clinical trial in men with androgenic alopecia (AGA) for its topical anti-androgen Clascoterone (Breezula®) solution. The results show statistically significant improvement versus vehicle (placebo) for Target Area Hair Count (TAHC) for every dose tested along with directional improvement for Hair Growth Assessment (HGA). The results also indicate an excellent safety profile, similar to vehicle, for both adverse events and local skin reactions, even after 12 months treatment.

This phase II dose ranging trial, recruiting more than 400 subjects in Germany, was aimed to evaluate the efficacy and safety of four different doses of Clascoterone compared to vehicle in male subjects 18-55 years of age with mild to moderate androgenetic alopecia in the temple and vertex region. All subjects applied Clascoterone or vehicle to the balding areas of the scalp twice daily for a total of 12 months. The eligible subjects were randomly assigned to one of the following five treatment groups: 2.5% solution BID; 5.0% solution BID; 7.5% solution BID; 7.5% solution QD (once a day) and vehicle solution; vehicle solution BID.

The co-primary efficacy endpoints evaluated in the trial were: (1) change in non-vellus TAHC (target area hair count) at month 12 and (2) HGA (hair growth assessment) score at month 12. The target area is defined as an area of one square centimeter.

The main secondary endpoints included (1) Changes from Baseline in non-vellus TAHC and HGA score at months 3, 6 and 9, and (2) Changes from Baseline in non-vellus TAHW (target area hair width) at Months 3, 6, 9, and 12.

Efficacy Results

TAHC

For the TAHC, statistically highly significant changes vs. vehicle were observed in all active groups with the highest change observed in the 7.5% BID group, which reached statistical significance at all timepoints, beginning with the third month (first follow-up visit), while the placebo group had a decrease in TAHC, representing the progression of AGA over time if left untreated. These results indicate that Clascoterone stops the loss of hair and grows new hair.

Per Protocol (344 subjects) **At 12 months**	Clascoterone 2.5% BID	Clascoterone 5% BID	Clascoterone 7.5% BID	Clascoterone 7.5% QD
Mean changes from vehicle TAHC (n.)	10.2	13.8	14.3	12.7
P value (vs. vehicle)	0.0087	0.0006	0.0003	0.0016

HGA

The HGA assessment represents the opinion of the patient on hair growth, expressed with a questionnaire. More subjects in all active groups saw an increase in their hair growth compared to the vehicle.

HGA **Per Protocol (344 subjects)**	Clascoterone 2.5% BID	Clascoterone 5% BID	Clascoterone 7.5% BID	Clascoterone 7.5% QD	Vehicle
At 12 months					
Favorable HGA (+1, +2, +3)	60.8%	60.0%	61.8%	56.1%	50.0%

TAHW

For the TAHW, statistically highly significant changes vs. vehicle were observed in all active groups with the highest change observed in the 7.5% BID group, which reached borderline statistical significance since the third month (first follow-up visit) and statistical significance at months 6, 9 and 12.

TAHW **Per Protocol (344 subjects)** **At 12 months**	Clascoterone 2.5% BID	Clascoterone 5% BID	Clascoterone 7.5% BID	Clascoterone 7.5% QD
Mean changes from vehicle TAHW (µm)	521.1	615.0	762.5	658.8
P value (vs. vehicle)	0.0105	0.0034	0.0003	0.0018

Meanwhile, the placebo group had a significant decrease in the TAHC and TAHW, representing the progression of AGA over time if left untreated. Also, these data confirm that Clascoterone stops the loss of hair and grows new hair.

Safety Results

The results indicate an excellent safety profile, similar to vehicle for both adverse events and local skin reactions, even after 12 months treatment. There were no treatment-related serious adverse events among patients treated with Clascoterone.

Since the chemical structure of Clascoterone is similar to that of a steroid while its function is not, cortisol levels were tested in a sub-group of patients to verify that Clascoterone is free from systemic steroid activity. The mean absolute changes of cortisol values throughout the study were similar among groups, proving that Clascoterone has no systemic effect on cortisol.

Comments
After reviewing the data, Maria Hordinsky, MD, Professor and Head of the Department of Dermatology at the University of Minnesota Medical School, and acting President of the American (North, South and Central America) Hair Research Society, commented: “After reviewing the data, it is clear there is now the potential to have a new, safe and effective topical anti-androgen in our armamentarium to treat as well as stabilize androgenetic alopecia. The data nicely show that patients with Hamilton types 3, 4 and 5 demonstrate an increase in hair counts compared to placebo treated subjects. This positive effect can also be demonstrated with evaluation of clinical photography and an increase in hair growth noted by study subjects and investigators. I look forward to seeing this topical medication being successfully used to treat our patients.”

Diana Harbort, CEO of Cassiopea, said: “We are very pleased by these excellent results which show that our topical anti-androgen is efficacious in the treatment of AGA with side effects similar to placebo and importantly without any systemic side effects. Based on these results, we plan to meet with the FDA mid-year to discuss the planned six-month Phase III trials in men. Hopefully, we will begin our Phase III program in 4Q 2019. We also plan to begin – as soon as practicable – a POC study in women, which would enlarge significantly the potential of the product. The global hair loss market is very large and very underserved with only OTC products and generic therapies available, therefore this product, if approved, could serve a global audience.”

If approved, Clascoterone would be the first FDA-approved topical anti-androgen for the treatment of androgenetic alopecia and the first novel new drug approved for AGA since 1997.

Cassiopea plans to present this data at future medical meetings and also for consideration for publication in a peer-reviewed journal.

Next Steps
Based on these results, Cassiopea will proceed with a proof of concept clinical trial in women and an end of phase II meeting with the FDA in advance of the Phase III trials in men.

About Clascoterone (Breezula®)
Clascoterone, a new chemical entity, is a topically applied anti-androgen in late stage development for the treatment of acne (in a 1 % cream) and androgenetic alopecia (in a higher strength solution). When applied directly to the skin surface, Clascoterone penetrates the skin to reach the androgen receptors within the sebaceous glands and hair follicles. Clascoterone is on track to becoming the first effective and safe topical anti-androgen without systemic side effects.

In androgenetic alopecia (AGA), high local concentrations of dihydrotestosterone (DHT) bind to androgen receptors within the scalp hair follicles, resulting in shortening of the hair cycle and gradual miniaturization scalp follicles. Over time, these progressively smaller, thinner hair follicles are unable to produce new hair, thus resulting in AGA’s characteristic patterned baldness. DHT dependent effects are considered, in most cases, reversible, such that AGA could be responsive to medical treatment with drugs such as Clascoterone. By blocking DHT interaction with the specific hair follicle
androgen receptors, Clascoterone, if successful, would be the only topical antiandrogen approved for use in AGA that could potentially be used in both men and women.

Cassiopea believes that topical Clascoterone (Breezula®) will not have the contraindications and safety warnings of the orally administered androgen modulator approved for the treatment of men with AGA. Clascoterone does not interfere with the hormonal and, in particular, testosterone profiles of male subjects; libido and sexual behavior changes have not been observed in clinical trials to date. Clascoterone is quickly metabolized to cortexolone, a naturally occurring metabolite found throughout all human tissues, cells, blood

and urine; cortexolone's safety and metabolic fate are well characterized. Due to its rapid metabolism and local activity, Clascoterone does not produce systemic side effects.

About Cassiopea

Cassiopea SpA is a clinical-stage specialty pharmaceutical company focused on developing and commercializing innovative and differentiated medical dermatology products. Our focus is on the topical treatment of acne, androgenic alopecia (or AGA) and genital warts. The portfolio comprises four unencumbered clinical candidates, for which Cassiopea owns the worldwide rights. The company plans to commercialize the products directly in the US and partner the products outside of the US. For further information on Cassiopea, please visit www.cassiopea.com.

Next events

Jefferies Global Health Care Conference, New York	4-6 June
Half Year Report 2019	July
Jefferies Global Health Care Conference, London	13-14 November
Credit Suisse Small & Mid Cap Conference, Zurich	13-15 November

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