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PSORIASIS

TOO MUCH

INNOVATION

NOT ENOUGH TIME

I have received funding either as an investigator, consultant, or a speaker from the following pharmaceutical companies:

- Abbott
- Abbvie
- Ablynx
- Acambis
- Aclaris
- Allergan
- Almirall
- Alumis
- Anaptys
- Amgen
- Anacor
- Apogee Therapeutics
- Arcutis, Inc.
- Apollo Therapeutics
- Aqua
- Astellas
- Asubio
- Bayer
- Beiersdorf, Inc
- Biofrontera
- BMS
- Berlex
- Biogen-Idec
- Biolife
- Biopelle
- Boehringer-Ingleheim
- Botanix Pharmaceuticals
- Breckenridge Pharma
- Brickell
- Cassiopea
- Cellceutix
- Celgene
- Centocor
- ChemoCentryx
- Cipher
- Coherus
- Colbar
- Collagenex
- Combinatrix
- Connetics
- Coria
- Dermata Therapeutics
- Dermavant
- Dermik
- Dermira
- Dow
- Dusa Pharmaceuticals
- Eli Lilly
- Embil Pharmaceuticals
- Enveda Biosciences
- Exeltis
- EOS
- Feldan Therapeutics
- Ferndale
- Galderma
- Genentech
- Glaxo-Smith Kline
- HealthPoint
- Idera
- Incyte Corportation
- Intendia
- Innovail
- Isdin
- Johnson & Johnson
- Kymera Therapeutics
- Laboratory Skin Care
- 3M
- Leo
- L'Oreal
- MC-2
- Maruho
- Medical International technologies
- Medicis
- Merck
- Merck Serono
- Merz
- NanoBio
- Nektar Therapeutics
- Novartis
- Novan
- Nucryst
- Obagi
- Onset Therapeutics
- Organon Biosciences SRL
- Ortho Dermatologics
- OrthoNeutrogena
- Oruka Therapeutics
- PediaPharma
- Pelthos
- Pfizer
- PharmaDerm
- Promius
- Puracap
- QLT
- Quatrix
- Quinnova
- Regeneron
- Sagimet Biosciences
- Sandoz, a Novartis Company
- Sanofi
- Serono
- SkinMedica
- Stiefel
- Sun Pharma
- Takeda Pharmaceuticals USA
- Taro
- TolerRx
- Triax Pharmaceuticals
- UCB
- Valeant
- Vellera
- Warner & Chilcott
- Xenoport
- ZAGE
- Zalicus

JAMA Dermatology | Consensus Statement

Defining On-Treatment Remission in Plaque Psoriasis

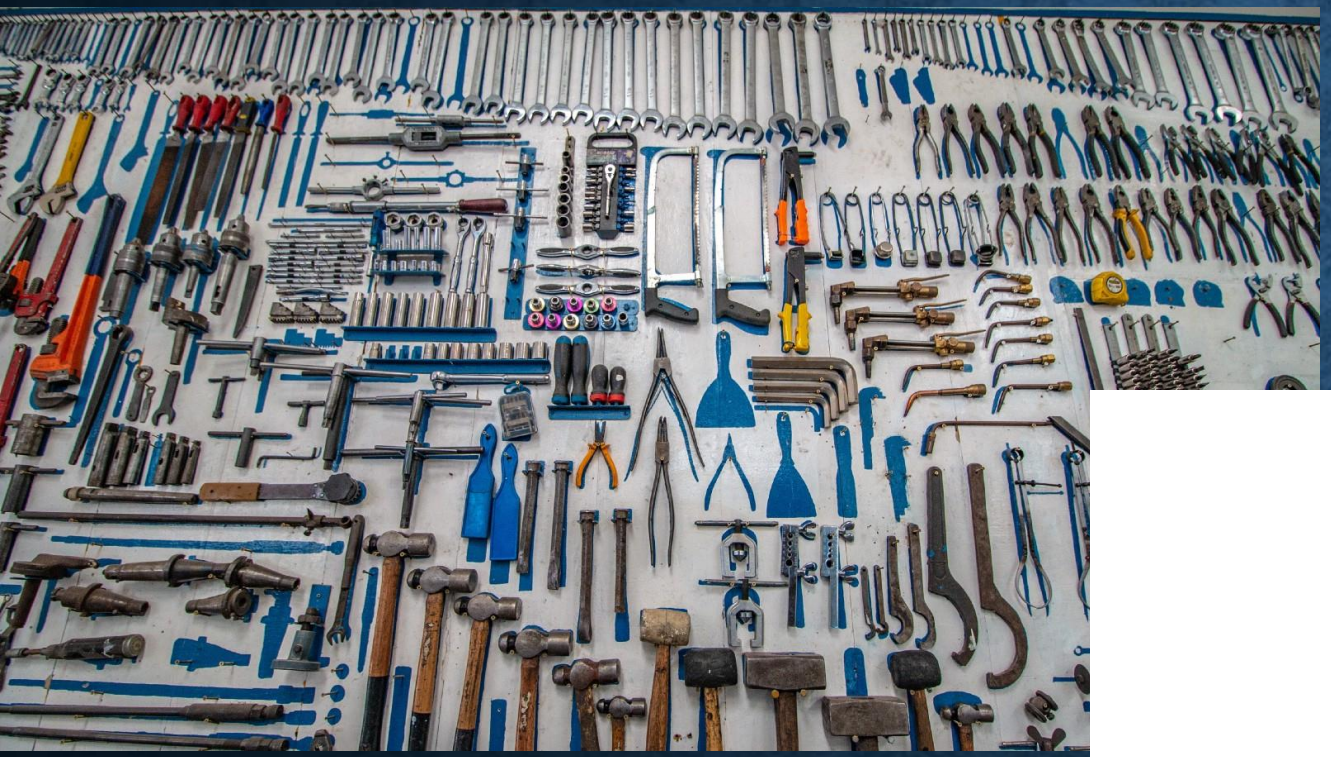
A Consensus Statement From the National Psoriasis Foundation

April W. Armstrong, MD, MPH; George C. Gondo, MA; Joseph F. Merola, MD, MMSc; Alyssa M. Roberts, BS; Lourdes M. Pérez-Chada, MD, MMSc; Deepak M. W. Balak, MD, PhD; Guy S. Eakin, PhD; Charlotte Read, MD, PhD; Stephanie T. Le, MD; Yasmin Gutierrez, MD; Tina Bhutani, MD; Andrew Blauvelt, MD, MBA; Kristina Callis Duffin, MD, MS; Steven Fakharzadeh, MD, PhD; Steven R. Feldman, MD, PhD; Joel M. Gelfand, MD, MSCE; Dafna D. Gladman, MD; Brad Glick, DO, MPH; Lawrence J. Green, MD; George Han, MD, PhD; Jason E. Hawkes, MD, MS; Samuel T. Hwang, MD, PhD; Nicole Johnsen, BS; Robert E. Kalb, MD; Leon Kircik, MD; Richard G. Langley, MD; Mark G. Lebwohl, MD; G. Michael Lewitt, MD; Emanual Maverakis, MD; Ronald Prussick, MD; Soumya M. Reddy, MD; Cheryl F. Rosen, MD; Jose U. Scher, MD; Evan L. Siegel, MD; Elizabeth B. Wallace, MD; Jeffrey M. Weinberg, MD; Paul S. Yamauchi, MD, PhD; Gil Yosipovitch, MD; Wilson Liao, MD; for the Remission Workgroup of the National Psoriasis Foundation

CONCLUSIONS AND RELEVANCE

Through a Delphi consensus process, on-treatment remission for plaque psoriasis was defined as patients maintaining a **BSA involvement of 0% or IGA of 0 for at least 6 months while on treatment.** This clear and standardized benchmark is applicable to both research and practice settings.

TOPICAL TREATMENT IS THE FOUNDATION OF DERMATOLOGIC THERAPY



WHAT DO I DO?

BIOLOGICS TOPICALS

SYSTEMIC TOPICALS

LIGHT TOPICALS

TOPICALS

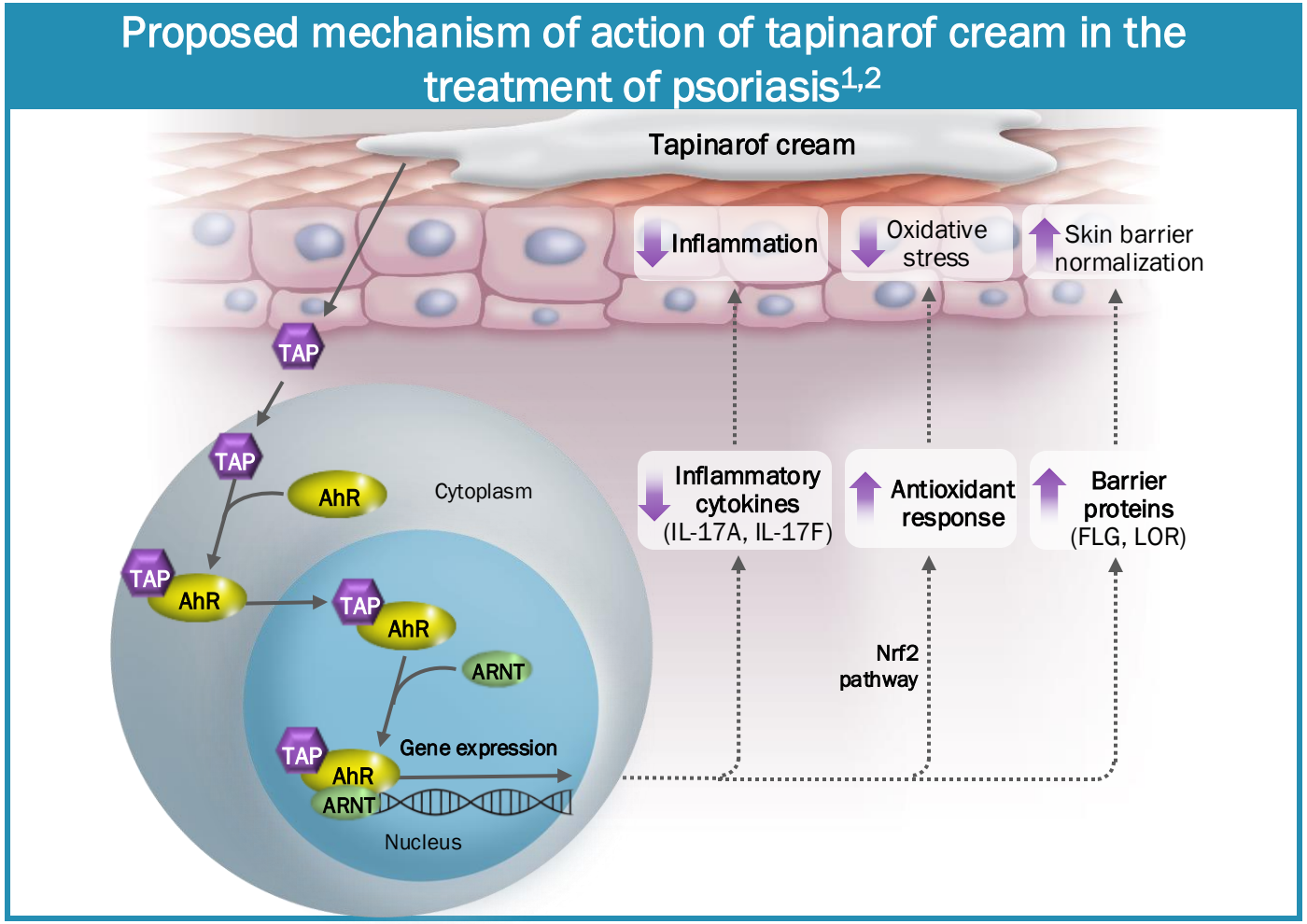
I DON'T WANT TO BE ON STEROIDS

UNMET NEED

NEW CHEMICAL ENTITIES

Tapinarof is a First-in-Class, Topical Therapeutic Aryl Hydrocarbon Receptor Modulating Agent (TAMA)

Proposed mechanism of action of tapinarof cream in the treatment of psoriasis[1,2]



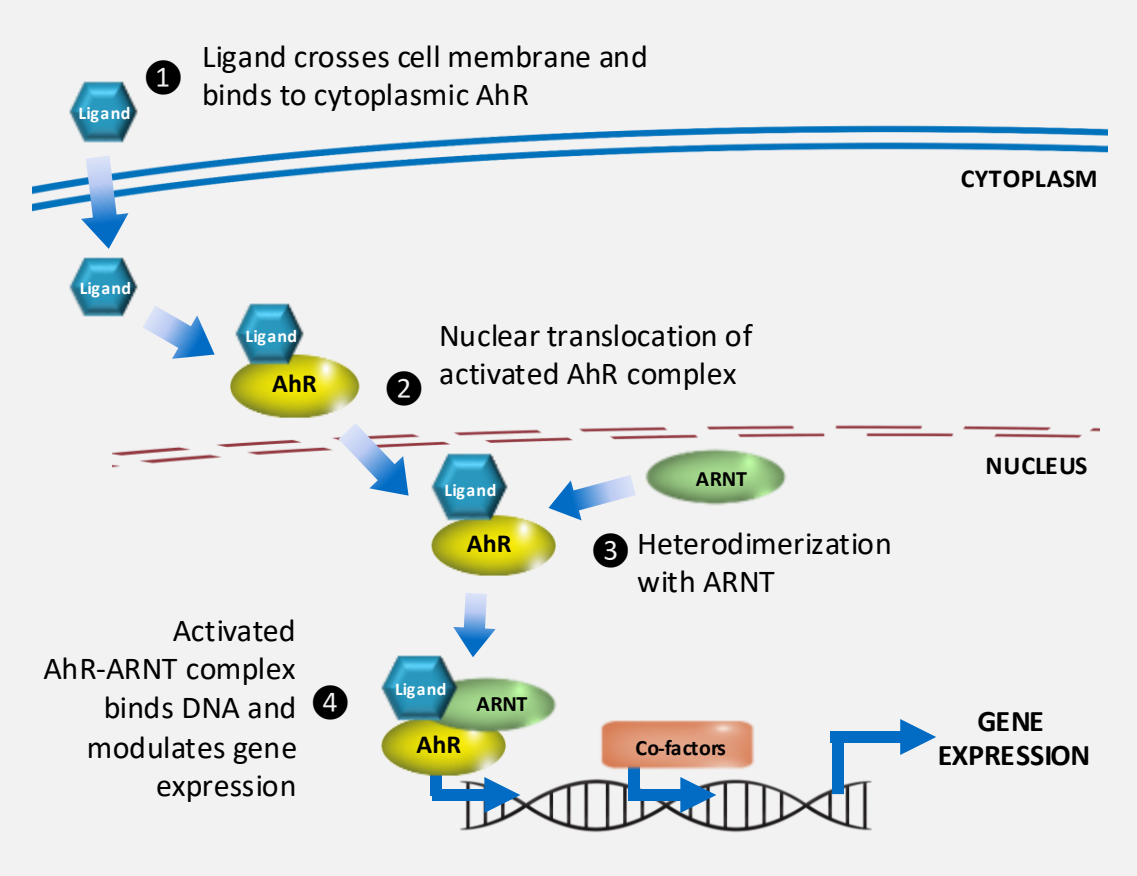
AhR, aryl hydrocarbon receptor; ARNT, aryl hydrocarbon receptor nuclear translocator; FLG, filaggrin; IL, interleukin; LOR, loricrin; Nrf2, nuclear factor erythroid 2-related factor 2; TAP, tapinarof.

1. Smith SH, et al. *J Inv Dermatol.* 2017;137:2110–2119; 2. Furue M, et al. *J Dermatological Sci.* 2015;80:83–88.

Tapinarof: Therapeutic AhR Modulating Agent (TAMA)

- Tapinarof is a topical, small molecule TAMA that directly binds to and activates AhR transcription factor[1]
- AhR activation via tapinarof *in vitro* and animal models leads to:
  - Reduction of Th17 cytokine expression[1]
  - Reduction of Th2 cytokine expression[1,2]
  - Decreased oxidative stress[1]
  - Increased skin barrier proteins[1]

AhR pathway[3]



AhR, aryl hydrocarbon receptor; ARNT, aryl hydrocarbon receptor nuclear translocator; TAMA, therapeutic aryl hydrocarbon receptor modulating agent; Th, T helper cell.

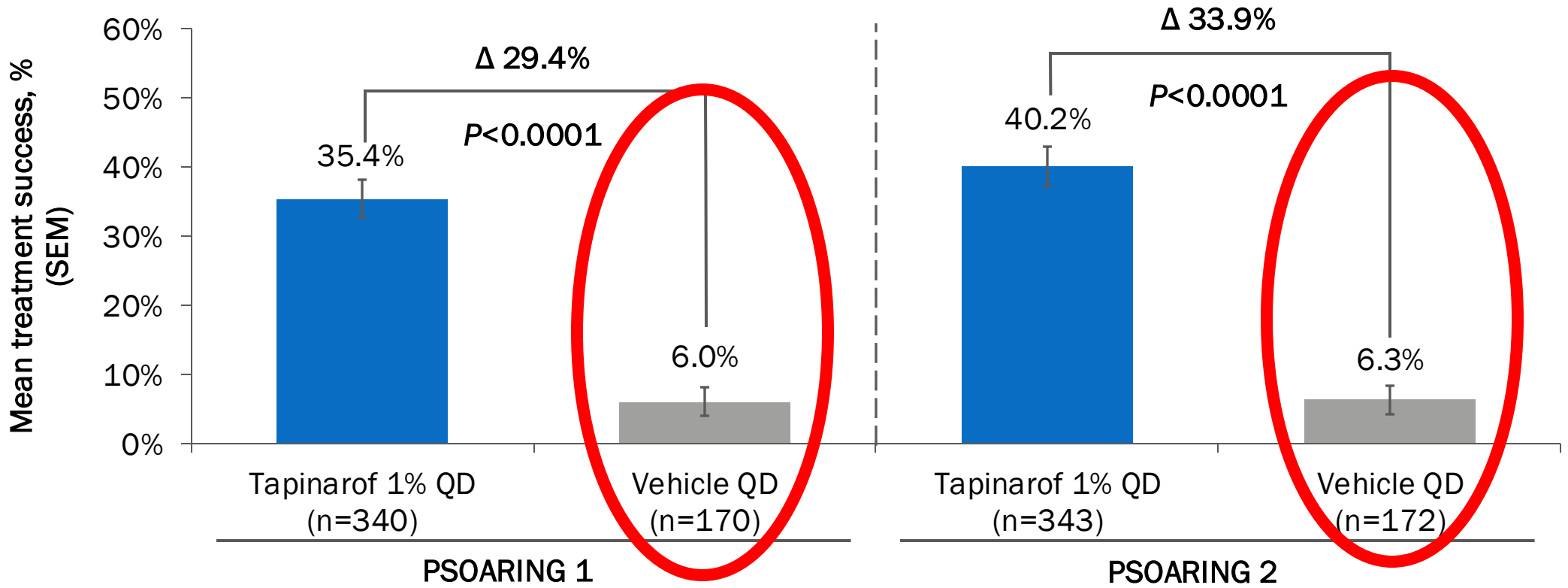
1. Smith SH et al. *J Inv Dermatol* 2017;137:2110–2119; 2. Negishi T et al. *J Immunol.* 2005;175;7348–7356; 3. Furue M et al. *J Dermatological Sci*. 2015;80:83–88.

Tapinarof Cream 1% QD for the Treatment of Plaque Psoriasis: Efficacy and Safety in Two Pivotal Phase 3 Trials

Mark Lebwohl,[1] Linda Stein Gold,[2] Bruce Strober,[3] Kim Papp,[4] April Armstrong,[5] Jerry Bagel,[6] Leon Kircik,[1,7] Benjamin Ehst,[8] H Chih-ho Hong,[9] Jennifer Soung,[10] Jeff Fromowitz,[11] Scott Guenthner,[12] Stephen C Piscitelli,[13] David S Rubenstein,[13] Philip M Brown,[13] Anna M Tallman,[13] Robert Bissonnette[14]

[1]Icahn School of Medicine, Mount Sinai, New York, NY, USA; [2]Henry Ford Health System, Detroit, MI, USA; [3]Yale University, New Haven and Central Connecticut Dermatology Research, Cromwell, CT, USA; [4]Probity Medical Research, Waterloo, ON, Canada; [5]Keck School of Medicine University of Southern California, Los Angeles, CA, USA; [6]Psoriasis Treatment Center of Central New Jersey, NJ, USA; [7]Skin Sciences, PLLC, Louisville, KY, USA; [8]Oregon Medical Research Center, Portland, OR, USA; [9]University of British Columbia and Probity Medical Research, Surrey, BC, Canada; [10]Southern California Dermatology, Santa Ana, CA, USA; [11]Dermatology of Boca, Boca Raton, FL, USA; [12]The Indiana Clinical Trials Center, PC, Plainfield, IN, USA; [13]Dermavant Sciences, Inc., Durham, NC, USA; [14]Innovaderm Research Inc., Montreal, QC, Canada

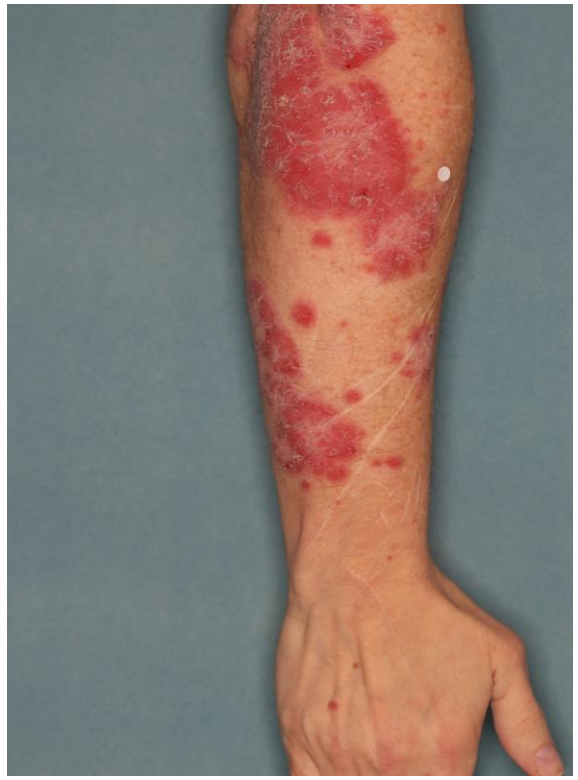
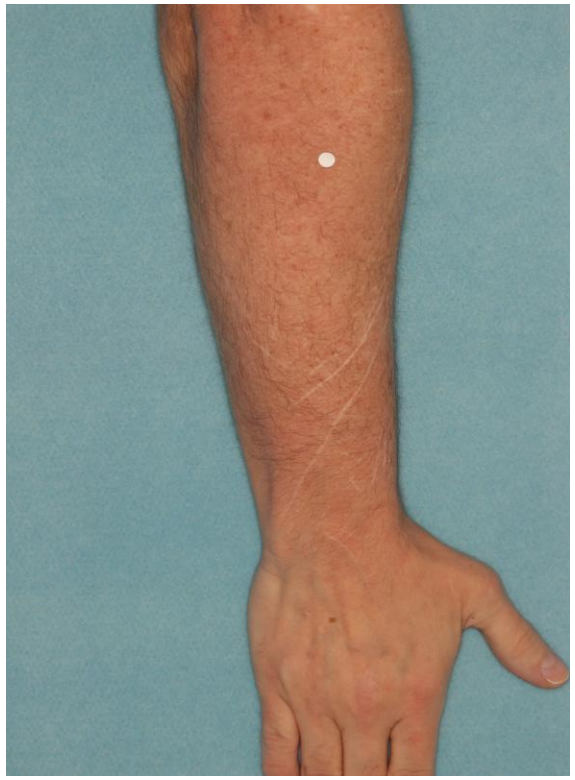
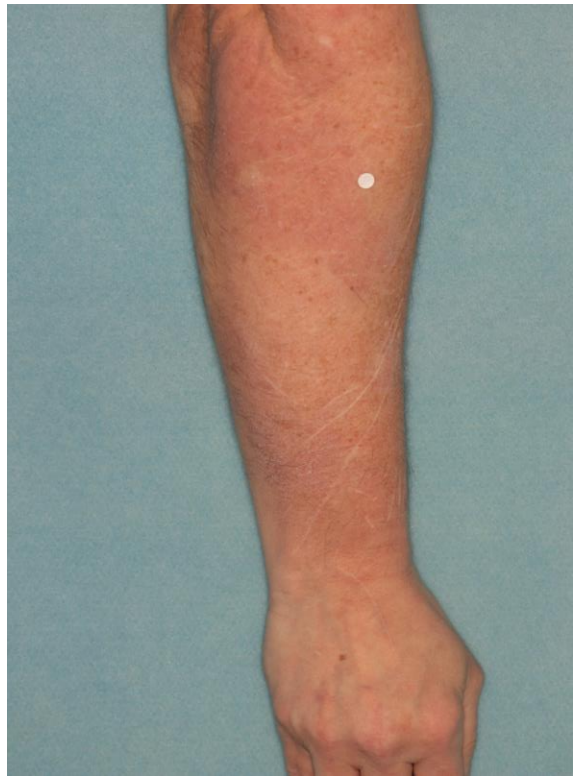
Tapinarof 1% QD: Primary Endpoint of PGA Response at Week 12 was Achieved in Both Studies



PGA response rate* was highly statistically significant in the tapinarof cream 1% QD group versus vehicle in both PSOARING 1 and 2: 35.4% vs 6.0% (*P*<0.0001) and 40.2% vs 6.3% (*P*<0.0001), respectively

*PGA of 0 or 1 and ≥2-grade improvement at Week 12.
ITT population. *P* value based upon Cochran-Mantel-Haenszel analysis stratified by baseline PGA score.
ITT, intent-to-treat; PGA, Physician Global Assessment; QD, once daily; SEM, standard error of mean

Tapinarof 1% QD Clinical Response of Patient with Plaque Psoriasis who Achieved Primary and Secondary Efficacy Endpoints at Week 12

Baseline	Week 4	Week 12
		
• PGA = 3 • PASI = 17.6	• PGA = 2 • PASI = 4	• PGA = 0 • PASI = 0

PGA and PASI are global efficacy assessments. Example of one representative target lesion of a patient treated with tapinarof 1% QD; individual results may vary. Photographs demonstrate improvement in PGA and PASI at Week 4 and 12.
PASI, Psoriasis Area and Severity Index; PGA, Physician Global Assessment; QD, once daily.

Demonstrates ~25- to >300-fold higher potency than currently available PDE-4 inhibitors[3]

Roflumilast Cream, a Once-Daily, Potent Phosphodiesterase-4 Inhibitor, in Chronic Plaque Psoriasis Patients: Efficacy and Safety From DERMIS-1 and DERMIS-2 Phase 3 Trials

Mark Lebwohl,[1] Leon H. Kircik,[2] Angela Moore,[3] Linda Stein Gold,[4] Zoe D. Draelos,[5] Melinda J. Gooderham,[6] Kim A. Papp,[7] Jerry Bagel,[8] Neal Bhatia,[9] James Del Rosso,[10] Laura K. Ferris,[11] Lawrence J. Green,[12] Adelaide A. Hebert,[13] Terry Jones,[14] Steven E. Kempers,[15] David M. Pariser,[16] Paul S. Yamauchi,[17] Matthew Zirwas,[18] Patrick Burnett,[19] Robert C. Higham,[19] Lynn Navale,[19] David R. Berk[19]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Icahn School of Medicine at Mount Sinai, New York, NY, Indiana Medical Center, Indianapolis, IN, Physicians Skin Care, PLLC, Louisville, KY, and Skin Sciences, PLLC, Louisville, KY, USA; [3]Arlington Research Center, Arlington, TX, USA, Baylor University Medical Center, Dallas, TX, USA; [4]Henry Ford Medical Center, Detroit, MI, USA; [5]Dermatology Consulting Services, High Point, NC, USA; [6]SkiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; [7]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [8]Psoriasis Treatment Center of Central New Jersey, Windsor, NJ, USA; [9]Therapeutics Clinical Research, San Diego, CA, USA; [10]JDR Dermatology Research Center, LLC, Las Vegas, NV, USA; [11]University of Pittsburgh, Department of Dermatology, Pittsburgh, PA, USA; [12]George Washington University School of Medicine, Rockville, MD, USA; [13]UT Health McGovern Medical School, Houston, TX, USA; [14]U.S. Dermatology Partners Bryan, Bryan, TX, USA; [15]Minnesota Clinical Study Center, Fridley, MN, USA; [16]Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, VA, USA; [17]David Geffen School of Medicine at UCLA, Los Angeles, and Dermatology Institute & Skin Care Center, Inc., Santa Monica, CA, USA; [18]Dermatologists of the Central States, Probity Medical Research, and Ohio University, Bexley, OH, USA; [19]Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA

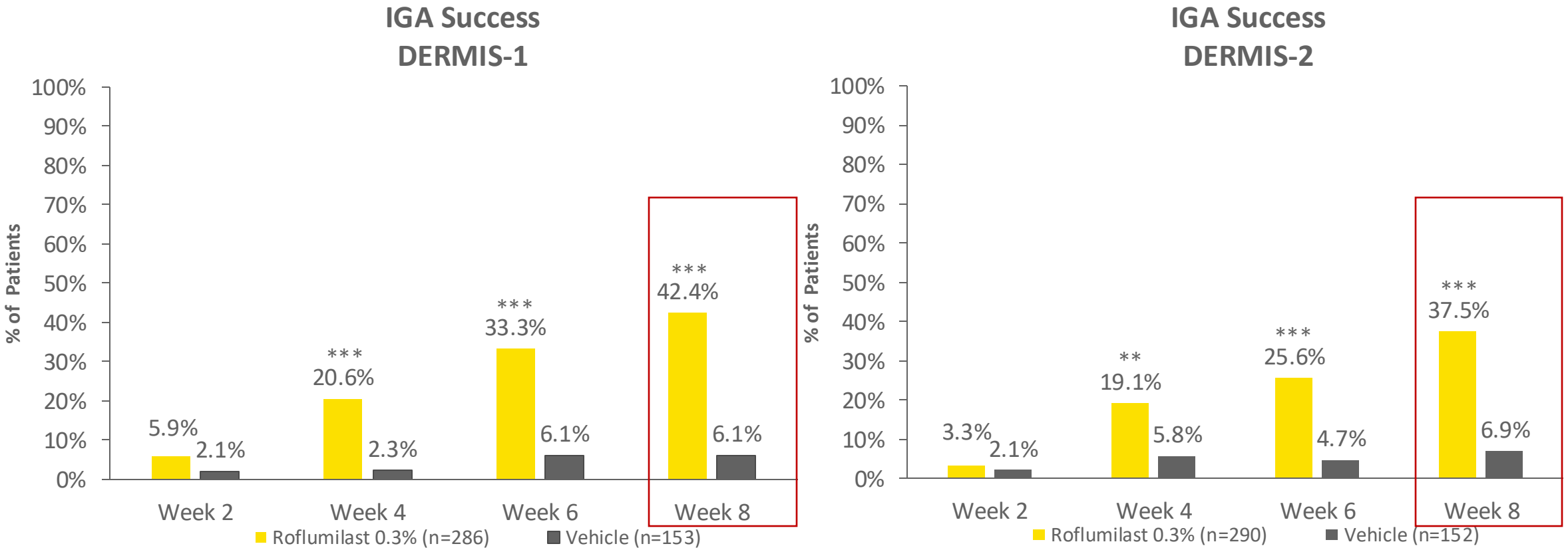
Disclosures: Mark Lebwohl, Leon H. Kircik, Angela Moore, Linda Stein Gold, Zoe D. Draelos, Melinda J. Gooderham, Kim A. Papp, Jerry Bagel, Neal Bhatia, James Del Rosso, Laura K. Ferris, Lawrence J. Green, Adelaide A. Hebert, Terry Jones, Steven E. Kempers, David M. Pariser, Paul S. Yamauchi, and Matthew Zirwas are investigators and/or consultants for Arcutis Biotherapeutics, Inc. and received grants/research funding and/or honoraria; Robert C. Higham, Lynn Navale, and David R. Berk are employees of Arcutis Biotherapeutics, Inc. Additional disclosures provided on request.

This work was supported by Arcutis Biotherapeutics, Inc.

Writing support was provided by Christina McManus, PhD, Alligent Biopharm Consulting LLC, and funded by Arcutis Biotherapeutics, Inc.

Robust Efficacy on IGA Success in Both Phase 3 Studies

IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline



* p<0.05; ** p<0.01; *** p<0.001

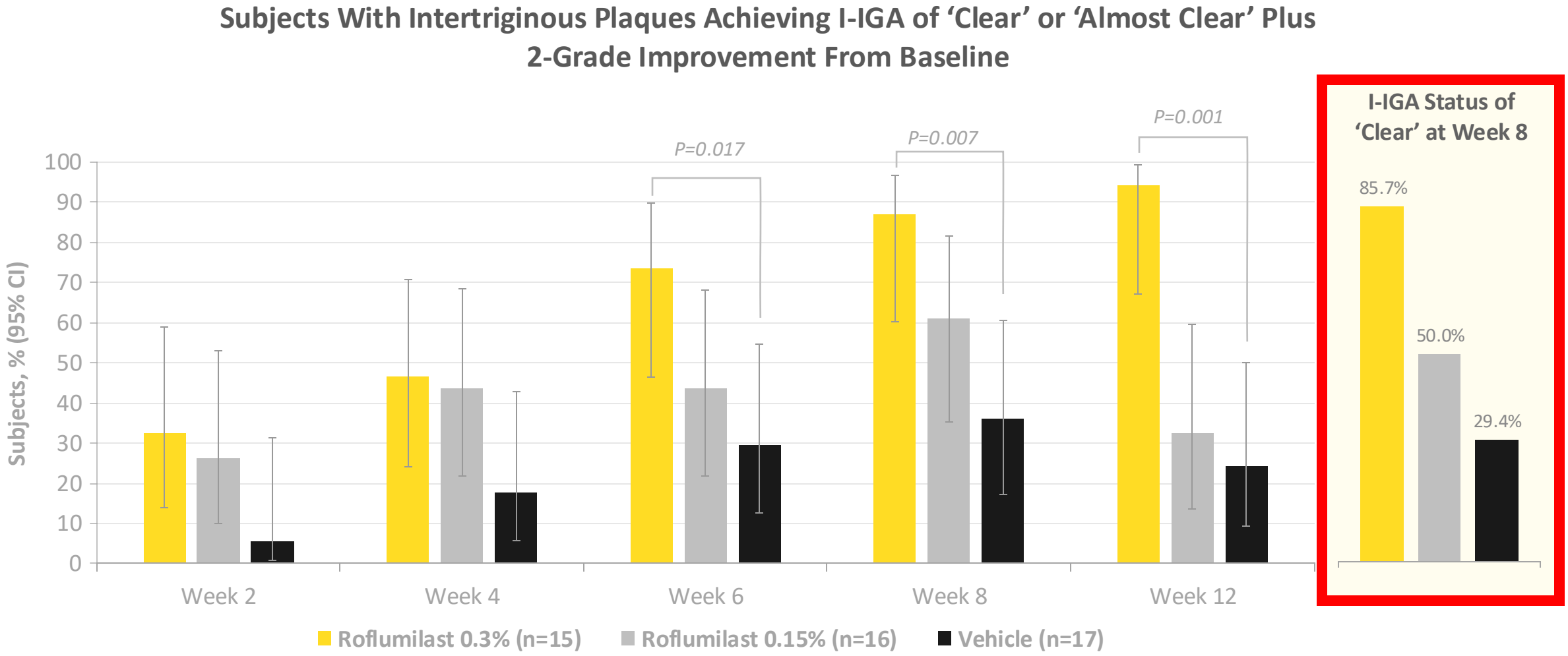
The primary endpoint was achieved in both DERMIS-1 and DERMIS-2

Intent-to-treat population; missing scores imputed using multiple imputations

IGA: Investigator's Global Assessment

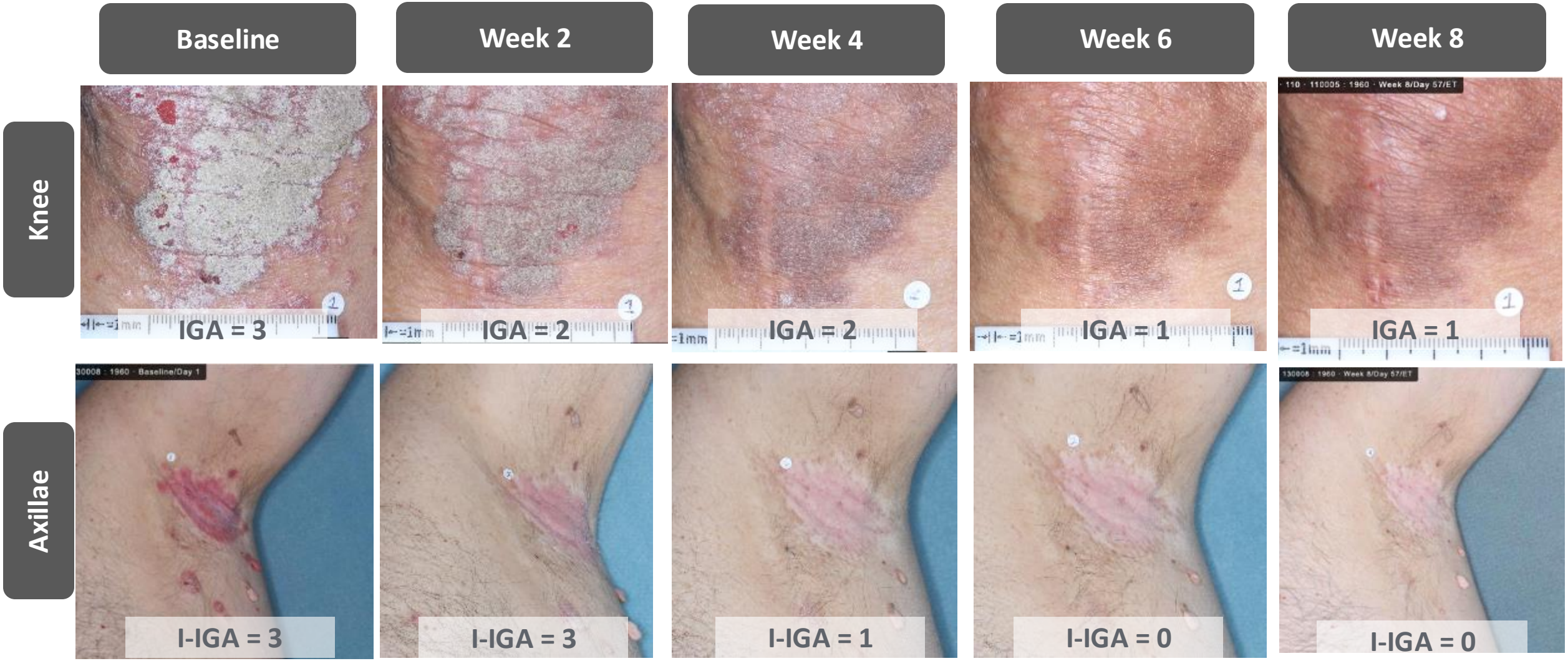
Presented at the European Academy of Dermatology and Venereology Spring Symposium 2021, 06-07 May 2021

Most Subjects With Intertriginous Plaques Treated With Roflumilast Cream Achieved I-IGA Success by Week 6 With Continued Improvement Through Week 12



Data are presented for intent-to-treat population. CI: confidence interval; I-IGA: Intertriginous Investigator Global Assessment.

Patient Examples Illustrating Efficacy of Roflumilast Cream 0.3% From DERMIS-1 & DERMIS-2



IGA: Investigator's Global Assessment; I-IGA: intertriginous-IGA

Presented at the European Academy of Dermatology and Venereology Spring Symposium 2021, 06-07 May 2021

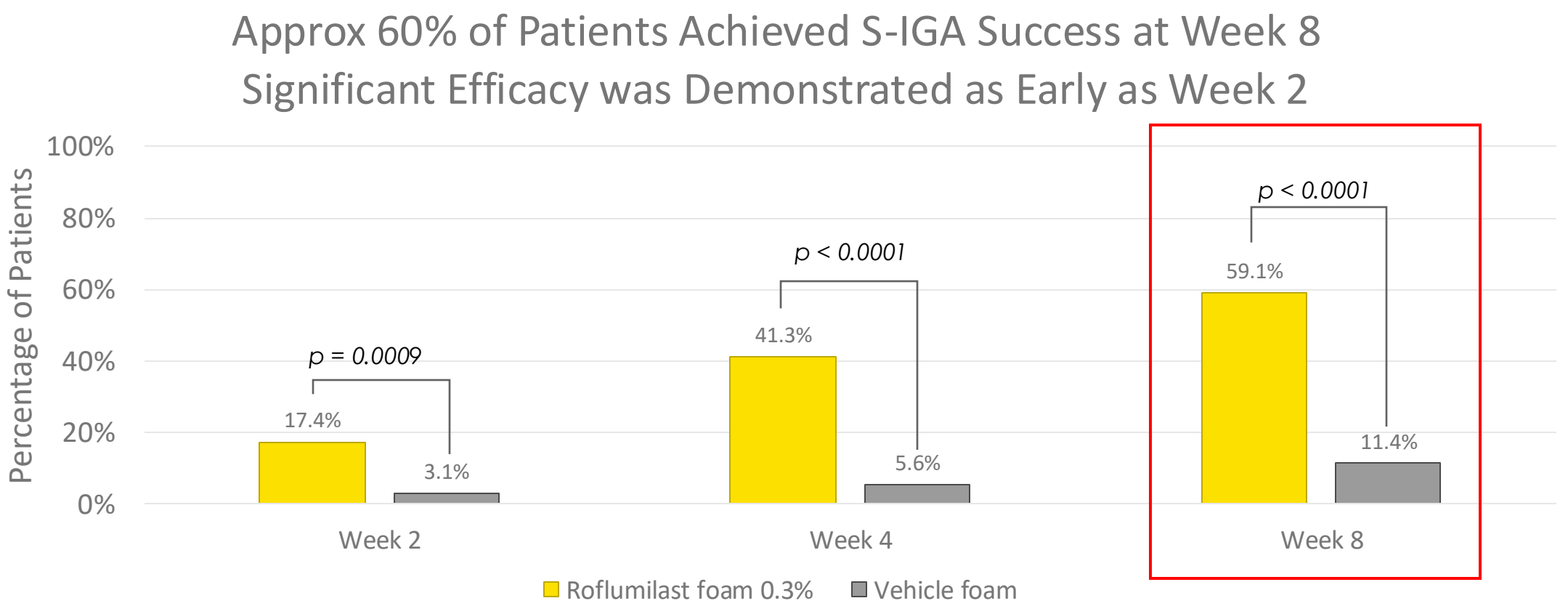
Once-daily Roflumilast Foam 0.3% for Scalp and Body Psoriasis: A Randomized, Double-blind, Vehicle-controlled Phase 2b Study

Leon H Kircik[1], Angela Moore[2], Neal Bhatia[3], Alim R Devani[4], Zoe D Draelos[5], Janet DuBois[6], Melinda J Gooderham[7], Steven E Kempers[8], Edward Lain[9], Mark Lee[10], Dedee F Murrell[11], Kim A Papp[12], David M Pariser[13], Rodney Sinclair[14], Matthew Zirwas[15], Patrick Burnett[16], Robert C Higham[16], Lynn Navale[16], David R Berk[16]

[1]Icahn School of Medicine at Mount Sinai, NY, Indiana Medical Center, Indianapolis, IN, Physicians Skin Care, PLLC, Louisville, KY, and Skin Sciences, PLLC, Louisville, KY, USA; [2]Arlington Research Center, Arlington, TX, USA, and Baylor University Medical Center, Dallas, TX; [3]Therapeutics Clinical Research, San Diego, CA, USA; [4]Dermatology Research Institute, Skin Health & Wellness Centre and Probity Medical Research, Calgary, AB, Canada; [5]Dermatology Consulting Services, High Point, NC, USA; [6]DermResearch, Inc., Austin, TX, USA; [7]SkiN Centre for Dermatology, Probity Medical Research and Queen's University, Peterborough, ON, Canada; [8]Minnesota Clinical Study Center, Fridley, MN, USA; [9]Sanova Dermatology, Austin, TX, USA; [10]Progressive Clinical Research, San Antonio, TX, USA; [11]UNSW, Sydney, Australia; [12]Probity Medical Research and K Papp Clinical Research, Waterloo, ON, Canada; [13]Eastern Virginia Medical School and Virginia Clinical Research, Inc., Norfolk, VA, USA; [14]Sinclair Dermatology, East Melbourne, Australia; [15]Dermatologists of the Central States, Probity Medical Research, and Ohio University, Bexley, OH, USA; [16]Arcutis Biotherapeutics, Inc., Westlake Village, CA, USA

This study was supported by Arcutis Biotherapeutics

Roflumilast Foam Significantly Increased the Percentage of Patients with S-IGA Success at Week 8 (Primary Endpoint)



34.3% of patients on roflumilast achieved S-IGA = 0 (clear) versus 3.4% on vehicle

IGA Success = Clear or Almost Clear with at least a 2-grade improvement from baseline

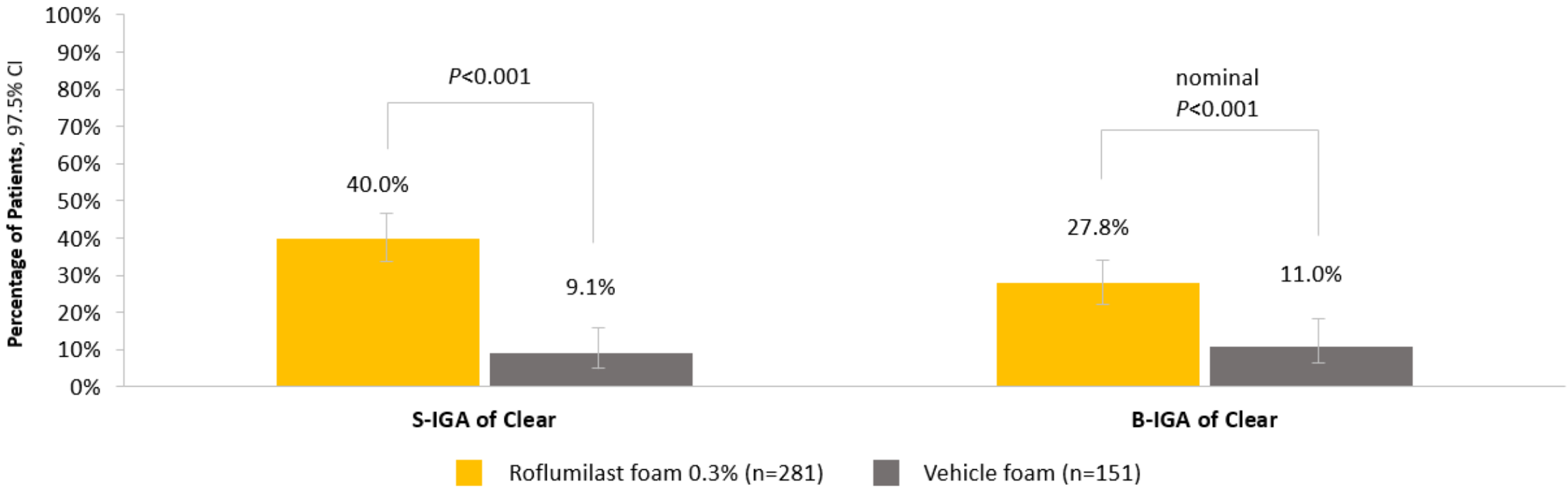
Intent-to-treat population

S-IGA: Scalp-Investigator's Global Assessment

Efficacy and Safety of Roflumilast Foam 0.3% in Patients With Scalp and Body Psoriasis (ARRECTOR)

Clearance of Scalp and Body Psoriasis at Week 8

Percentage of Patients Achieving S-IGA or B-IGA Status of Clear (0) at Week 8



B-IGA, Body-Investigator Global Assessment; CI, confidence interval; S-IGA, Scalp-Investigator Global Assessment.
Gooderham MJ, et al. *JAMA Dermatol*. Published online May 07, 2025. doi: 10.1001/jamadermatol.2025.1136.

Patient With Psoriasis Treated With Roflumilast Foam 0.3%

Black/African American Male

Baseline	Week 2	Week 4	Week 8
			
S-IGA: 4 SI-NRS: 9	S-IGA: 3 SI-NRS: 4	S-IGA: 1 SI-NRS: 2	S-IGA: 1 SI-NRS: 0

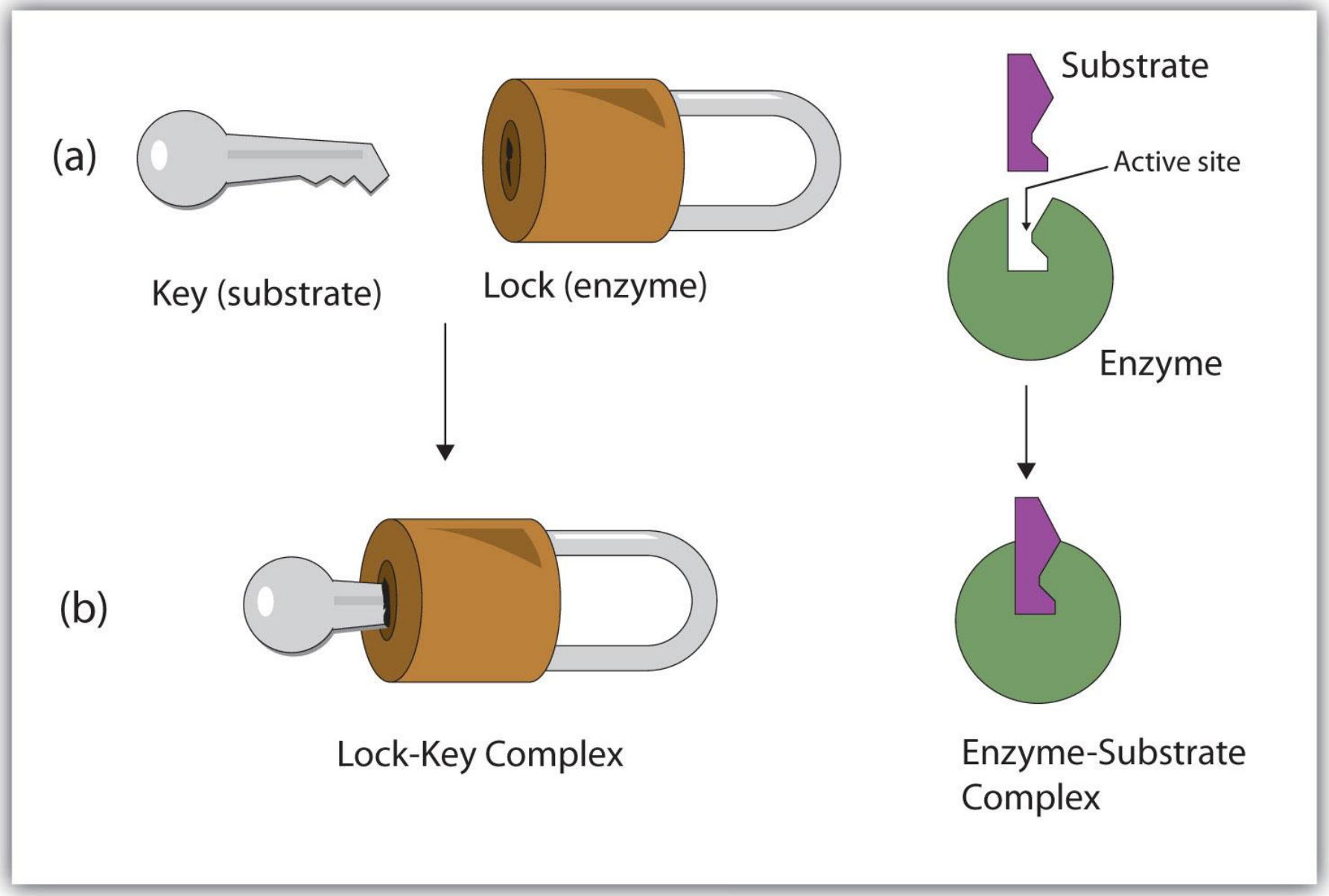
S-IGA, Scalp-Investigator Global Assessment; SI-NRS, Scalp Itch-Numeric Rating Scale.

Gooderham MJ, et al. *JAMA Dermatol*. Published online May 07, 2025. doi: 10.1001/jamadermatol.2025.1136.

GAME CHANGER IN PSORIASIS AND ATOPIC DERMATITIS TREATMENT

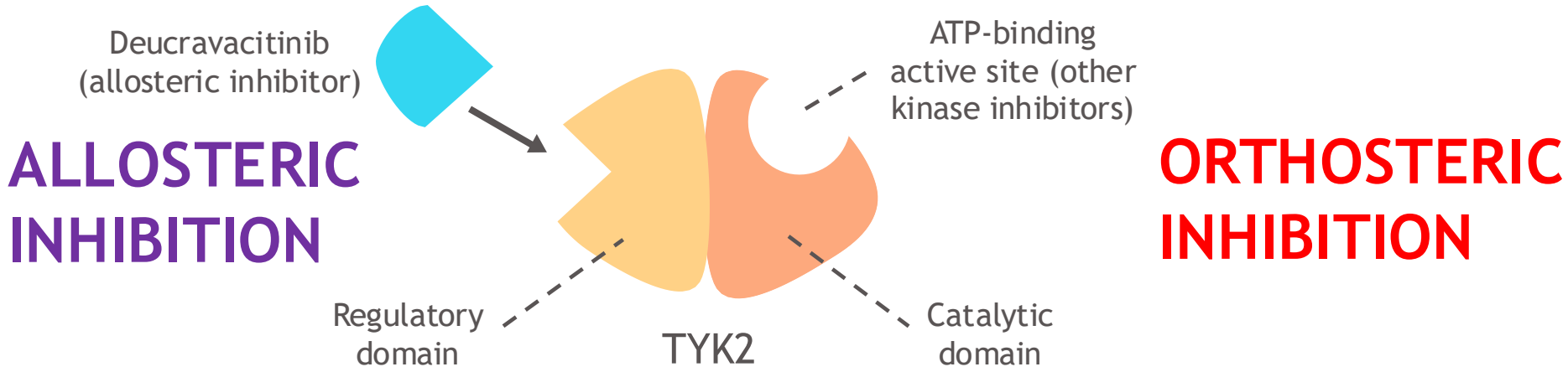
HOW ARE THE TYK2 AND JAK 1/2/3 KINASES DIFFERENT FROM EACH OTHER?

HIGH SCHOOL CHEMISTRY



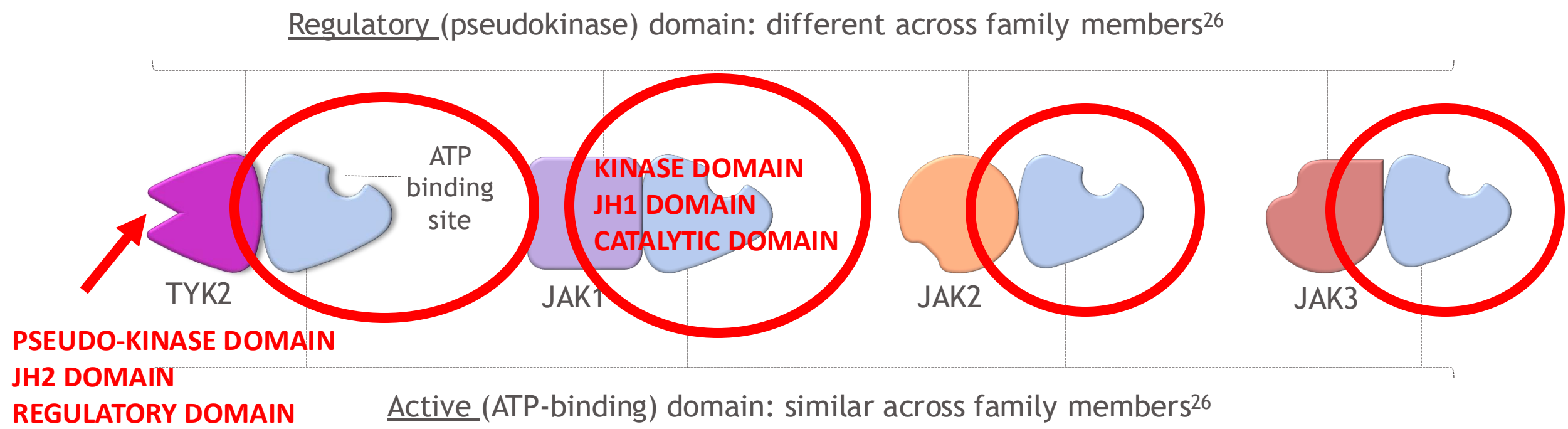
Introduction

- Deucravacitinib
  - Novel, oral, selective tyrosine kinase 2 (TYK2) inhibitor with a unique mechanism of action distinct from Janus kinase (JAK) 1, 2, 3 inhibitors[1]
    - Binds to the TYK2 regulatory domain with high selectivity and inhibits TYK2 via an allosteric mechanism[1]
      - ≥100-fold greater selectivity for TYK2 vs JAK1/3 and ≥2000-fold greater selectivity for TYK2 vs JAK2[1,2]
    - Inhibits TYK2-mediated signaling by cytokines involved in psoriasis pathogenesis (eg, IL-23, IL-12, and Type 1 interferon)[1]
  - Previously demonstrated efficacy and tolerability in Phase 2 trials in moderate to severe plaque psoriasis[3] and active psoriatic arthritis[4]



1. Burke JR et al. *Sci Transl Med*. 2019;11:1-16; **2**. Wrobleski ST et al. *J Med Chem*. 2019;62:8973-8995; **3**. Papp K et al. *N Engl J Med*. 2018;379:1313-21; **4**. Mease PJ et al. Presented at Annual Scientific Meeting of the American College of Rheumatology; Nov 5-9, 2020.

TYK2 and JAK1/2/3 kinases are *structurally* different from each other[26]

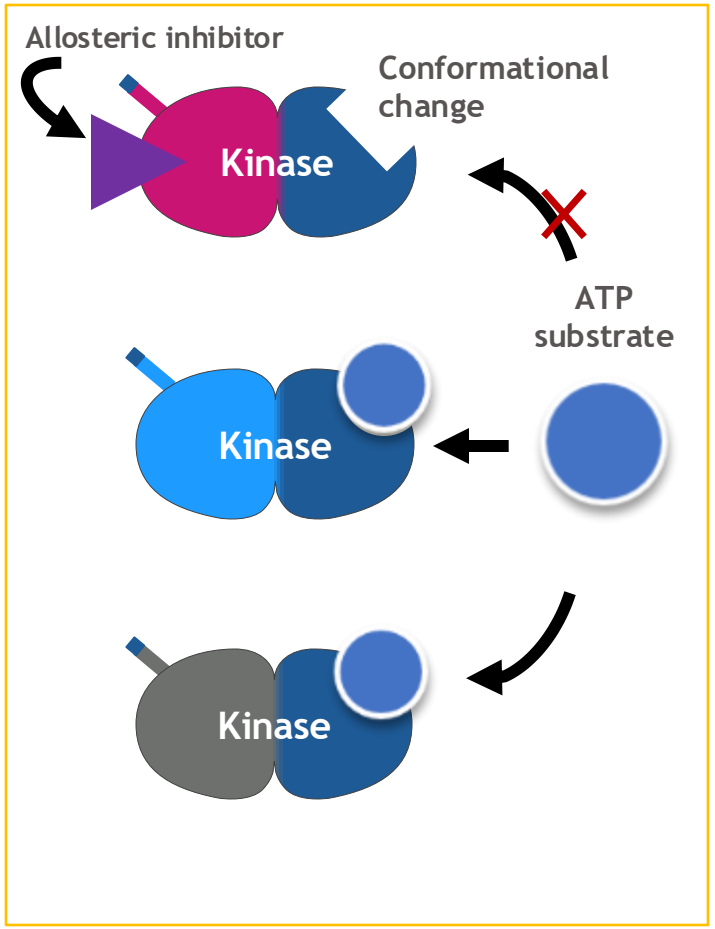


ATP=adenosine triphosphate; JAK=Janus kinase; TYK2=tyrosine kinase2.

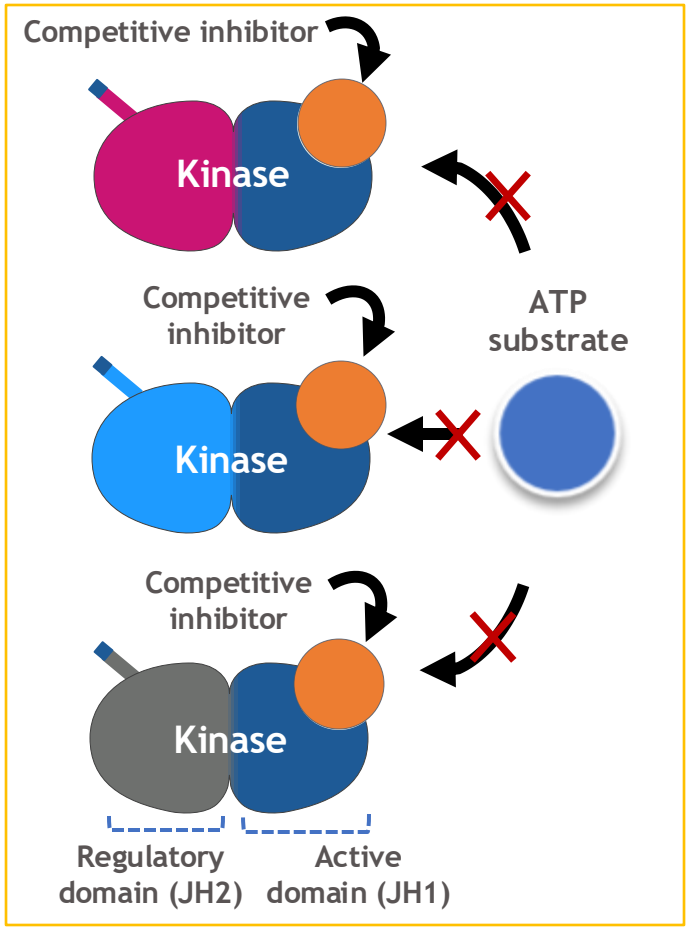
US Immunology

Allosteric kinase inhibition by small molecules[1,2]

Allosteric inhibitors bind to a site other than the active site[1,3-5]



Competitive inhibitors bind to the conserved active site[1,3-5]



- Allosteric inhibition can prevent ATP from binding to the active domain in several ways[1,4]:
  - Inducing a conformational change to the active site construction
  - Blocking access to the active site
- Allosteric inhibitors tend to target less conserved sites versus competitive inhibitors and therefore can have a higher degree of specificity for a particular enzyme[1]

ATP=adenosine triphosphate.

1. Nussinov R, Tsai C-J. *Cell*. 2013;153:293-305. 2. Imai K, Takaoka A. *Nat Rev Cancer*. 2006;6:714-727. 3. Berg JM et al. *Biochemistry*. 5th ed. 2002. 4. Strelow J et al, In: Markossian S et al, eds. *Assay Guidance Manual*. 2012. 5. Lu X et al. *Angew Chem Int Ed Engl*. 2020;59:1-13. doi.org/10.1002/anie.201914525.

Achievement of Treat-to-Target Thresholds with Envudeucitinib in Moderate-to-Severe Plaque Psoriasis: Results from STRIDE and OLE

April Armstrong[1], Benjamin D. Ehst[2], Jason E. Hawkes[2], Grace Ma[3†], Yuri Klyachkin[3†], Elena Hitraya[3†], and Kim A. Papp[4#*]

Disclosures: Commercial support was provided by Alumis Inc.

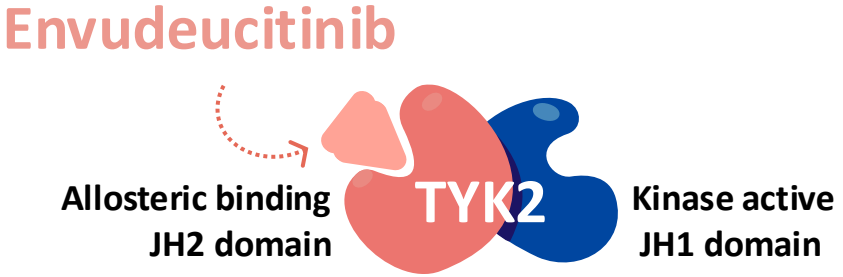
[#] Received honoraria as a scientific speaker and adviser from multiple Pharma companies
** Received research grants and funding from multiple Pharma companies*
[†] Author is employed by Alumis Inc.

Background

- **Treat-to-target thresholds** in psoriasis (PsO) help to guide therapeutic decisions by defining clinically meaningful improvements in symptoms and quality of life (QoL).

- **Psoriasis Area Severity Index (PASI), body surface area (BSA), and Dermatology Life Quality Index (DLQI)** are validated scores used to define treatment success, with treat-to-target thresholds for PASI of 0, ≤1, ≤2, ≤3, and ≤5, BSA of ≤1% and ≤3%, and DLQI of 0 and 0/1 being recognized in clinical guidelines and real-world practice.[1,2,3,4]

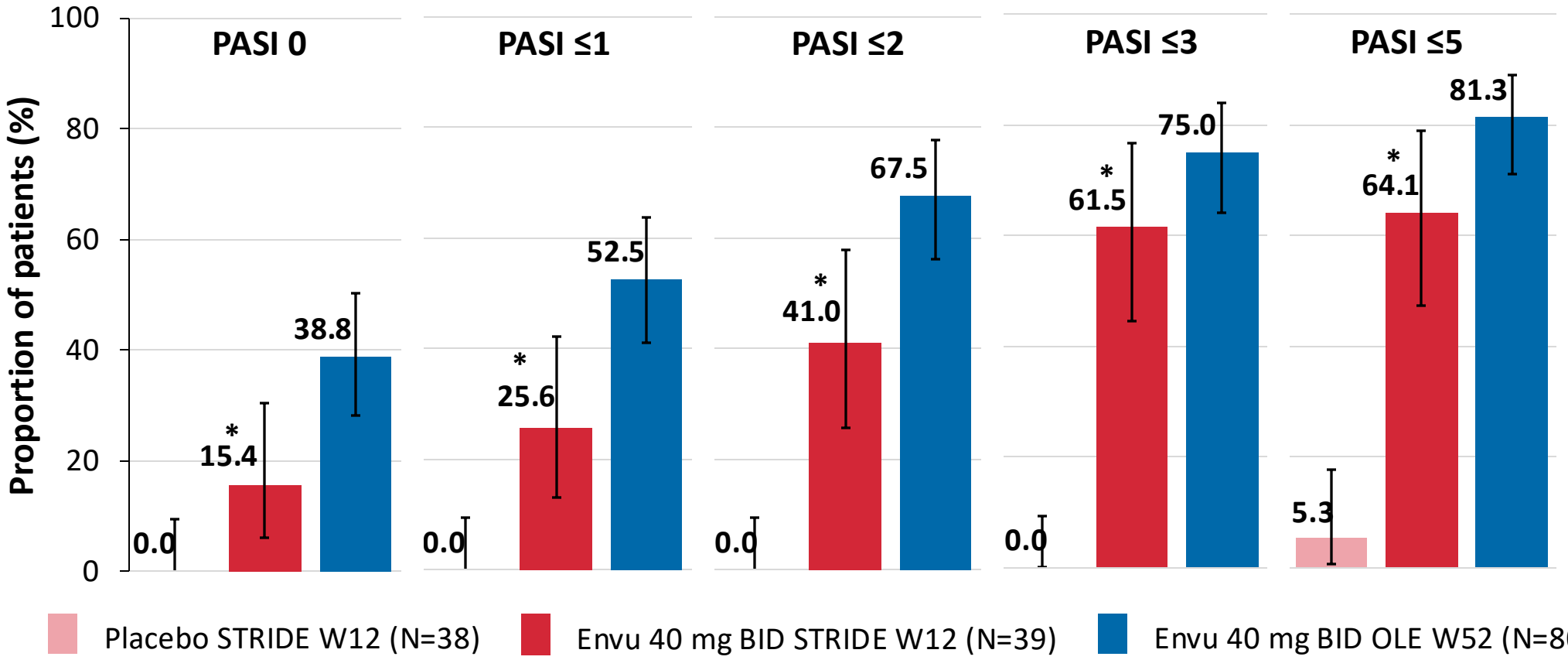
- **Envudeucitinib*** (formerly known as ESK-001), a highly selective allosteric tyrosine kinase 2 (TYK2) inhibitor, has shown efficacy and a favorable safety profile in Phase 2 clinical trials, demonstrating its potential to achieve treat-to-target goals in moderate-to-severe plaque PsO.



**Envudeucitinib is investigational and has not been approved by any regulatory authority.*

1. *Armstrong AW et al. J Am Acad Dermatol. 2017;76(2):290-298.* ***2.*** *Mahil SK et al. Br J Dermatol. 2020;182(5):1158-1166.* ***3.*** *Gisondi P et al. Dermatol Ther (Heidelb). 2021;11(1):235-252.* ***4.*** *Golbari NM et al. J Eur Acad Dermatol Venereol. 2021;35(2):417-421.*

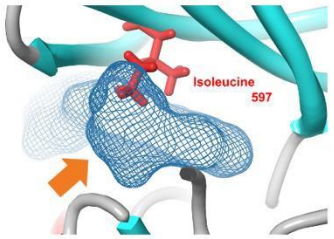
Consistent improvement in absolute PASI thresholds over time with envudeucitinib through 52 weeks



*Error bars represent the 95% CI. * p<0.013 versus placebo (STRIDE).*

Zasocitinib

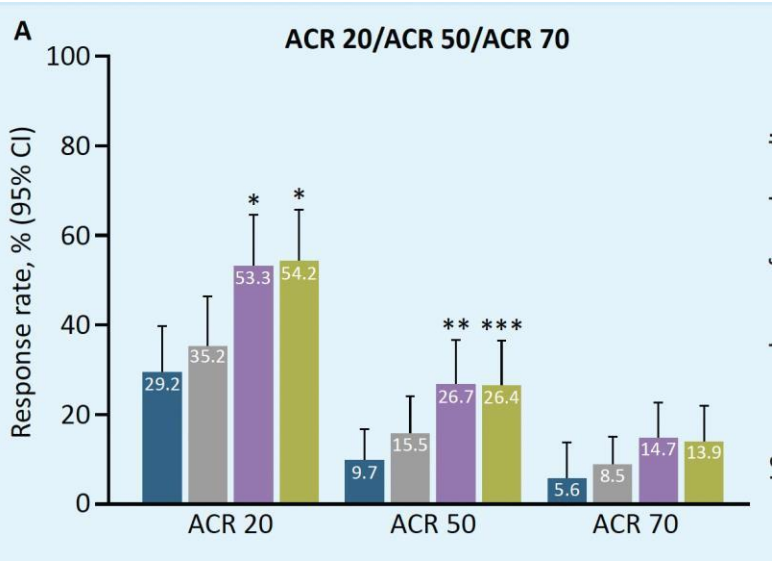
TAK-279 is a highly selective oral allosteric TYK2 inhibitor



TAK-279
Prohibited from Binding
in JAK1 Allosteric (JH2) Pocket

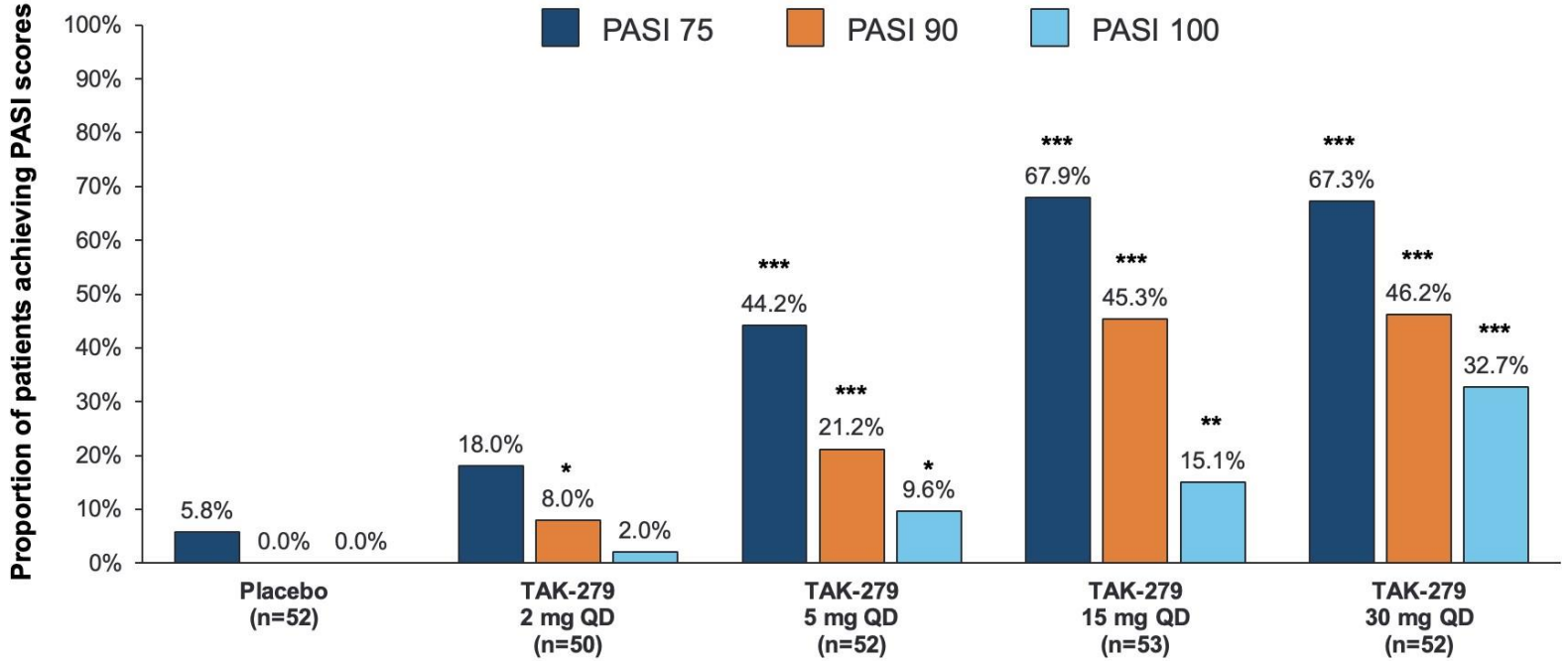
TAK-279 is excluded from the allosteric binding pocket of JAK1 owing to a single amino acid difference from TYK2

TYK2–JH2 binding K_d	0.034 nM
JAK1–JH2 binding K_d	5000 nM
Biochemical selectivity (fold)	1 470 588



Patients achieving PASI 75, 90 or 100 at Week 12

NRI analysis



Armstrong A. et al. AAD March 17–21, 2023, New Orleans, LA, USA
Kivitz, A et al. et al. ACR March 2023, San Diego, CA USA

- *Both studies met their co-primary and all 44 ranked secondary endpoints, including PASI 90, PASI 100 and sPGA 0, validating what we saw in our Phase 2b study.*

- *More than half of study participants treated with zasocitinib achieved clear or almost clear skin (PASI 90), and on average about 30 percent achieved completely clear skin (PASI 100) by week 16, showing the potential of a convenient once-daily pill to deliver complete skin clearance.*

- *Zasocitinib was generally well tolerated with a safety profile consistent with previous clinical studies. No new safety signals were identified.*

- *We plan to present the full Phase 3 results at upcoming medical congresses and submit an NDA to the U.S. FDA and other regulatory authorities starting in fiscal year 2026. We will keep this group updated, as appropriate.*

Icotrokinra Demonstrated Superior Responses Compared With Placebo and Deucravacitinib in the Treatment of Moderate-to-Severe Plaque Psoriasis

Results Through Week 24 of the Phase 3 ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2 Studies

Linda Stein Gold,[1] April W. Armstrong,[2] Robert Bissonnette,[3] Nina Magnolo,[4] Ronald B. Vender,[5] Michael Sebastian,[6] Maria Laura Galimberti,[7] Athanasios Tsianakas,[8] Marcelo Arnone,[9] Paul Wallace,[10] Margrit Simon,[11] Josep Riera-Monroig,[12] Bassey Effiom Edem,[13] Jennifer Campbell,[14] Ofelia Reyes-Servin,[15] Lea Kephart,[15] Yaung-Kaung Shen,[15] Kellen Cresswell,[15] Kim A. Papp[16]

[1]Henry Ford Health System, West Bloomfield, MI, USA; [2]Department of Dermatology, University of California Los Angeles, Los Angeles, CA, USA; [3]Innovaderm Research, Montreal, QC, Canada; [4]University Hospital Muenster, Muenster, Germany; [5]McMaster University and Dermatrials Research Inc., Hamilton, ON, Canada; [6]Dermatological Practice Dr. med. Michael Sebastian, Mahlow, Germany; [7]Hospital Italiano de Buenos Aires, Buenos Aires, Argentina; [8]Fachklinik Bad Bentheim, Bad Bentheim, Germany; [9]Hospital das Clínicas of University of São Paulo Medical School, São Paulo, Brazil; [10]Wallace Skin & Body Institute and Wallace Skin Research Center, Los Angeles, CA, USA; [11]Practice Dr. med. Margrit Simon, Berlin, Germany; [12]Dermatology Department, Hospital Clinic de Barcelona, University of Barcelona, Spain; [13]Johnson & Johnson, Leiden, The Netherlands; [14]Johnson & Johnson, Cambridge, MA, USA; [15]Johnson & Johnson, Spring House, PA, USA; [16]Alliance Clinical Trials and Probity Medical Research, Waterloo, ON, Canada and Division of Dermatology, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

This presentation was sponsored by Johnson & Johnson.
Adapted from presention by L. Stein Gold at the EADV Congress; September 17-20, 2025; Paris, France.

US-SFM-7338 09/25

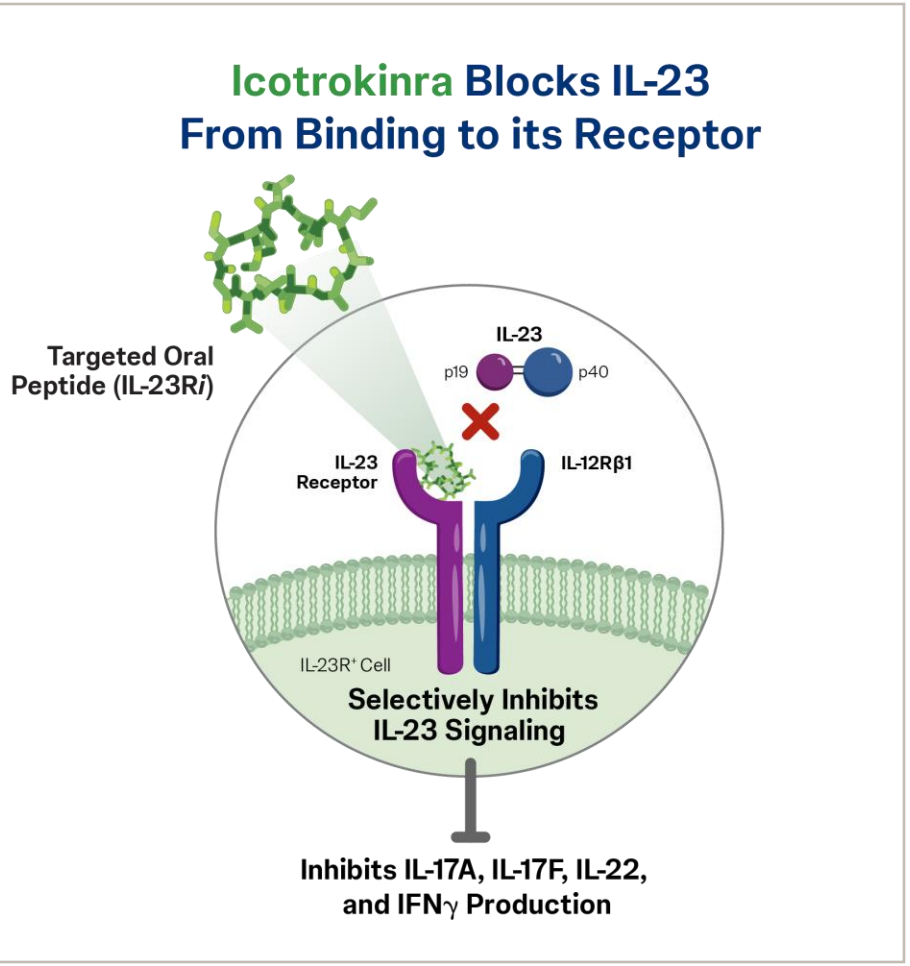
Background and Objective

Icotrokinra for plaque psoriasis

- Patients with moderate-to-severe plaque psoriasis (PsO) are limited to injectable therapies to achieve high-level efficacy with a favorable safety profile

Icotrokinra (ICO) is a first-in-class targeted oral peptide that:

- Selectively binds the interleukin (IL)-23 receptor and inhibits IL-23 pathway signaling[1]
- Demonstrated significantly higher response rates vs placebo (PBO) at Week (W)16 in adults & adolescents with moderate-to-severe plaque PsO (ICONIC-LEAD) and in those with high-impact site PsO involving the scalp and genitals (ICONIC-TOTAL); no safety signals have been identified[2,3]

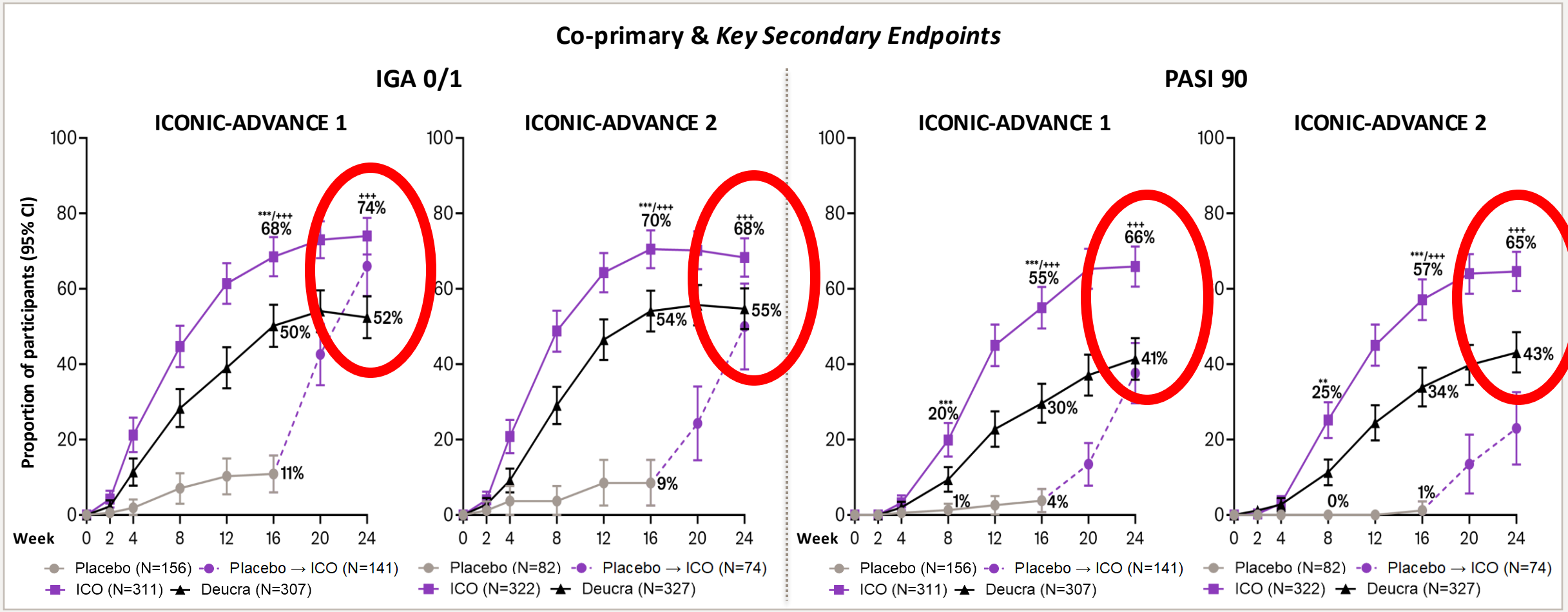


Objective

- Report key clinical and participant-reported outcomes (PROs) and safety findings from ICONIC-ADVANCE 1 and ICONIC-ADVANCE 2, the first PBO-controlled ICO trials to also include an active comparator arm vs deucravacitinib (Deucra)

[1]Fourie AM, et al. *Sci Rep*. 2024;14:17515. [2]Bissonnette R, et al. Presented at: AAD Annual Meeting; March 8, 2025; Orlando, FL, USA.[3]Gooderham M, et al. SID Annual Meeting; May 7-10, 2025; San Diego, CA, USA. **IFN**=interferon, **IL-12Rβ1**=interleukin-12 receptor beta 1, **IL-23R**=interleukin-23 receptor, **IL-23Ri**=interleukin-23 receptor inhibitor.

ICO demonstrated significantly higher rates of IGA 0/1 and PASI 90 vs PBO at W16 (co-primary endpoints) & vs Deucra at W16 and W24

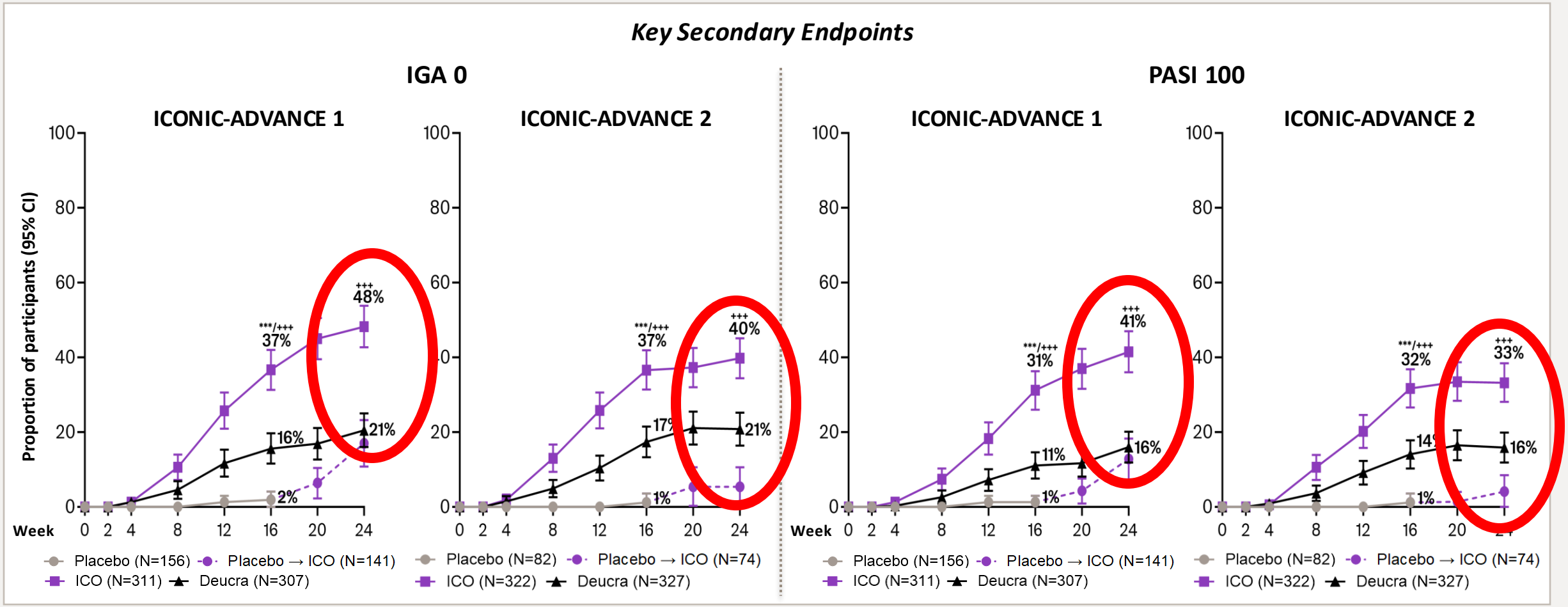


Multiplicity-adjusted **p*<0.05, ***p*<0.01, ****p*<0.001 vs PBO; multiplicity-adjusted ^{+}p<0.05, ^{++}p<0.01, ^{+++}p<0.001 vs Deucra

ICO showed early separation from PBO for achievement of PASI 90 at W8

P-values based on Cochran-Mantel-Haenszel chi-square test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region. **CI**=confidence interval, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **IGA 0/1**=IGA score 0/1 & ≥2-grade improvement from baseline, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.

ICO demonstrated significantly higher rates of complete skin clearance vs PBO at W16 & vs Deucra at W16 and W24



Multiplicity-adjusted *p<0.05, **p<0.01, ***p<0.001 vs PBO; multiplicity-adjusted ^{+}p<0.05, ^{++}p<0.01, ^{+++}p<0.001 vs Deucra

Rates of completely clear skin were ~2-fold or greater for ICO- vs Deucra-treated participants at W16 and W24

P-values based on Cochran-Mantel-Haenszel chi-square test stratified by baseline weight category (≤90 kg, >90 kg) and geographic region. **CI**=confidence interval, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **IGA**=Investigator's Global Assessment, **PASI**=Psoriasis Area and Severity Index, **PBO**=placebo, **W**=week.

ICO AE profile was similar to PBO through W16

Combined ICONIC-ADVANCE 1 & 2 AEs[a]	PBO-Controlled (W0-16)			Active Comparator-Controlled (W0-24)	
	PBO (N=237)	ICO (N=632)	Deucra (N=634)	ICO (N=632)	Deucra (N=634)
Mean weeks/total PY of follow-up	15.5 / 70.5	15.9 / 192.7	15.8 / 191.6	23.6 / 285.2	23.3 / 283.1
Any AE	136 (57%)	303 (48%)	360 (57%)	**359 (57%)**	**411 (65%)**
Incidence/100 PY (95% CI)[b]	**314 (254, 361)**	**225 (200, 251)**	300 (268, 330)	**201 (180, 221)**	**263 (237, 288)**
Serious AE	4 (2%)	14 (2%)	14 (2%)	18 (3%)	20 (3%)
Incidence/100 PY (95% CI)[b]	**6 (<1, 9)**	**7 (3, 11)**	7 (4, 11)	6 (3, 9)	7 (4, 10)
Serious infection[c]	1 (<1%)	1 (<1%)	4 (1%)	3 (<1%)	4 (1%)
Incidence/100 PY (95% CI)[b]	**1 (0, 9)**	**1 (0, 3)**	2 (1, 6)	1 (<1, 3)	1 (<1, 4)
Malignancy[d]	1 (<1%)	3 (<1%)	1 (<1%)	3 (<1%)	2 (<1%)
Incidence/100 PY (95% CI)[b]	**1 (0, 9)**	**2 (<1, 5)**	1 (0, 3)	1 (<1, 3)	1 (<1, 3)
AE leading to discontinuation	12 (5%)	13 (2%)	14 (2%)	15 (2%)	17 (3%)
Incidence/100 PY (95% CI)[b]	**17 (6, 24)**	**7 (3, 10)**	7 (4, 11)	5 (3, 8)	6 (3, 9)

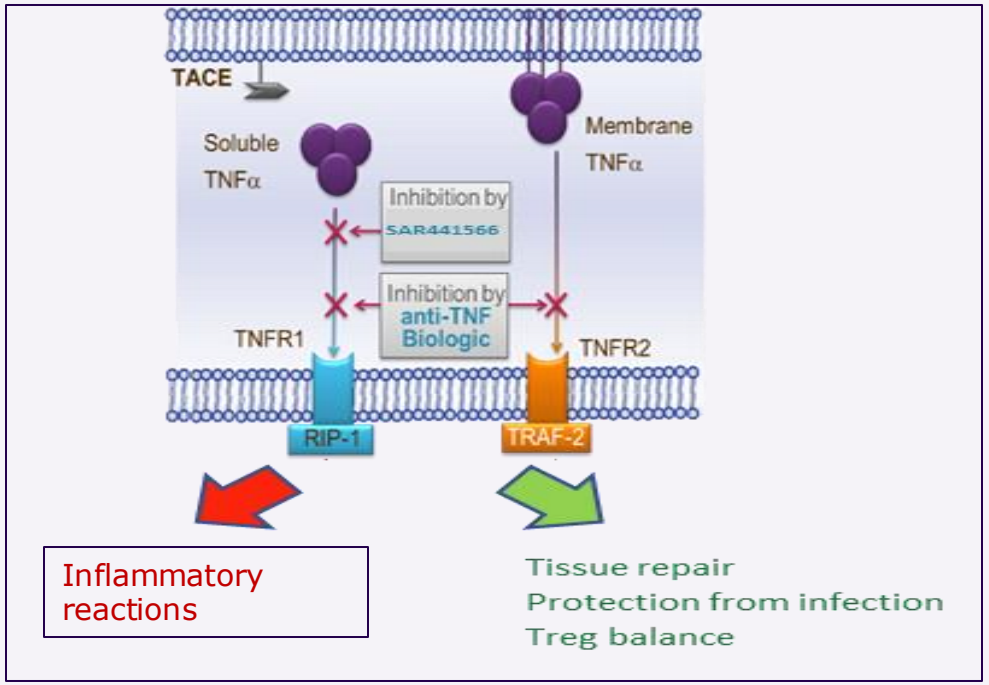
Overall AE rates through W24 were lower with ICO than Deucra

Values are n (%) unless otherwise noted. [a]Safety analysis set included all randomized and treated participants (pts); ICONIC-ADVANCE 1 & 2: PBO=155/82, ICO=310/322, Deucra=307/327. [b]Incidence/100 PY: number of pts with AEs/total PY at risk × 100; CI based on study-size adjusted Wald statistics. [c]Included arthritis bacterial in the PBO group, infective exacerbation of chronic obstructive airways disease and pneumonia in the ICO group, and campylobacter colitis, lower respiratory tract infection, viral infection, and viral upper respiratory tract infection in the Deucra group. [d]Included invasive ductal breast carcinoma in the PBO group, pancreatic carcinoma and hepatic metastases, breast cancer, and keratoacanthoma in the ICO group, and buccal squamous cell carcinoma and malignant melanoma in situ in the Deucra group; all considered unrelated to study treatment by investigators. **AE**=adverse event, **CI**=confidence interval, **Deucra**=deucravacitinib, **ICO**=icotrokinra, **PBO**=placebo, **PY**=participant-years, **W**=week.

ORAL TNF INHIBITORS

Selective inhibition of TNFR1 signal

Current TNF inhibitors target both TNFR1 and TNFR2 signal



TNF subtype	Receptor	Function
sTNF	TNFR1	• Pro-inflammatory responses • Promotes tissue destruction
mTNF	TNFR2	• Tissue regeneration • Regulatory T-cell function • Host-pathogen defense • Potential role in some immune-mediated diseases

Potential Advantages

- Reduced risk of serious infections*
- Reduced exacerbations of autoimmune disease*
- Improved efficacy maintenance through Treg activation

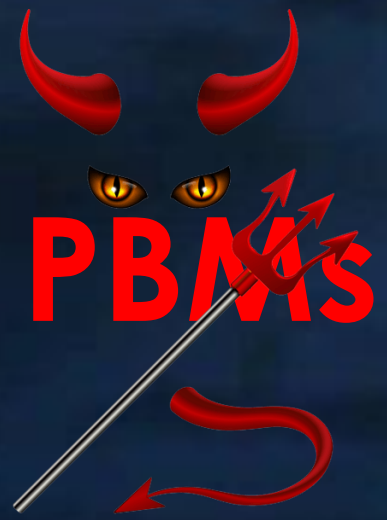
We are lucky to have new vehicles and new molecules in Dermatology.

HOWEVER…

IS MEDICAL PRACTICE CATCHING UP WITH MEDICAL INNOVATION?

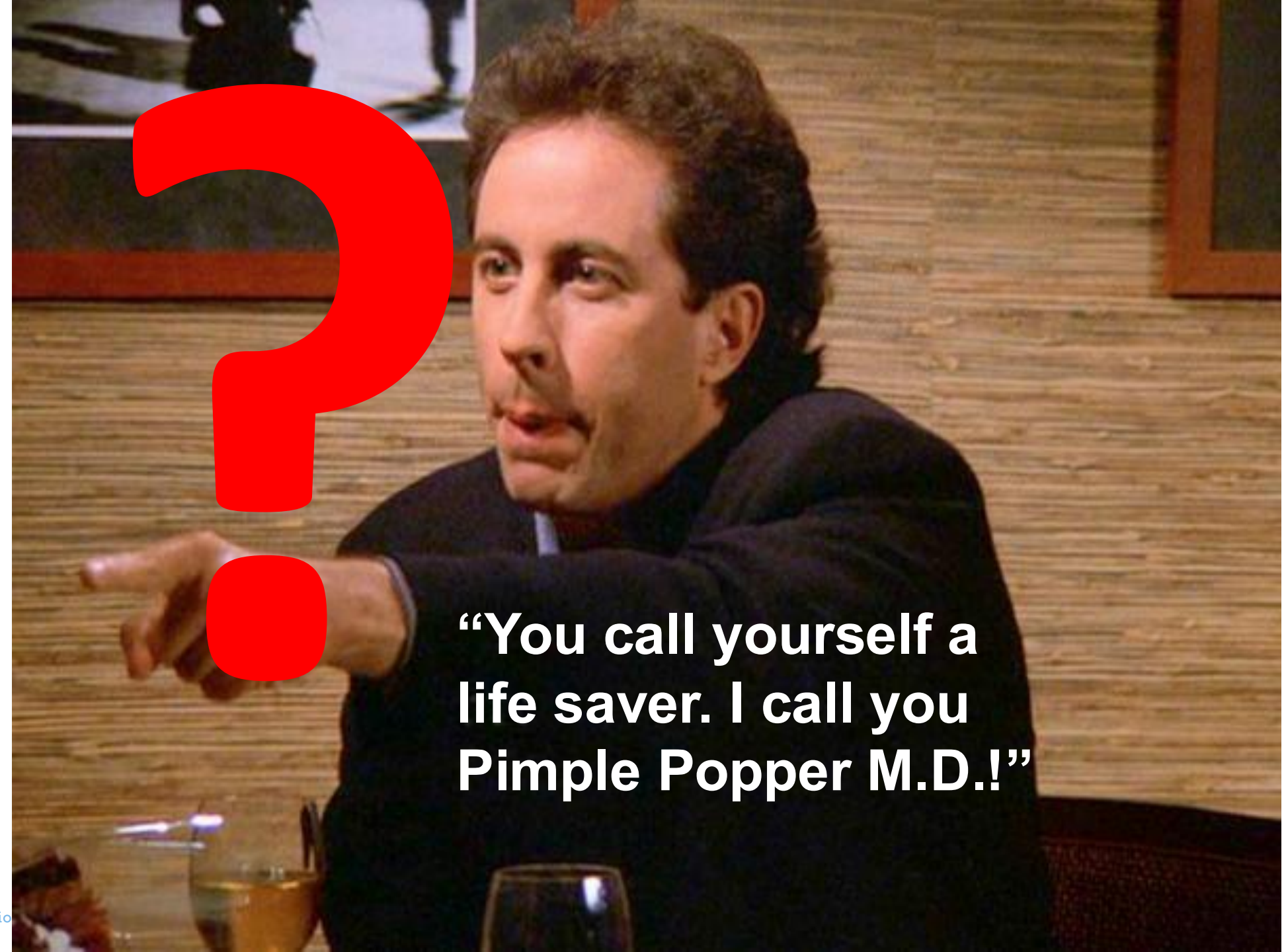
IS MEDICAL PRACTICE CATCHING UP WITH MEDICAL INNOVATION?

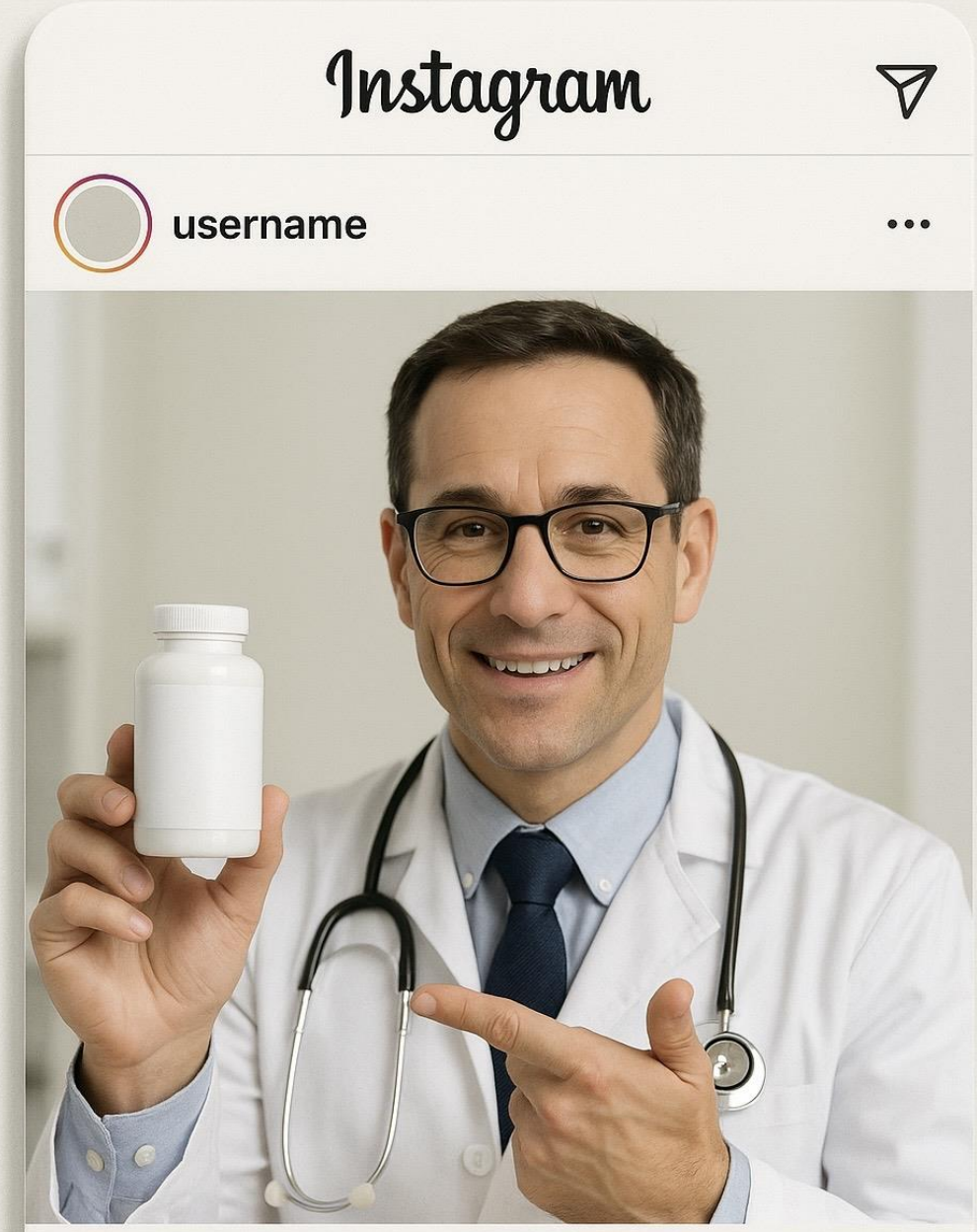
1.PRIOR AUTHORIZATION
2.THIRD PARTY PAYERS
3.DEDUCTIBLES
4.COPAYS



IS THIS THE END OF R&D FOR DERM IN USA?

DERMATACOSMETICS VS PRESCRIPTION TREATMENTS

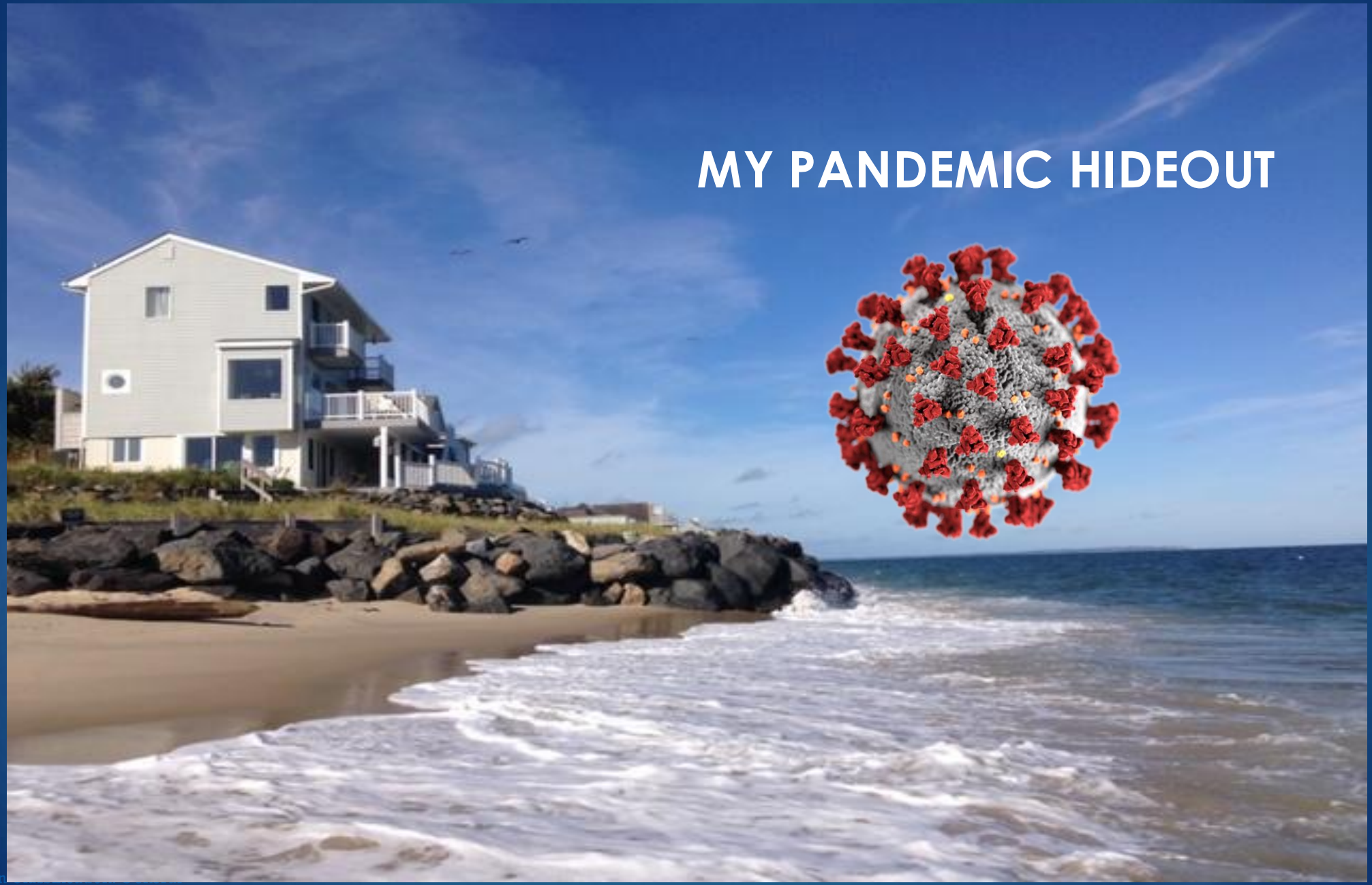




MEDICAL DERMATOLOGY CAN NOT BE TAKEN CARE OF BY INFLUENCERS OR SOCIAL MEDIA

MEDICAL DERMATOLOGY CAN ONLY BE TAKEN CARE OF IN OUR OFFICES BY SEEING PATIENTS

MY PANDEMIC HIDEOUT



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