Creating Innovation in Dermatology

JEFFERIES HEALTHCARE CONFERENCE

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Balanced Pipeline with Key Upcoming Events

Product	Pre-Clinical	Phase I	Phase II	Phase III	MA / Expected Launch	Next Catalyst	Market Opportunity
Winlevi® ACNE Anti-androgen **NCE**(1)				H2 2017	4Q2019/ 1Q2020	H1 2018 (Ph 3 data)	**US only:** $5bn(2)
Breezula® ALOPECIA Anti-androgen **NCE**(1)			POC completed DR H2 2018	2019-2020	2021	H1 & 2 2018 (Ph II interim and full DR data)	$1.9bn(3) (surgical) $600m(4) (drugs)
CB-06-01 ACNE Antibiotic **NCE**			POC completed DR 2019	2020-2021	2022	H2 2019 (Ph II DR data)	**US only:** US$5bn(2)
CB-06-02 HPV Integrin activator **NCE**			POC 2017 DR 2019	2020-2021	2022	H1 2018 (POC)	**US only:** c.14m new infections each year(5)

POC = Proof of Concept
DR = Dose Ranging

(1) Winlevi® and Breezula® are different formulations of the same NCE, for different indications.
(2) Management estimates based on IMS Health, IMS SMART MVP Solutions. Comprised of USC3 Classification 37100 Acne Therapy, Prescription Only, plus antibiotics Doryx, Monodox, Solodyn and Tazorac – Manufacturing prices increased by 20%.
(3) International Society of Hair Restoration Surgery. Note: 2012 survey figure.
(4) EvaluatePharma.
(5) Centers for Disease Control and Prevention.

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Well managed cost base

EUR/1,000	30.06.17	30.06.16
Revenues	**0**	**0**
Other income	0	0
Cost of sales	(0)	(0)
Research and development costs	(6,452)	(6,602)
Selling, general and administrative costs	(818)	(1.035)
Net Operating expenses	**(7,270)**	**(7,637)**
Operating Result	***(7,270)***	***(7,637)***
Financial income	265	152
Financial expenses	(2,262)	(993)
Profit (loss) Before Taxes	***(9,267)***	***(8,478)***
Income tax expenses	(0)	(0)
Profit (loss) For The Period	***(9,267)***	***(8,478)***
EUR/1,000	**30.06.17**	**30.06.16**
Profit (loss) for the period (A)	**(9,267)**	**(8,478)**
Other comprehensive income that will be not reclass. to P/L	0	0
Other comprehensive income that will be reclassified to P/L	0	0
Total other comprehensive income, net of tax (B)	**0**	**0**
Total comprehensive income (A)+(B)	**(9,267)**	**(8,478)**

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Sufficient funds to end 2018

EUR/1,000	30.06.17	31.12.16
Tangible and intangible assets	380	358
Tax receivables	5,011	5,583
Total non-current assets	**5,391**	**5,941**
Other receivables and other current assets	2,555	2,328
Cash and cash equivalents	25,083	33,656
Total current assets	**27,638**	**35,984**
Total assets	**33,029**	**41,925**
Total Non-current liabilities	0	0
Total Current liabilities	2,744	2,776
Total liabilities	**2,744**	**2,776**
Total equity	**30,285**	**39,149**
Total equity and liabilities	**33,029**	**41,925**

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Cassiopea's Pipeline

Creating a New Class of Drugs for Acne: The First Topical Anti-Androgen

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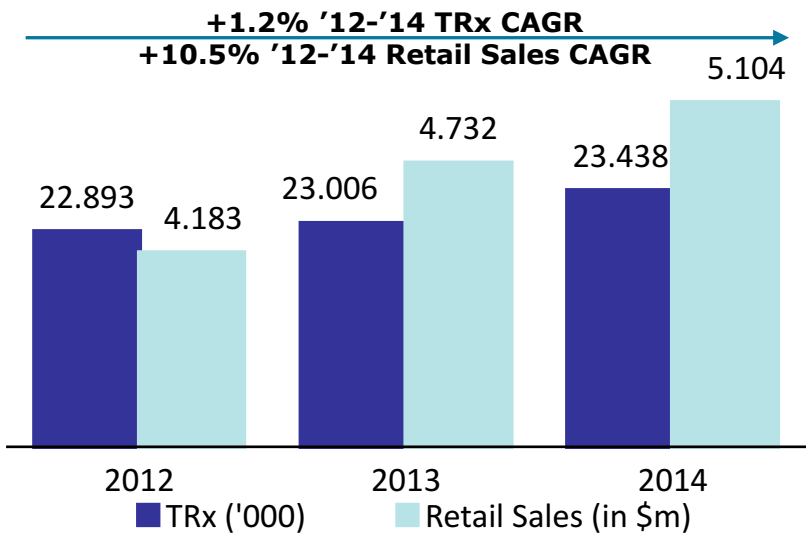
US Acne Market Overview

Acne market dynamics & opportunity

- affects 40m-50m people annually(1) – c.15% of the population(2)
  - 85% of all people aged 12-24 get acne(1)
- ~24m prescriptions(3) are written annually, mostly of older molecules as there are no new drugs

US Acne Market 2012-2014(3)



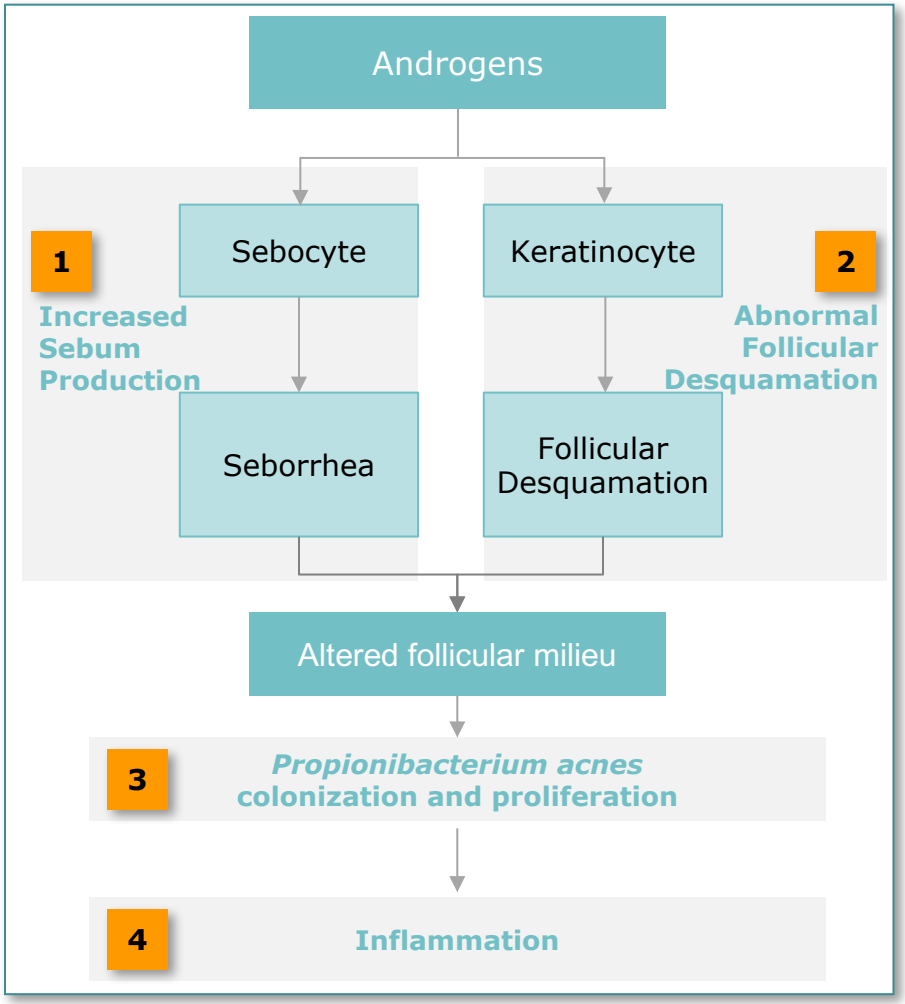
Dermatology market has had little innovation

- No NCE in acne in the US market since the mid 1990s (Differin and Tazorac launched in '95 and '97)
- AAD guidelines recommend acne treatment should target as many pathogenic factors as possible
- Derms generally prescribe 2-3 products with complementary MoAs at the same time as the cause of acne is multifactorial
- Dermatology is lower risk area: Historically low clinical trial failure rate
- Acne medications in the US are subject to reimbursement
- Avg branded products have annual revenues of $250-400MM
- Major topical prescription sellers are the anti-infectives EPIDUO and Aczone

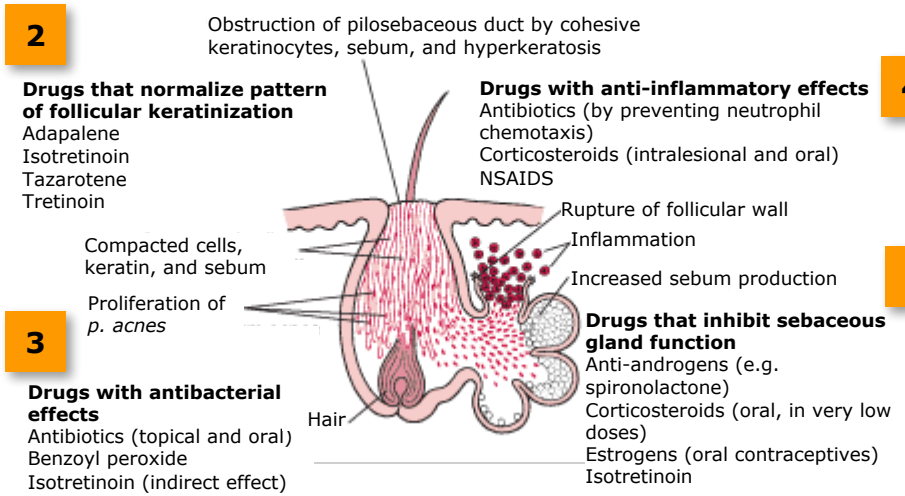
(1) American Academy of Dermatology.
(2) United States Census Bureau, US 2013 population of 317m.
(3) Management analysis of data from IMS Health, IMS SMART MVP Solutions. TRx and Retail sales comprised of USC3 classification 37100 Acne Therapy, Prescription Only, in all specialties; selected anti-acne products Doryx, Monodox, Solodyn and Tazorac, in all specialties; TRx and Retail sales within the Dermatology specialty only for Doxycycline HYC DR, Doxycycline Hyclat, Doxycycline Monohyd, Minocycline HCl, Minocycline HCl ER, and Spironolactone.

Overview Of Acne Pathogenesis

The 4 pathways of Acne pathogenesis



Acne formation(1)



1 **Seborrhea**

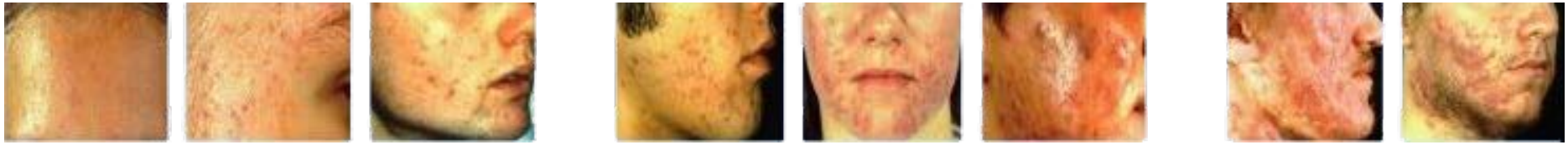
2 **Obstruction**

3 ***P. acnes***

4 **Inflammation**

(1) Merck Manual.

Acne Treatment Algorithm



	Mild		Moderate		Severe
	Non-inflammatory	**Inflammatory**	**Inflammatory**	**Inflammatory**	**Inflammatory**
	Comedonal	**Papular/pustular**	**Papular/pustular**	**Nodular**	**Nodular/conglobate**
First choice	Topical retinoid	Topical retinoid + topical antimicrobial	**Oral** antibiotic + topical retinoid +/- BPO	**Oral** antibiotic + topical retinoid +/- BPO	**Oral** isotretinoin
Alternatives (males and females)	Azelaic acid or salicylic acid	Alt. topical antimicrobial agent + all. topical retinoid or azelaic acid	Alt. **oral** antibiotic + alt. topical retinoid +/- BPO	Oral isotretinoin or alt. **oral** antibiotic alt. topical retinoid +/- BPO/azelaic acid	High-dose **oral** antibiotic + topical retinoid + BPO
Alternatives (females only)	See first choice	See first choice	**Oral** anti-androgen(1) + topical retinoid/ azelaic acid +/- BPO	**Oral** anti-androgen(2) + topical retinoid +/- oral antibiotic +/- alt. antimicrobial	**High-dose oral anti-androgen**(2) + topical retinoid +/- alt. topical Antimicrobial
Maintenance therapy	Topical retinoid		Topical retinoid +/- BPO		

Notes: BPO = Benzoyl peroxide.

(1) Expert Rev Clin Pharmacol 2010 Expert Reviews Ltd.

(2) Off-label spironolactone.

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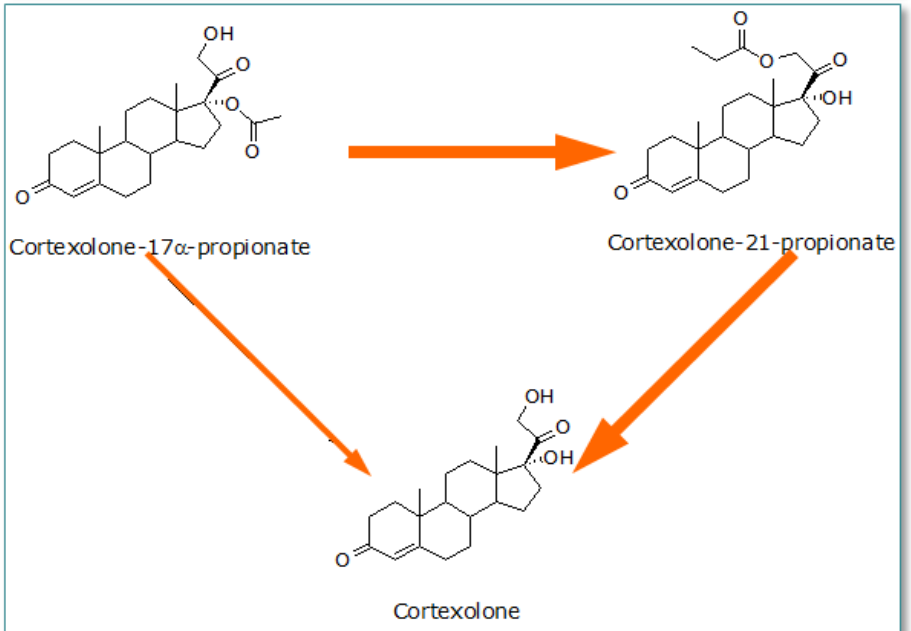
Winlevi Mechanism of Action

Mechanism of Action

- A topical anti-androgen would prevent the cascade of physiological events that leads to acne formation
- Winlevi™ displaces the androgen hormones from the androgen receptors located at the sebaceous gland and hair follicle
- This reduces sebum secretion and follicle cell keratinization
- As a result, the follicle is not obstructed, preventing colonization by *p. acnes* and subsequent inflammation
- Winlevi™ is metabolized to cortexolone, a physiological component of the body's endogenous pool of corticosteroids

Metabolic Pathway



- The final compound is cortexolone, whose safety profile is well known
- The aim is to achieve high local activity without systemic effects due to the in vivo hydrolysis pattern

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Winlevi Safety Summary

- CB-03-01/ Winlevi® aims to be the first effective and safe topical anti-androgen devoid of systemic effects
- Unlike other hormonal therapies for acne, CB-03-01 can be used in both males and females
- Following topical application, CB-03-01 is rapidly metabolized in skin and plasma to cortexolone, resulting in very low systemic bioavailability (<1% of applied dose) and minimal plasma levels
- Cortexolone as a major metabolite is a physiological component of the pool of endogenous corticosteroids and exhibits limited glucocorticoid activity and has no anti-androgenic properties
- Based on safety to date, and low levels of systemic exposure, FDA granted a waiver for the typically required systemic 2-year carcinogenicity study
- Safety data in >1000 subjects, treated up to 1 year, shows an AE profile and local skin reactions (LSR's) similar to placebo

Because CB-03-01 pharmacological action is targeted at the local site of application, its use is expected to avoid the side effects associated with systemic exposure to hormonal agents currently used in the treatment of acne

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Winlevi Highlights

Key Takeaways

- If approved, will be the first ever topical anti-androgen, fully developed in-house
- A new chemical entity (NCE) with a new mechanism of action
- Expansive to the existing acne market
- Clean safety profile
- An active anti-inflammatory agent
- Clinically superior and better tolerated than topical tretinoin (based on our trial results)
- Has the potential to be used in combination with other drugs such as anti-infectives or retinoids

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Note: These properties are all as seen in trials thus far but testing / development are not complete and final clinical results may vary.

Winlevi Phase III Program Ongoing

Phase III Program and Trial Design

- Special Protocol Assessment (SPA) approved by FDA in July 2015
- Winlevi® 1% cream applied twice-daily for 12 weeks in subjects with facial acne
- FDA requires at least 1,000 patients treated for safety evaluation
- 2 pivotal trials (sites in both US + EU) with 700 patients/each
  - FPI November 2015 /Complete enrollment in H2 2017
  - Enroll subjects from 9 years of age and older with moderate to severe acne (Grades 3 and 4 on IGA)
  - Data expected to be available H1 2018
- 1 longterm open label safety trial: 300+ subjects 6 months, 100 subjects 12 months exposure
- NDA filing targeted for H2 2018

Study Endpoints

Primary

- Proportion of subjects with IGA score of 0 (clear) or 1 (almost clear) and at least a two-point reduction in IGA compared to baseline
- Absolute change from baseline in non-inflammatory lesion count at week 12
- Absolute change from baseline in inflammatory lesion count at week 12

Secondary

- Absolute and % Change from baseline in total lesion count at week 12
- %age change from baseline in non-inflammatory lesion count at week 12
- %age change from baseline in inflammatory lesion count at week 12

IGA = Investigator Global Assessment.

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Phase 3 Acne Studies

97% enrolled

03 November 2017

Study 25 US

• 33 sites actively recruiting	
• Randomized subjects	643
• Completed	391

Study 26 EU

• 34 sites actively recruiting	
• Randomized subjects	714
• Completed	454

Study 27 EU/US Open Label Long Term Safety Study

• Rolled over from Studies 25 and 26	564
• Rolled over from 25 study	239
• Rolled over from 26 study	325

Cassiopea's Pipeline

Breezula

A Novel Approach To Alopecia In Phase II

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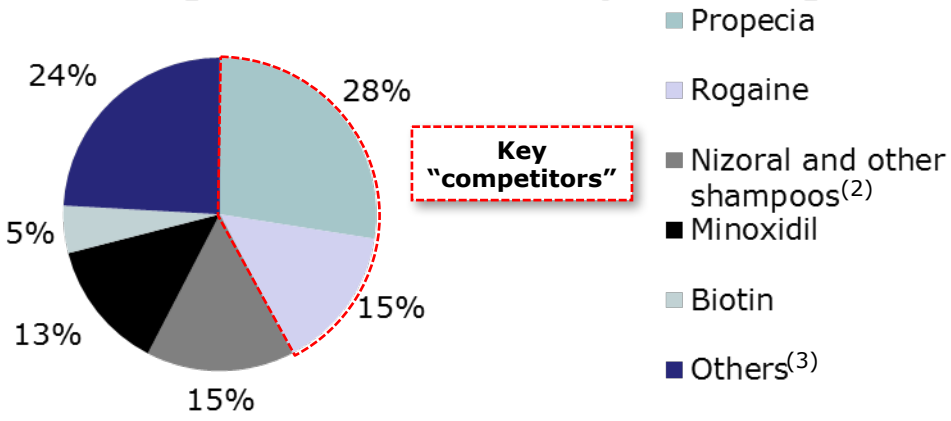
Alopecia Market Overview

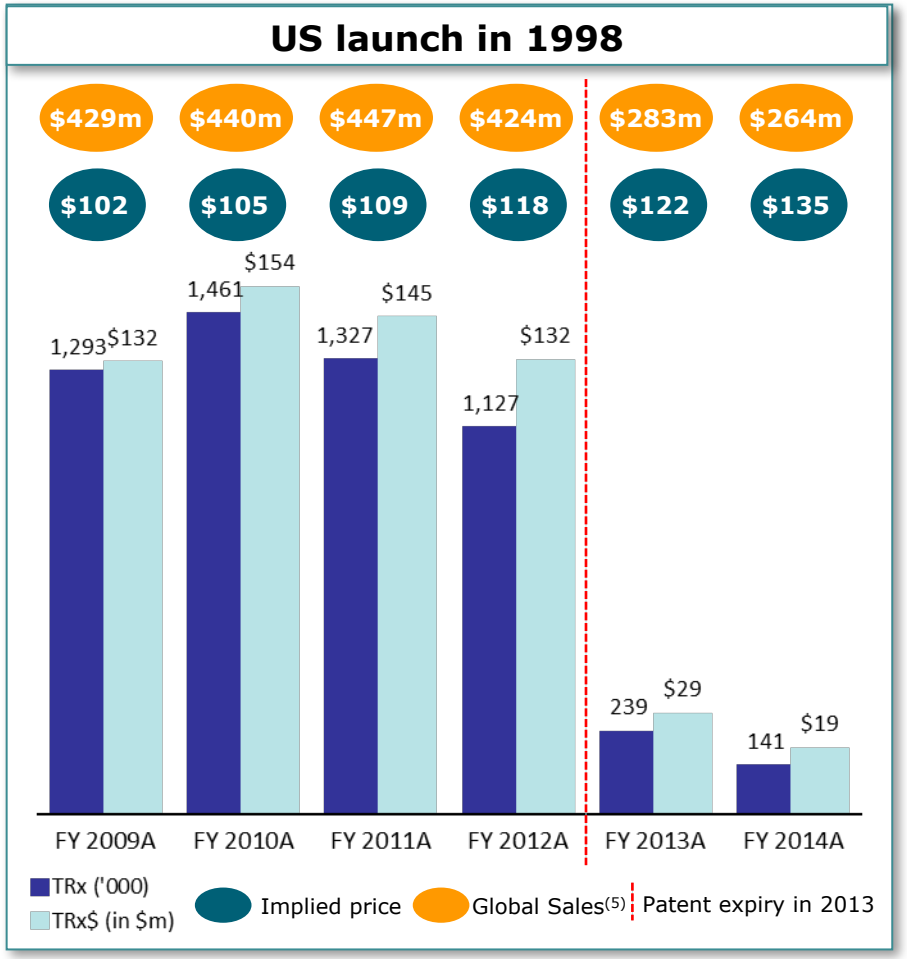
Competitive Landscape

Non-Surgical Patient Prescription Usage[1]



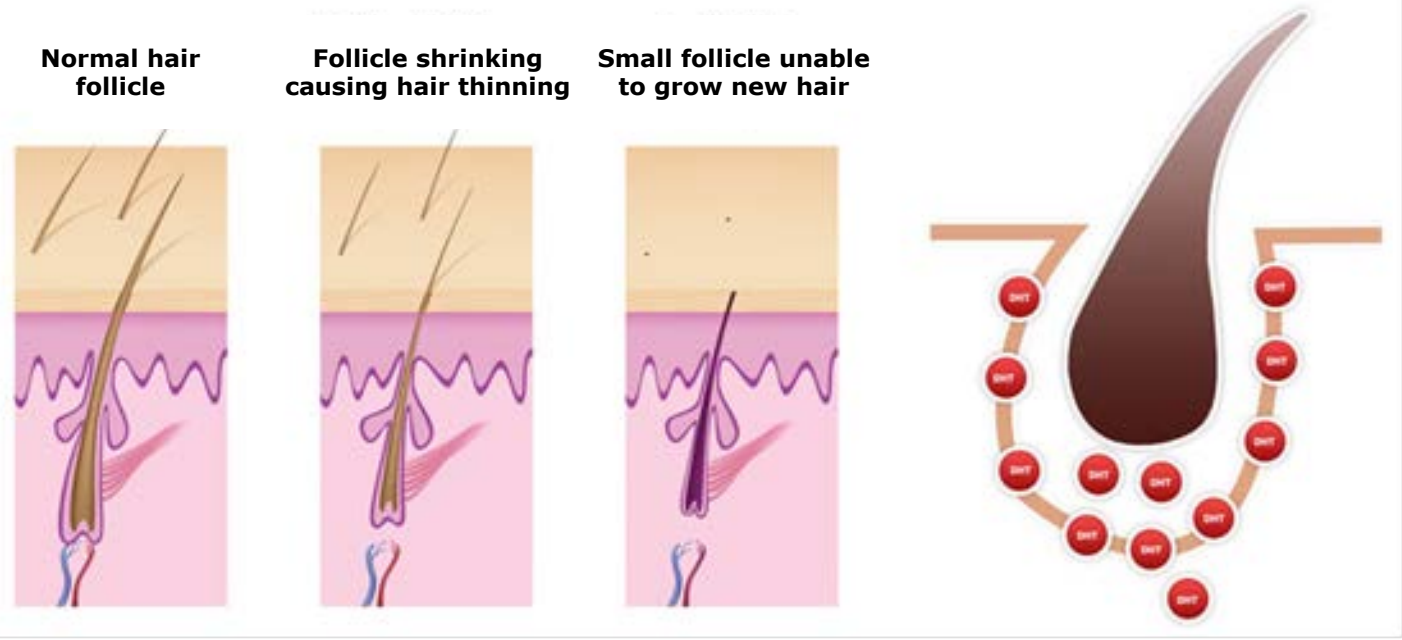
- Overview of key competitors:
  - Rogaine (topical): shows a vasodilator effect, ensuring a better flow of nutrients to the papilla
  - Propecia (oral): Shows anti-androgenic activity on follicle, however, serious side effects due to systemic hormonal imbalance. Not indicated for women

US Propecia Case Study[4]



(1) International Society of Hair Restoration Surgery, 2014.
(2) Other shampoos include Nioxin, other special shampoos and Head & Shoulders.
(3) Other treatments include Proscar, Compounded minoxidil with additives, home and clinical low level laser therapy, herbs & vitamins and Avodart.
(4) IMS Health, IMS SMART MVP Solutions.
(5) EvaluatePharma.

Breezula Overview Of Existing Drugs



Existing Treatments

Propecia™ (finasteride)

- Shows anti-androgenic activity on follicle
- However, serious side effects due to hormonal imbalance
- Not indicated for women

Minoxidil©

- Shows a vasodilator effect, ensuring a better flow of nutrients to the papilla

Breezula® A Novel Anti-androgen

Breezula

- Antagonizes DHT's negative effects on dermal papilla
- Reduces hair miniaturization
- Reduces dermal inflammation

DHT = Dihydrotestosterone

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Breezula Highlights

Key Takeaways

- Positive POC results in androgenic alopecia
- NCE(1) with topical anti-androgenic properties
- All available alopecia treatments have a very low and transient (treatment-lasting) efficacy
- Large opportunity in a significantly underexploited market
- Can be used by men and women
- Can be used in sunlight exposure
- Chronic treatment
- No significant systemic side effects

Mechanism of Action

- Breezula® is formulated to act at cutaneous (scalp) level:
  - Antagonizes DHT's negative effects on dermal papilla
  - Reduces prostaglandin D2 production by human skin fibroblasts
  - Controls sebum secretion
  - Reduces hair miniaturization
  - Reduces dermal inflammation
- No exhibited interference with the hormonal (testosterone) profile of patients (libido and sexual behaviour unaffected) in trials to date

Note: These properties are all as seen in trials thus far but testing / development are not complete and final clinical results may vary.

(1) Winlevi® and Breezula® are different formulations of the same NCE, for different indications.

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Positive PH2 POC Results

Trial Highlights

- Double blind, 3 parallel arms, Breezula 5% (N=31), placebo (N=33) and Minoxidil 5% (N=31), 6 mo treatment, BID, conducted 10/2014-12/2015, males 18-50, 95 enrolled, 78 completed, 73 per protocol efficacy analysis
- Both actives (Minoxidil and Breezula) showed directional superiority (study was not sized for statistical significance) over Vehicle at Month 6 in term of TAHC
- Minoxidil showed significance on TAHC, compared to baseline, (p=0.0006) and CB-03-01 approaches significance (p=0.0780), Vehicle was not effective (p=0.4274)
- Data by subjects HGA correlates with the hair count outcomes for all treatment groups
- Local skin reactions observed for all treatment groups were mostly minimal or mild and decreased over time, no significant systemic AEs

Results of the primary endpoints

Change from Baseline in Non-Vellus TAHC (co-primary endpoint)

PP	BREEZULA	MINOXIDIL	VEHICLE
Mean	12.7%	18.8%	2.9%

Hair Growth Assessment (HGA) increased (co-primary endpoint)

PP	BREEZULA	MINOXIDIL	VEHICLE
% of Subjects	39.1%	36%	16%

- Maximal effect with Breezula TBD; may not have been reached at Month 6. For Oral Finasteride (antiandrogen) significant increase is observed at Month 6 with peak effect seen at 12 months (75% of peak effect at month 6)
- Overall, results of this POC study indicate a favorable efficacy profile of Breezula 5% with potential of showing greater and sustained efficacy long-term, without having the systemic effects of oral finasteride

Phase 2 DR Study Ongoing

- Single 12-month study with interim analysis at 6 months
- Male subjects 18-55 years of age with mild to moderate AGA
- Co-Primary Endpoints:
  - Changes from Baseline in TAHC [in number of non-vellus hairs] at Month 12
  - The subject's evaluation of treatment benefit via the HGA question at Month 12
- 400 subjects, 80 per treatment arm
- 5 arms: 2.5%, 5.0%, 7.5%, vehicle BID and 7.5% QD
- CRO: bioskin; 6 German sites and 1 Back up site
- First Patient In June 2017
- 326 of 400 patients enrolled as of 3 Nov 17
- Enrollment should be complete by year end 2017
- Interim results due 2Q 2018 and Topline 12 month results due 4Q 2018

Cassiopea's Pipeline
CB-06-01

A NCE In Phase II POC For Acne

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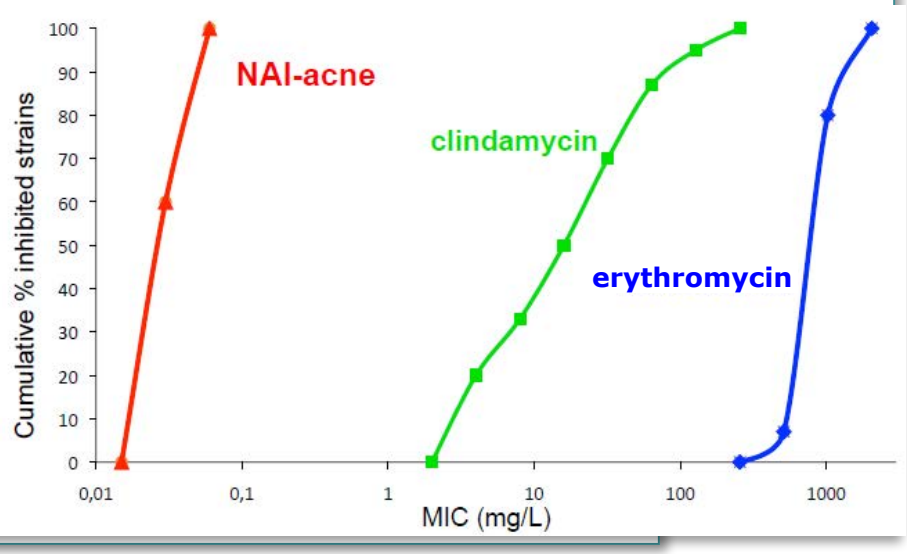
CB-06-01 Highlights

Key Takeaways

- Topical antibiotic for the treatment of Acne; inhibits bacterial protein synthesis
- NCE with very potent and selective properties
- Effective on bacterial strains resistant to certain other antibiotics
- PoC shown with a gel formulation in 2016
- Complementary to Winlevi®
- In-licensed worldwide from Italian company Naicons

Specifically more effective on *p. acnes* than currently available alternatives

- Incidence of erythromycin-resistant *p. acnes* can be as high as 70%
- Most erythromycin-resistant strains are cross-resistant to clindamycin



Note: These properties are all as seen in trials thus far but testing / development are not complete and final clinical results may vary.

CB-06-01 Phase II POC Results

Trial Highlights

- Double-blind randomized placebo controlled trial
- 90 patients (Slovakia)
- 12 weeks of treatment
- 3% gel treatment twice per day
- No adverse events
- Results announced October 2016

Top Line Results

Primary

- Absolute and percent change in inflammatory lesion count from baseline to week 12 compared between treatments:
- **Median reduction of ILC by 66,2%, 9% greater than vehicle**

Secondary

- Absolute and percent change in total lesion count from baseline
- **Median reduction of TLC by 61,3%, 17% greater than vehicle**
- Proportion of subjects with IGA score reduction of at least 2 (defined as a success) from baseline
- **17.8% of patients on CB-06-01 vs 6.7% on vehicle**

Safety

- Evaluation of safety, tolerability and local tolerability as compared to the matching placebo
- **No Serious Adverse Events were reported, no increased local skin reactions vs vehicle**

IGA= Investigator Global Assessment.
CADI= Cardiff Acne Disability Index (Quality of life index).

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CB-06-01 Status

Development activities

- **API manufacturing development:**
  - Produce a new GMP batch of API to be used as active substance for the new clinical batch of gel
- **Formulation development:**
  - Optimize the formulation in order to:
    - Improve the penetration of the active substance in the follicles, increasing its effectiveness against Propionibacterium acnes
    - Improve its cosmetic appearance, increasing patients' compliance

Cassiopea's Pipeline
CB-06-02

A NCE In Phase II POC For Genital Warts

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CB-06-02 Highlights

Key Takeaways

- Genital warts market consists of products with low efficacy and high recurrence rates
- Tellurium-based topical product for treatment of HPV ano-genital warts
- Proven anti-viral agent on cutaneous viral warts caused by HPV, most commonly located on the skin and genitalia
- Demonstrated safety in hundreds of patients in different topical formulations for dermatological indications (Verruca vulgaris, Condiloma Acuminata)
- 75.7% of all patients treated (n=74) were completly cured(1)
- In-licensed worldwide from Israeli company BioMas

Mechanism of Action

- Acts as a low toxicity immunomodulator in supporting the natural immune response against HPV and its warts for quicker clearance and reduced recurrence(2)

Phase II POC Trial Design

- POC Phase II ongoing in Israel on 30 + 30 patients, double blind, parallel arms, 14 weeks of treatment + 3 months of follow up, endpoints on remission and recurrence rates
- Trial completion anticipated by H2 2017, Results expected H12018

Note: These properties are all as seen in trials thus far but testing / development are not complete and final clinical results may vary.

(1) Friedmann N., British Journal (2009), 160, 403-8.

(2) BioMas preclinical study.

Key Future Milestones

2017

- Q4 Complete enrolment in Winlevi Phase 3 Trials
- Q4 Complete enrolment in Breezula Dose Ranging Study
- Complete enrolment in CB06-02 Genital Warts POC Study

2018

- H1 Winlevi® Phase 3 Results
- H1 PoC data CB-06-02 HPV
- H1 Breezula Phase 2 Six Month Interim Results
- H2 Pre NDA Meeting Winlevi
- H2 Breezula Phase 2 DR results
- Q4 2018/Q1 2019 NDA filing Winlevi®

Note: Current timing is based on certain assumptions with regards to progression through clinical trials and may be subject to delays.

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