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

QTORIN™ Rapamycin Pipeline Expansion
September 24, 2025

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QTORIN™ Rapamycin Pipeline Expansion: Today's Attendees

Wes Kaupinen
CEO

Jeff Martini, PhD
Chief Scientific Officer

Matt Korenberg
CFO

Bohan Wei
VP Corporate Development & New Product Planning

James Treat, MD

- Pediatric dermatologist at Children's Hospital of Philadelphia (CHOP)
- Clinical dermatologist at the Comprehensive Vascular Anomalies Program at CHOP
- Professor of Clinical Pediatrics and Dermatology, Perelman School of Medicine at the University of Pennsylvania
- Member of Palvella Medical and Scientific Advisory Board

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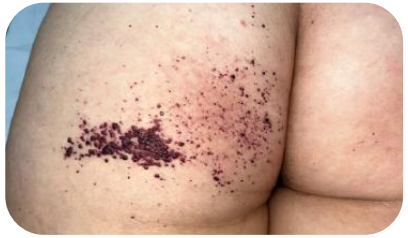
Four High-Impact Milestones Between Now and End of Q1 2026

TODAY | Q4 2025 | 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

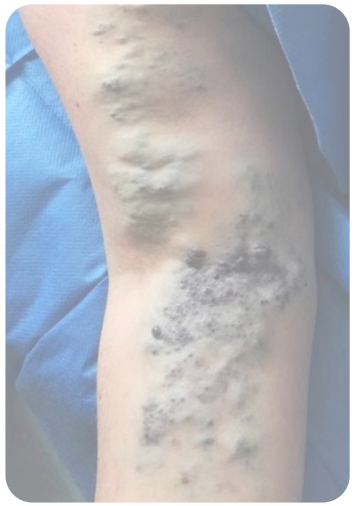
- ✓ Serious, rare, no FDA-approved therapies
- ✓ Clear biology
- ✓ Commercially attractive
- ✓ Targeting <$10mm and <2.5 years to Phase 2 POC data

QTORIN™ PLATFORM

3 Phase 2 Topline Data in Cutaneous VMs

FULLY ENROLLED

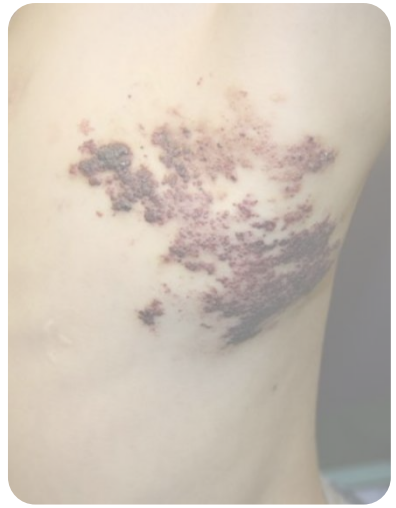
- ✓ 16 subjects



4 Phase 3 Topline Data in Microcystic LMs

EXCEEDED ENROLLMENT TARGET

- ✓ 51 subjects



QTORIN™ 3.9% rapamycin anhydrous gel is for investigational use only and has not 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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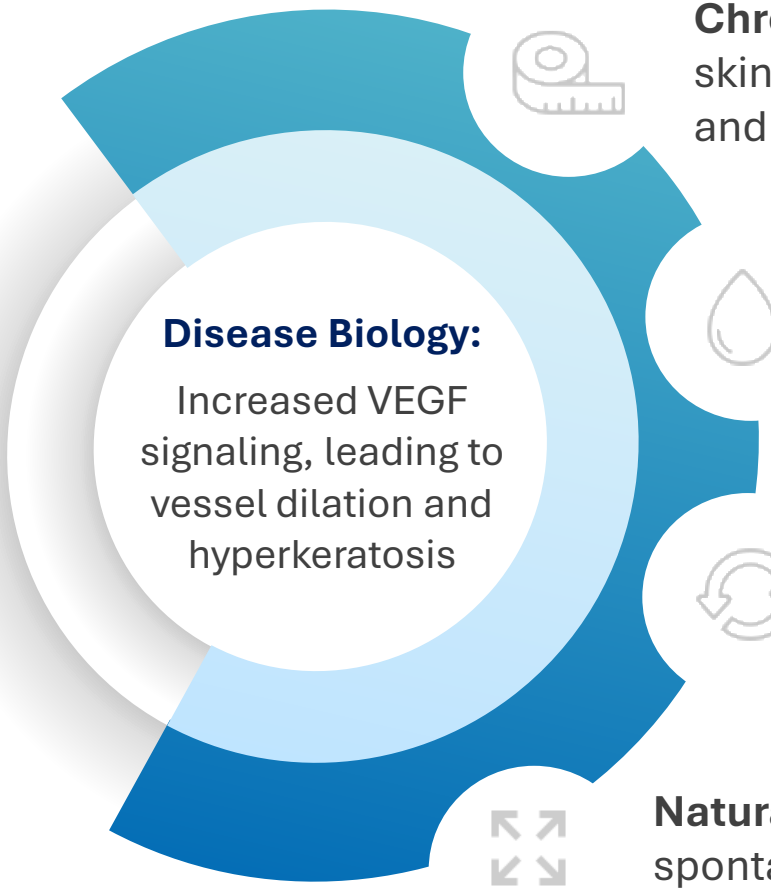
Clinically Significant Angiokeratomas:
Superficial Vascular Malformations of Lymphatic Origin

Palvella's focus to include Fordyce, Solitary, Mibelli, and Circumscriptum subtypes



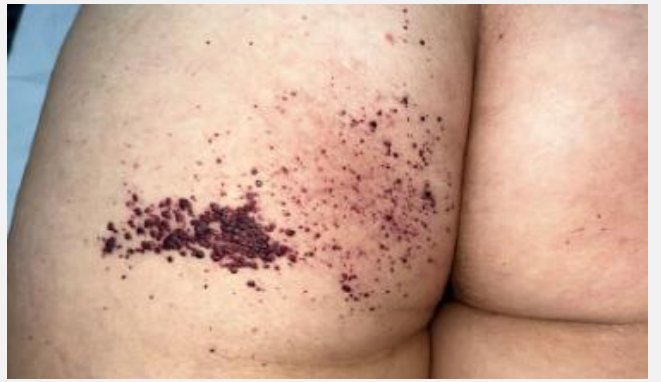
Chronically debilitating lymphatic-derived skin lesions associated with bleeding, pain, and functional impairment

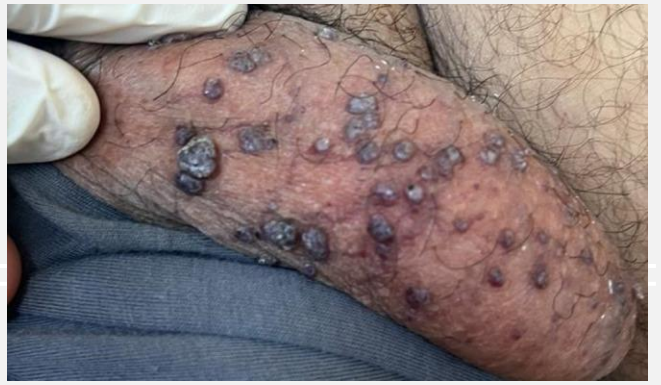
Recurrent bleeding: Friction can cause fragile lesions to frequently bleed

Persistent and extensive: Lesions can be large and increase in size, number, and extent over time

Natural history: No tendency for spontaneous regression

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





No FDA-approved therapies

Current options:
laser therapy, electrosurgery, cryotherapy, and surgical excision

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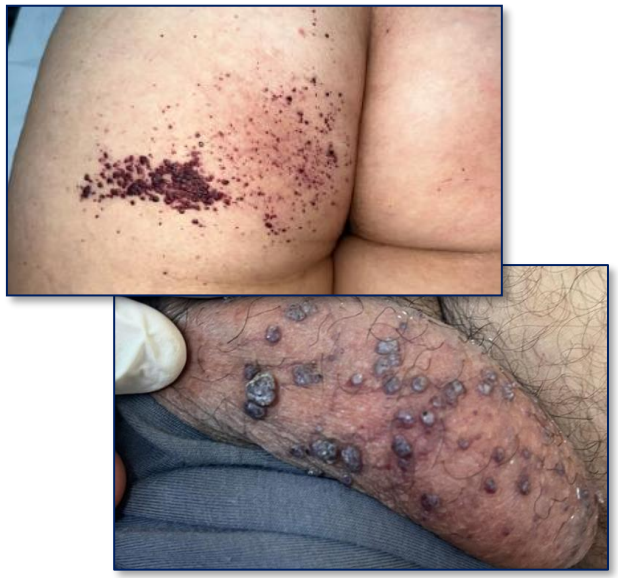
Wang et al., *Journal of Cutaneous Pathology*, (2014); Trinidade et al., *Am J Dermopathol*, (2014); Prindaville et al., *Pediatric Dermatology*, (2017); Singh et al, *Indian Journal of Dermatology*, (2023); Molla, *Clinical, Cosmetic and Investigative Dermatology*, (2024). Ivy H, Julian CA. Angiokeratoma Circumscriptum. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
1. Clarity Pharma research (July 2025), n=643 physicians surveyed.

QTORIN™ Rapamycin for Clinically Significant Angiokeratomas



1. **Unmet need:** Serious, debilitating disease with no FDA-approved therapies

2. **Scientific overview:** Superficial malformations of lymphatic origin with shared clinical features to microcystic LMs

3. **Commercial:** Estimated > 50k diagnosed U.S. patients[1], currently with no FDA-approved therapies

4. **Streamlined development plan:** Planned initiation of Phase 2 trial in 2H 2026

QTORIN™ rapamycin has the potential to be the first FDA-approved therapy for clinically significant angiokeratomas

1. Clarity Pharma research (July 2025), n=643 physicians surveyed.

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1 Clinically Significant Angiokeratomas: An Unmet Medical Need

James Treat, MD

- Pediatric dermatologist at Children's Hospital of Philadelphia (CHOP)
- Clinical dermatologist at the Comprehensive Vascular Anomalies Program at CHOP
- Professor of Clinical Pediatrics and Dermatology, Perelman School of Medicine at the University of Pennsylvania
- Member of Palvella Medical and Scientific Advisory Board

Chronic, debilitating, hyperkeratotic lesions prone to bleeding with minor trauma

Can cause significant impact on quality of life

A significant percentage of angiokeratomas are clinically significant

L. Lacina, O. Kodet and J. Štork, "Angiokeratoma and conditions accompanied by its multiple occurrence," *Dermatology for Practice,* vol. 11, no. 3, pp. 110-114, 2017.
Singh S, Sharma A, Malhi K, De D, Handa S, Mahajan R, et al. Sirolimus in dermatology: Jack of many trades. *Indian J Dermatol Venereol Leprol.* 2025;91:S32-S34. doi: 10.25259/IJDVL_869_2023.

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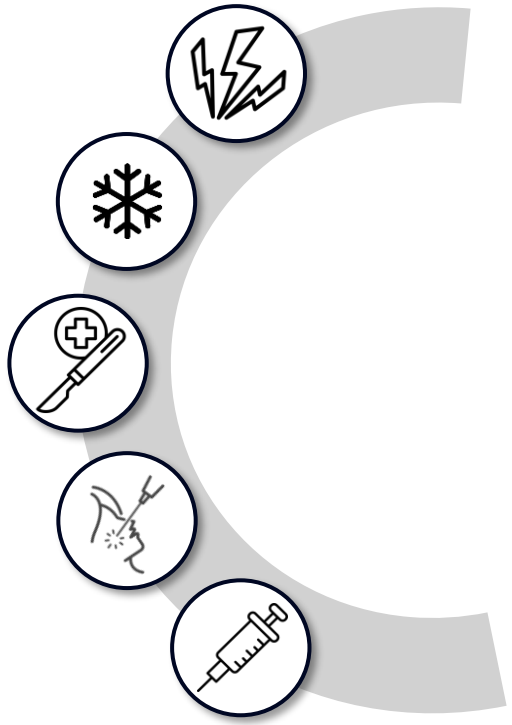
1 Clinically Significant Angiokeratomas: An Unmet Medical Need

Current Treatment Paradigm

- **No FDA-approved medical therapies**
- **Existing approaches for clinically significant angiokeratomas can be invasive and inadequate**
  - Laser therapy, electrosurgery, cryotherapy, and surgical excision are often destructive procedural interventions with potential for disease recurrence
  - Further limitations include pain and scarring
- **No ongoing clinical trials of pharmacotherapies[1]**



An unmet medical need exists for a targeted pharmacotherapy to treat clinically significant angiokeratomas

1. As of 9/23/2025.

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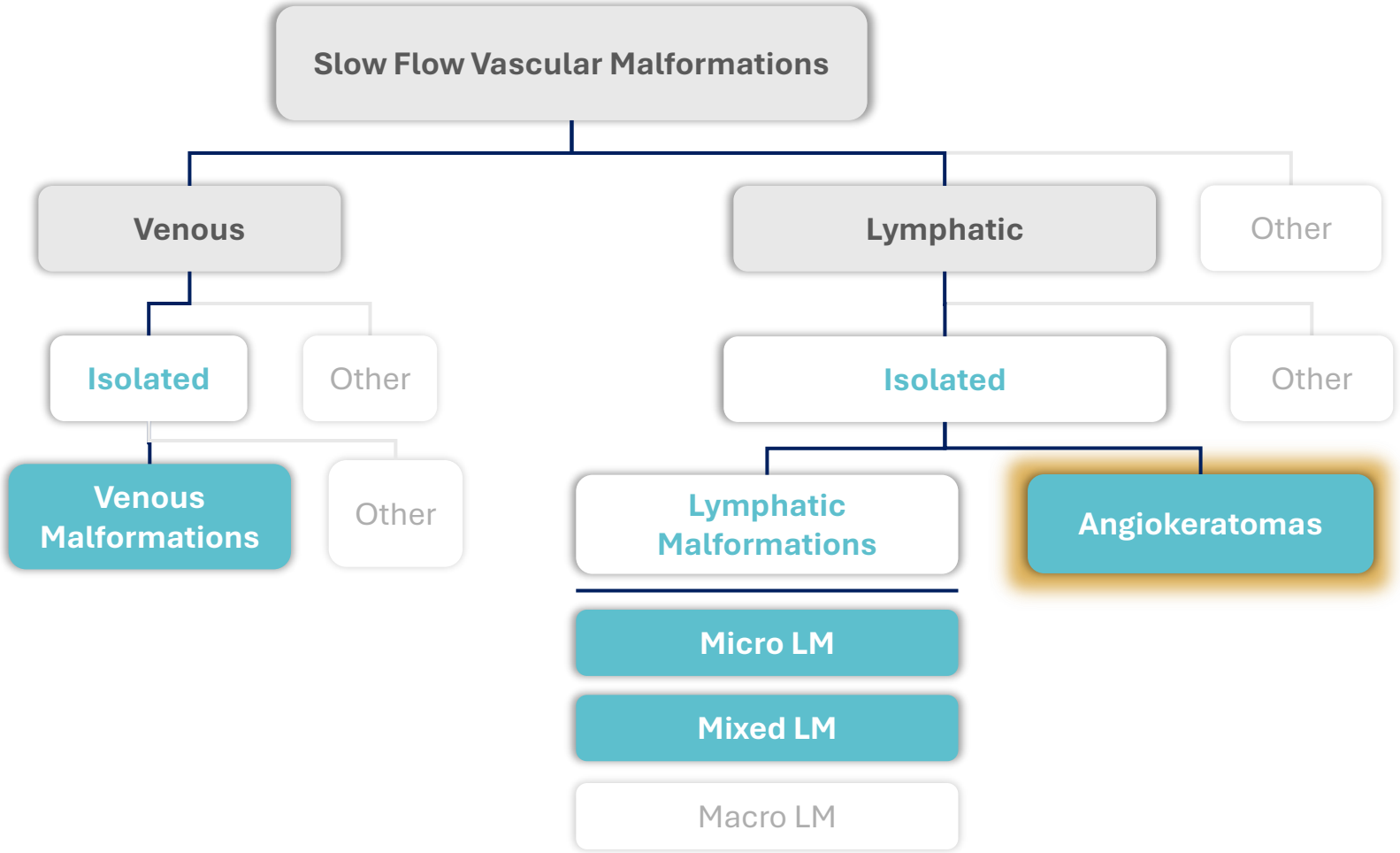
❷ Angiokeratomas are Superficial Vascular Malformations of Lymphatic Origins



Recently classified as **Isolated Lymphatic Malformations** in 2025 by ISSVA*

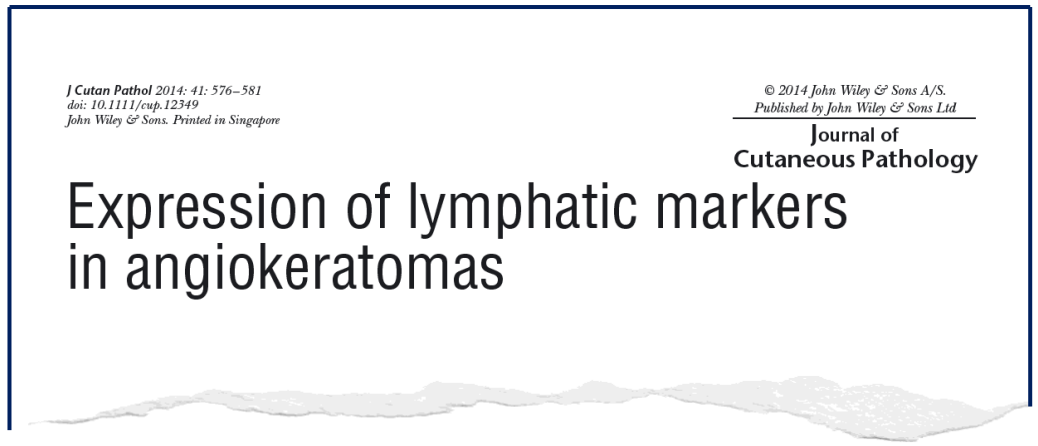
Growing mechanistic and real-world evidence supporting use of rapamycin in lymphatic and venous malformations

Denotes Palvella programs

ISSVA: International Society for the Study of Vascular Anomalies

❷ Scientific Discoveries Elucidate Angiokeratomas As Superficial Vascular Malformations of Lymphatic Origin

Journal of Cutaneous Pathology



J Cutan Pathol 2014: 41: 576–581
doi: 10.1111/cup.12349
John Wiley & Sons. Printed in Singapore

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Published by John Wiley & Sons Ltd

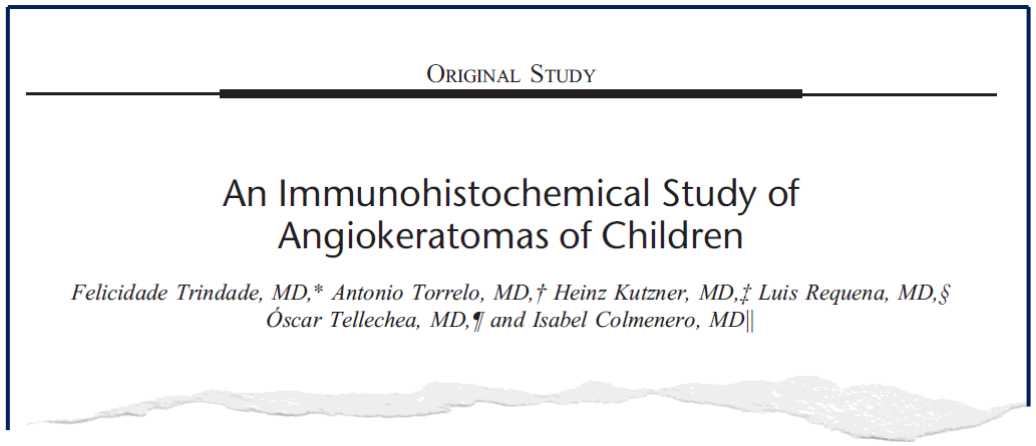
Journal of
Cutaneous Pathology

Expression of lymphatic markers in angiokeratomas

"All the cases showed positive staining for Prox1, ***thus suggesting lymphatic lineage****."*

Wang et al

The American Journal of Dermopathology



ORIGINAL STUDY

An Immunohistochemical Study of Angiokeratomas of Children

Felicidade Trindade, MD, Antonio Torrelo, MD,† Heinz Kutzner, MD,‡ Luis Requena, MD,§ Óscar Tellechea, MD,¶ and Isabel Colmenero, MD‖*

*"The lymphatic component of angiokeratoma is demonstrated by positivity and/or focal expression for lymphatic markers (prodoplanin and Prox1)…****These findings suggest that angiokeratomas in children are superficial lymphatic malformations****."*

Trindade et al

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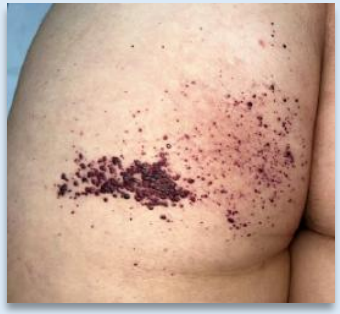
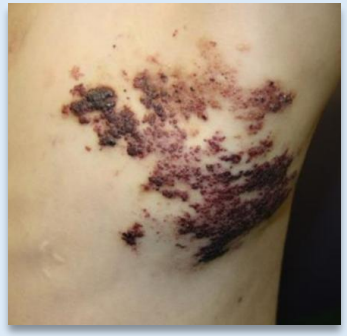
❷ **Clinically Significant Angiokeratomas:** Superficial Vascular Malformations of Lymphatic Origin

Shared Clinical Features between Clinically Significant Angiokeratomas and Microcystic LMs



Angiokeratomas

✓	Lymphatic origin[1,5]	✓
✓	Scientific rationale and real-world evidence supporting targeted therapy with rapamycin[2,5]	✓
✓	Superficial dermal location[3,5]	✓
✓	Clinically impactful, causing bleeding, functional impairment, and risk of infection[4,5]	✓



Microcystic LMs

1. Trindade F, et al. *Am J Dermatopathol*, Sep 30, 2014. 2. Bell KA, et al. *JAAD Case Reports*, Nov 30, 2020; Camacho I, et al. *Dermatologic Therapy*, Jun 27, 2020; Moeineddin F, et al. *Clinical Case Reports*, May 31, 2024; Farajzadeh S, et al. *Indian J Dermatol Venereol Leprol*, Jun 20, 2023; Fernández Ginés Fd, et al. *Eur J Hosp Pharm*, Feb 28, 2018; Kang Y, et al. *J Korean Association of Oral Maxillofacial Surgery* July 12, 2014. 3. Trindade F, et al. *Am J Dermatopathol*, Sep 30, 2014. 4. Philip C, et al. *Dermatological Therapeutics* March 31, 2020; Hobbs et al, *Journal of Dermatology Surg Onco*, 1987. 5. Teng et al, *Lymphatic Research and Biology*, 2022.

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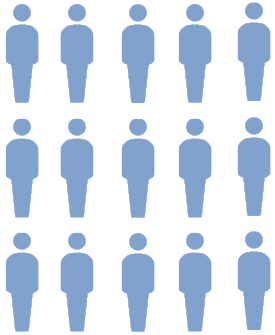
3 **Commercial Opportunity:** Clinically Significant Angiokeratomas Expand Potential Pool of Addressable Patients for QTORIN™ Rapamycin

= 5k

30k+

Microcystic LMs

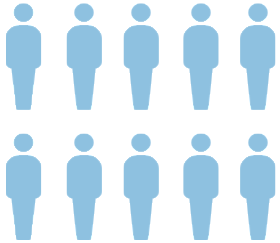
75k+



Cutaneous VMs

Announced
September 2025

50k+[1]



Clinically Significant Angiokeratomas

TODAY

Targeting announcement
in 2026 and beyond

200k+

Additional Potential Future Indications[2]

FUTURE

Estimated timeline for potential regulatory approval

2027 | 2029 | 2031+ | 2032+

1. Clarity Pharma research (July 2025), n=643 physicians surveyed. 2. Lapa et al., *Journal of Cutaneous Medicine and Surgery*, (2025).

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❸ Commercial Opportunity for Clinically Significant Angiokeratomas

Estimated Diagnosed U.S. Prevalence	>50k clinically significant angiokeratomas in the U.S. based on nationally representative, blinded, real-world observational study conducted July 2025 (n=643 physicians)[1]
Pricing	Anticipate drug pricing similar to QTORIN™ rapamycin for Microcystic LMs and Cutaneous VMs based on disease severity and lack of FDA-approved therapies
Market Research[2] *(n=50 physicians)*	**96%** would incorporate Product X (topical 3.9% rapamycin gel) into their practice **85%** believe there is unmet need for a novel treatment across all subtypes *"A topical application that was basically asymptomatic in terms of its application…would be ideal for these intractable cases"*

1. Clarity Pharma research (July 2025), n=643 physicians surveyed. 2. Medacorp Survey (September 2025), n=50 physicians surveyed.

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4 QTORIN™ Rapamycin as a "Pipeline-in-a-Product": Advancing Program to Angiokeratoma Patients

Leveraging established aspects of QTORIN™ rapamycin program

- QTORIN™ 3.9% rapamycin formulation
- Drug supply ready to deploy to clinic
- Open IND with FDA Division of Dermatology and Dentistry
- Existing intellectual property coverage

FDA meeting planned 1H 2026

- Discuss proposed Phase 2 study design
- Longer-term, supplemental NDA (sNDA) submission planned (if approval achieved) in microcystic LMs and/or cutaneous VMs
- Discuss eligibility for expedited programs (Fast Track Designation)

Planned Phase 2 study initiating in 2H 2026

- Single arm, baseline-controlled study with n=~10-20 patients
- Microcystic LM efficacy endpoints potentially applicable based on clinical overlap

GOAL: Initiate Phase 2 clinical development in 2H 2026

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Clinically Significant Angiokeratomas:
Aligned With Palvella's QTORIN™ Rapamycin Pipeline Strategy

Lymphatic Malformations

	Microcystic LMs	Clinically Significant Angiokeratomas	Cutaneous VMs	
Serious	✓	Chronically debilitating with frequent bleeding	✓	*Significant unmet medical need*
Rare	✓	>50k U.S. patients	✓	
No FDA-approved Therapies	✓	None; no ongoing clinical trials	✓	
Strong Scientific & Biologic Rationale	✓	Increased VEGF signaling, leading to vessel dilation and hyperkeratosis	✓	*Optimizing likelihood of clinical success*
Published Case Studies & Use of Off-label Rapamycin	✓	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 estimates and third-party prevalence and drug pricing estimates.

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Thank You

Striving to be first for rare disease patients

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