Leon H. Kircik, MD, FAAD

Clinical Professor of Dermatology
Icahn School of Medicine at Mount Sinai, New York, NY
Indiana University Medical Center, Indianapolis, IN
Medical Director
Physicians Skin Care, PLLC Louisville, KY
DermResearch, PLLC, Louisville, KY
Skin Sciences, PLLC, Louisville, KY

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- Acambis
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- Allergan
- Almirall
- Amgen
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- Asubio
- BMS
- Berlex
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- Brickell
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- Triax Pharmaceuticals
- UCB
- Valeant
- Warner & Chilcott
- Xenoport
- ZAGE

RETINOIDS

Inhibition of Toll-like receptor (TLR)-2[1,2]

Reduction in inflammatory signaling from *C. acnes**[6]

Reduced Formation of Hyperproliferative Keratins (K6, K16)[3,4]

Normalize Differentiation[7]

Inhibition of AP-1 Pathway[5]

Reduction in inflammatory signaling associated with collagen degradation and scarring[8]

*previously referred to as *P. acnes*

1. Kim J, et al. *J Immunol*. 2002;169(3):1535-1541.**2.** Bunimovich et al. *J Am Acad Dermatol.* 2007;56(2)(suppl 2):AB13. American Academy of Dermatology 65th Annual Meeting poster abstract. **3.** Gregoriou S, et al. *Clin Cosmet Investig Dermatol*. 2014;7:165-170. **4.** Korge B, et al. *J Invest Dermatol*. 1990;95(4):450-455. **5.** Leyden et al. *Dermatol Ther (Heidelb).* 2017;7(3):293-304. **6.** McInturff JE, et al *J Invest Dermatol*. 2005;125(1):1-8. **7.** Lee DD, et al. *J Cell Physiol*. 2009;220(2):427-439. **8.** Chien A. *J Drugs Dermatol*. 2018;17(12):s51-s55.

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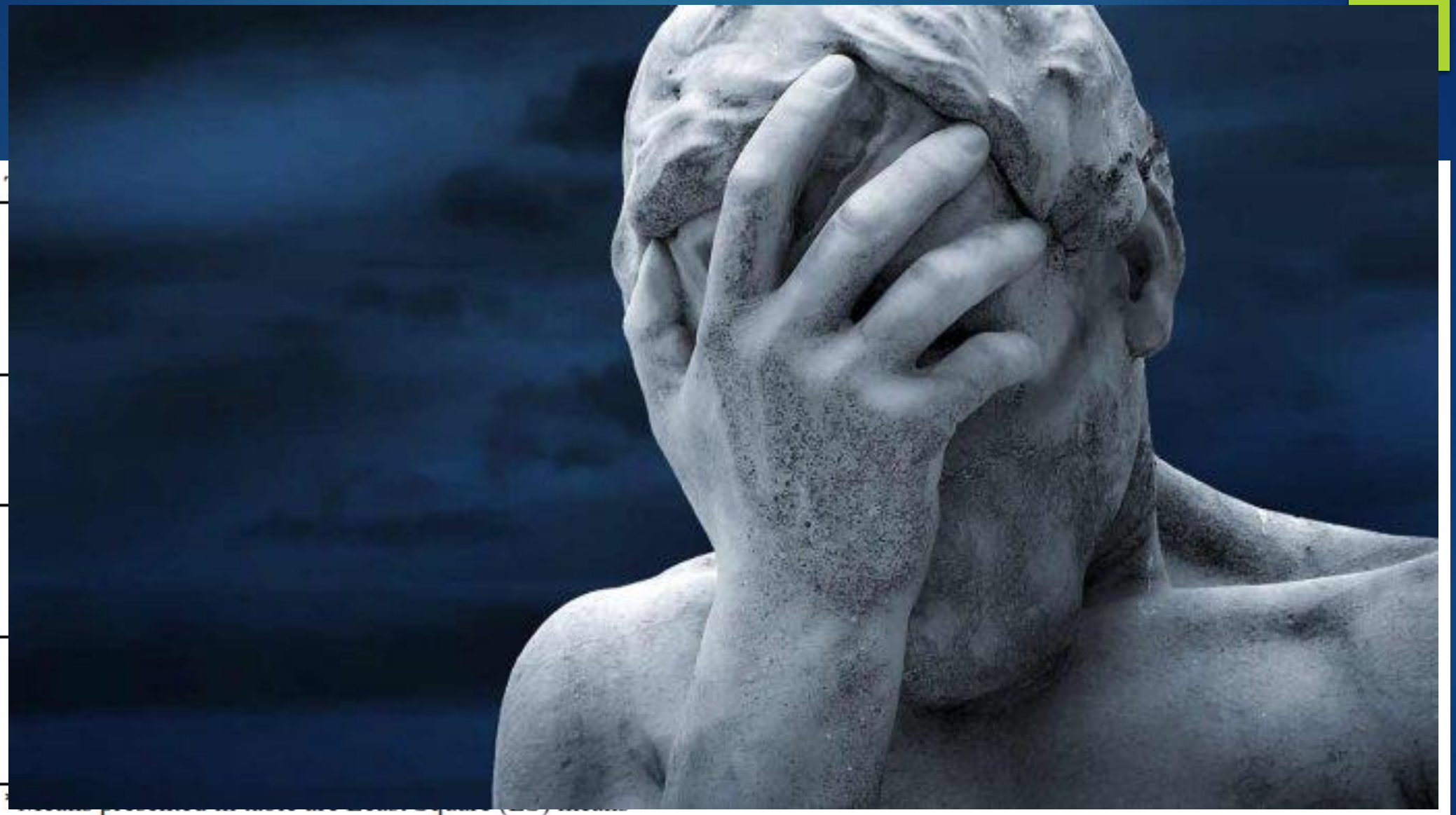


AKLIEF PACKAGE INSERT

VEHICLE MATTERS

TRIFAROTENE

Table 2. Application Site Tolerability Reactions at Any Post Baseline Visit

Face	AKLIEF N=1214 Maximum Severity during Treatment			Vehicle Cream N= 1194 Maximum Severity during Treatment		
	Mild	Moderate	Severe	Mild	Moderate	Severe
Erythema 59%	30.6%	28.4%	6.2%	21%	6.8%	0.8%
Scaling 65%	37.5%	27.1%	4.9%	23.7%	5.9%	0.3%
Dryness 69%	39%	29.7%	4.8%	29.9%	6.8%	0.8%
Stinging/Bur 56%	35.6%	20.6%	5.9%	15.9%	3.8%	0.5%
Trunk	**N=1202**			**N=1185**		
Erythema	26.5%	18.9%	5.2%	12.7%	4.4%	0.4%
Scaling	29.7%	13.7%	1.7%	13.2%	2.6%	0.1%
Dryness	32.9%	16.1%	1.8%	17.8%	3.9%	0.1%
Stinging/Burning	26.1%	10.9%	4.3%	9.2%	2.2%	0.5%

AKLIEF PACKAGE INSERT

TAZAROTENE FOAM

TAZAROTENE LOTION?

A Comparative Clinical Demonstration of the Spreadability of Tazarotene Lotion 0.045% versus Trifarotene Cream 0.005%

Zoe D Draelos, MD[1]; Emil A Tanghetti, MD[2]

[1]Dermatology Consulting Services, PLLC, High Point, North Carolina; [2]Center for Dermatology and Laser Surgery, Sacramento, CA

SYNOPSIS

- The ability of a topical medication to spread is an important parameter, since only the thinnest layer of medication contacting the skin is physiologically active
- A thinner film is just as effective as a thicker film from an efficacy standpoint, but a thinner film will spread farther—exhibiting superior spreadability and increasing the number of applications while decreasing the cost per application
- From a rheological perspective, products exhibiting low yield stress and lower intrinsic viscosity will have better spreadability and require less effort to spread at the surface of the skin[1,2]
  - Yield stress is the minimum force required to make a structured fluid flow
  - Viscosity describes a fluid's resistance to flow (eg, the "thickness" of a fluid)

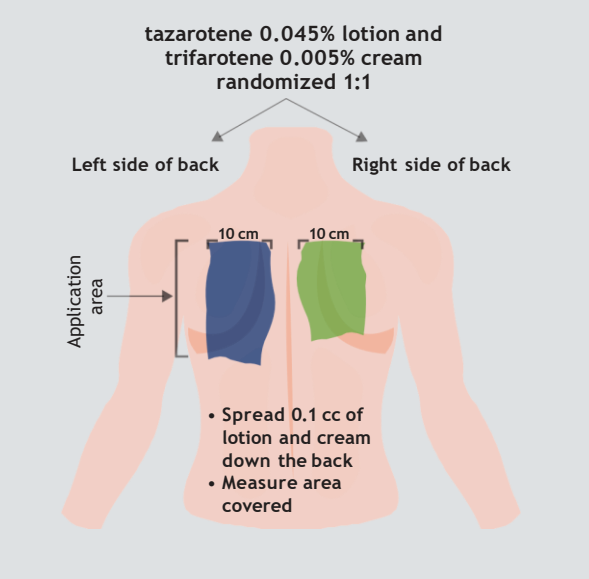
OBJECTIVE

- To compare the spreadability of two topical formulations: tazarotene 0.045% polymeric emulsion lotion versus trifarotene 0.005% cream
- To relate the rheological profile of topical products to their spreadability

METHODS

- This double-blind, split-body study enrolled male or female adults ≥18 years of age with normal back skin
  - Participants, who provided written informed consent, were assessed for limited back hair which would prevent application of the study products
- Tazarotene 0.045% lotion was applied to one randomized half of the back and trifarotene 0.005% cream was applied to the opposite randomized half of the back (**Figure 1**)
  - The back was divided at the vertebral column into right and left
  - Drugs were randomized for right or left application; however, the left back product was always pigmented blue and the right back product was always pigmented green. One toothpick tip of blue or green food-coloring gel was used to pigment the drugs
- The blinded dermatologist investigator was presented with 0.1 cc (0.1 mL) of each of the drugs for application by the unblinded coordinator
- Two 10 cm wide application areas were marked with a gentian violet marker, one on each side of the back; this mark defined the lateral bounds over which the lotion or cream were spread
- The investigator applied the products with a gloved hand to obtain an even film, moving study product down the back until it would no longer spread
- The lower extent of the study product application was marked with a gentian violet marker and measured in centimeters
- A two-tailed Student's t-test was used to assess the spreadability data

FIGURE 1. Study Schematic



RESULTS

- A total of 30 participants were included in the study
- Participants ranged from 18 to 59 years of age; 26 (87%) were female
- Tazarotene 0.045% lotion spread over an average area measuring 10 cm x 16.70 cm (167.0 cm^2) while the trifarotene 0.005% cream spread over an average area measuring 10 cm x 13.03 cm (130.3 cm^2; $P<0.001$; **Figure 2**)
- No adverse reactions or adverse events occurred during the conduct of the study

FIGURE 2. Mean Spreadability of Tazarotene 0.045% Lotion and Trifarotene 0.005% Cream (N=30)

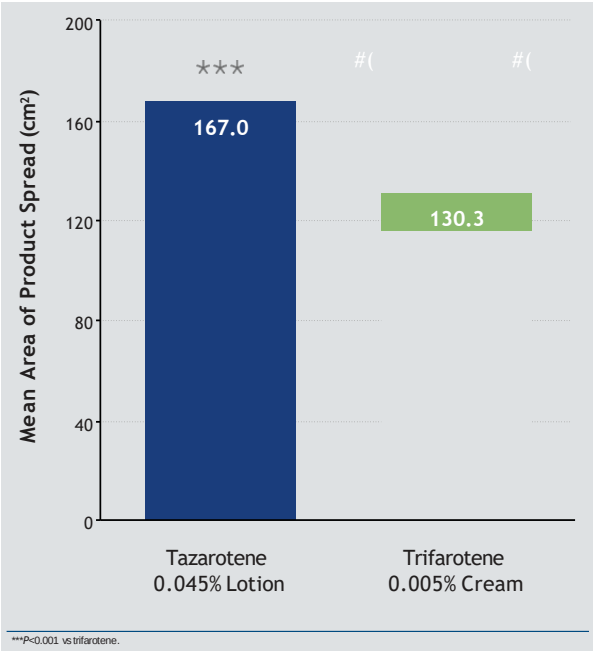
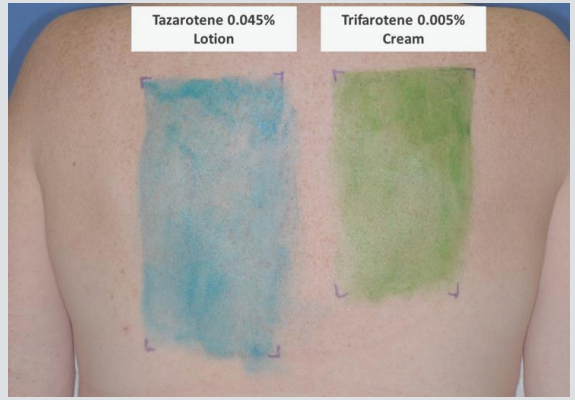


FIGURE 3. Spreadability of Tazarotene 0.045% Lotion and Trifarotene 0.005% Cream on a Participant



CONCLUSIONS

- The tazarotene 0.045% lotion spread on average 36.7 square centimeters farther than the trifarotene 0.005% cream
- These results are supported by the differences in the rheological profiles of the two products, in which tazarotene lotion exhibits lower yield stress and lower intrinsic viscosity versus trifarotene cream[3]

REFERENCES

1. Adeyeye MC, et al. *AAPS PharmSciTech*. 2002;3(2):E8.
2. Kryscio DR, et al. *AAPS PharmSciTech*. 2008;9(1):84-86.
3. Data on File. Ortho Dermatologics.

AUTHOR DISCLOSURES

ZDD received funding from Ortho Dermatologics to conduct the research presented in this poster. EAT has served as speaker for Novartis, Ortho Dermatologics, Sun Pharmaceuticals, Lilly, Galderma, AbbVie, and Dermira; served as a consultant/clinical studies for Hologic, Ortho Dermatologics, and Galderma; and is a stockholder for Accure.

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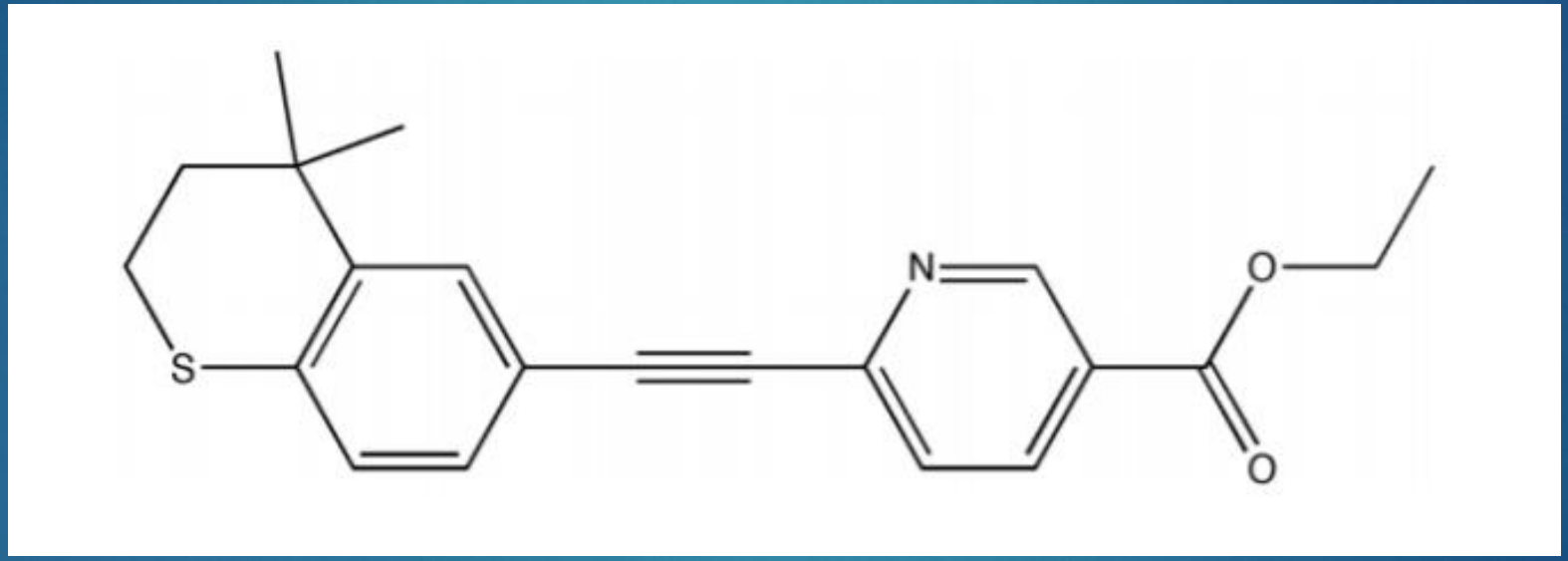
TAZAROTENE



VEHICLE MATTERS

TAZAROTENE 0.045% LOTION

Novel Polymeric Emulsion Lotion Formulation

1. Tazarotene encapsulated in oil droplets, with moisturizing ingredients (light mineral oil, diethyl sebacate)
2. Oil droplets uniformly dispersed within O/W emulsion & separated 3-dimensional mesh matrix or honeycomb-like structure
3. Humectant –sorbitol – dispersed in water phase
4. Mesh network allows the oil droplets and moisturizing components to spread uniformly onto the skin.
5. Mesh breaks upon contact with salts on the skin surface, depositing all the ingredients uniformly onto the skin.

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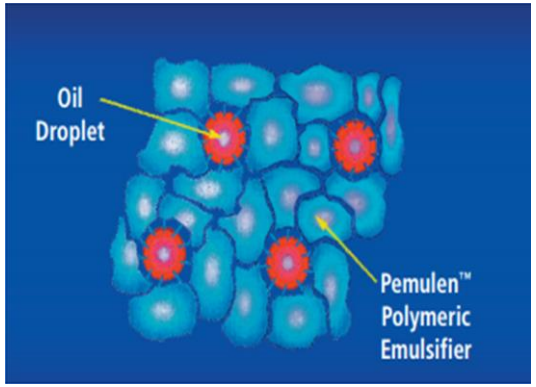
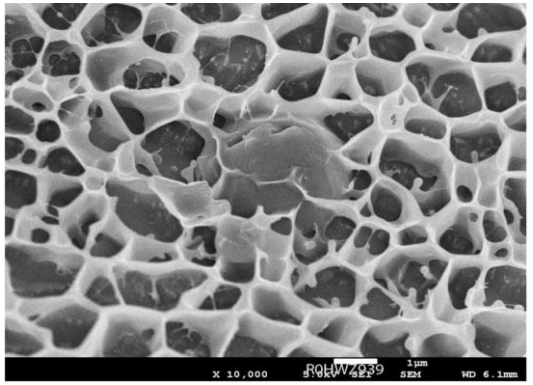




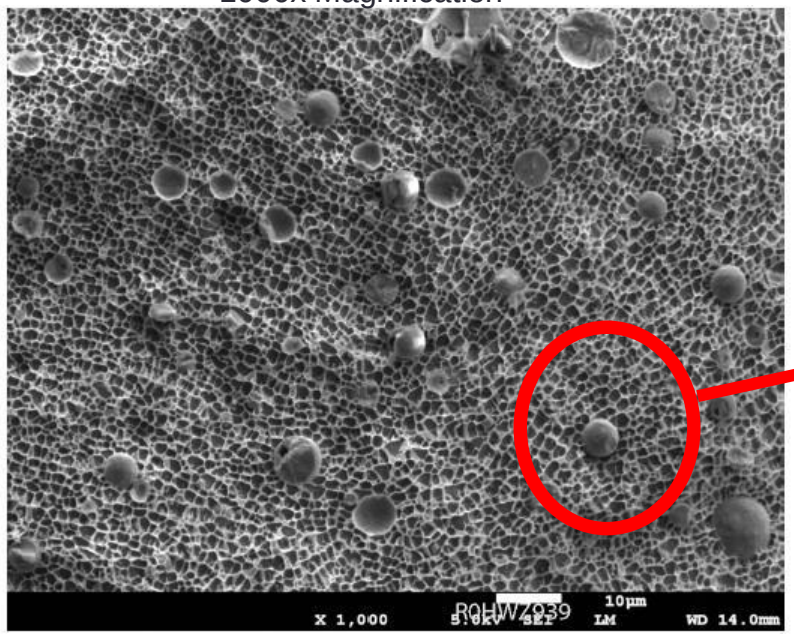
10,000X magnification of honeycomb mesh showing emulsion droplet

A More Efficient Delivery System for Active and Functional Excipients

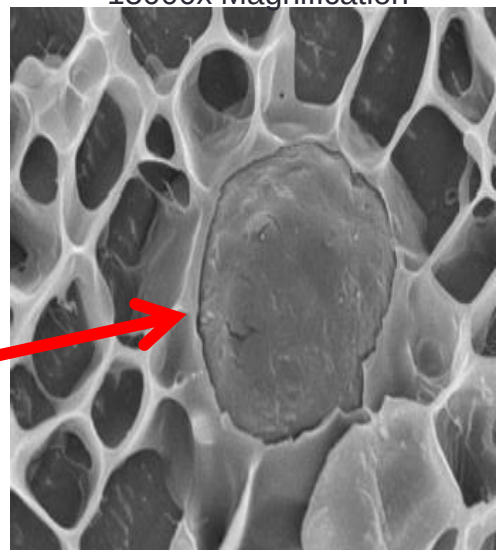
Vehicle formulation

Cryo Scanning Electron Microscopy

1000x Magnification



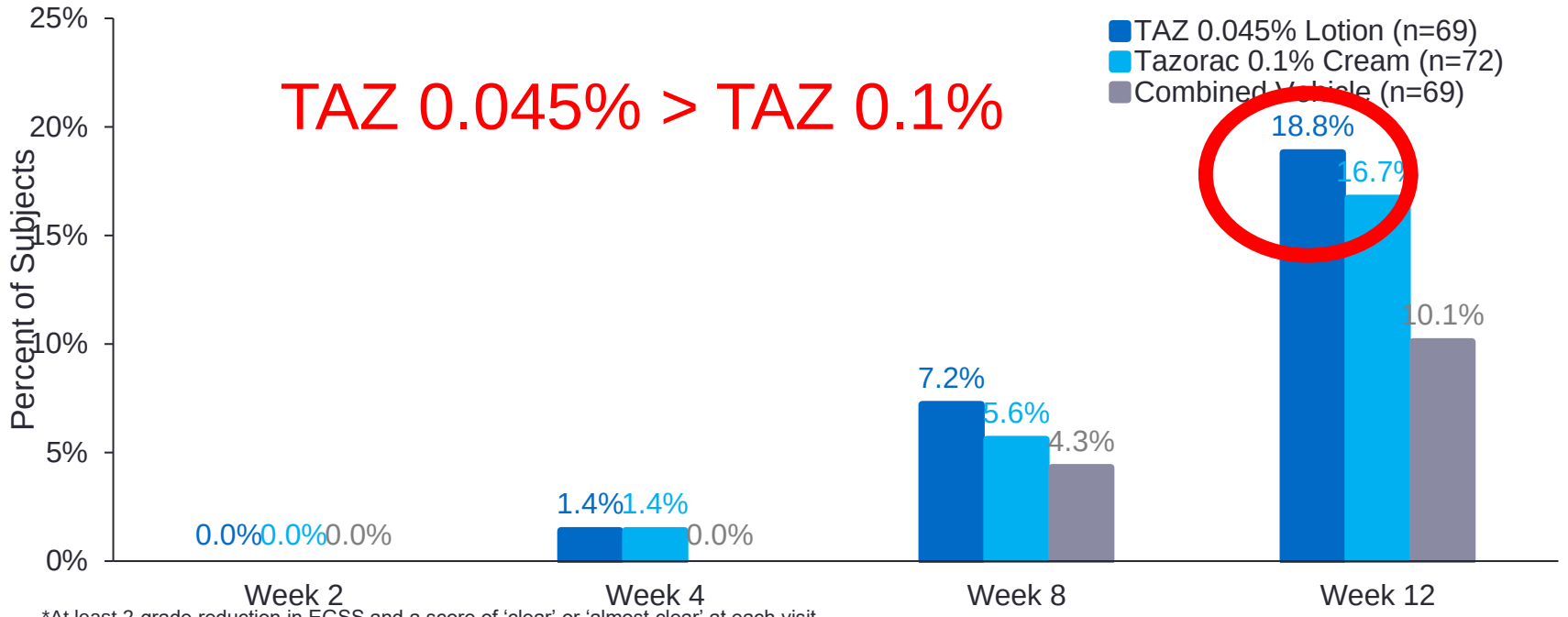
15000x Magnification



Tazarotene is solubilized within oil droplets

Data on file, Ortho Dermatologics

Percent of Subjects With Treatment Success



*At least 2-grade reduction in EGSS and a score of 'clear' or 'almost clear' at each visit.
EGSS, Evaluator's Global Severity Score; TAZ, tazarotene.

Phase 2 Safety Data

Treatment-Emergent and Related Adverse Events Through Week 12

	Tazarotene 0.045% Lotion (n=68)	Tazorac 0.1% Cream (n=71)	Combined Vehicle (n=67)
Subjects reporting any TEAE	**10 (14.7%)**	**19 (26.8%)**	**9 (13.4%)**
Subjects reporting any SAE	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subjects who discontinued due to TEAE	0 (0.0%)	1 (1.4%)	0 (0.0%)
Severity of AEs reported			
Mild	6 (8.8%)	12 (16.9%)	9 (13.4%)
Moderate	2 (2.9%)	7 (9.9%)	0 (0.0%)
Severe	2 (2.9%)	0 (0.0%)	0 (0.0%)
Relationship to study drug			
Related	2 (2.9%)	4 (5.6%)	0 (0.0%)
Unrelated	8 (11.8%)	15 (21.1%)	9 (13.4%)
Treatment Related AEs reported by ≥1% subjects			
Application site pain	2 (2.9%)	3 (4.2%)	0.(0.0%)
Application site erythema	0 (0.0%)	1 (1.4%)	0 (0.0%)
Application site exfoliation	0 (0.0%)	1 (1.4%)	0 (0.0%)
Application site dryness	0 (0.0%)	1 (1.4%)	0 (0.0%)
Erythema	0 (0.0%)	1 (1.4%)	0 (0.0%)

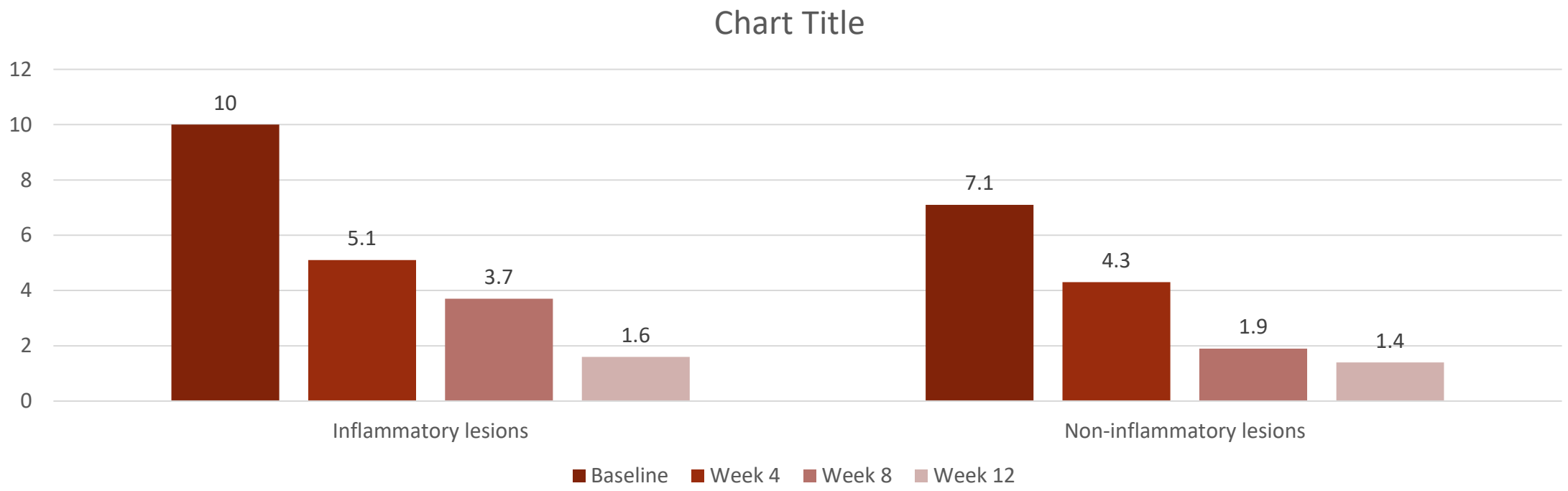
No deaths occurred in this study.
AE, adverse event; TEAE, treatment-emergent adverse event; SAE, serious [illegible] event.

Efficacy and Safety of Tazarotene lotion, 0.045% in the Treatment of Truncal Acne Vulgaris

IGA Scores

89% CLEAR/ALMOST CLEAR

Mean Lesion Counts



FMX101

FX2017-22 Results

Topical Minocycline Foam 4%
For Moderate-to-Severe Acne

Novel Patented Foam Technology

Would Enable First Topical Minocycline Product

Natural triglyceride-based foam technology

- Hydrophobic composition allows for stable and efficient delivery of inherently unstable active pharmaceutical ingredients (APIs) such as minocycline
- Free of primary irritants such as surfactants and short chain alcohols
- Unique physical foam characteristics
  - Foam structure maintained from dispensing to application
- Facilitates ease of application and absorption at target sites

First stable micronized topical minocycline formulation

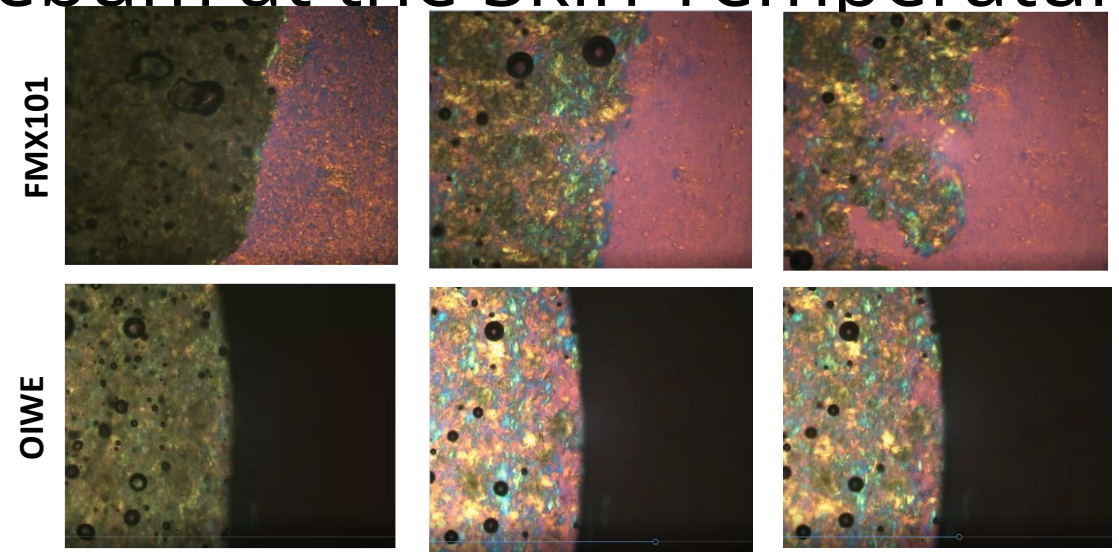
Epidermis and Dermis Distribution

- **For FMX101, it is estimated that, after a single application, the concentration of minocycline is[2]:**
  - 500 mcg/g in epidermis
  - 28 mcg/g in dermis
  - Greater than 100 mcg/g in the sebaceous appendage

Minocycline Concentration (mcg/g tissue) After 21 Oral Doses (n=4)[1]

Tissue	Day 0 Mean (min, max)	Day 8 Mean (min, max)	Day 21 Mean (min, max)
Epidermis (oral delivery)	0 (0, 0)	7.91 (3.02, 13.10)	3.74 (3.07, 4.17)
Dermis (oral delivery)	0 (0, 0)	2.98 (1.72, 3.84)	2.28 (1.79, 3.20)

Miscibility of Oil-Based FMX-101 Formulation With Sebum at the Skin Temperature (35°C)



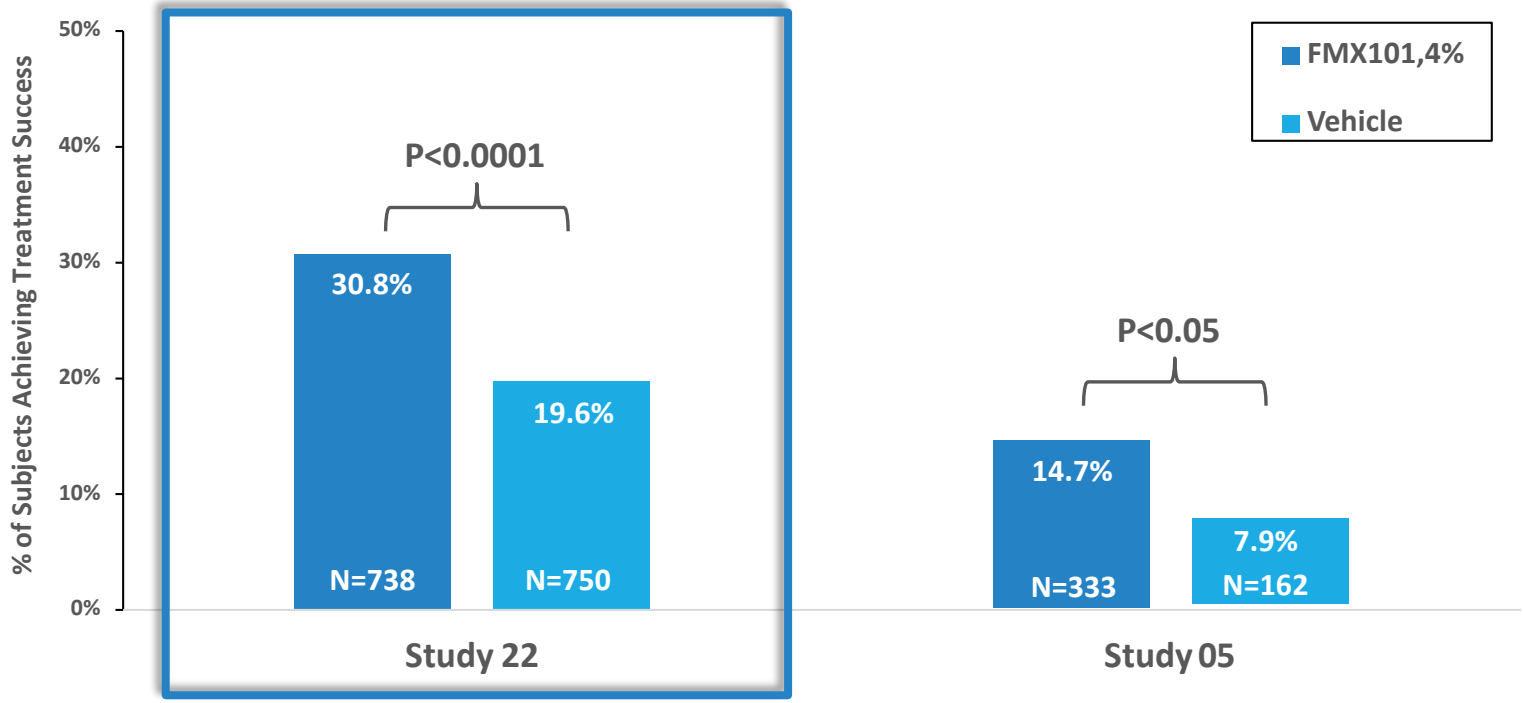
Sample of sebum (left) was placed side by side with sample of FMX101 vehicle or OIWE (right)– the photomicrographs were taken at 25°C before heating

Photomicrograph is taken at 35°C, heating at 2°C/min – immediately after reaching 35°C

Photomicrographs was taken after sample reached 35°C and held for 1 min at 35°C

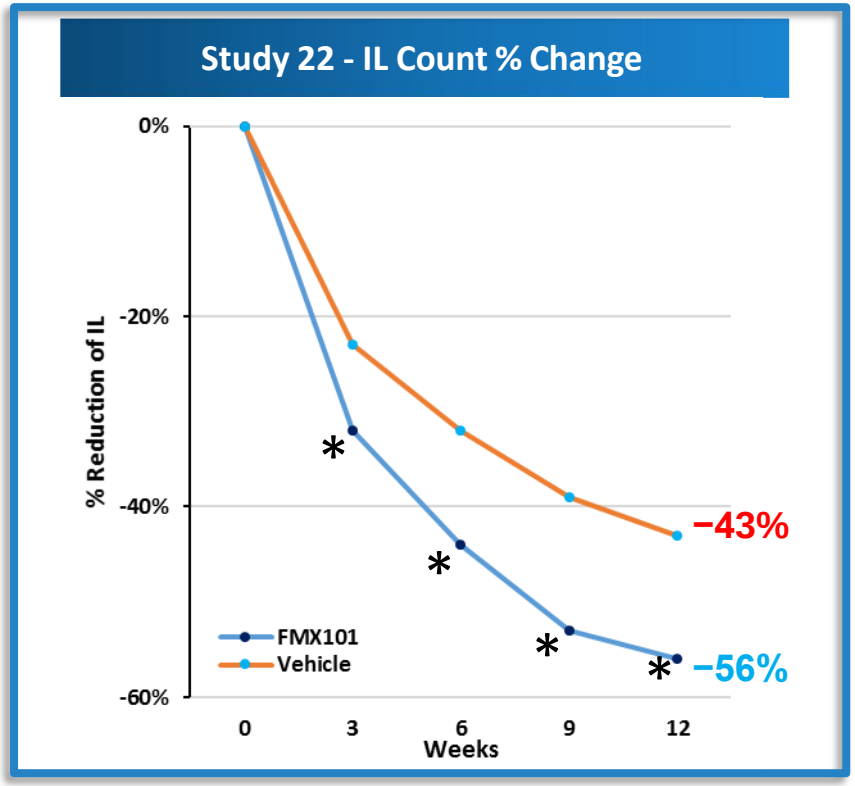
VEHICLE MATTERS

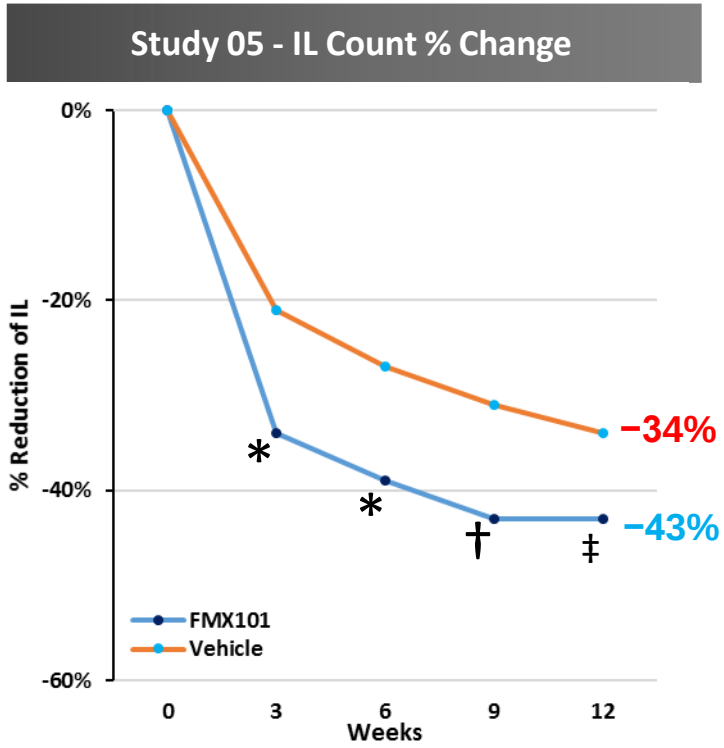
Co-primary endpoint:
IGA Treatment Success at Week 12 [Score Clear (0) or Almost Clear (1)]



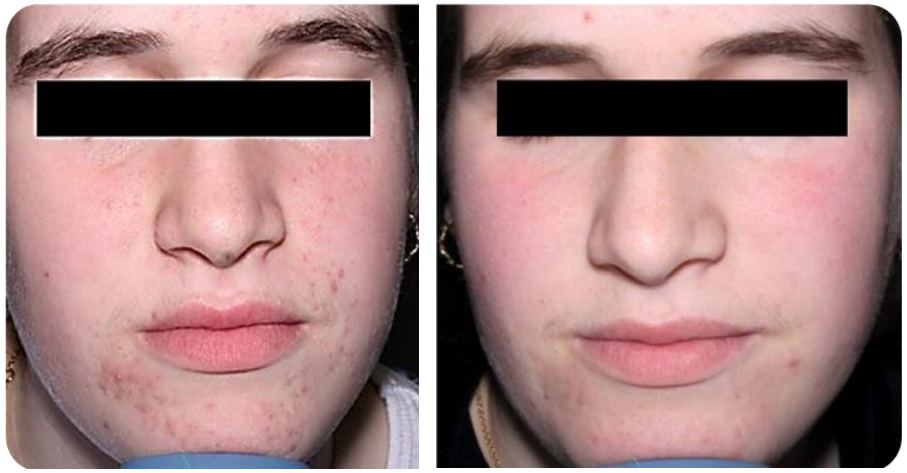
- **In Study 22, IGA Treatment Success for FMX101, 4% treatment group was 30.80% versus 19.63% in vehicle treatment group (p<0.0001)**
- **In Study 05, IGA Treatment Success for FMX101, 4% treatment group was 14.67% versus 7.89% in vehicle treatment group (p=0.0423)**
- In Study 22 including subject data from disqualified site (N=19), IGA Treatment Success for the FMX101, 4% treatment group (N=748) was 30.58% versus 19.41% in vehicle treatment group (N=759) (p<0.0001)

Key secondary endpoint:
Percent Change of Inflammatory Lesion Count at Weeks 3, 6, 9 & 12

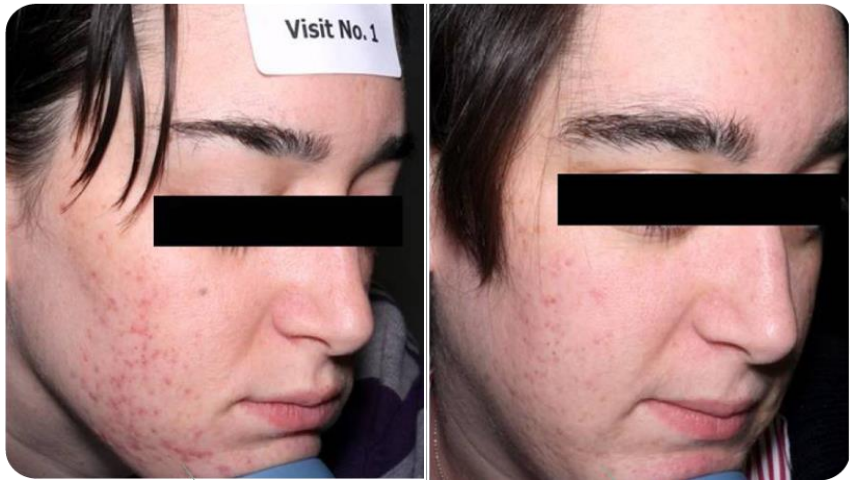




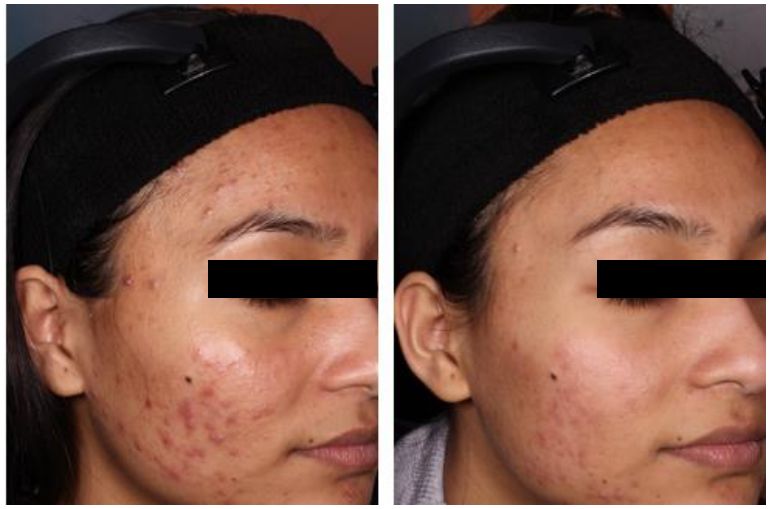
- In Study 22, percent change in inflammatory lesion count for the FMX101, 4% treatment group at week 12 was -56% versus -43% in vehicle ($p<0.0001$)
- In Study 05, percent change in inflammatory lesion count for the FMX101, 4% treatment group at week 12 was -43% versus -34% in vehicle ($p=0.0097$)
- Statistical significance demonstrated at all timepoints, beginning at Week 3, for both studies



Baseline 12 Weeks



Baseline 12 Weeks

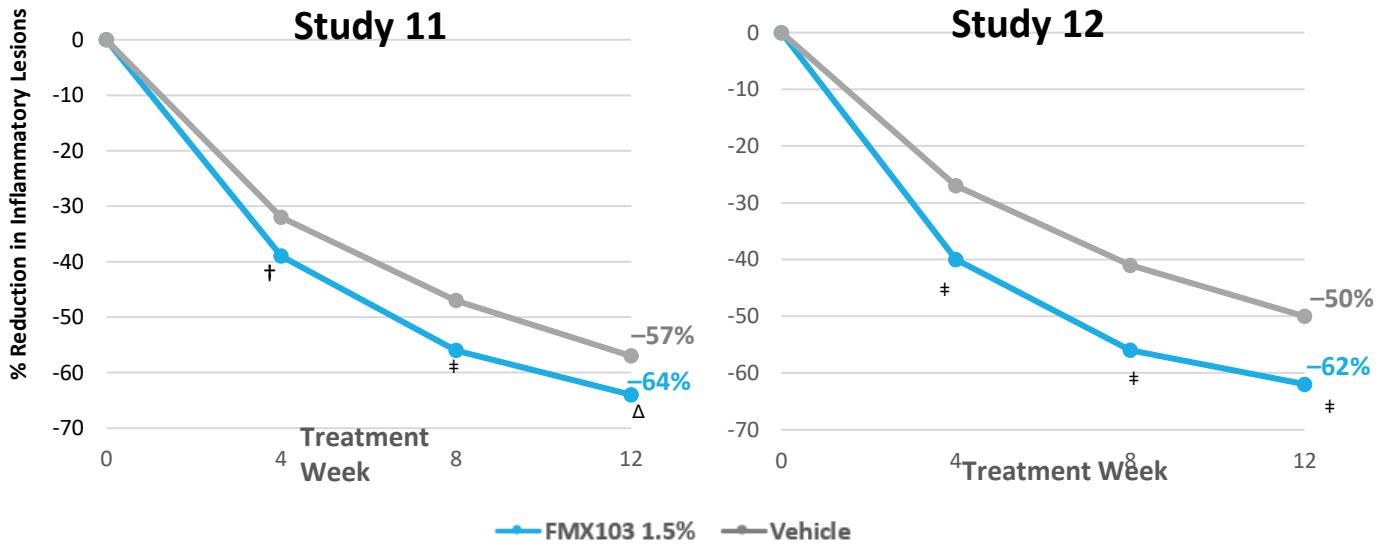


Baseline 12 Weeks

Baseline 12 Weeks

Percentage Change From Baseline to Week 12 in Inflammatory Lesions by Visit*

- Percentage reduction in inflammatory lesions was statistically significant for FMX103 1.5% at all visits in both studies – weeks 4, 8, and 12



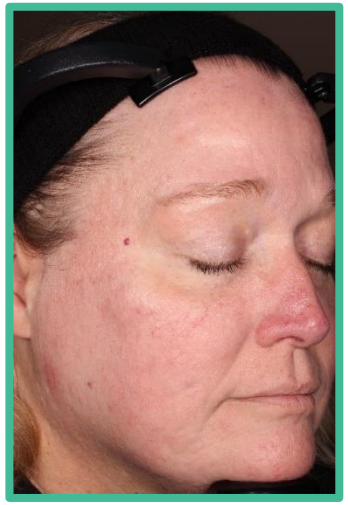
PHASE 3 ROSACEA STUDY

Phase 3 Rosacea Results

Baseline

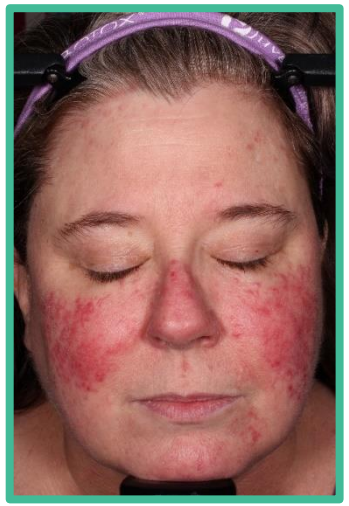
IGA=3

Week 12



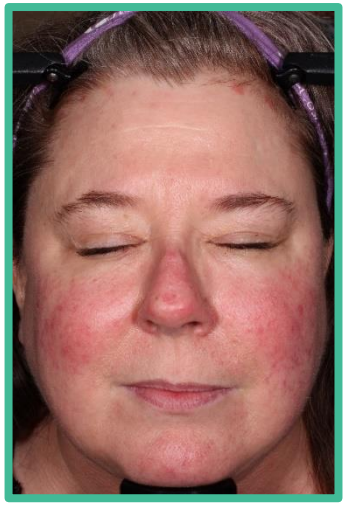
IGA=0

Baseline



IGA=3

Week 12



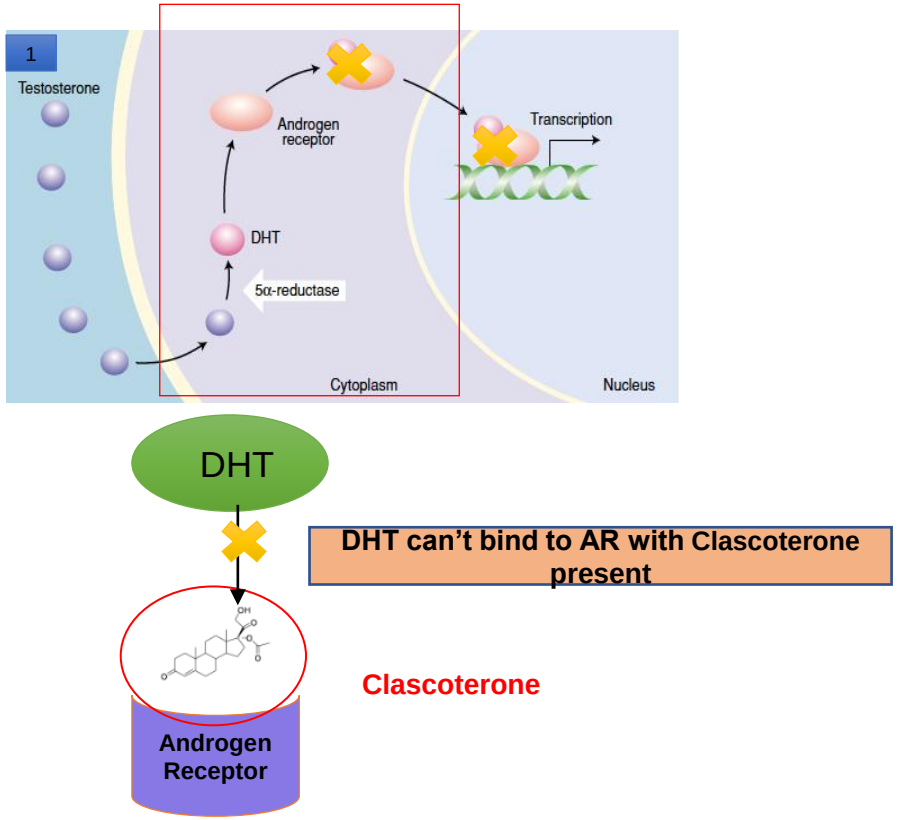
IGA=2

NEW CHEMICAL ENTITIES

Clascoterone exhibits strong, selective anti-androgen activity by targeting AR in the skin, not systemically

Clascoterone competes with DHT for binding to the AR

- AR/Clascoterone complex limits or blocks transcription of androgen responsive genes[2]
- Modification specific gene expression[2]
- Downstream impact on sebum & inflammation [2]



1. Figure from: Ellis JA. Expert Rev Mol Med. 2002; https://www.ncbi.nlm.nih.gov/pubmed/14585162
2. Data on File. CB-03-01 2017. Cassiopea SpA.

MY BALD HEAD

GAME CHANGER IN ACNE TREATMENT


DREAMS
COME TRUE

IDP-126 GEL
(0.15% ADAPALENE/1.2% CLINDAMYCIN PHOSPHATE/3.1% BPO)

FIRST TRIPLE COMBO

Efficacy and Safety of a Fixed-Dose Clindamycin Phosphate 1.2%, Benzoyl Peroxide 3.1%, and Adapalene 0.15% Gel for Moderate-to-Severe Acne: Randomized Phase 2 and Phase 3 Studies of the First Triple-Combination Drug

Linda Stein Gold, MD[1]; Leon H. Kircik, MD[2-4]; Emil A Tanghetti, MD[5]; Hilary Baldwin, MD[6,7]; Zoe D Draelos, MD[8]; Michael Gold, MD[9]; Edward Lain, MD, MBA[10]; David M. Pariser, MD[11,12]; Neil Sadick, MD[13,14]; Radhakrishnan Pillai, PhD[15]; Varsha Bhatt, PhD[15]

[1]Henry Ford Hospital, Detroit, MI; [2]Indiana University School of Medicine, Indianapolis, IN; [3]Physicians Skin Care, PLLC, Louisville, KY; [4]Icahn School of Medicine at Mount Sinai, New York, NY; [5]Center for Dermatology and Laser Surgery, Sacramento, CA; [6]The Acne Treatment and Research Center, Brooklyn, NY; [7]Robert Wood Johnson University Hospital, New Brunswick, NJ; [8]Dermatology Consulting Services, PLLC, High Point, NC; [9]Tennessee Clinical Research Center, Nashville, TN; [10]Austin Institute for Clinical Research, Austin, TX; [11]Eastern Virginia Medical School, Norfolk, VA; [12]Virginia Clinical Research, Inc., Norfolk, VA; [13]Department of Dermatology, Weill Cornell Medical College, New York, NY; [14]Sadick Dermatology, New York, NY; [15]Bausch Health US, LLC, Petaluma, CA. **Bausch Health US, LLC is an affiliate of Bausch Health Companies Inc. Ortho Dermatologics is a division of Bausch Health US, LLC.*

LSG has served as investigator/consultant or speaker for Ortho Dermatologics, LEO Pharma, Dermavant, Incyte, Novartis, AbbVie, Pfizer, Sun Pharma, UCB, Arcutis and Lilly. LHK has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. EAT has served as speaker for Novartis, Ortho Dermatologics, Sun Pharma, Lilly, Galderma, AbbVie, and Dermira; served as a consultant/clinical studies for Hologic, Ortho Dermatologics, and Galderma; and is a stockholder for Accure. HB has served as advisor, investigator, and on speakers' bureaus for Almirall, Cassiopea, Foamix, Galderma, Ortho Dermatologics, Sol Gel, and Sun Pharma. ZDD has received funding from Ortho Dermatologics. MG has acted as an investigator, advisor, speaker, and consultant for Ortho Dermatologics. EL has nothing to disclose. DMP has served as consultant to Atacama Therapeutics, Bickel Biotechnology, Biofrontera AG, Celgene, Dermira, LEO Pharma, Regeneron, Sanofi, TDM SurgiTech, TheraVida, and Ortho Dermatologics; investigator for Abbott Laboratories, Almirall, Amgen, AOBiome, Asana Biosciences, Bickel Biotechnology, Celgene, Dermavant, Dermira, Eli Lilly, LEO Pharma, Menlo Therapeutics, Merck & Co., Novartis, Novo Nordisk A/S, Ortho Dermatologics, Pfizer, Regeneron, and Stiefel; on advisory board for Pfizer; and on the data monitoring board for BMS. NS has served on advisory boards, as a consultant, investigator, speaker, and/or other and has received honoraria and/or grants/research funding from Almirall, Actavis, Allergan, Anacor Pharmaceuticals, Auxilium Pharmaceuticals, Bausch Health, Bayer, Biorasi, BTG, Carma Laboratories, Cassiopea, Celgene Corporation, Cutera, Cynosure, DUSA Pharmaceuticals, Eclipse Medical, Eli Lilly and Company, Endo International, EndyMed Medical, Ferndale Laboratories, Galderma, Gerson Lehrman Group, Hydropeptide, Merz Aesthetics, Neostrata, Novartis, Nutraceutical Wellness, Palomar Medical Technologies, Prescriber's Choice, Regeneron, Roche Laboratories, Samumed, Solta Medical, Storz Medical AG, Suneva Medical, Vanda Pharmaceuticals, and Venus Concept. RP and VB are an employees of Bausch Health US, LLC and may hold stock and/or stock options in its parent company.

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Background/Rationale

- A three-pronged approach to acne treatment—combining an antibiotic, antibacterial, and retinoid—may provide greater efficacy and tolerability than single/double treatments while potentially reducing antibiotic resistance and increasing compliance[1-3]
- Clindamycin phosphate 1.2%/BPO 3.1%/adapalene 0.15% (IDP-126) gel, once approved, will be the first triple-combination, fixed-dose topical acne product that addresses the major pathophysiological abnormalities in patients with acne

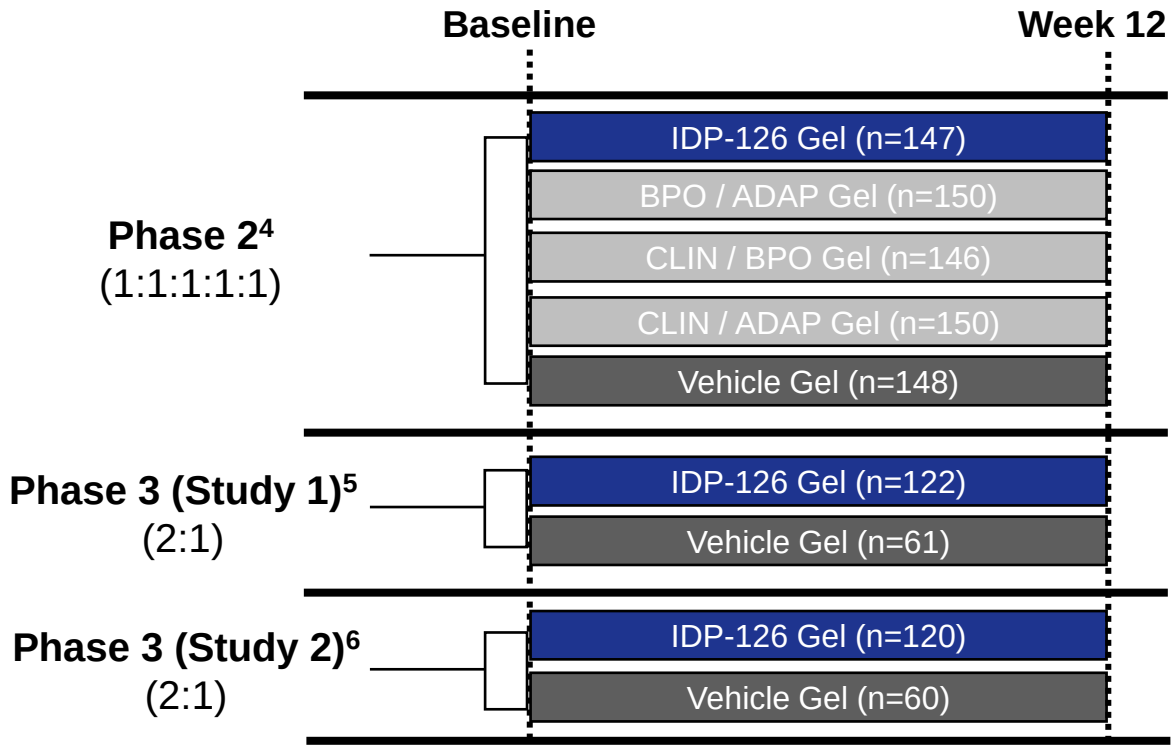
Objectives

- To evaluate efficacy, adverse events, and tolerability of once-daily IDP-126 gel in one phase 2 and two phase 3 studies of patients with moderate-to-severe acne

Eligibility

- Aged ≥9 years and EGSS = 3 (moderate) or 4 (severe)
- Inflammatory lesion counts: 30–100
- Noninflammatory lesion counts: 35–150

Study Designs



N values shown for randomized populations

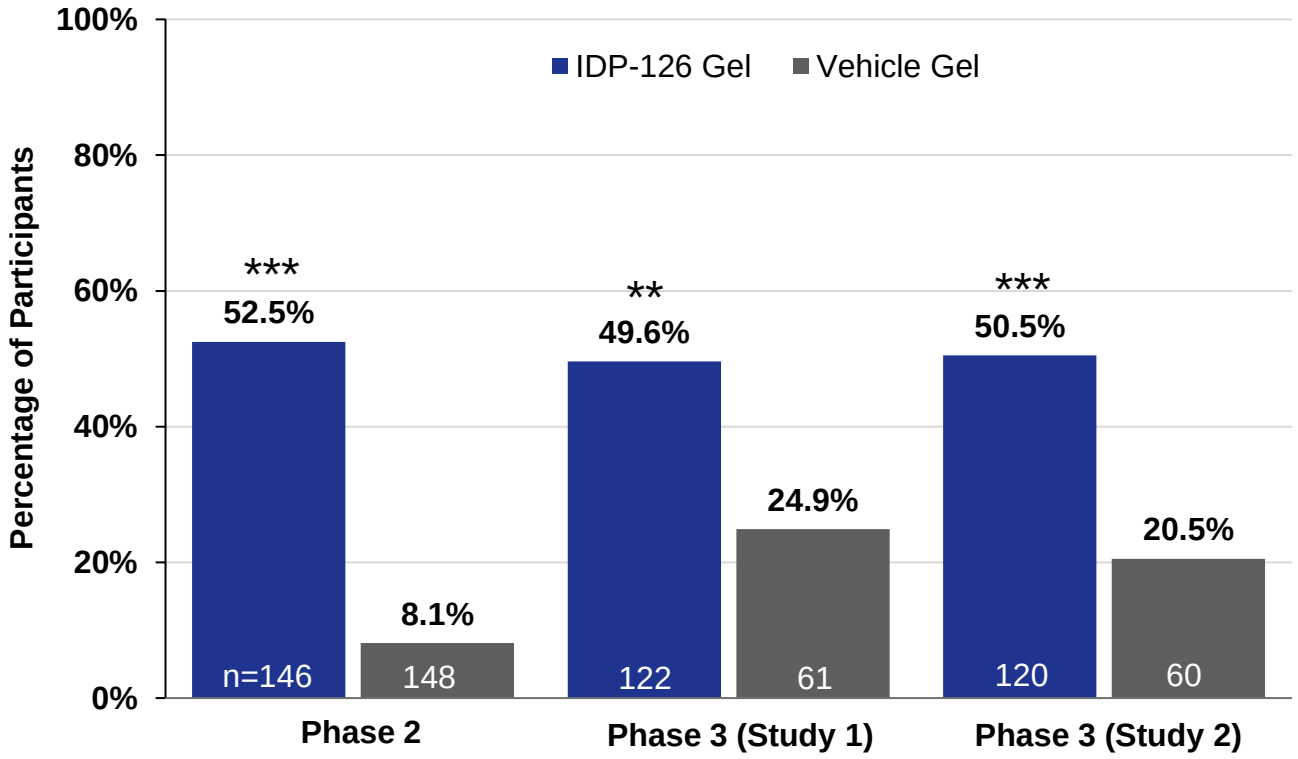
Baseline Demographics/Characteristics

- Mean age ranged from 19.2–21.4 years across all studies
- The majority were female, White, and non-Hispanic, with EGSS=3 (moderate)

ADAP, adapalene 0.15%; BPO, benzoyl peroxide 3.1%; CLIN, clindamycin phosphate 1.2%; EGSS, Evaluator's Global Severity Score.

1. Zaenglein, A.L., et al., *J Am Acad Dermatol*. 2016;74(5):945-73. 2. Kirck, L. *J Clin Aesthet Dermatol*. 2011;4(11):30-3. 3. Leyden, J.L., et al. *Cutis*. 2008;82(6):417-21. 4. Stein Gold, L., et al. *Am J Clin Dermatol*. 2021; doi: 10.1007/s40257-021-00650-3. 5. Clinical Study Comparing the Efficacy and Safety of IDP-126 Gel in the Treatment of Acne Vulgaris (NCT04214639). https://clinicaltrials.gov/ct2/show/NCT04214639. 6. Clinical Study Comparing the Efficacy and Safety of IDP-126 Gel in the Treatment of Acne Vulgaris (NCT04214652). https://clinicaltrials.gov/ct2/show/NCT04214652.

Treatment Success[a] at Week 12 with IDP-126



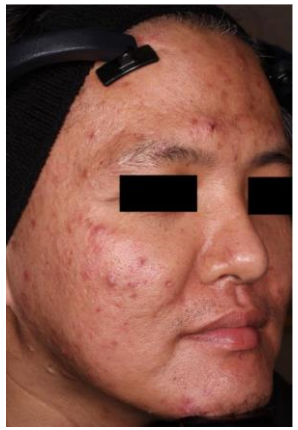
About half of participants achieved treatment success with IDP-126

**P<0.01; ***P≤0.001 versus vehicle.
[a]Defined as percentage of participants achieving ≥2-grade reduction from baseline in Evaluator's Global Severity Score and a score of 0 (clear) or 1 (almost clear).
Values have been adjusted for multiple imputation. Data shown for intent-to-treat populations.
IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel.

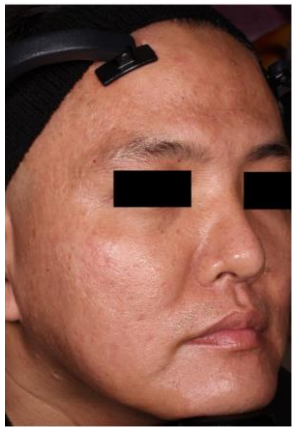
Improvements with IDP-126

44-Year-Old Male – Asian/Non-Hispanic

Baseline: EGSS 3 (moderate)
IL: 48; NIL: 49

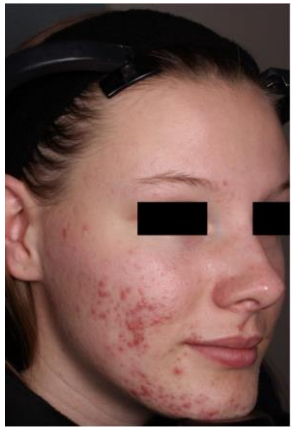


Week 12: EGSS 0 (clear)
IL: 0 (-100%); NIL: 2 (-96%)

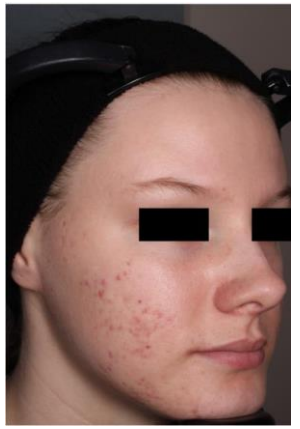


18-Year-Old Female – White/Non-Hispanic

Baseline: EGSS 3 (moderate)
IL: 40; NIL: 69

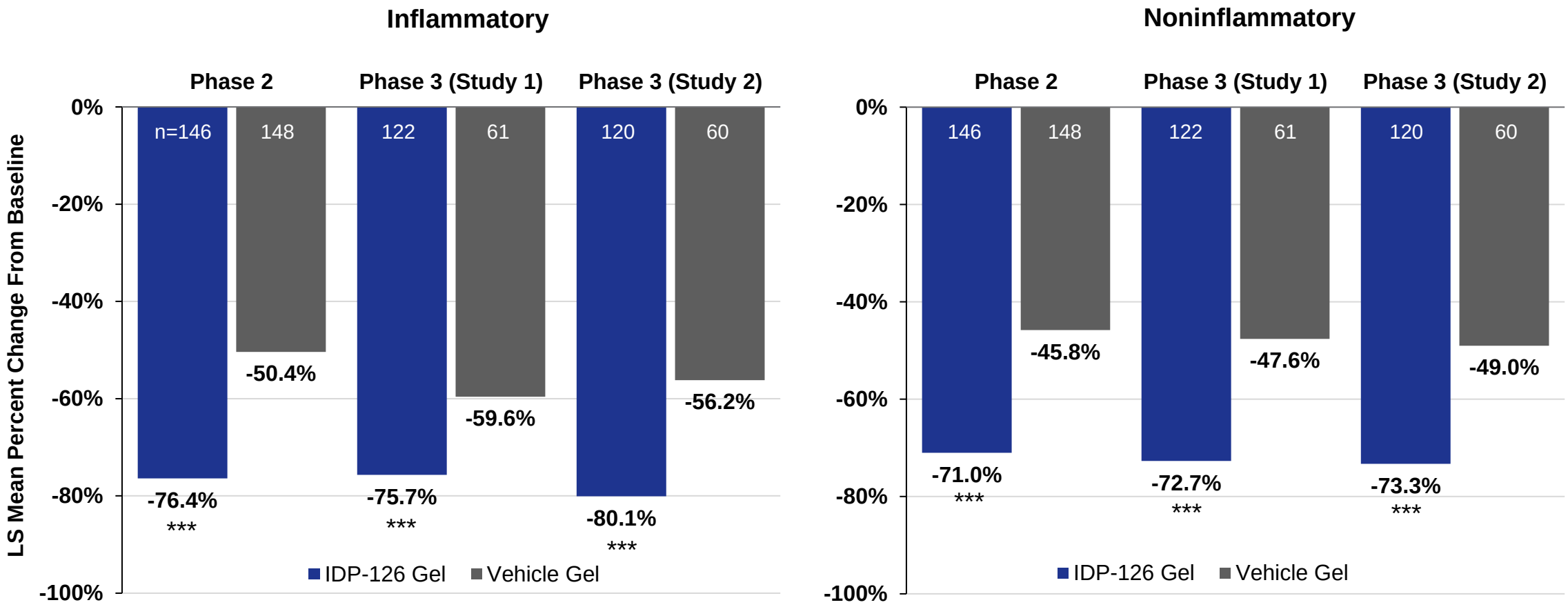


Week 12: EGSS 1 (almost clear)
IL: 3 (-93%); NIL: 9 (-87%)



EGSS, Evaluator's Global Severity Score; IL, inflammatory lesions; NIL, noninflammatory lesions.

IDP-126 Reduced Inflammatory and Noninflammatory Lesions at Week 12



IDP-126 resulted in **over 70% reductions** of inflammatory and noninflammatory lesions

****P*<0.001 vs vehicle.
Values have been adjusted for multiple imputation. Data shown for intent-to-treat populations.
IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel; LS, least-squares.

IDP-126 Was Well Tolerated

- Most TEAEs were of mild-moderate severity
- Less than 4% of participants discontinued studies/ treatment due to AEs
- Cutaneous safety/tolerability mean scores were <1 (mild)

n (%)	Phase 2		Phase 3			
			Study 1		Study 2	
	IDP-126 (n=141)	VEH (n=146)	IDP-126 (n=122)	VEH (n=61)	IDP-126 (n=120)	VEH (n=60)
TEAEs	51 (36.2)	22 (15.1)	30 (24.6)	5 (8.2)	36 (30.0)	5 (8.3)
Related	28 (19.9)	2 (1.4)	22 (18.0)	0	26 (21.7)	2 (3.3)
Not related	23 (16.3)	20 (13.7)	8 (6.6)	5 (8.2)	10 (8.3)	3 (5.0)
Serious AEs[a]	1 (0.7)	0	0	0	0	0
Discontinued drug or study due to AE	4 (2.8)	2 (1.4)	3 (2.5)	0	4 (3.3)	0
Most common treatment-related TEAEs (≥3% participants in any treatment)						
AS pain	11 (7.8)	1 (0.7)	13 (10.7)	0	18 (15.0)	1 (1.7)
AS dryness	9 (6.4)	0	2 (1.6)	0	5 (4.2)	0
AS exfoliation	5 (3.5)	1 (0.7)	4 (3.3)	0	0	0
AS irritation	3 (2.1)	0	1 (0.8)	0	4 (3.3)	0
Erythema	1 (0.7)	0	6 (4.9)	0	0	0

CONCLUSIONS

- In all three studies at week 12, **about half of participants achieved treatment success** with IDP-126 versus less than one-fourth with vehicle
- IDP-126 resulted in **over 70% reductions of inflammatory and noninflammatory lesions** at week 12
- IDP-126 was **well tolerated**, with most TEAEs of mild-moderate severity
- The innovative fixed-dose, triple-combination IDP-126 gel was efficacious and well tolerated in 3 clinical studies including children, adolescents, and adults with moderate-to-severe acne
- To our knowledge, acne improvements with IDP-126 were greater than any FDA-approved topical acne treatment, though patient populations may differ across studies

[a]No serious AEs were considered related to treatment.
Data shown for safety populations.
AE, adverse event; AS, application site; IDP-126, clindamycin phosphate 1.2%/benzoyl peroxide 3.1%/adapalene 0.15% gel; TEAE, treatment-emergent adverse event; VEH, vehicle.

GAME CHANGER IN ACNE TREATMENT

OLDIE

BUT

GOODIE

Isotretinoin LD Capsules: The Only Micronized Isotretinoin[1-3]

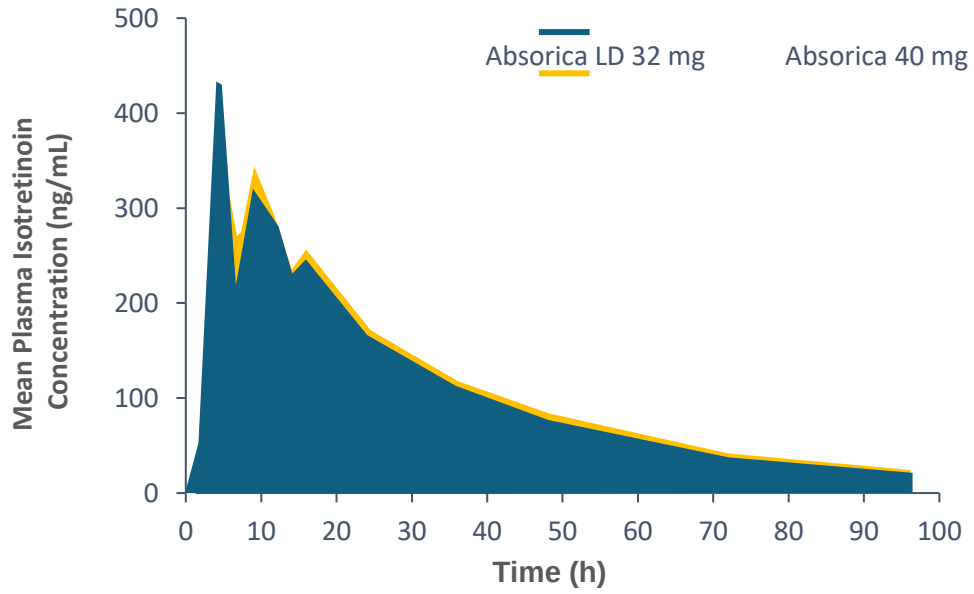
Maximized Absorption in Low-Dose Formulation

- Physical process of reducing drug particles to micrometer size[2]
- Micronization of isotretinoin substantially increases surface area per particle compared to other isotretinoin formulations[3-5]
- Micronization increases the rate of drug dissolution[2,4,5]
- Isotretinoin LD demonstrates twice the plasma levels of isotretinoin compared with Isotretinoin (isotretinoin) capsules in a fasted state[3]

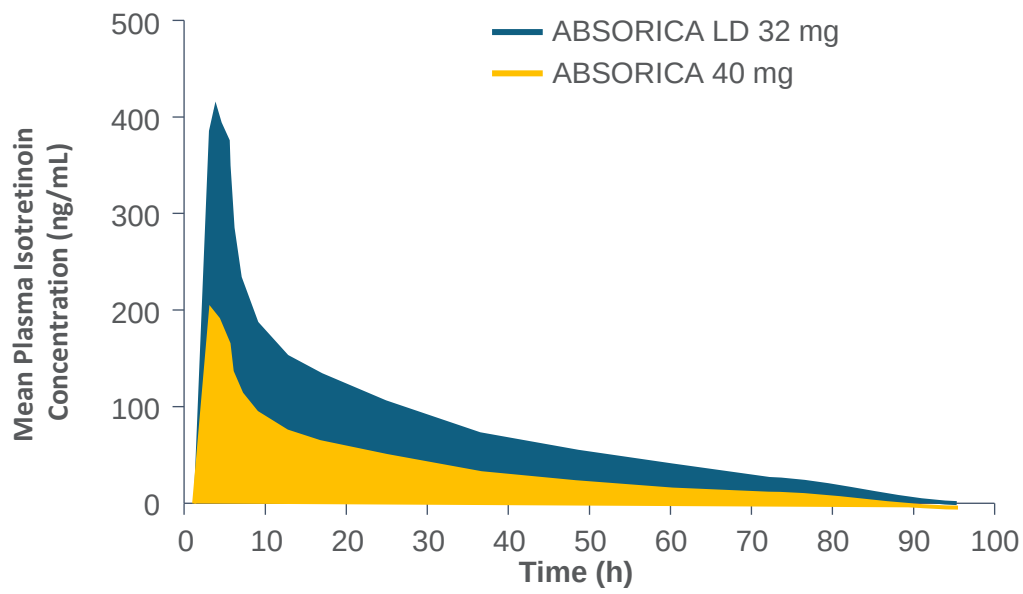
1. ABSORICA/ABSORICA LD [prescribing information]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc; 2019. 2. Madan HK, et al, inventors; Sun Pharmaceutical Industries Limited, assignee. Low dose oral pharmaceutical composition of isotretinoin. US patent 9,750,711. September 5, 2017. 3. Madan S, et al. Poster presented at: 7th Annual Maui Derm NP+PA Summer Meeting; June 19-22, 2019; Colorado Springs, CO. 4. Choudhary S, et al. *Front Pharmacol*. 2017;8:261. 5. Blagden N, et al. *Adv Drug Deliv Rev*. 2007;59(7):617-630. 5.

Isotretinoin LD Capsules 32 mg Deliver 2 Times More Isotretinoin Than Isotretinoin Capsules 40 mg in the Absence of Food

Fed State



Fasting State



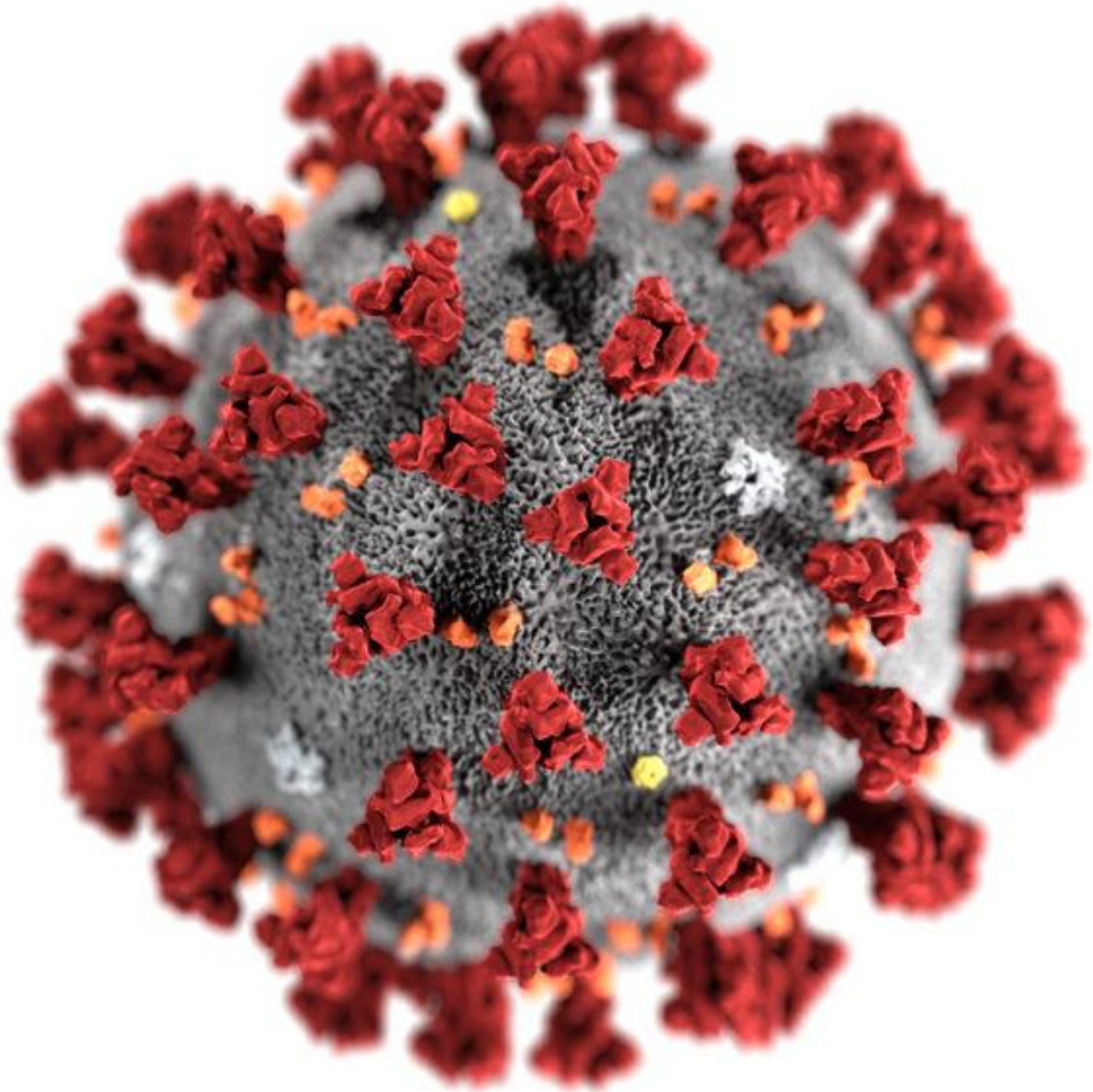
Human Microbiome Project[1]

1. The NIH HMP Working Group et al. Genome Res. 2009;19:2317-2323

On the horizon…

EMERGING THERAPIES

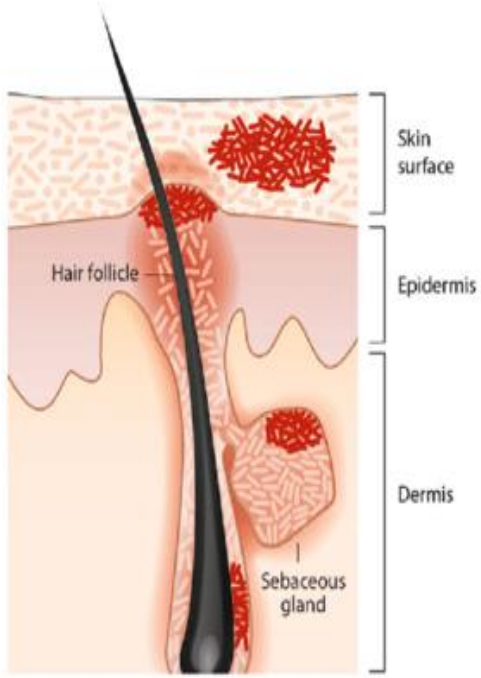
BREAKING NEWS!!!!



Biofilm Also Reduces the Effect of Antibiotics

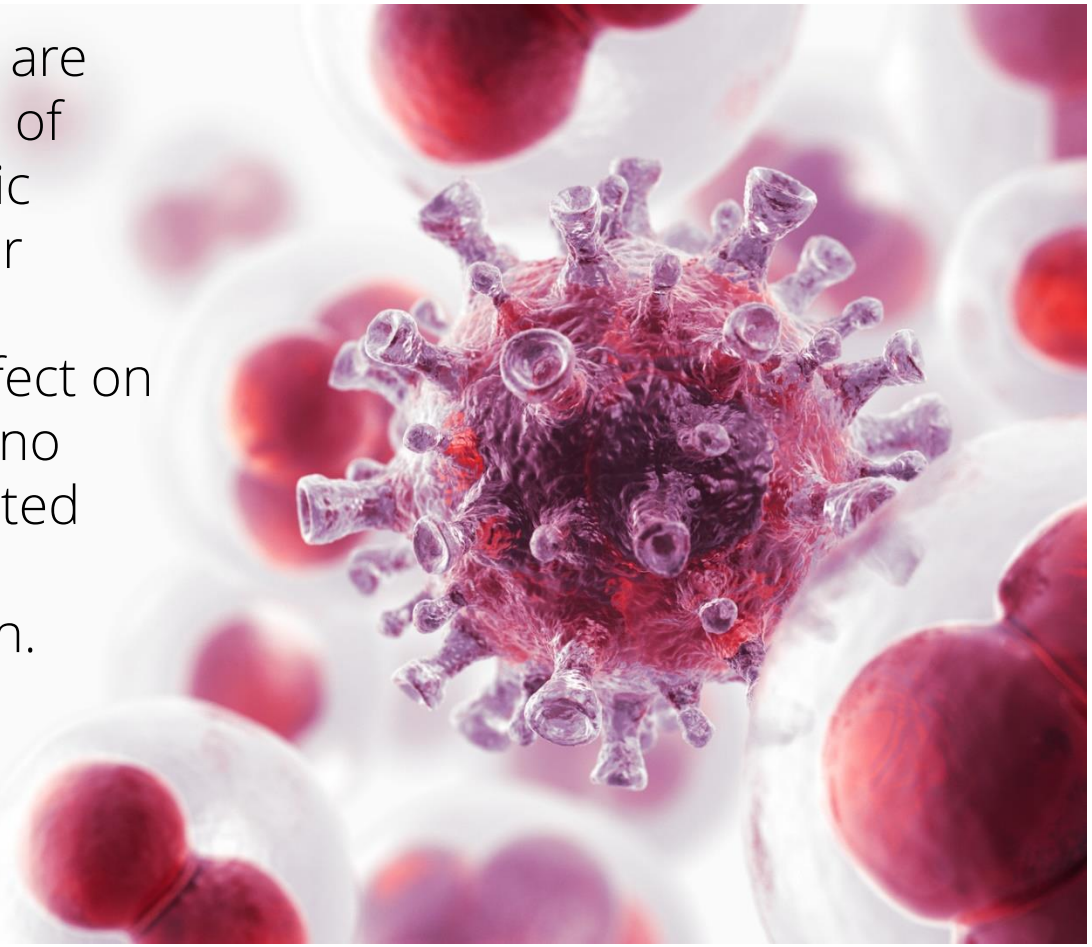
- *C. acnes* on skin form a polysaccharide protective mesh, named biofilm
- Biofilm prevents antibiotics effect– a physical barrier to effective penetration
- In the last decade biofilm has been shown also to accumulate in the pilosebaceous unit

Illustration of biofilm on skin surface and within pilosebaceous unit



Linfante et al. (2017), Journal of Clinical & Experimental Dermatology Research

Well-nested in the biofilm, the bacteria are mechanically protected from the effect of antimicrobials, maintain a low metabolic state, and express the ability to transfer antibiotic resistance genes. Many antimicrobials that have a profound effect on killing planktonic P. acnes have little or no effect on the sessile, biofilm-encapsulated microbes, requiring many months of antibiotics with little or no success seen.



Increased phage abundance in healthier skin

Greater phage abundance in healthy skin

A recent study published in Scientific Reports (34 healthy individuals, 38 acne patients)

- ✓ Increased phage abundance in healthy individuals
- ✓ Increased phage abundance in older individuals

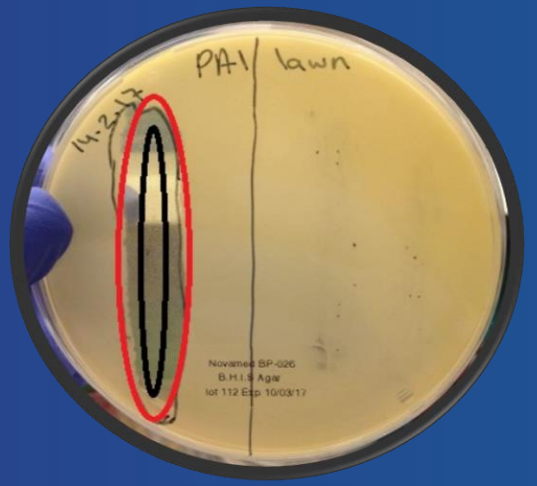
"Barnard, E., Shi, B., Kang, D., Craft, N., & Li, H. (2016). The balance of metagenomic elements shapes the skin microbiome in acne and health. Scientific Reports, 6, 39491"

BX001 – A novel natural product for acne prone skin

A topical gel with a proprietary phage cocktail to control P. acnes

- ✓ **Balances skin phage microbiome**
- ✓ **Targets causative bacteria**
- ✓ **Penetrates biofilm**
- ✓ **Active against antibiotic resistant bacteria**

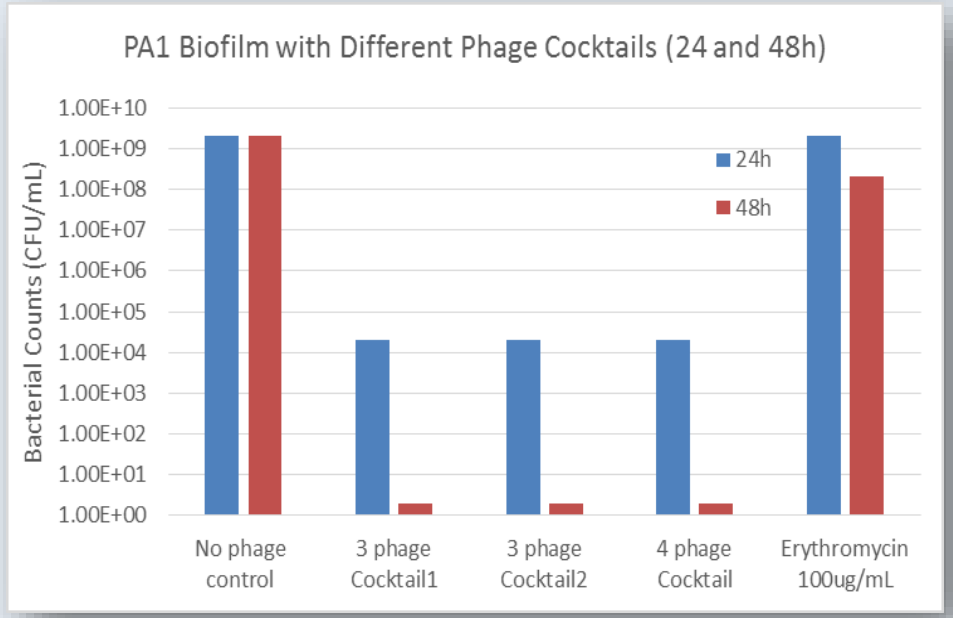
BX001 on a lawn of P. acnes



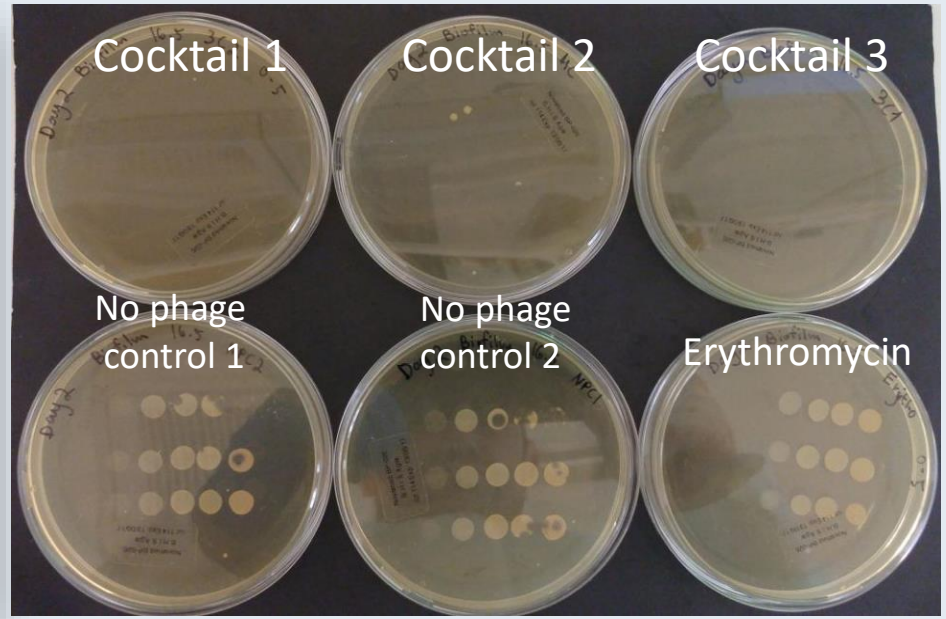
Black – Area BX001 gel applied
Red – Area of activity (eradication P.acnes)

BX001 penetrates biofilm

Results – Bacteria counts



Results – 48 hours after phage treatment



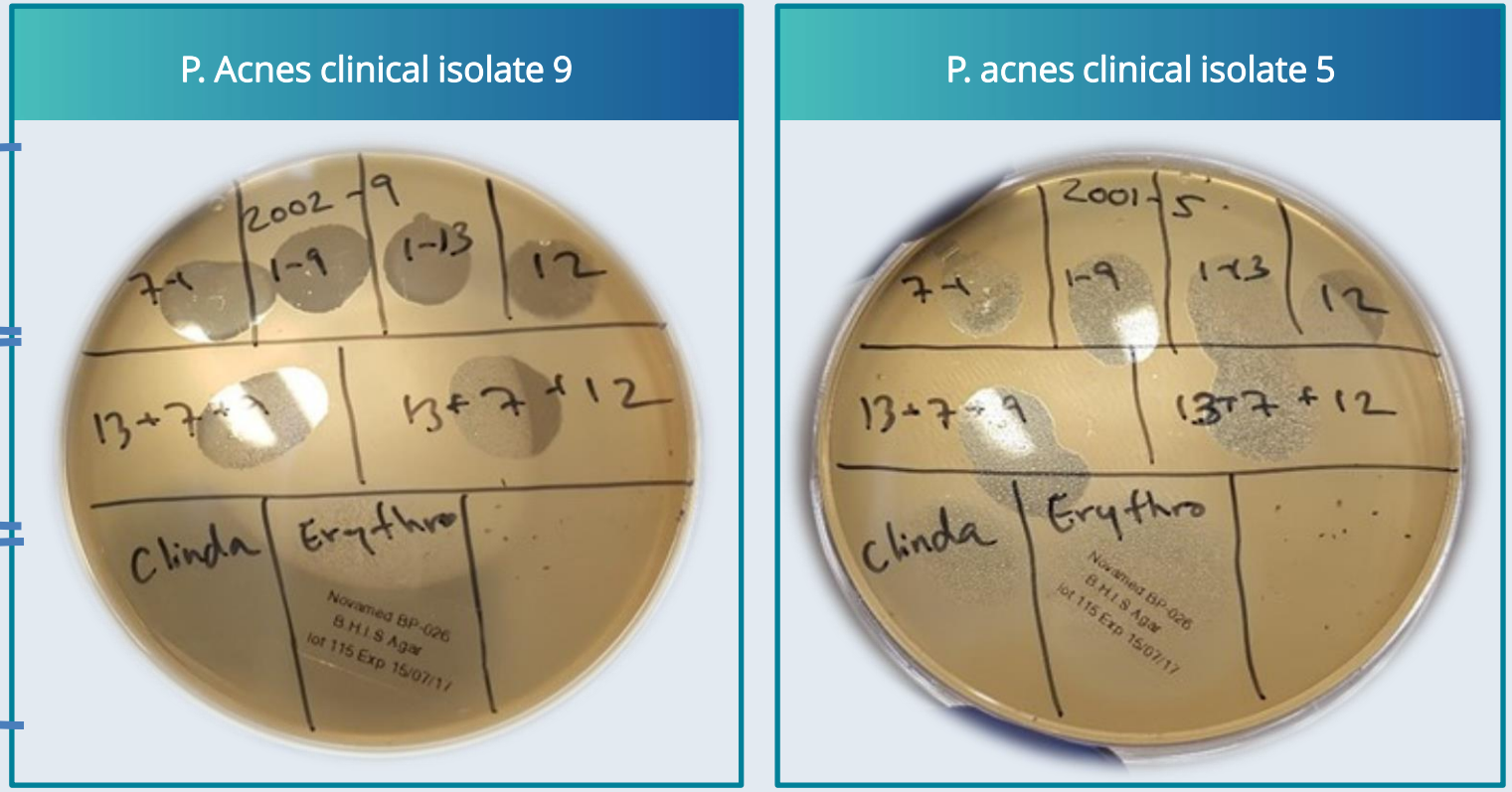
Successful penetration of biofilm in contrast to antibiotics

BX001 eradicates antibiotic resistant clinical strains

Individual phages

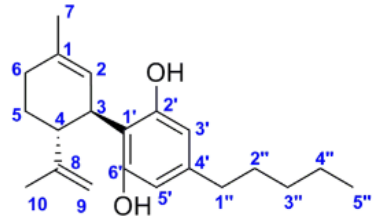
Phage cocktails

Antibiotics



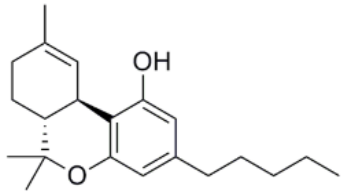
Cannabinoid Research Advances

Cannabidiol
(also known as CBD)



CBD

(-)-trans-Δ^9-tetrahydrocannabidiol
(also known as Δ^9-THC)



Δ^9-THC

- Cannabidiol is one of ~ 113 types of cannabinoids identified in the *cannabis sativa* plant
- Accounts for up to 40% of natural plant extract
- Unlike tetrahydrocannabinol (THC), CBD is non-psychoactive
- CBD has broad mechanisms of action, including immune modulation, anti-inflammatory effects and anti-microbial activity

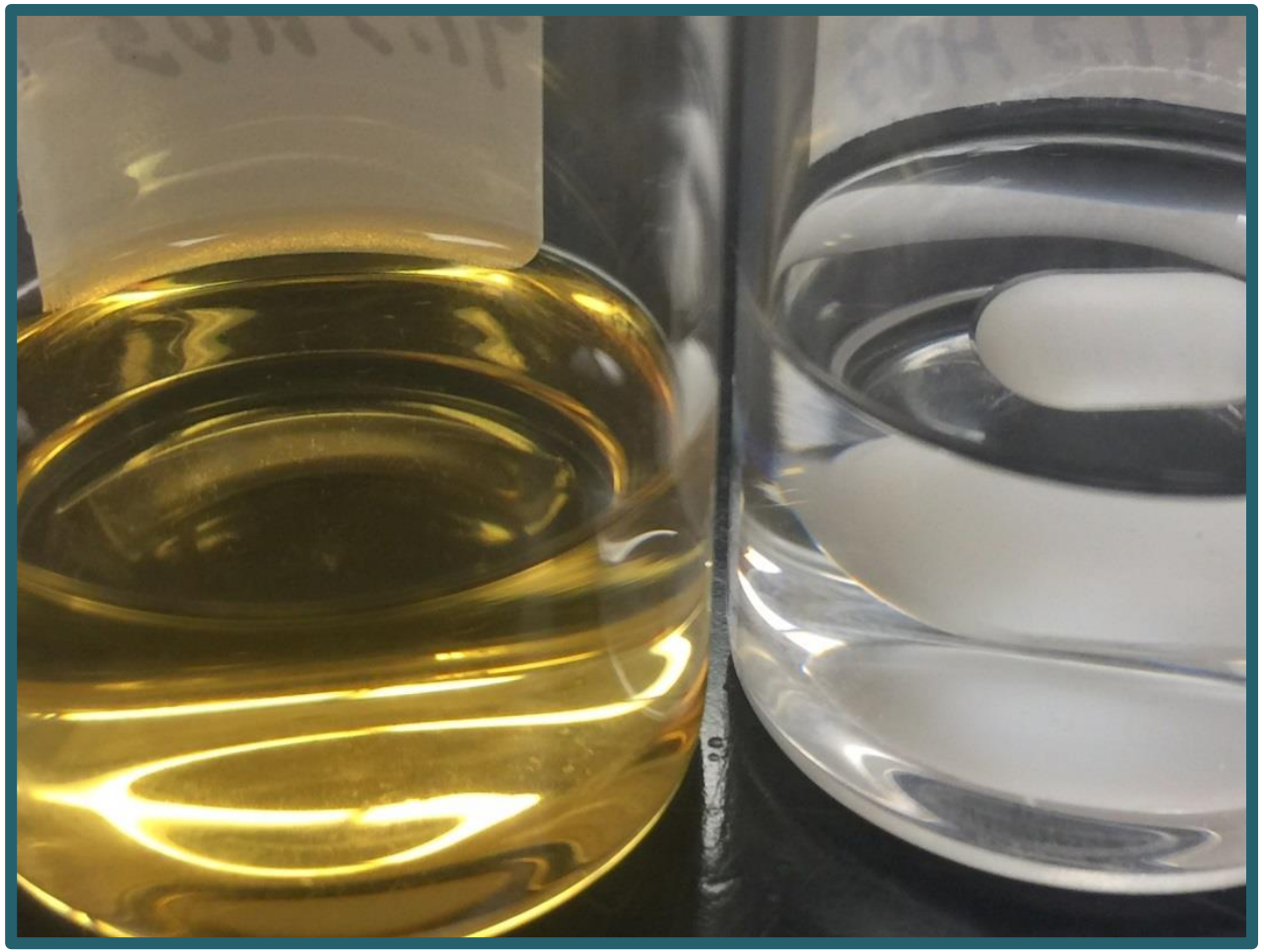
- As more clinical studies are validated and with the recent FDA approval of Epidiolex® (cannabidiol) Oral Solution, cannabinoids are attracting strong interest in drug development
- There are more than 100 active clinical trials for cannabidiol (CBD), ***but only 1 trial in acne vulgaris and 1 trial in atopic dermatitis***
  - Both are Phase 2 trials using synthetic CBD

Plant Extract CBD versus Synthetic CBD

Synthetic derivates are aimed to improve efficacy, pharmacokinetic properties and potency of CBD

Plant Extract CBD

- Extracted and purified
- 100+ chemicals
- Multiple impurities
- Not registered with FDA

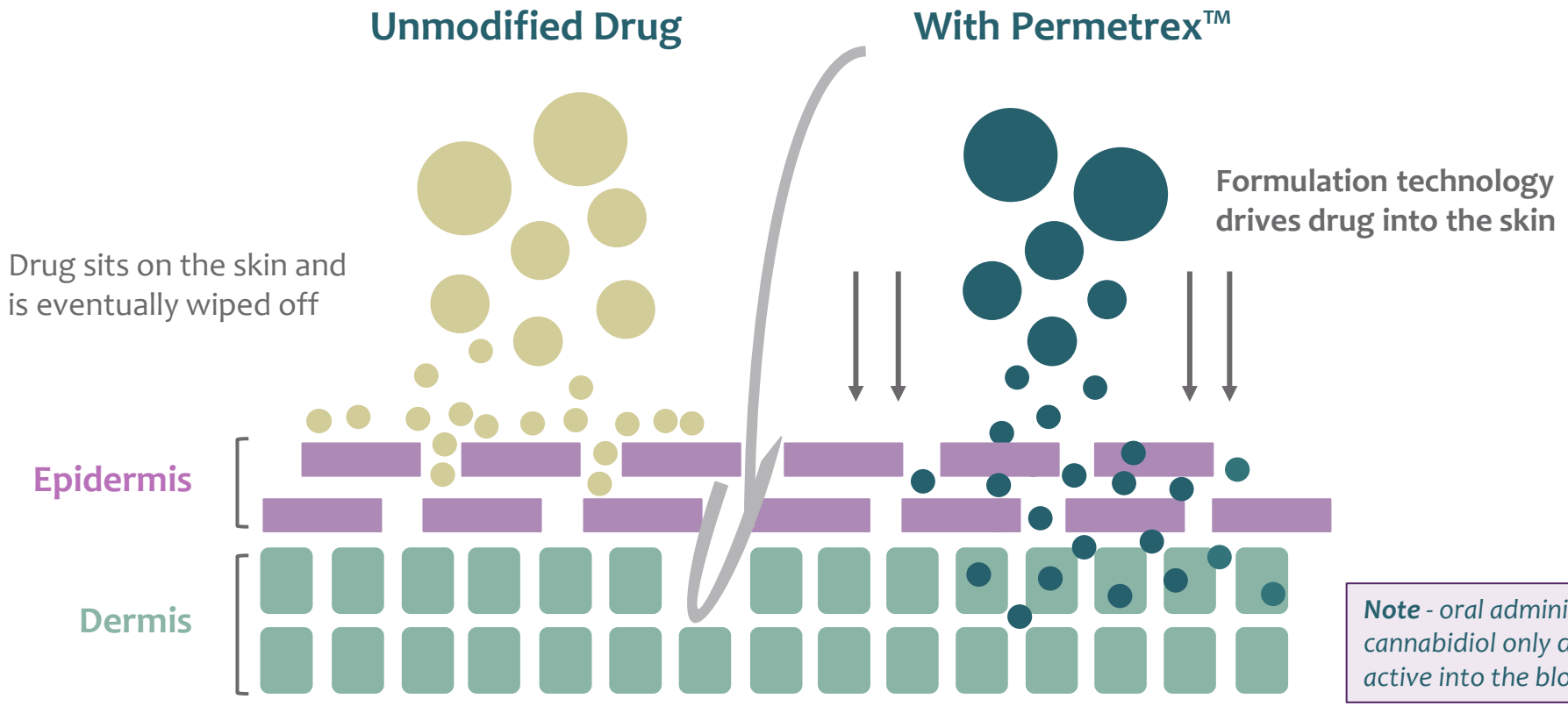


Synthetic CBD

- Synthetically manufactured
- Only 1 chemical
- 100% pure
- Registered with FDA

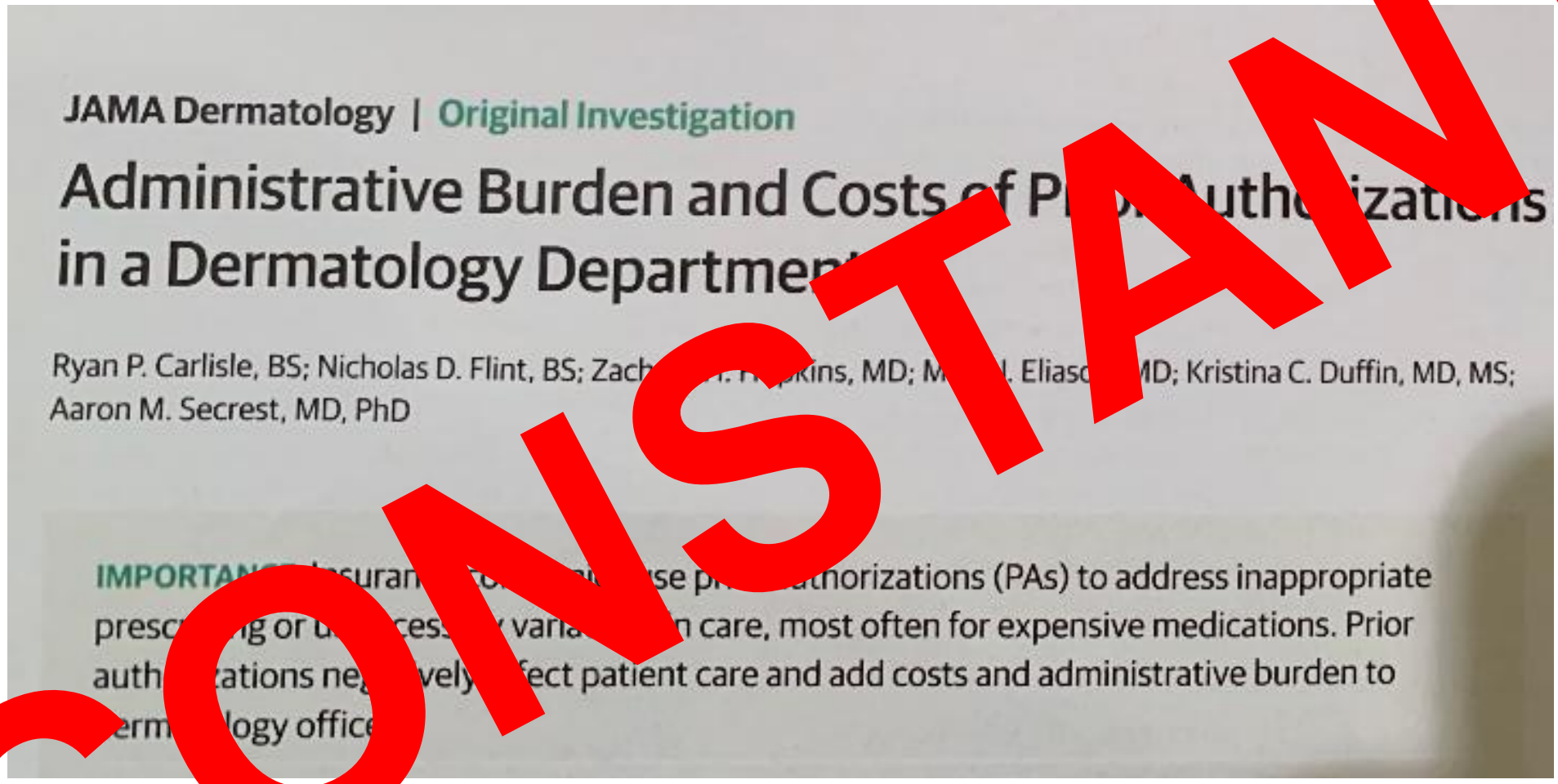
Permetrex™ Patented Skin Delivery Technology

Proprietary Permetrex™ technology delivers high doses of drug into the layers of the skin without use of permeation enhancers, preservatives, or the use of irritating alcohol/petrolatum additives



***Note** - oral administration of cannabidiol only delivers ~6% drug active into the blood stream*

FUTURE OF DERMATOLOGY?



JAMA Dermatology | Original Investigation

Administrative Burden and Costs of Pr[illegible]Authorizations in a Dermatology Departmen[illegible]

Ryan P. Carlisle, BS; Nicholas D. Flint, BS; Zach[illegible]kins, MD; M[illegible]Eliasc[illegible]MD; Kristina C. Duffin, MD, MS; Aaron M. Secrest, MD, PhD

IMPORTANC[illegible]surar[illegible]se pr[illegible]thorizations (PAs) to address inappropriate presc[illegible]g or u[illegible]ces[illegible]varia[illegible]n care, most often for expensive medications. Prior auth[illegible]cations neg[illegible]vely[illegible]fect patient care and add costs and administrative burden to derm[illegible]logy office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wedoderm@yahoo.com