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First-in-disease therapies for patients with rare skin diseases

QTORIN™ Pitavastatin: Developing the First Pathogenesis-directed Therapy for Disseminated Superficial Actinic Porokeratosis

November 5, 2025

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QTORIN™ Pitavastatin Program: Today's Attendees

Keith Choate, MD, PhD

Yale SCHOOL OF MEDICINE

- Aaron B. and Marguerite Lerner Professor and Chair of Dermatology
- Professor of Genetics and Pathology
- Associate Dean for Physician-Scientist Development
- President of the Pediatric Dermatology Research Alliance (PeDRA)
- Consultant to Palvella

Wes Kaupinen
Founder & CEO

Jeff Martini, PhD
Chief Scientific Officer

David Osborne, PhD
Chief Innovation Officer

Matt Korenberg
CFO

Bohan Wei
VP Corporate Development & New Product Planning

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Multiple High-Impact Milestones Between Now and End of Q1 2026

✓ SEPTEMBER 2025

TODAY

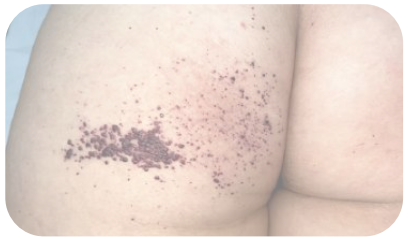
MID-DECEMBER 2025

Q1 2026

1

Third Planned Indication for QTORIN™ Rapamycin: Clinically Significant Angiokeratomas

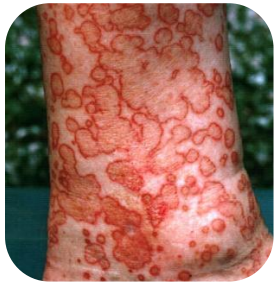
- ✓ Serious, rare, no FDA-approved therapies
- ✓ Commercially attractive



2

New QTORIN™ Program: QTORIN™ Pitavastatin for DSAP* & Other Porokeratosis

- ✓ Serious, rare, no FDA-approved therapies
- ✓ Clear biology
- ✓ Commercially attractive: >50k U.S. patients
- ✓ Projected <2.5 years to Phase 2 POC data

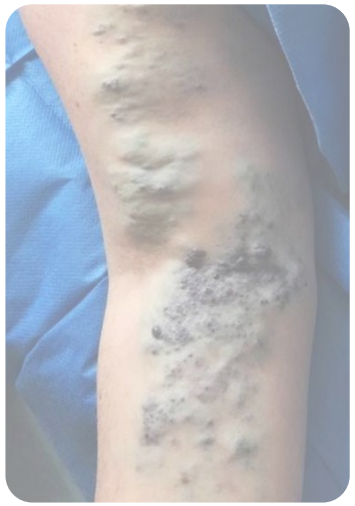


3

Phase 2 Topline Data in Cutaneous VMs

FULLY ENROLLED

- ✓ 16 subjects

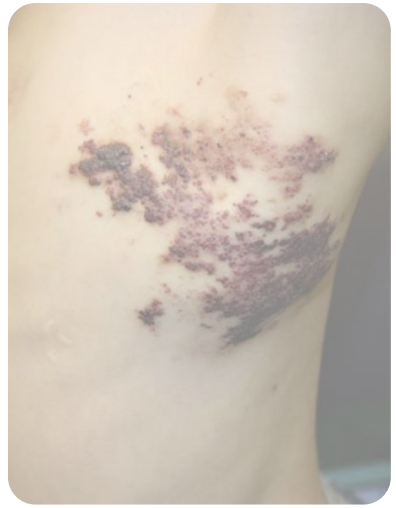


4

Phase 3 Topline Data in Microcystic LMs

EXCEEDED ENROLLMENT TARGET

- ✓ 51 subjects



*DSAP = Disseminated Superficial Actinic Porokeratosis. *QTORIN™ 3.9% rapamycin anhydrous gel and QTORIN™ pitavastatin are for investigational use only and neither has been approved or cleared by the FDA or by any other regulatory agency. The safety or efficacy has not been established for any use.*

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QTORIN™ Pitavastatin for
Disseminated Superficial Actinic Porokeratosis

Disease Overview & Scientific Rationale

Dr. Keith Choate,
Yale School of Medicine

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Disseminated Superficial Actinic Porokeratosis (DSAP) is a Serious Disease with No FDA-Approved Therapy

Keith Choate, MD, PhD

Yale SCHOOL OF MEDICINE

- Aaron B. and Marguerite Lerner Professor and Chair of Dermatology
- Professor of Genetics and Pathology
- Associate Dean for Physician-Scientist Development
- President of the Pediatric Dermatology Research Alliance (PeDRA)
- Consultant to Palvella

High impact to patient quality of life with meaningful risk of malignant transformation to squamous cell carcinomas

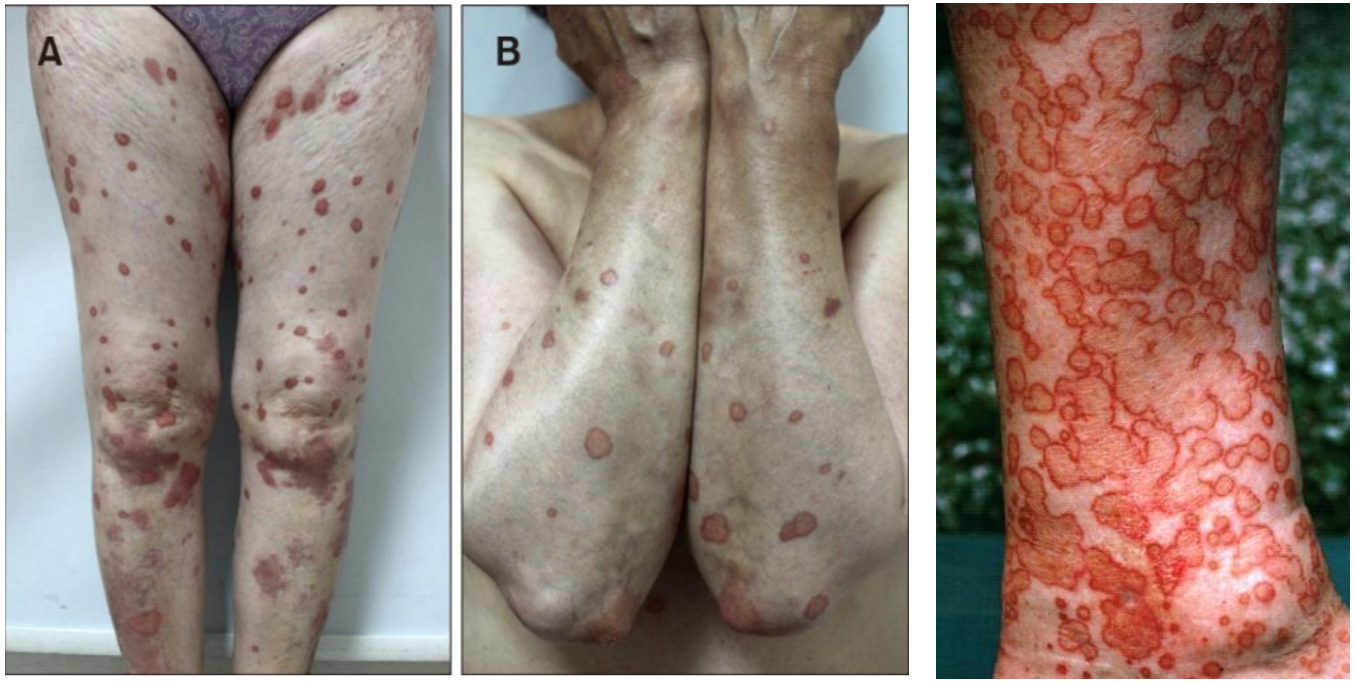

Image sources: Sim et al, Ann Dermatol, (2018) and Dr. Keith Choate presentation to Palvella (2025).

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Disseminated Superficial Actinic Porokeratosis (DSAP):
Progressing to the First Potential Pathogenesis-directed Therapy

1893

Vittorio Mibelli
Italian Dermatologist

First discovered porokeratosis – from Greek meaning *"abnormal keratinization disorder"*

2011

Amy Paller, MD
Member of Palvella MSAB
Northwestern Medicine
Feinberg School of Medicine

Discovery that **mutations in the mevalonate pathway** are responsible for many genetic skin diseases

2019-2020

Keith Choate, MD, PhD
Yale SCHOOL OF MEDICINE

Breakthrough discovery that **second hit mutation underlies porokeratosis** and translated those findings into a proof-of-concept study in patients with porokeratosis

2025

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Jeff Martini, PhD
Chief Scientific Officer

David Osborne, PhD
Chief Innovation Officer

Extensive formulation development completed with plans to enter clinic in 2H 2026 – **potential to be first FDA-approved therapy**

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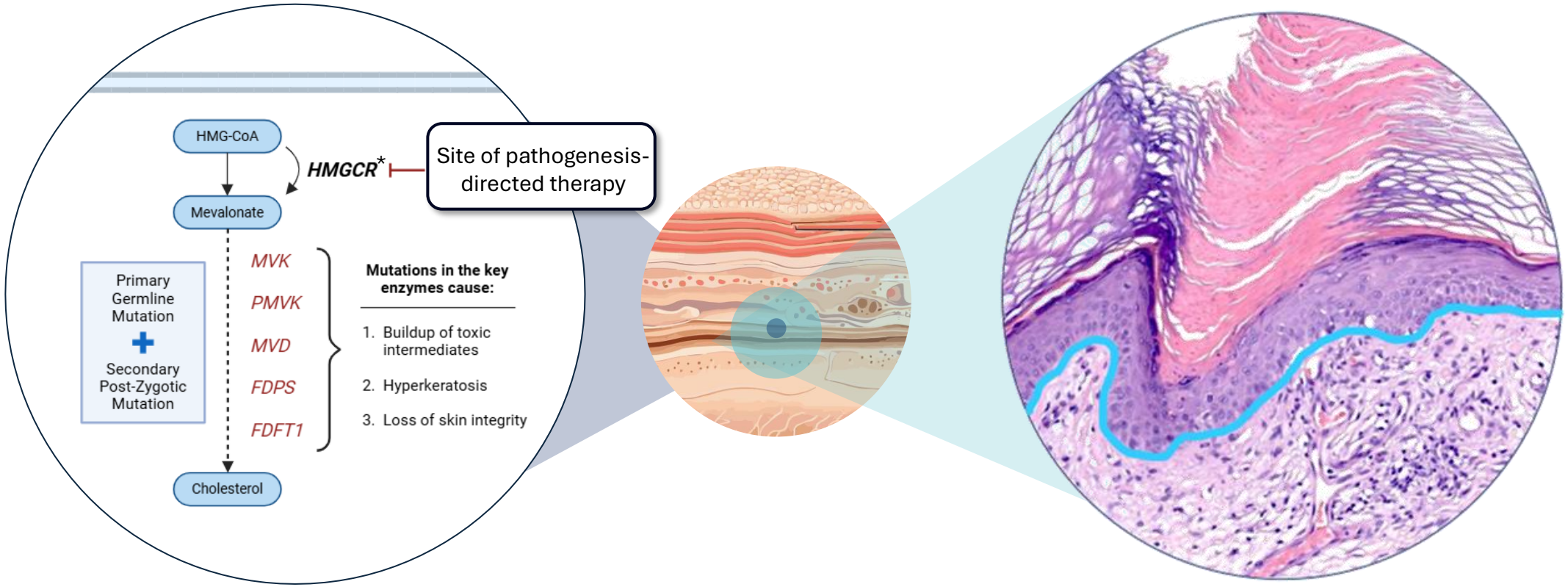
Bagherani et al, *Glob Dermatol*, (2015); Paller et al, *J Invest Dermatol*, (2011); Atzmony et al, *J Invest Dermatol,* (2019); Atzmony et al, *J Am Acad Dermatol*, (2020).

Clear Biology: Targeting the Causal Mevalonate Pathway

Target: Mevalonate Pathway

Tissue: Epidermis & Dermis



An on-target, in-tissue approach could result in significant clinical improvement

*HMGCR = 3-hydroxy-3-methylglutaryl-coenzyme A reductase. Image sources: Milani D, Warbasse E, Chen WS. Porokeratosis. PathologyOutlines.com website.

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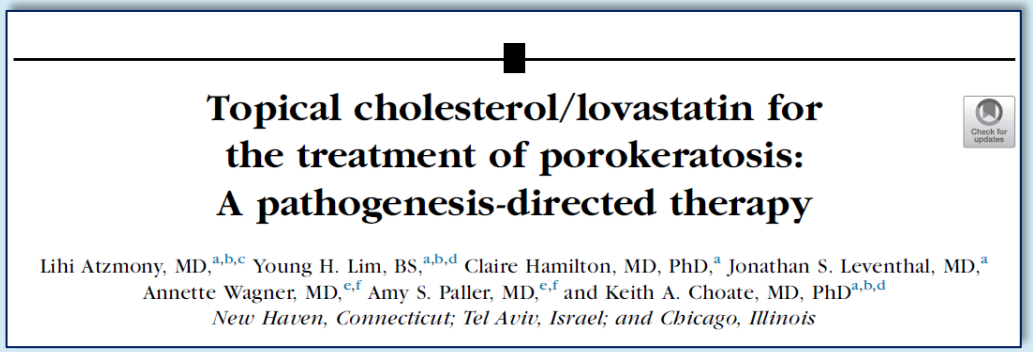
Unmet Need for First FDA-approved Topical Mevalonate Pathway Inhibitor for DSAP

Oral statins are not a viable therapeutic option in DSAP:

High first pass metabolism and/or sub-therapeutic biodistribution to the skin



Topical cholesterol/lovastatin for the treatment of porokeratosis: A pathogenesis-directed therapy

Lihi Atzmony, MD,[a,b,c] Young H. Lim, BS,[a,b,d] Claire Hamilton, MD, PhD,[a] Jonathan S. Leventhal, MD,[a] Annette Wagner, MD,[e,f] Amy S. Paller, MD,[e,f] and Keith A. Choate, MD, PhD[a,b,d]

New Haven, Connecticut; Tel Aviv, Israel; and Chicago, Illinois

Proof-of-concept study, demonstrating a plausible mechanistic approach

>20 subsequent supportive studies of off-label use of topical statin therapy in porokeratosis…

…however, today **poor patient outcomes persist** due to lack of access and known variability in unapproved formulations which can limit safety, efficacy, and quality

Significant need for an FDA-approved topical mevalonate pathway inhibitor

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QTORIN™ Pitavastatin for
Disseminated Superficial Actinic Porokeratosis

QTORIN™ Pitavastatin Formulation Development

Dr. David Osborne,
Chief Innovation Officer

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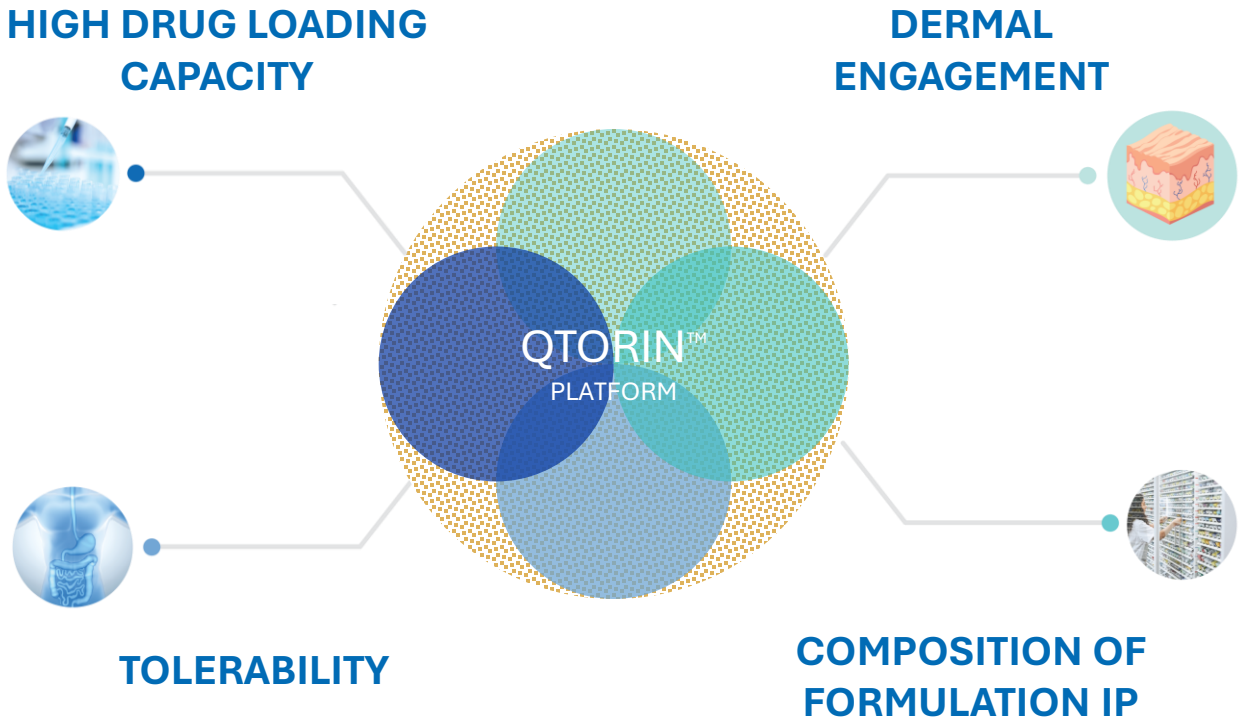
QTORIN™ Platform: Application to Mevalonate Pathway Inhibitors

David Osborne, PhD

Chief Innovation Officer

- Recognized formulation expert with 35+ years of industry-leading experience in topical drug development
- Founding scientist and CTO at Arcutis Biotherapeutics (NASDAQ: ARQT)
- Contributed to the development of three dozen topical therapies, incl. ZORYVE® (roflumilast) cream and foam



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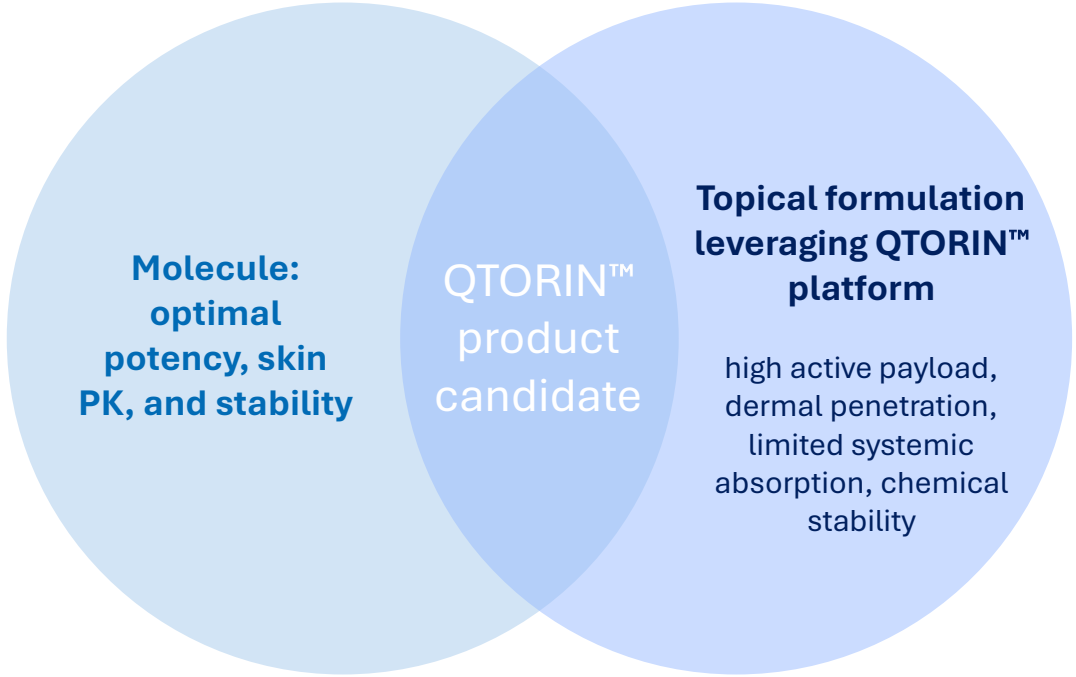
Developing the First Pathogenesis-directed Therapy For DSAP



Target Product Profile Established in 2024

- Chemical & formulation stability
- Targeted dermal penetration
- High potency
- Optimized release from vehicle
- Designed for patient adherence

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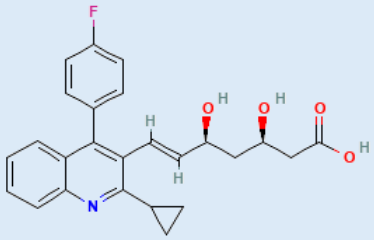
QTORIN™ Pitavastatin: On Target, In Tissue

Using QTORIN™, we considered and tested a wide range of mevalonate pathway inhibitors

Molecule	Potency	Optimal Skin PK	Stability
Pitavastatin	✓	✓	✓
Mev. Inhibitor 2	*Did not meet some or all pre-defined target product attributes*		
Mev. Inhibitor 3			
Mev. Inhibitor 4			
Mev. Inhibitor 5			
Mev. Inhibitor 6			
Mev. Inhibitor 7			

QTORIN™

PITAVASTATIN



- **Pitavastatin is an FDA-approved next-generation oral statin** for patients with primary hyperlipidemia and mixed dyslipidemia
- **Superior inhibition of the mevalonate pathway compared to all molecules evaluated**
- **Key characteristics:**
  - Payload: > 2% concentration achieved
  - Dermal penetration: *in vitro* penetration test confirms > IC90
  - Low systemic absorption
  - Encouraging preliminary drug stability
  - IP: Filed formulation & method of use IP and licensed Yale IP

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QTORIN™ Pitavastatin for
Disseminated Superficial Actinic Porokeratosis

Clinical Development Plan

Dr. Jeff Martini,
Chief Scientific Officer

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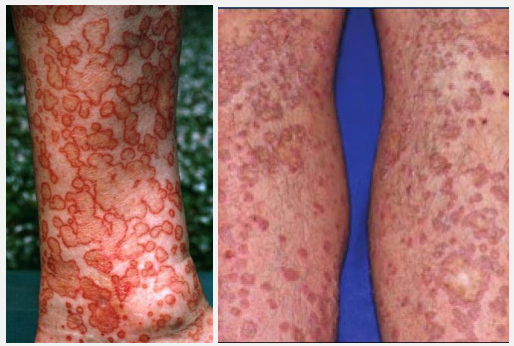
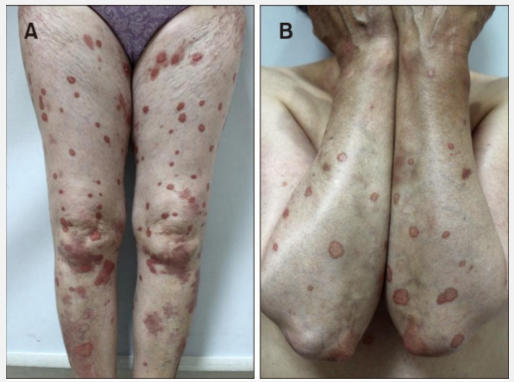
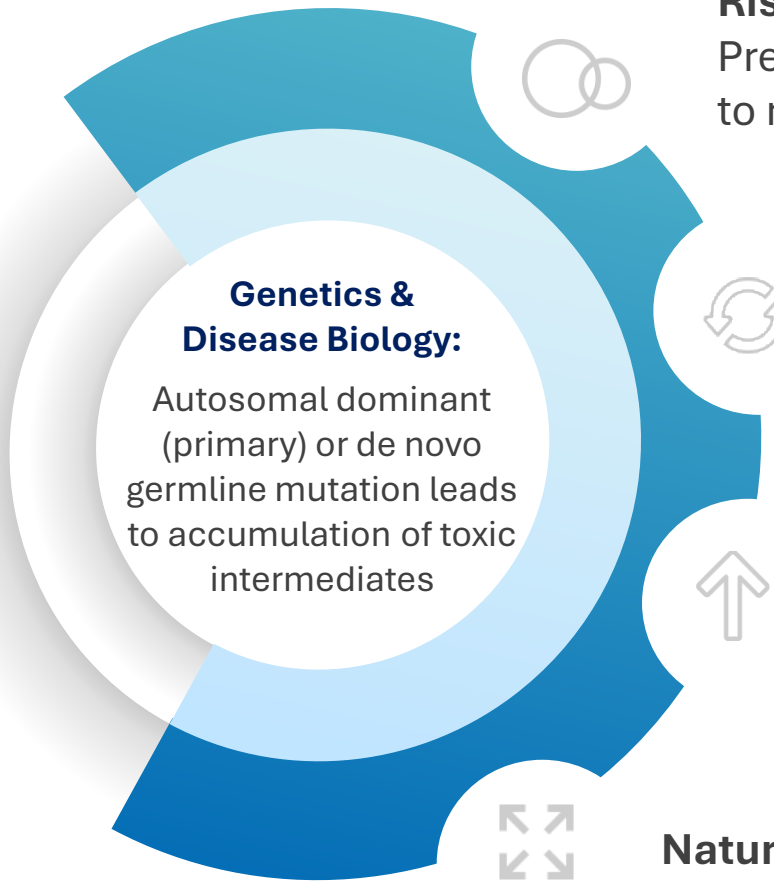
Disseminated Superficial Actinic Porokeratosis (DSAP):
Chronic, Pre-Cancerous, and Progressive

> 50k patients
ESTIMATED IN THE U.S.[1]







Risk of malignant transformation: Premalignant disease with transformation to non-melanoma skin cancers[2]

Significant impact to quality of life: clinical signs include skin disfigurement, burning, and persistent itch

Persistent and extensive: Clonal proliferation of abnormal keratinocytes leads to increased number and size of lesions

Natural history: Spontaneous regression is extremely rare[2]

No FDA-approved therapies

Current options:
Laser, surgery, and off-label topical chemo agents & mevalonate pathway inhibitors

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1. Clarity Pharma research (April 2025), n=277 physicians surveyed. 2. Williams, Grant M., et al. “Porokeratosis.” StatPearls Publishing, 2024.

QTORIN™ Pitavastatin Clinical Pathway:
Planned Initiation of Phase 2 in 2H 2026

QTORIN™ Pitavastatin: From Concept to Clinic

- Targeting <2.5 years to Phase 2 POC data
- QTORIN™ pitavastatin optimized for stability and drug delivery
- Working with FDA Division of Dermatology and Dentistry
- Filed intellectual property

FDA meeting planned 1H 2026

- Discuss proposed Phase 2 study design
- Discuss eligibility for expedited programs (Fast Track Designation)

Initiation of Proposed Phase 2 study anticipated in 2H 2026

- Phase 2 protocol drafted
- Endpoint development nearing completion with extensive input from key opinion leaders and patients

GOAL: Initiate Phase 2 clinical development in 2H 2026

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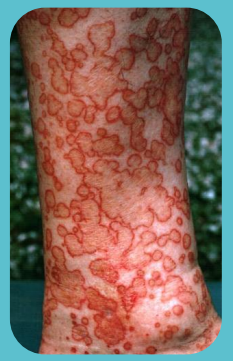
QTORIN™ Pitavastatin: Future Expansion Opportunities

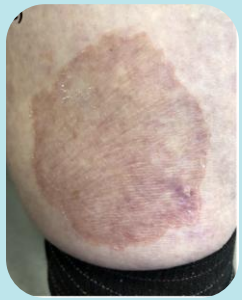
First Clinical Trial: DSAP Patients



DSAP:

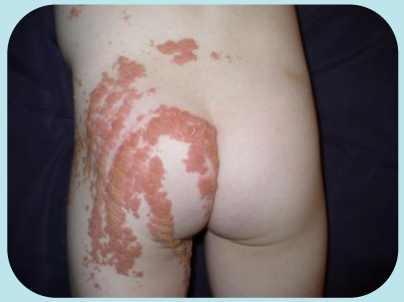
50k+ U.S. pts

Subsequent Studies: Expand into Other Porokeratosis Subtypes



Porokeratosis of Mibelli:

20k+ U.S. pts



Other subtypes (incl. linear porokeratosis):

10k+ U.S. pts

Clarity Pharma (September 2025), n=277 physicians surveyed, MedaCorp Survey (August 2025), n=55 physicians surveyed.

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QTORIN™ Pitavastatin for
Disseminated Superficial Actinic Porokeratosis

Commercial Opportunity

Matt Korenberg
Chief Financial Officer

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Attractive U.S. Commercial Opportunity for DSAP

>50k

diagnosed DSAP patients in the U.S. based on two sources (Clarity Pharma, n=277 physicians; Zagoras et al, 2023) and confirmed by KOL calls

Orphan Pricing

anticipated based on disease severity and lack of FDA-approved therapies

Market research (n=55 physicians)[1]:

100%

of physicians would incorporate Product X (topical mevalonate pathway inhibitor) into their practice

96%

of physicians would consider Product X as a first line therapy for DSAP patients

1. MedaCorp Survey (August 2025), n=55 physicians surveyed.

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QTORIN™ Pitavastatin for
Disseminated Superficial Actinic Porokeratosis

Key Takeaways

Wes Kaupinen
Founder & Chief Executive Officer

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QTORIN™ Pitavastatin for DSAP: Key Program Milestones Achieved

1 Scientific & Medical

- ✓ **Strong KOL support -** Dr. Keith Choate, Dr. Amy Paller, Dr. Dirk Elston, Dr. Jim Treat, Dr. John Doux, and others
- ✓ **Known genetics and clear biology confirmed**
- ✓ **Analyzed published case studies of off-label statin use, confirming proof-of-principle**

2 Commercial

- ✓ **No FDA-approved therapies and low competition**
- ✓ **Prospective epidemiology work** confirmed commercially attractive opportunity
- ✓ **Initial physician market research and patient-based market research completed**

3 Product Development

- ✓ **QTORIN™ formulation:** High concentration of drug, dermal penetration, stable
- ✓ **Safety:** *in silico* testing completed
- ✓ **IP licensed from Yale** (Inventor: Dr. Keith Choate)
- ✓ **IP filed on formulation and method of use**

4 Regulatory

- ✓ **Planned 505(b)(2) pathway**
- ✓ **Potentially eligible for expedited programs** (Fast Track Designation)
- ✓ **Potentially eligible for orphan designation**

Life cycle management opportunities for other porokeratosis subtypes

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Disseminated Superficial Actinic Porokeratosis (DSAP):
Aligned With Palvella's Pipeline Strategy

	QTORIN™ Rapamycin	QTORIN™ Pitavastatin	
	Microcystic LMs, Cutaneous VMs, Clinically Significant Angiokeratomas	DSAP	
Serious	✓	Chronic, extensive lesions, malignant transformation	*Significant unmet medical need*
Rare	✓	>50k U.S. patients	
No FDA-approved Therapies	✓	None	
Strong Scientific & Biologic Rationale	✓	Mutations in mevalonate pathway lead to accumulation of toxic intermediates	*Optimizing likelihood of clinical success*
Published Case Studies & Off-label Use of API	✓	Multiple published case studies + use in academic centers	
Commercially Attractive	✓	Opportunity to be first-in-disease and SOC	*Multi-billion dollar U.S. TAM[1]*

1. Based on internal and third-party estimates.

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Thank You

Striving to be first for rare disease patients

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