Cassiopea announces attainment of all primary and secondary endpoints and highly satisfactory safety data in its Phase 3 for Winlevi (Clascoterone) cream in Treating Acne

Lainate, Italy – 18 October 2018 – Cassiopea SpA (SIX: SKIN), a clinical-stage specialty pharmaceutical company focused on developing and commercializing innovative and differentiated medical dermatology products, today announced that the results of its two pivotal phase 3 clinical trials for its topical anti-androgen Clascoterone (Winlevi® cream 1%) demonstrated highly statistically significant improvements for all primary and secondary clinical end points and that the drug is generally safe and well tolerated. The results of both the primary and secondary endpoints are consistent with the Special Protocol Assessment agreed to with the FDA prior to the start of the study.

"This robust efficacy data confirms our most optimistic expectations" said Cassiopea CEO, Diana Harbort. "The US dermatology market has not seen a new mechanism for acne since the 1980s. If approved, Winlevi® will be the first topical antiandrogen. Winlevi® works at the top of the cascade of the events generating acne devoid of any significant hormonal side effect. Therefore, if approved, we expect high interest from doctors and patients."

Upon reviewing the data, James Leyden, MD, Emeritus Professor CE of Dermatology, University of Pennsylvania, one of the world's foremost authorities on acne remarked: "Over my nearly 50 years investigating acne, I have said many times that the Holy Grail of acne therapy is an effective topical anti-androgen that inhibits sebaceous gland activity. There have been many attempts. This is the first molecule to show clear clinically relevant efficacy. This drug will represent a major advance in acne therapy."

Clinical Trial Design

In two clinical trials (study 25 and 26) a total of 1440 subjects were enrolled in 112 sites in the US and Europe. The trials were identical in design and evaluated the safety and efficacy of Clascoterone compared to vehicle (placebo) in acne patients ages > 9 years with an IGA score of 3 or 4. Subjects applied Winlevi® 1% cream or placebo twice daily for 12 weeks. Upon completion of the clinical trials 604 subjects were rolled over into an open label long term safety trial (study 27) to assess the safety of the treatment for a total duration of 12 months and 345 patients completed the study. Results will be available in the 4th quarter for study 27.

The primary endpoints evaluated in the trials were: (1) the proportion of subjects in each treatment group with at least a two point reduction on IGA (Investigator Global Assessment) compared to baseline and an IGA score of 0 (clear) or 1 (almost clear) at week 12, (2) the absolute change from baseline in non-inflammatory lesion counts (NILC) in each treatment group at week 12, and (3) the absolute change from baseline in inflammatory lesion counts (ILC) in each treatment group at week 12. The secondary endpoints evaluated in the trials

were: (1) absolute reduction in total lesion counts at week 12, (2) percentage reduction in total lesion counts at week 12, (3) percentage reduction in non-inflammatory lesion counts at week 12, (4) percentage reduction in inflammatory lesion counts at week 12.

Efficacy Results Primary End Points

IGA treatment success ITT population

In Study 25, IGA Treatment Success for Winlevi 1% treatment group was 16.1% versus 7.0% in vehicle (p=0.0008)

In Study 26, IGA Treatment Success for Winlevi 1% treatment group was 18.7% versus 4.7% in vehicle (p<0.0001)

IGA treatment success PP population

In Study 25, IGA Treatment Success for Winlevi 1% treatment group was 20.4% versus 7.3% in vehicle (p<0.0001)

In Study 26, IGA Treatment Success for Winlevi 1% treatment group was 22.2% versus 5.5% in vehicle (p<0.0001)

Absolute reduction in non-inflammatory lesions ITT population

In Study 25, absolute change in non-inflammatory lesion count for the Winlevi 1% treatment group was -19.4 versus -13.1 in vehicle (p=0.0016)

In Study 26, absolute change in non-inflammatory lesion count for the Winlevi 1% treatment group was -19.4 versus -10.9 in vehicle (p<0.0001)

Absolute reduction in non- inflammatory lesions PP population

In Study 25, absolute change in non-inflammatory lesion count for the Winlevi 1% treatment group was -20.0 versus -11.5 in vehicle (p=0.0001)

In Study 26, absolute change in non-inflammatory lesion count for the Winlevi 1% treatment group was -21.7 versus -11.6 in vehicle (p<0.0001)

Absolute reduction in inflammatory lesions ITT population

In Study 25, absolute change in inflammatory lesion count for the Winlevi 1% treatment group was -19.4 versus -15.5 in vehicle (p=0.0029)

In Study 26, absolute change in inflammatory lesion count for the Winlevi 1% treatment group was -20.0 versus -12.6 in vehicle (p<0.0001)

Absolute reduction in inflammatory lesions PP population

In Study 25, absolute change in inflammatory lesion count for the Winlevi 1% treatment group was -20.7 versus -16.1 in vehicle (p=0.0005)

In Study 26, absolute change in inflammatory lesion count for the Winlevi 1% treatment group was -21.5 versus -13.4 in vehicle (p<0.0001)

Efficacy Results Secondary End Points

Absolute reduction of total lesions counts at week 12 ITT population

In Study 25, absolute change in total lesion count for the Winlevi 1% treatment group was -39.2 versus -28.9 in vehicle (p=0.0002)

In Study 26, absolute change in total lesion count for the Winlevi 1% treatment group was -40.3 versus -23.7 in vehicle (p<0.0001)

Percentage reduction of total lesions counts at week 12 PP population

In Study 25, percentage change in total lesion count for the Winlevi 1% treatment group was -37.1% versus -28.5% in vehicle (p=0.0016)

In Study 26, absolute change in total lesion count for the Winlevi 1% treatment group was -37.7% versus -22.2 in vehicle (p<0.0001)

Percentage reduction of non-inflammatory lesions count at week 12 ITT population
In Study 25, percentage change in non-inflammatory lesion count for the Winlevi 1% treatment group was -30.7% versus -21.9% in vehicle (p=0.0141)
In Study 26, percentage change in non-inflammatory lesion count for the Winlevi 1% treatment group was –29.3% versus -15.8% in vehicle (p<0.0001)

Percentage reduction of inflammatory lesion count at week 12 ITT population
In Study 25, percentage change in inflammatory lesion count for the Winlevi 1% treatment group was -44.8% versus -36.6% in vehicle (p=0.0070)
In Study 26, percentage change in inflammatory lesion count for the Winlevi 1% treatment group was -47.0% versus -29.8% in vehicle (p<0.0001)

Safety Data
Clascoterone 1% cream appeared to be generally safe and well tolerated with side effects similar to placebo. There were no treatment-related serious adverse events.

Percentage of subjects with treatment emergent adverse events
In Study 25, percentage of Treatment-Emergent Adverse Events for the Winlevi 1% treatment group was 11.3% (40 Subjects with 56 TEAE) versus 11.5% (41 Subjects with 52 TEAE) in vehicle
In Study 26, percentage of Treatment-Emergent Adverse Events for the Winlevi 1% treatment group was 11.4% (42 Subjects with 59 TEAE) versus 13.8% (50 Subjects with 87 TEAE) in vehicle

Treatment emergent adverse events by severity
In Study 25, percentage of severe, moderate and mild TEAE was 0%, 21%, 79% for the Winlevi 1% treatment group and 4%, 35%, 62% in vehicle – only 1 SAE in vehicle group
In Study 26, percentage of severe, moderate and mild TEAE was 0%, 22%, 78% for the Winlevi 1% treatment group and 1%, 24%, 75% in vehicle – only 1 SAE in vehicle group

Related treatment-emergent adverse events description
In Study 25, 4 subjects with 5 (9 with 11 for vehicle) related AEs all of them mild: 2 of them, each with 1 AE, continued the treatment (application site pain, application site dryness)
2 of them with 3 AEs withdrew the drug (application site hypersensitivity, oropharyngeal pain)
In Study 26, 8 subjects with 9 (13 with 15 for vehicle) related AEs: 7 of them mild and 2 moderate (acne, peritonsillar abscess): 6 of them with 7 AEs (1 subject with 2 AEs) continued the treatment (headache, eye irritation, application site hypertrichosis, acne – moderate, application site dryness + erythema (same subject), peritonsillar abscess – moderate). 2 of them with 2 AEs withdrew the drug (contact dermatitis, hair color change)

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

About Clascoterone
Clascoterone, is a new chemical entity topical anti-androgen in late stage development for the treatment of acne (in a 1% cream) and androgenetic alopecia (in a higher strength solution). It is a topically delivered small molecule that penetrates the skin to reach the

androgen receptors of the sebaceous gland. It aims to be the first effective and safe topical anti-androgen that does not have systemic effects.

Clascoterone helps to prevent that cascade of events that leads to acne. It displaces the androgen hormones from the androgen receptors on the sebaceous gland within the hair follicle. Clascoterone is metabolized quickly to cortexolone, a physiological component of the body's endogenous pool of corticosteroids, thus attaining high local activity without having any systemic effects.

A different formulation containing a higher strength of clascoterone is also in Phase 2 clinical development for the treatment of androgenetic alopecia.

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

Credit Suisse Healthcare Conference, Zurich	November 14, 2018
Jefferies Global Healthcare Conference, London	November 15, 2018
Annual Report 2018	March 2019

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