mc2 therapeutics

Pioneering novel treatment paradigms within Immunology and Inflammation

Global company presentation
2024

Two (Ph2 stage) first-in-class “pipeline in a product” are driving value creation

1

Two first-in-class and novel MOA drug candidates – “I&I pipeline in a product”

MC2-32: Oral HSP90 Inhibitor – unique pharmacological profile (even within the HSP90 class):

- ✓ Specific Tissue Targeting profile – enables a favorable safety profile
- ✓ Novel MOA modulating multiple pro-inflammatory pathways is providing formidable effect

MC2-25: Topical Iso-cyanate Scavenger for multiple urea associated skin diseases

2

Mature programs addressing “blue ocean” indications with high value potential

MC2-32 for Hidradenitis Suppurativa Ph2b (HiSCR75) in planning (Ph2a data in JAMA Dermatology Dec 2023)
MC2-32 for Indication 2 and Indication 3 (IND’s Ph2a anticipated in 2025)
MC2-25 for Vulvar Lichen Sclerosus (Ph2a ongoing)

3

Marketed psoriasis drug Wynzora® Cream (psoriasis) - recurring revenue stream

Partnerships in US, Europe, China and ASEAN (covering ~2.5B people)
Represents a significant growth opportunity

4

Solid long lasting intellectual property

Strong portfolio of drug patents and applications into 2040’ies
For topicals, PAD Technology™ enables a new standard of products

5

Experienced team with proven drug development and regulatory competences

Developed Wynzora® from idea to approval, manufacturing and launches in EU and US
Robust clinical and drug development capabilities and commercialization insights

Attractive pipeline: Near term value catalyzers within multiple I&I indications

Program	Active Ingredient MoA	Indication	MC2 Rights	Pre-Clinical IND prep.	Phase 1	Phase 2	Phase 3	Next milesone	Market Size 2030[2]
MC2-32 Oral	HSP90 Inhibitor • First-in-class • New MoA • Tissue specific targeting	Hidradenitis Suppurativa	WW ex. CN 2044			1		IND Ph2b H2 2024	~2% ~$10B[3]
		Indication 2 TBD - rare	WW ex. CN 2044		Covered by HS file			IND Ph2a 2025	Rare disease
		Indication 3 TBD	WW ex. CN 2044		Covered by HS file			IND Ph2a 2025	~X% ~$YYB
MC2-25 Topical	Iso-cyanate scavenger • First-in-class • New target and MoA	Vulvar Lichen Sclerosus	Worldwide 2040					Ph2a data H2 2024	~1% >$5B

MC2-32 has “Pipeline in a product” potential in >10 I&I indications
MC2-25 also represents a potential to address multiple urea associated skin diseases

[1] Ph2a is completed, data in JAMA Dermatology here; [2]US, EU, CN and JP Est.; [3] Market analyses by Jefferies (2023) and Cowen (2022)

High execution leadership through diverse experiences and professional owner

Executive Management

Jesper J. Lange, LLM
Chief Executive Officer

KROMANN REUMERT | LUNDGRENS

Casper Møller
Chief Financial Officer

EY Building a better working world

Lars Iversen, Prof.
Chief Medical Officer

AARHUS UNIVERSITY

Frédéric Gomez
Investor Relations

BNP PARIBAS | NOVAGALI PHARMA

Morten Præstegaard
Chief Operating Officer

ThermoFisher SCIENTIFIC | novo nordisk®

Christopher Billis
Chief Commercial Officer

BAYER | STIEFEL® Research in Dermatology

Board of Directors and Owner

Mads Clausen
Chairman and Owner
MS in Biotechnology, John Hopkins Uni.
MS in Engineering, DTU
MBA from the London Business School

Clausen Family | Danfoss

Tomas Dahl Mikkelsen
Director Elsmark

Anders D. Hove
Director
Founder of Acorn Bioventure

venrock

John Haurum
Director

Company and investment highlights

- Domiciled in Copenhagen, DK and Guildford, UK
- >$110M contributed to equity capital
- Cost-efficient set-up – cash burn in 2023 of ~$15M
- Runway supported by owner and Wynzora® revenues

MC2-32: Novel HSP90 Inhibitor – first-in-class

Potential to become the leading oral therapy in multiple I&I indications

Ph2a data in Hidradenitis Suppurativa

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Key take aways on first-in-class oral MC2-32 HSP90 Inhibitor

1. **New MOA**: High affinity for HSP90α and HSP90β modulating multiple pro-inflammatory pathways

2. **Uniquely specific tissue targeting** (differentiated from other HSP90 inhibitors and small molecules)
   - ✓ Higher drug concentration in the target tissue vs plasma **allows a broader immune-modulation with low systemic effects**

3. **Pipeline in a drug:** MOA is relevant in various I&I indications – including neutrophilic dermatoses rare diseases

4. **Clinical efficacy and safety is documented** in a Ph2a in hidradenitis suppurativa trial and in plaque psoriasis

5. **Clinical safety supported by data from 185 patients** involved in clinical trials in oncology, PsO and HS

MC2-32 Hidradenitis Suppurativa: First-in-class oral therapy with unique MoA

Introduction to Hidradenitis Suppurative (HS)[7,8]

Most commonly affected areas

Symptoms

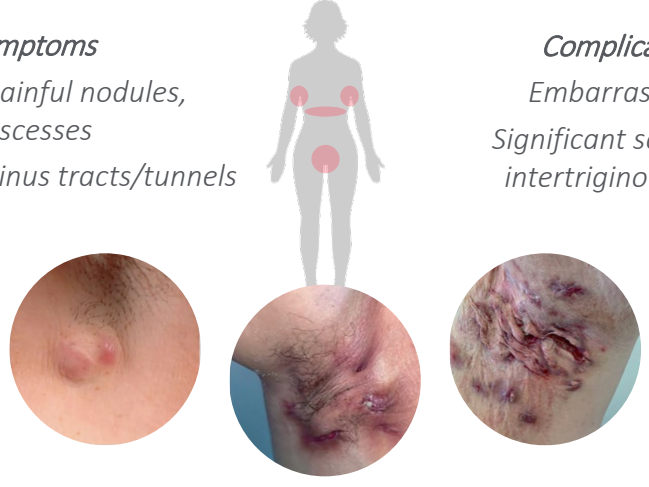
Chronic, painful nodules, abscesses

Suppurating sinus tracts/tunnels

Complications

Embarrassment

Significant scarring in intertriginous areas



- Debilitating inflammatory disorder with few treatment options.
- HS is still under-diagnosed with an average time of diagnosis 7 years after diseases initiation[1,2].
- Diagnosed in Hurley stages 1 (mild), 2 (moderate) and 3 (severe).

Rationale: Unique MoA is a perfect match for HS

- Major need for new oral drugs within I&I including in HS
- Unique MoA is targeting multiple pro-inflammatory pathways - patent applications filed for 10 additional indications
- Ph2a data substantiates potential to become a leading oral drug for HS and multiple additional I&I indications

Major market potential in HS

~8M (~1-2% of population[1,2,3]) in US and EU alone; only 5-10% currently diagnosed[4]

~0.6M (55% of patients Hurley stage II (moderate) and III (severe))[5]

~$3B+ market (US and EU) in 2030[6]

1. Garg et al. JAAD 2017; 77(1): 118-122; 2. Jfri et al. JAMA Dermatol. 2021; 157(8): 1–8; 3.Prens et al. BJ Derm. 2022;186(5): 814–822J; 4. Garg et al. Dermatol Ther 2023;13(2):581-594; 5. Annika et al. Dermatology Letters 2018: 234:232-33; 6. Market analyses by Jefferies (2023) and Cowen (2022), 7. Sabat et al. Nature Rev Dis Prim 2020;6: 18; 8. Nguyen et al. JEADV 2021;35:50-61

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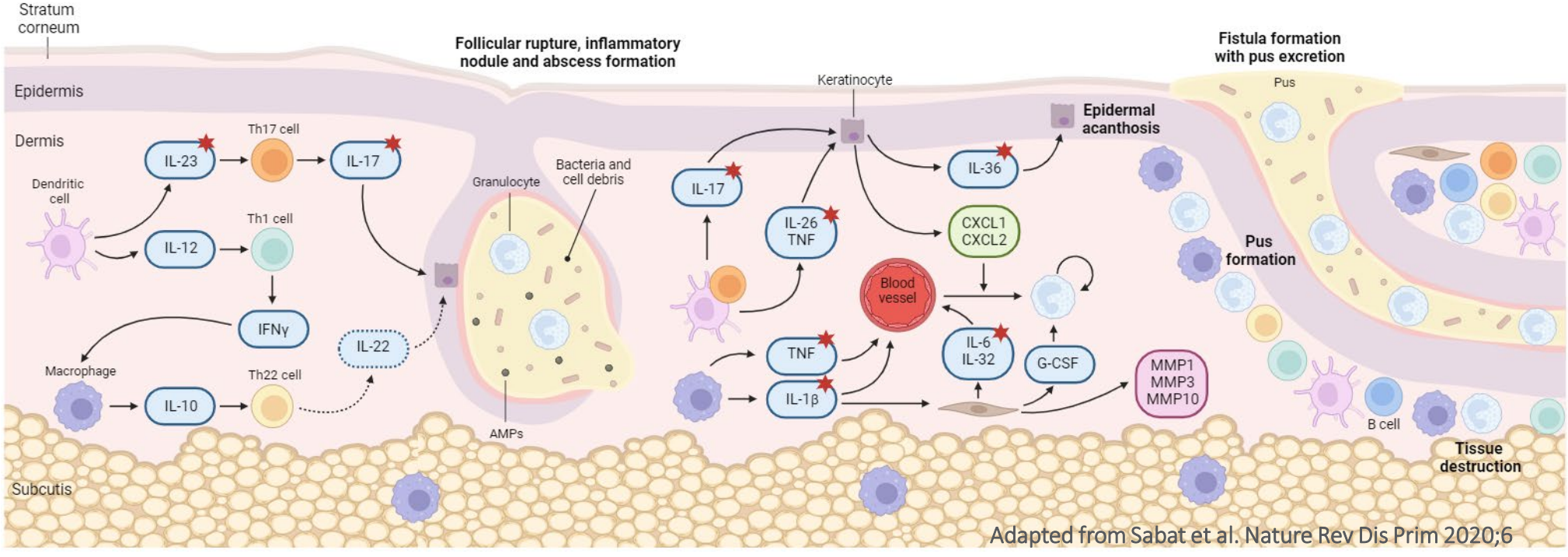
MC2-32 modulates multiple pro-inflammatory pathways relevant for I&I indications



Illustrates reduced expression after MC2-32 treatment as demonstrated both *in vitro* and *in vivo*[1-3]

References: 1) Bregnhøj et al. Br J Dermatol 2022;186:861-874; 2) Hansen et al. Exp Dermatol 2021;30:773-781; 3) Abdallah et al. Front Immunol. 14:1128897

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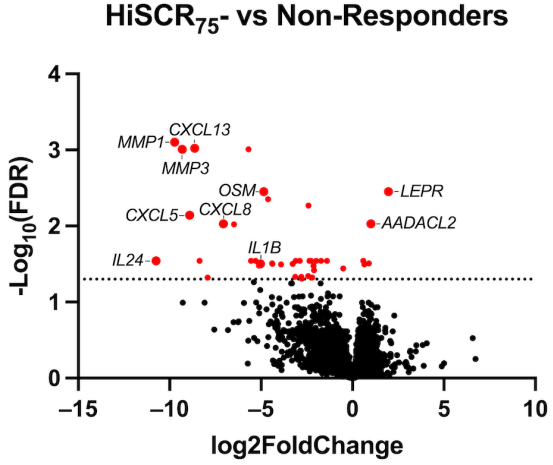
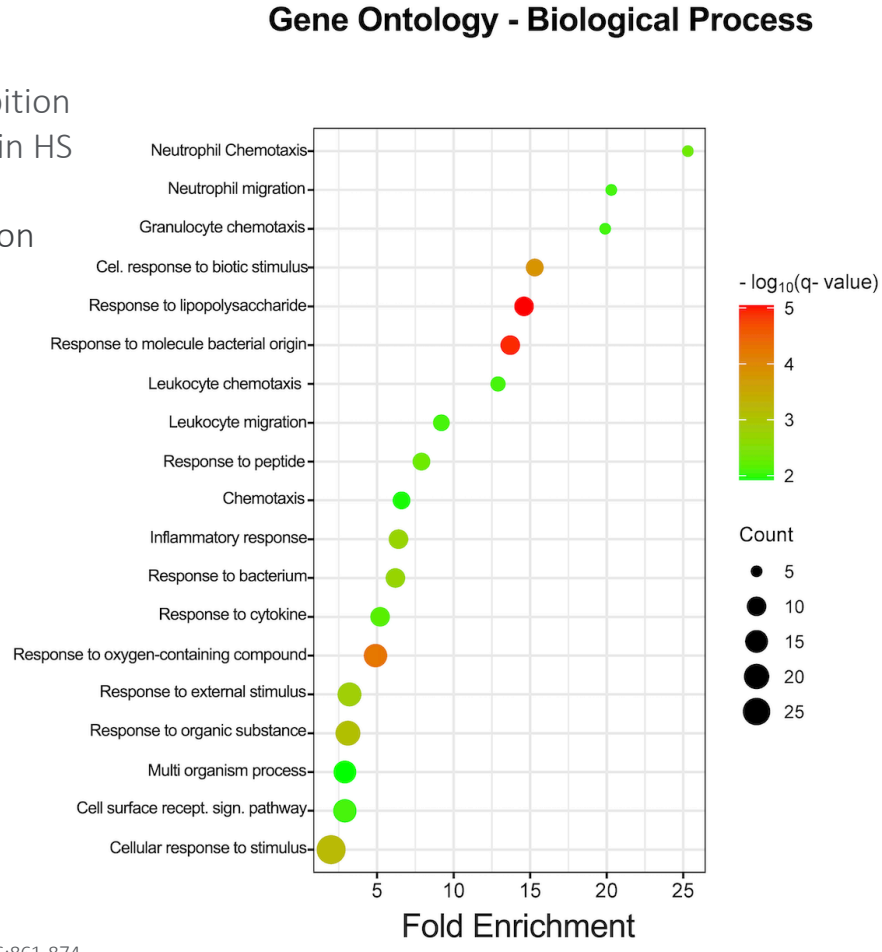
MC2-32 is highly relevant for neutrophilic dermatoses (ND)

Analysis of punch biopsies from the Ph2a HS trial

- Volcano plot and gene ontology enrichment analysis shows inhibition of neutrophil activation and recruitment in HiSCR75 responders in HS
- Inhibition of IL-1, IL-17, IL-36A, CXCL5 and CXCL8 mRNA expression
- MC2-32 has proven clinical efficacy in psoriasis[1] and HS – both neutrophilic dermatoses





1: Bregnhøj A et al. Br J Dermatol 2022;186:861-874

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Neutrophilic dermatoses (ND) are highly interesting and underserved I&I indications

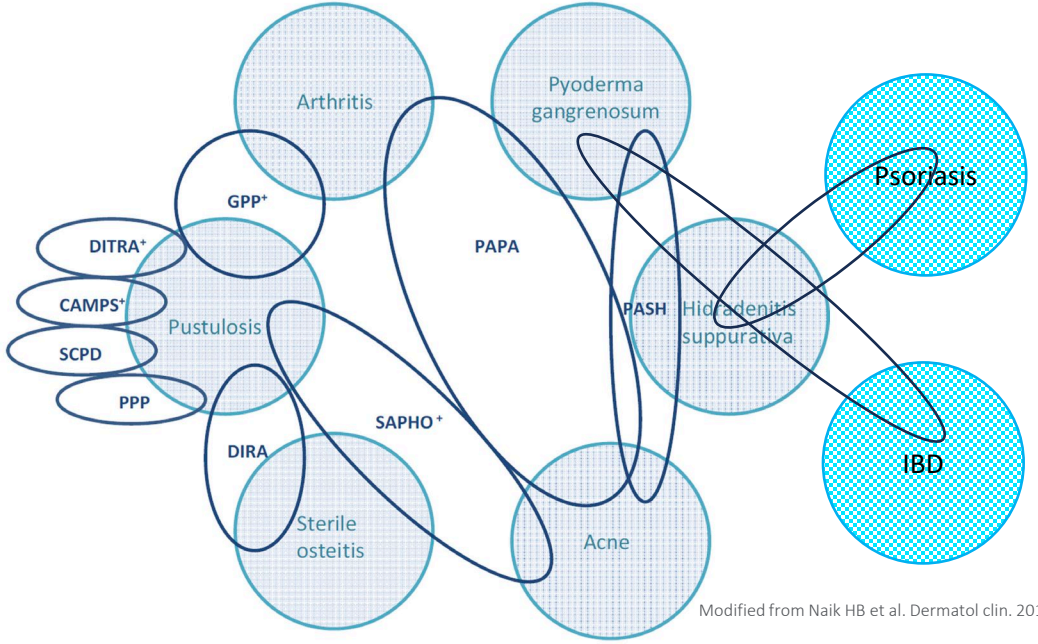
Examples of ND[3,4]:

- Hidadenitis suppurativa (HS)
- Palmoplantar pustular psoriasis
- Pustular psoriasis
- Pyoderma gangrenosum
- Sweet syndrome
- Behçet syndrome
- Neutrophilic eccrine hidradenitis

Other atypical ND:

- Psoriasis[5]

Neutrophilic / pustular dermatoses, syndromes and associated diseases:



Modified from Naik HB et al. Dermatol clin. 2013;31:405-425

CARD 14-mediated pustular psoriasis (CAMPS); deficiency of IL-1 receptor antagonist (DIRA); deficiency of the IL-36 receptor antagonist (DITRA); generalized pustular psoriasis (GPP); Inflammatory Bowel Disease (IBD); pyogenic arthritis, pyoderma gangrenosum, and acne (PAPA); pyoderma, acne and suppurative hidradenitis (PASH); palmoplantar pustulosis (PPP); synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO); subcorneal pustular dermatosis (SCPD).

1: Feldmeyer L et al. Clinics in Dermatology 2021;39:261-270 2: Marzano AV et al. Frontiers in Immunology 2019;10:Article number 1059 3: Rook's Textbook of Dermatology 9'th edition 2016, chapter 49
4: Shao S et al. J Allergy Clin Immunol 2022;149:1203-5 5: Czerwi´nska J et al. Int. J.Mol.Sci. 2022,23,1840. 6: Bregnhøj A et al. Br J Dermatol 2022;186:861-874

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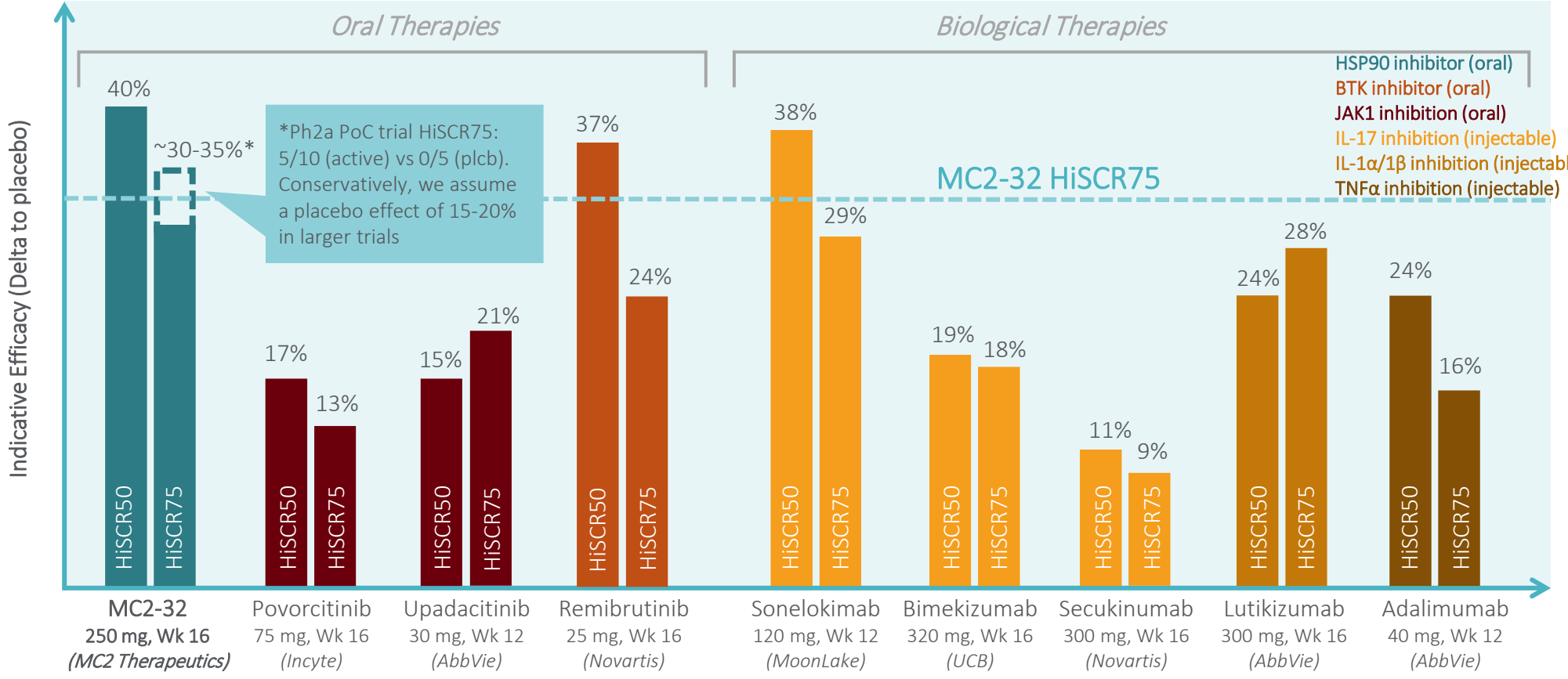
MC2-32 has the potential to become the leading HS therapy



Note: Several additional ongoing biologic or oral development programs in HS. Illustrated programs are those with substantial data.
This is a comparison across trials, with inherent limitations, i.e., not based on head-to-head trials. MC2-32: Trial NCT05286567; Late-breaking data Abdallah et al, EADV 2023, Abstract no 6471. Povorcitinib: Trial NCT04476043 (primary endpoint - mean AN count reduction). HiSCR50/HiSCR75 data from Kirby et al; EADV 2022, Poster P0004. Upadacitinib: Trial NCT04430855; Kimball et al, AAD 2023, Poster ID 43799. Chovatiya, Raj, Maui Derm Hawaii, Jan-2024. Remibrutinib: Late-breaking presentation at AAD 2024. Sonelokimab: Trial NCT05322473; MoonLake press release 11-Oct-2023. Bimekizumab: Mean of trials NCT04242446 and NCT04242498 (BE HEARD I/II); Kimball et al. AAD 2023 (late-breaking session). Secukinumab: Mean of trials NCT03713619 and NCT03713632 (SUNRISE/SUNSHINE); Kimball et al. Lancet 2023, 401(10378):747-761; Ingram,JR et al. EADV 2023, FC03.9. Lutikizumab: AbbVie press release 08-Jan-2024. Adalimumab mean of trials NCT01468207 and NCT01468233 (PIONEER I/II) for HiSCR50. Kimball et al, NEJM 2016, 375:422-434. HiSCR75 from Glatt et al, JAMA Dermatol. 2021,157(11):e212905. *Ph2a PoC trial demonstrated HiSCR75=50% (active) vs 0% (placebo). In larger trials a placebo effect of 15-20% is assumed.

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A randomized, double-blinded, placebo-controlled Ph2a trial in HS

Key inclusion criteria

- At least 18 years of age
- HS with at least 6 abscesses or inflammatory nodules in at least 2 distinct anatomic regions

Concomitant medication

No concomitant medication allowed. Systemic treatment for hidradenitis suppurativa was required to be discontinued at least 28 days before the baseline visit (12 weeks for biologics)

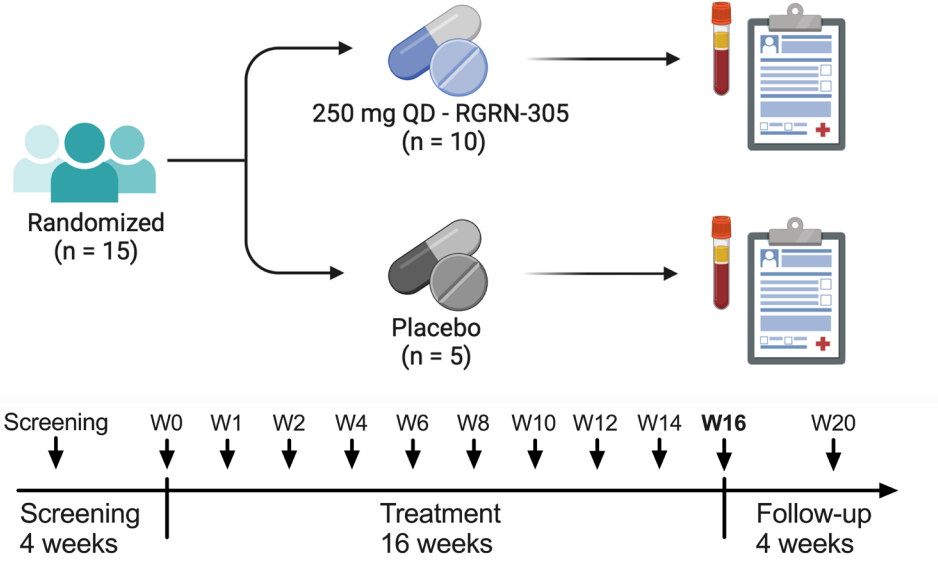
Endpoints

Primary endpoint: $HiSCR_{50}$ at week 16

Secondary efficacy endpoints : $HiSCR_{75}$, $HiSCR_{90}$, HS-PGA, DLQI (0-30), Pain-NRS (0-10)

Safety endpoints: SAE, TEAE, blood chemistry, ECGs

Study design



- Explorative study - Not powered to obtain statistical significance
- All patients completed the study as intended with no dropouts

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Compelling primary and secondary endpoint measures

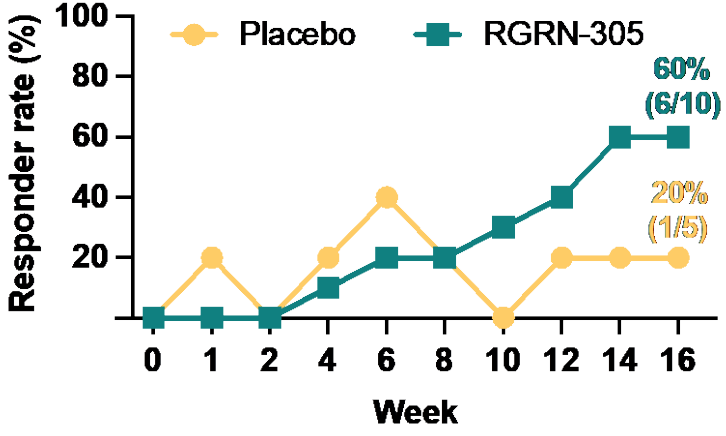
Hidradenitis Suppurativa Clinical Response (HiSCR)

The Hidradenitis suppurativa clinical response (HiSCR) is an outcome measure for HS used mainly in clinical trials

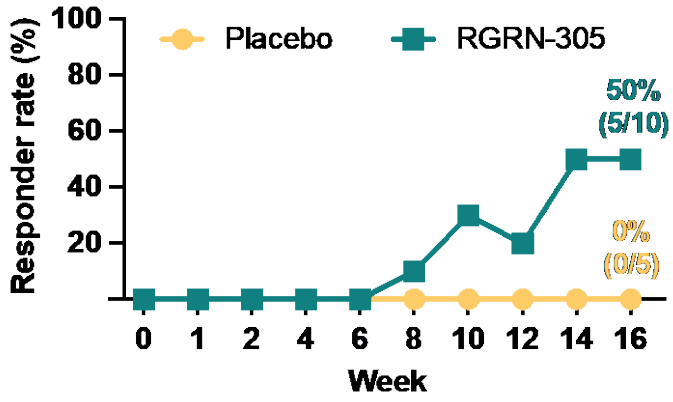
It focuses on the inflammatory changes in active HS

HiSCR is defined as a ≥ 50% reduction ($HiSCR_{50}$) in the abscess and inflammatory nodule (AN) count from Baseline Visit with no increase in abscesses and draining fistula count

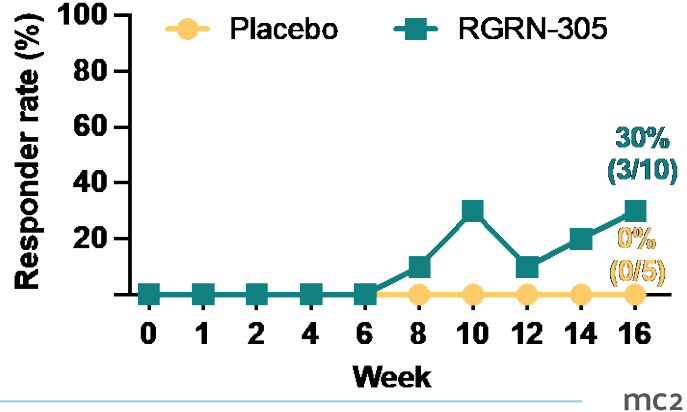
$HiSCR_{50}$



$HiSCR_{75}$

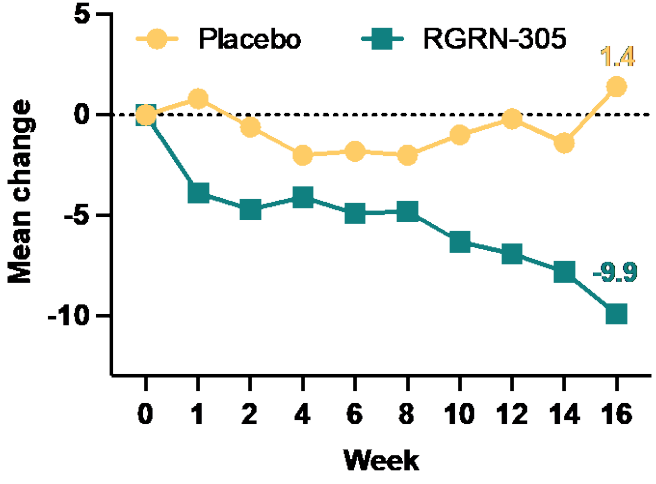


$HiSCR_{90}$

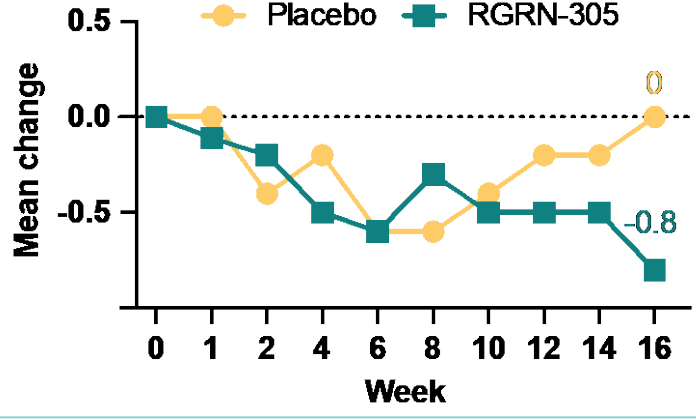


Secondary endpoints – IHS4, HS-PGA and PRO's are also promising

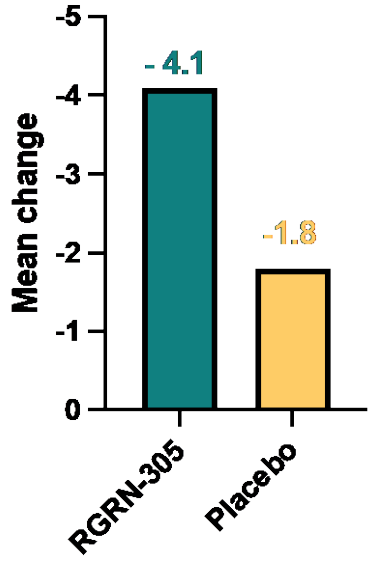
IHS4 (also including draining tunnels)



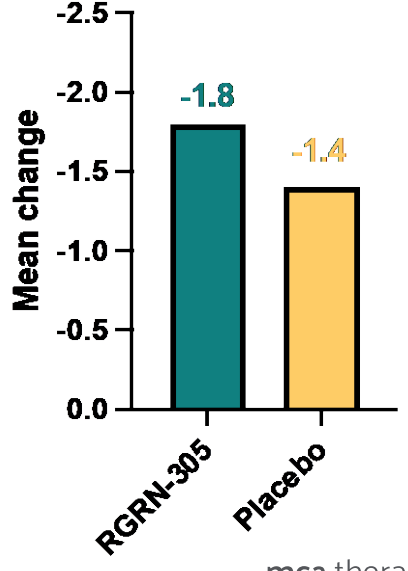
HS-PGA



DLQI change at W16



Pain NRS change at W16



Very favorable safety profile due to unique pharmacological profile

- No SAE's
- Similar frequency and profile of TEAEs between MC2-32/RGRN-305 and placebo
- All TEAEs in the MC2-32/RGRN-305 group were either mild or moderate
- No clinically relevant changes in blood biochemistry and ECGs

	No. (%) of patients with at least one TEAE [No. of events]	
	MC2-32/RGRN-305 (N=10)	Placebo (N=5)
Any TEAE	6 (60) [13]	5 (100) [7]
Upper respiratory infections	4 (40) [5]	2 (40) [2]
Headache	2 (20) [3]	1 (20) [1]
Diarrhea	2 (20) [2]	1 (20) [1]
Dizziness	1 (10) [1]	1 (20) [1]
Abdominal pain	1 (10) [1]	0 (0) [0]
Excessive sweating	1 (10) [1]	0 (0) [0]
Fatigue	0 (0) [0]	1 (20) [1]
Hemorrhoid	0 (0) [0]	1 (20) [1]

MC2-25: Iso-cyanate scavenger – First-in-class

Potential novel treatment paradigm
in multiple urea associated skin diseases

Ph2a trial ongoing in Vulvar Lichen Sclerosus

MC2 is investigating urea associated diseases for potentially multiple indications

MC2 research and discovery in urea related skin diseases

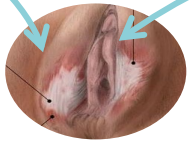
Urea is in equilibrium with highly reactive **iso-cyanate** that accumulates in the skin and causes carbamylation

MC2-25 is an iso-cyanate scavenger

Iso-cyanate

Amino Acid carbamylation

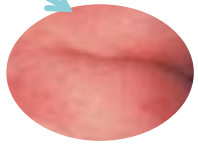
Protein carbamylation

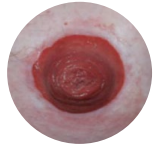


Inflamed fissured skin

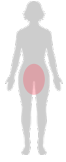
- ✓ Large indications with no or limited approved drugs
- ✓ Blue Ocean – favorable market access position
- ✓ Broad patent protection – prevention of carbamylation

Potential other indications





Potential multiple indications



Vulvar Lichen Sclerosus

Symptoms

Itching and pain. Painful sexual function, bleeding and blistering

Vulvar dermatitis

Symptoms

Incontinence, red skin itch, inflammation

ICD-10 L28

Diaper dermatitis

Symptoms

red skin, rash, itch and inflammation

ICD-10 L22

Peristomal LS

Symptoms

Lichen sclerosus painful red skin

ICD-10 L24.B3

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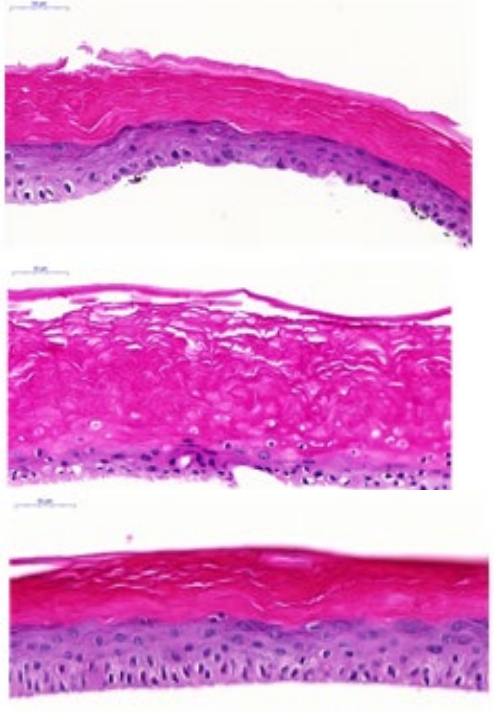
Carbamylation in skin is a potential new target

Histopathological analysis of skin samples

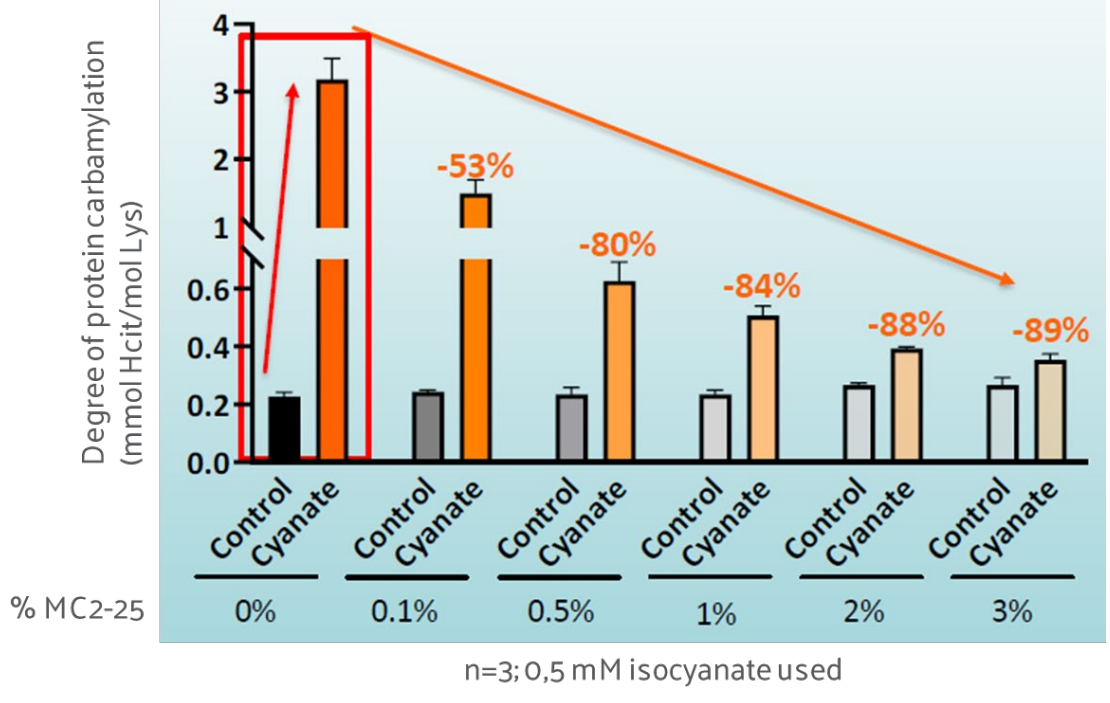


Control
In vitro reconstructed human epidermis from keratinocytes

Iso-cyanate treated

Iso-cyanate + MC2 Scavenger

Analysis of protein carbamylation



n=3; 0,5 mM isocyanate used

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MC2-25 Vulvar Lichen Sclerosus: Targeting first approved treatment

Introduction to Vulvar Lichen Sclerosus (VLS)

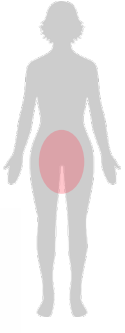
Most commonly affected areas

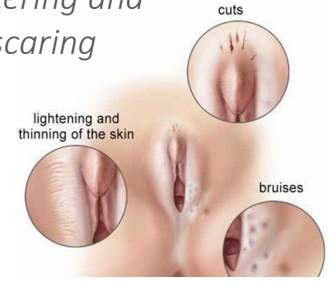
Symptoms

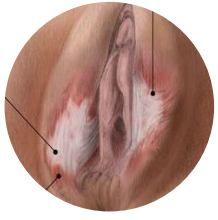
Redness - Itching

Discomfort/pain

Bleeding, blistering and scaring







Complications

Painful sexual function

Urinary retention

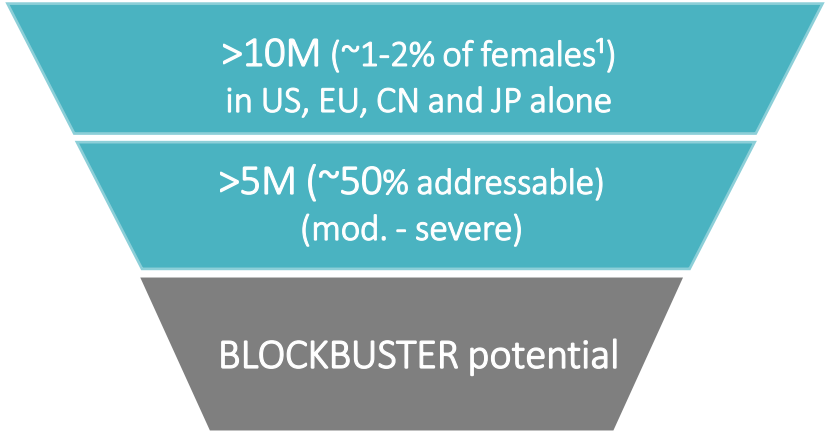
Increased risk of skin cancer[1]

- Lichen sclerosus most often appears in female genital epithelium for postmenopausal women[1]
- Causes of vulvar lichen sclerosus are until now unknown[1] and there are no approved therapies

Rationale: Addressing the likely root cause of VLS

- New mode of action addressing carbamylation of amino acids and proteins as a novel target
- Potential to become the first and leading approved therapy for VLS

Major market potential



1 Melnick et al. Lichen sclerosus among women in the US International Journal of Women's Dermatology, Volume 6, Issue 4, 2020, Pages 260-262,

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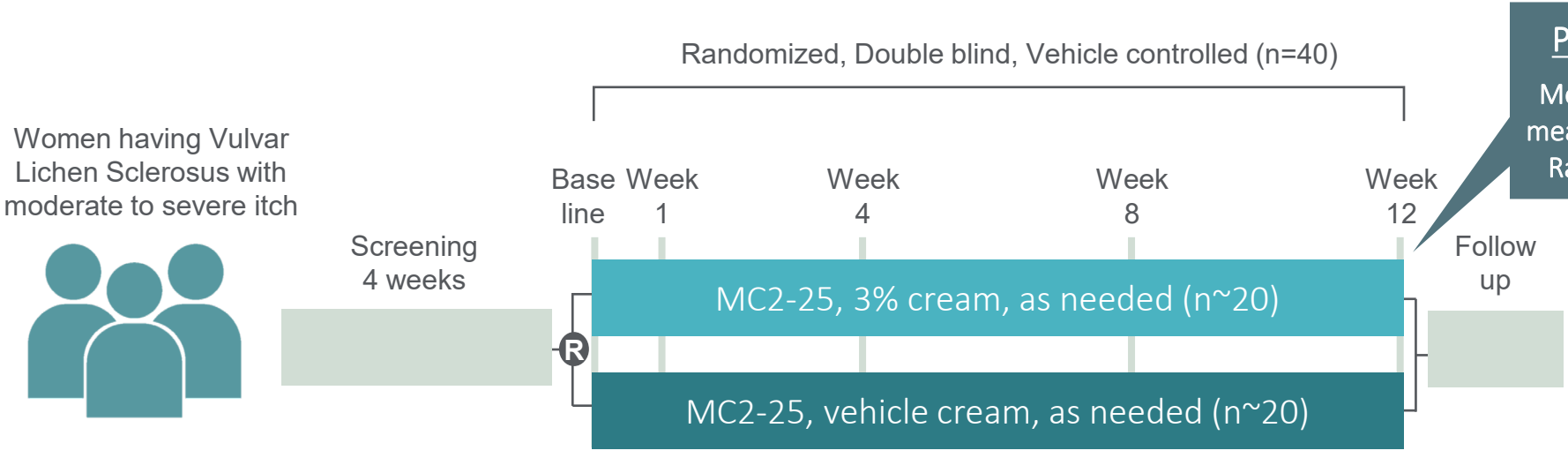
Ongoing Ph2a PoC trial in Vulvar Lichen Sclerosus



Primary Endpoint

Mean change in weekly mean Worst Itch Numeric Rating Score (WI-NRS)

Trial Status:

FPFV in Oct, 2023

Sized for statistical trends

Clinical sites in Denmark

Topline Ph2a PoC trial results expected in H2 2024

Secondary Endpoints

- Responder analyses in improvement of worst itch (WI-NRS)
- Additional patient and physician reported outcomes

Marketed drug Wynzora® Cream for treatment of plaque psoriasis in adults – launched in US and Europe and partnered in China

(0.005% w/w calcipotriene + 0.064% w/w betamethasone dipropionate cream)

Please see more at Wynzora.com

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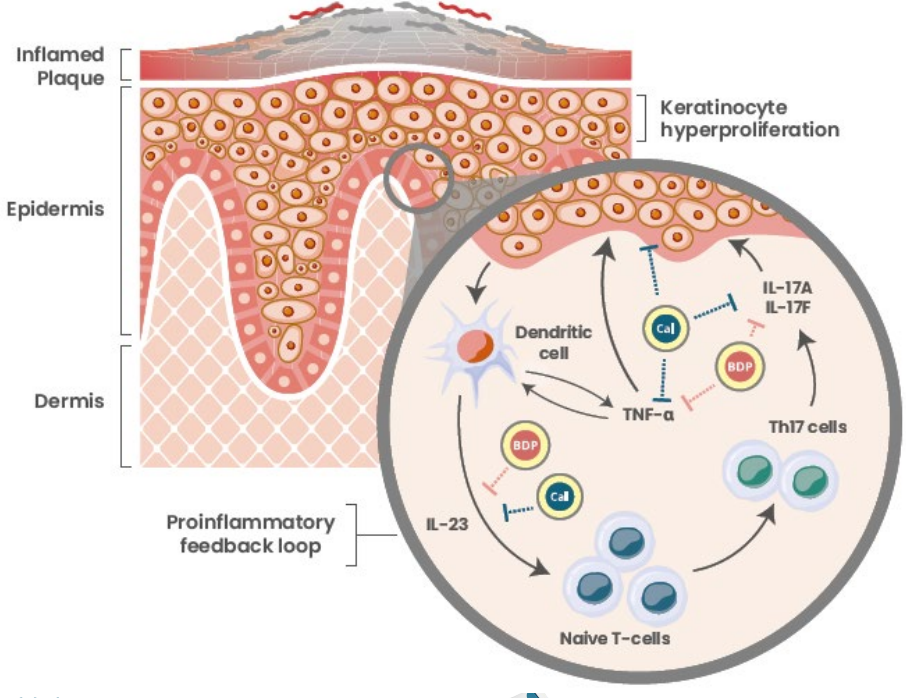
Marketed Wynzora® - potential to become world's leading topical psoriasis drug

Dual MoA of CAL & BDP targets hallmark cytokines, TNF-α, IL-23 and IL-17A/F



Wynzora®
(calcipotriene and betamethasone dipropionate)
Cream, 0.005%/0.064%

Patented until 2039

Marketed Wynzora® drug is developed from idea to approval by MC2 and partnered in major territories

almirall feel the science	Launched in EU under a License Agreement
mc2 therapeutics / mayne pharma	Owned by MC2 and distributed by local partner
HUADONG MEDICINE	In development under License Agreement
Hyphens	In development under License Agreement

Territories with ~2.5B people
Cash flow positive franchise