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First-in-disease therapies for patients with rare diseases

Corporate Presentation
May 2026

Forward Looking Statements

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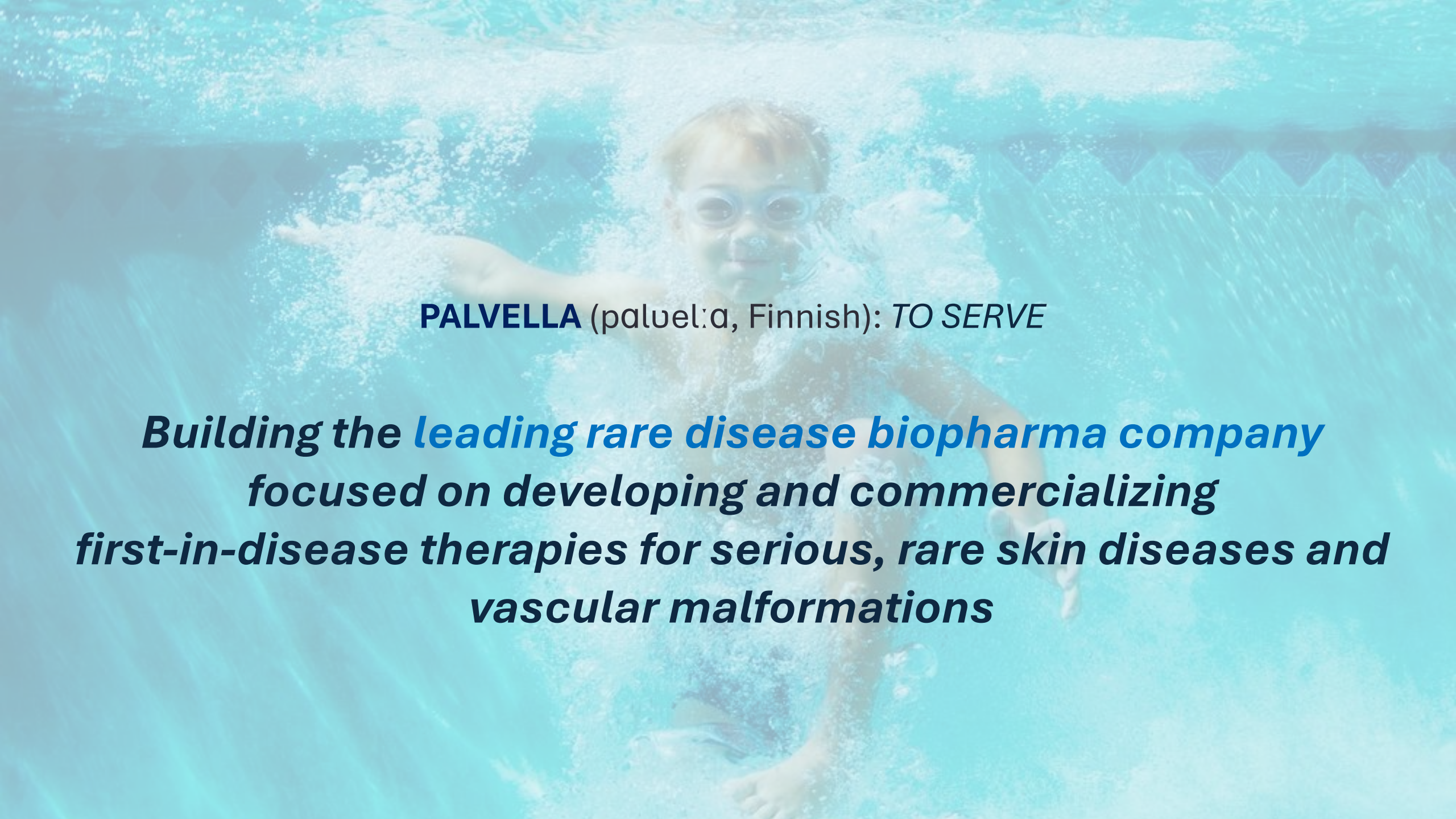

PALVELLA (palʋelːa, Finnish): *TO SERVE*

Building the leading rare disease biopharma company focused on developing and commercializing first-in-disease therapies for serious, rare skin diseases and vascular malformations

What Makes Palvella Stand Apart

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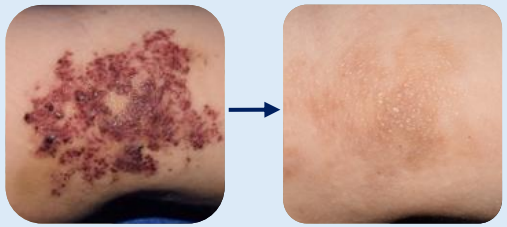
Repeatably unlocking multi-billion dollar market opportunities in previously untreated orphan diseases

1. **First-in-Disease Focus**
+
2. **Rare Diseases with Clear Disease Biology**
+
3. **Leveraging Existing Human Proof-of-Concept and Safety Data**
+
4. **Innovative QTORIN™ Platform: Durable IP Generation**

Veteran team executing rare disease model designed to reduce time and capital to FDA approval

Q1 2026 Achievements Position Company for First Potential Approval and Launch of QTORIN™ Rapamycin

Microcystic Lymphatic Malformations: Advancing Towards Potential 1H 2027 Approval

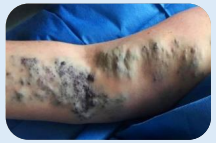


Phase 3 results exceeded upside case profile

NDA remains *on track* for 2H 2026

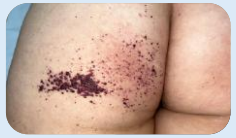
Exceptional veteran commercial leadership recruited; launch planning accelerating

Cutaneous VMs



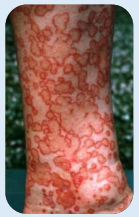
Phase 3 initiation on track for 2H 2026

Angiokeratomas



First patients dosed in Phase 2 ahead of schedule

DSAP



>40 patient inbounds for clinical trial

Review published in *Clinical and Experimental Dermatology*

$230mm raised in gross proceeds in upsized equity financing

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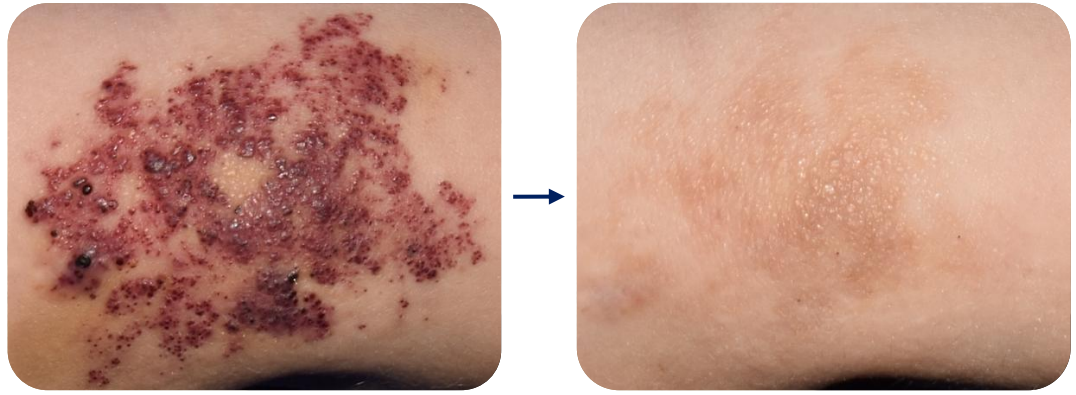
Microcystic Lymphatic Malformations: NDA Submission on Track for 2H 2026 with Anticipated U.S. Commercialization in 1H 2027

1

Microcystic Lymphatic Malformations

- ✓ Positive Phase 3 SELVA data
- ✓ In-person pre-NDA meeting granted by FDA, to occur in Q2 2026
- ✓ Findings presented at ISSVA World Congress, May 2026

- NDA submission on track for 2H 2026



Potential FDA approval and U.S. launch 1H 2027

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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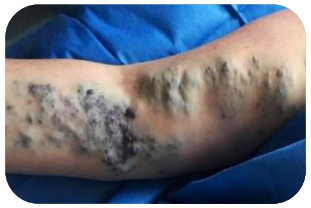
Multiple High-Impact Pipeline Milestones in 2026:
Density of Catalyst Creation Driven by QTORIN™

2

Cutaneous Venous Malformations

- ✓ Positive Phase 2 data
- ✓ BTD application submitted Q2 2026
- • P3 initiation expected 2H 2026



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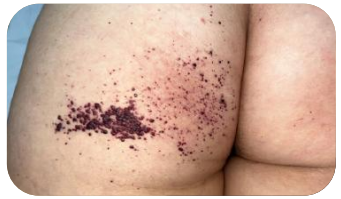
Clinically Significant Angiokeratomas

- ✓ Fast Track Designated
- ✓ Phase 2 initiated May 2026, ahead of schedule
- • Phase 2 data expected 2H 2027



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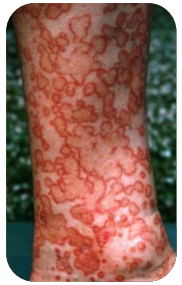
Disseminated Superficial Actinic Porokeratosis

- ✓ QTORIN™ pitavastatin formulation developed, IP filed
- • Phase 2 initiation expected 2H 2026



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QTORIN™ Third Program

- • Announcement expected 2H 2026
- • Potential pipeline-in-a-product

DAVID OSBORNE, PhD
Chief Innovation Officer

6

QTORIN™ Rapamycin Fourth Indication

- • QTORIN™ rapamycin fourth indication announcement expected 2H 2026

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OUR LEAD PRODUCT CANDIDATE

QTORIN™ 3.9% RAPAMYCIN ANHYDROUS GEL

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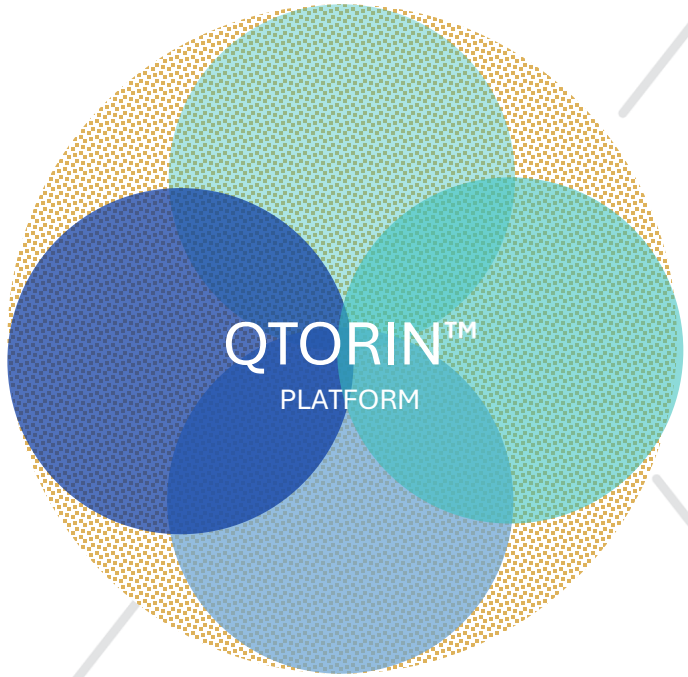
QTORIN™: Reproducible Platform for Generating Novel, Topical Product Candidates in a Capital Efficient Manner

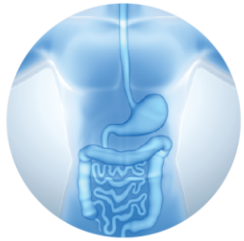
HIGH DRUG LOADING CAPACITY

High solubility → high concentrations → potential for rapid onset and large magnitude treatment effect



DERMAL ENGAGEMENT

Delivery to deeper layers of skin, often the site of disease pathophysiology



TOLERABILITY

Retaining active drug in the skin while minimizing systemic absorption

IP

Each QTORIN™ product candidate eligible for composition IP on formulation

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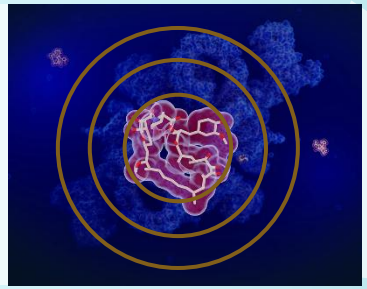
Our Breakthrough Innovation: QTORIN™ 3.9% Rapamycin Anhydrous Gel

Oral rapamycin is <u>not</u> a viable therapeutic option in skin diseases:

Systemic toxicities & low biodistribution to the skin

OPTIMIZED CONCENTRATION

QTORIN™ synergistic solubility results in *3.9%* concentration



DERMAL ENGAGEMENT

Rapamycin concentration in dermis exceeds IC90 for mTOR inhibition[1]

TOLERABILITY

No traditional penetration enhancers; limited systemic absorption[2]

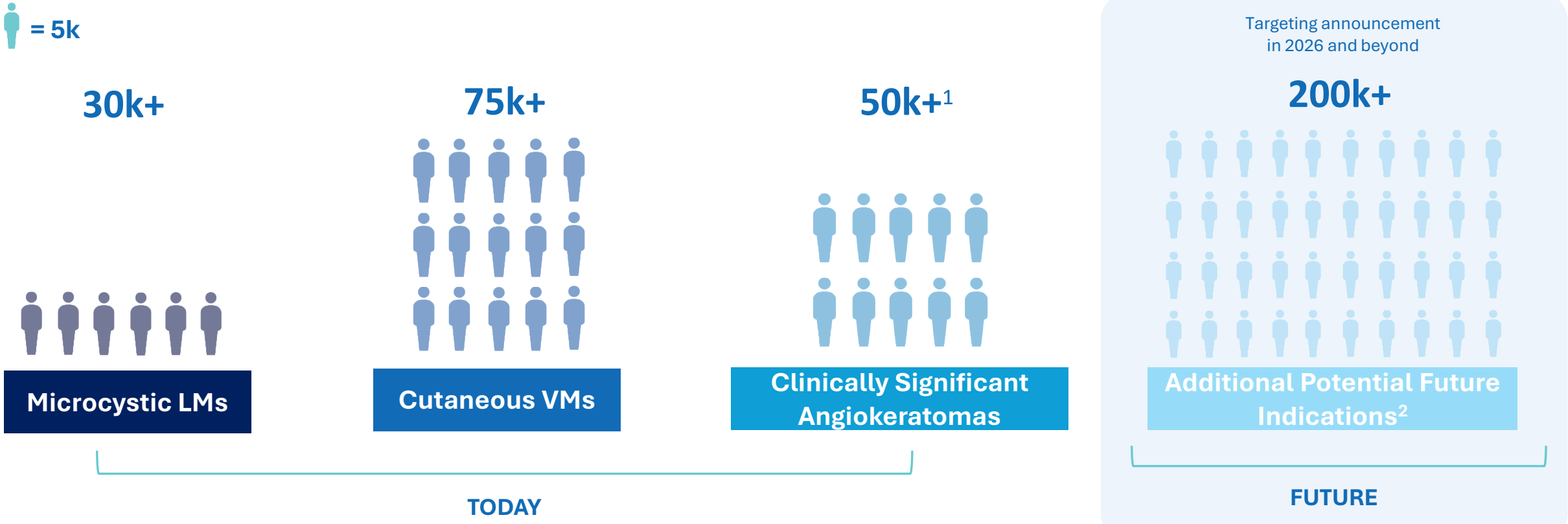
Intended for once daily at-home self-administration

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.

1. Data on file. 2.Clinical Study Report PALV-0609.

QTORIN™ Rapamycin: Fourth Indication Announcement in 2H 2026

Pipeline-in-a-product strategy expands addressable U.S. patient pool by 10x beyond initial indication



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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FOR

Microcystic Lymphatic Malformations

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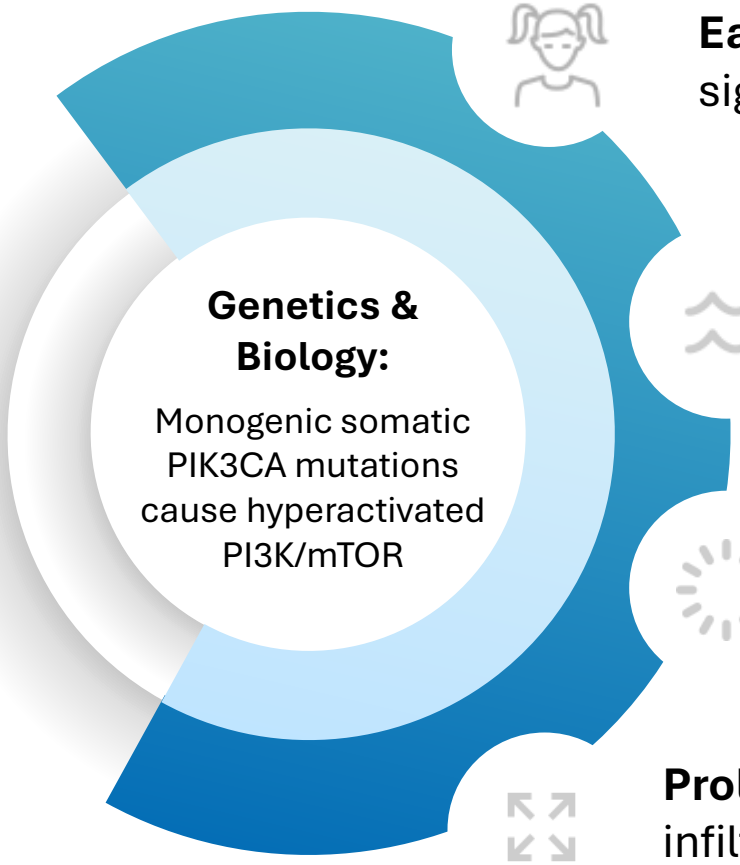
Microcystic Lymphatic Malformations:
Serious, Debilitating, and Lifelong



Early onset: Present at birth and significant impact to adolescents

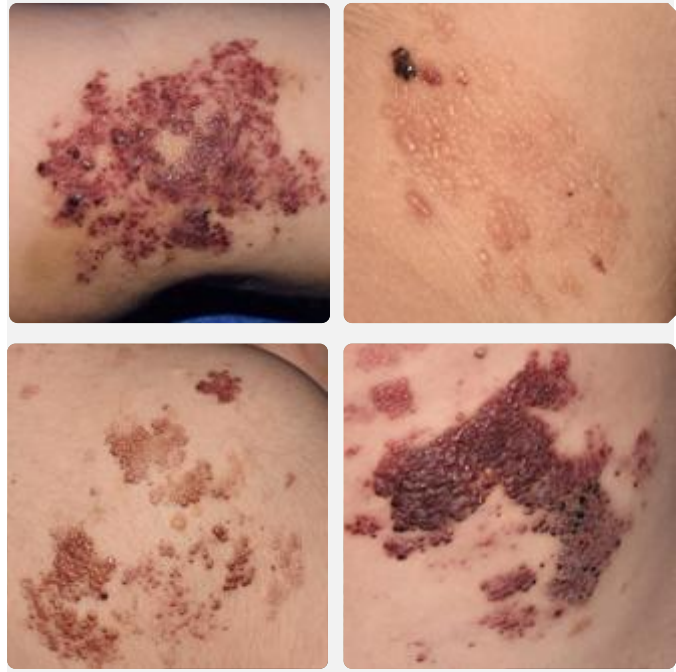
Lymphorrhea: Persistent discharge of lymphatic fluid through skin layers

Deep infections: Recurrent cellulitis and serious soft tissue infections, resulting in hospitalizations

Proliferative, progressive disease with infiltrative lesions and no spontaneous regression

> 30k patients
ESTIMATED DIAGNOSED IN THE U.S.[1]

No FDA-approved therapies



Breakthrough Therapy Designation

Fast Track Designation

Orphan Drug Designation

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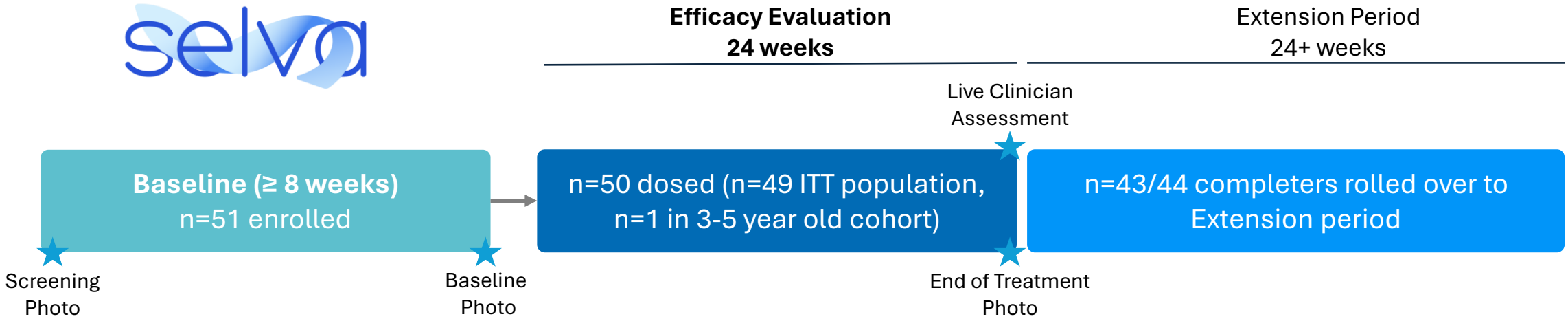
1. Incidence, prevalence, and care for patients with lymphatic malformations (LMs) in the U.S.: A claims-based analysis, Society of Investigative Dermatology, (2025) and Gallagher et al, *Orphanet Journal of Rare Diseases*, (2022). Includes microcystic LM and mixed LM (patients with both microcystic and macrocystic disease).

Phase 3 SELVA Trial Design

Single-arm, baseline-controlled, QD dose



Primary Endpoint: mLM-IGA (Investigator Global Assessment)

Key Secondary Endpoint: Blinded mLM Multi-Component Static Scale (mLM-MCSS): independent, blinded review of randomized Baseline and Week 24 photos evaluating three key signs of disease: Vesicle Appearance, Height, Leaking/Bleeding

Secondary Endpoints: Live mLM-MCSS, Patient Global Impression of Change (PGI-C), Clinician and Patient Global Impression of Severity (CGI-S, PGI-S), and Incidence and Severity of Adverse Events

Supported by FDA Orphan Products Grant:

Two tranches of non-dilutive funding received (most recent in Oct '25)

Note: Of the 51 participants enrolled, 50 initiated treatment, including 49 aged ≥6 years (ITT population). During the 24-week efficacy evaluation period, six participants discontinued treatment: four participants discontinued for reasons unrelated to adverse events, one participant discontinued due to an adverse event not related to study drug, and one participant discontinued due to an adverse event possibly related to study drug.

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selva : A Clear Path Forward for Patients

QTORIN™ Rapamycin at Week 24:

Highly statistically significant across primary, key secondary, and all four secondary endpoints (all p<0.001)

+2.13 Mean improvement on mLM-IGA primary endpoint (p<0.001)

Participants aged ≥ 6 who completed the efficacy evaluation period:

95% Improved on mLM-IGA

86% "Much Improved" (+2) or "Very Much Improved" (+3) on mLM-IGA

Potential to be first and only FDA-approved therapy for >30,000 diagnosed U.S. patients

mLM-IGA = Microcystic Lymphatic Malformation Investigator Global Assessment. Note: Data analyzed per statistical analysis plan; non-completer data imputed per statistical analysis plan for primary endpoint; endpoints tested according to pre-specified hierarchical testing procedure; statistical significance (p<0.05).

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selva : QTORIN™ Rapamycin Exceeded Upside Case Profile

Upside Target Clinical Profile	SELVA Outcome
Statistically significant primary endpoint with mean mLM-IGA of ≥+1.5 at Week 24	✓ **Highly statistically significant with mean mLM-IGA of +2.13 at Week 24 (p<0.001)**
Statistical significance on independent, blinded key secondary endpoint	✓ Highly statistically significant (p<0.001), including on all three clinical signs: vesicle appearance, height, leaking/bleeding
Rollover into extension period in line with best-in-class drugs for rare diseases	✓ 98% of Week 24 completers (43/44) rolled over to Extension period
Safety profile: well-tolerated and similar to previous clinical trials	✓ Well-tolerated across both adult and pediatric patients, supporting chronic administration

Note: Data analyzed per statistical analysis plan; non-completer data handled via multiple imputation per statistical analysis plan; endpoints tested sequentially according to pre-specified hierarchical testing; statistical significance (p<0.05). Week 24 completers included 43 participants ≥6 years old and 1 participant 3-5 years old.

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SELVA: Primary and Key Secondary Endpoints Achieved

	Mean Change at Week 24 (95% CI)	**p-value**
Primary Endpoint: Microcystic Lymphatic Malformation Investigator Global Assessment (mLM-IGA)*	**+2.13** (1.88, 2.38)	p<0.001
Key Secondary Endpoint: Blinded Microcystic Lymphatic Malformation Multi-Component Static Scale**	**-3.36** (-4.34, -2.38)	p<0.001

*Dynamic change scales (7-point scales ranging from "Very Much Worse" (-3) to "Very Much Improved" (+3); positive values indicate improvements from baseline)
**mLM-MCSS (Sum of three static severity scales: Height, Leaking/Bleeding, Vesicle Appearance: Each scale rated "Clear or Almost Clear" (1) to "Very Severe" (5); total score 3-15. Test baseline to Week 24 change; negative values indicate improvements from baseline)

Highly statistically significant across primary, key secondary, and all four secondary endpoints (all p<0.001)

Note: Data analyzed per statistical analysis plan; non-completer data imputed per statistical analysis plan for primary endpoint; endpoints tested according to pre-specified hierarchical testing procedure; statistical significance (p<0.05).

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Phase 3 Results: Well-Tolerated and Favorable Safety Profile

	Number of Participants (%)
Any Treatment-Emergent Adverse Event	35 (70%)
Severe (not related to study drug)	1 (2%)
Serious (not related to study drug)	4 (8%)
Any Treatment-Related[1] Adverse Event	17 (34%)
Severe	0 (0%)
Serious	0 (0%)
Treatment-Related[1] AEs with ≥ 5% Incidence	
Application site acne	3 (6%)
Application site discoloration	3 (6%)
Application site pruritus	3 (6%)
Possibly Treatment-Related AE Leading to Discontinuation	1 (2%)

Rapamycin levels were below 2 ng/mL in systemic circulation on for all participants at all timepoints in the study

Note: n=50 participants in efficacy evaluation evaluated for safety. 1. Denotes related or possibly related. 2. Validated assay of lower limit of quantification (100 pg/mL).

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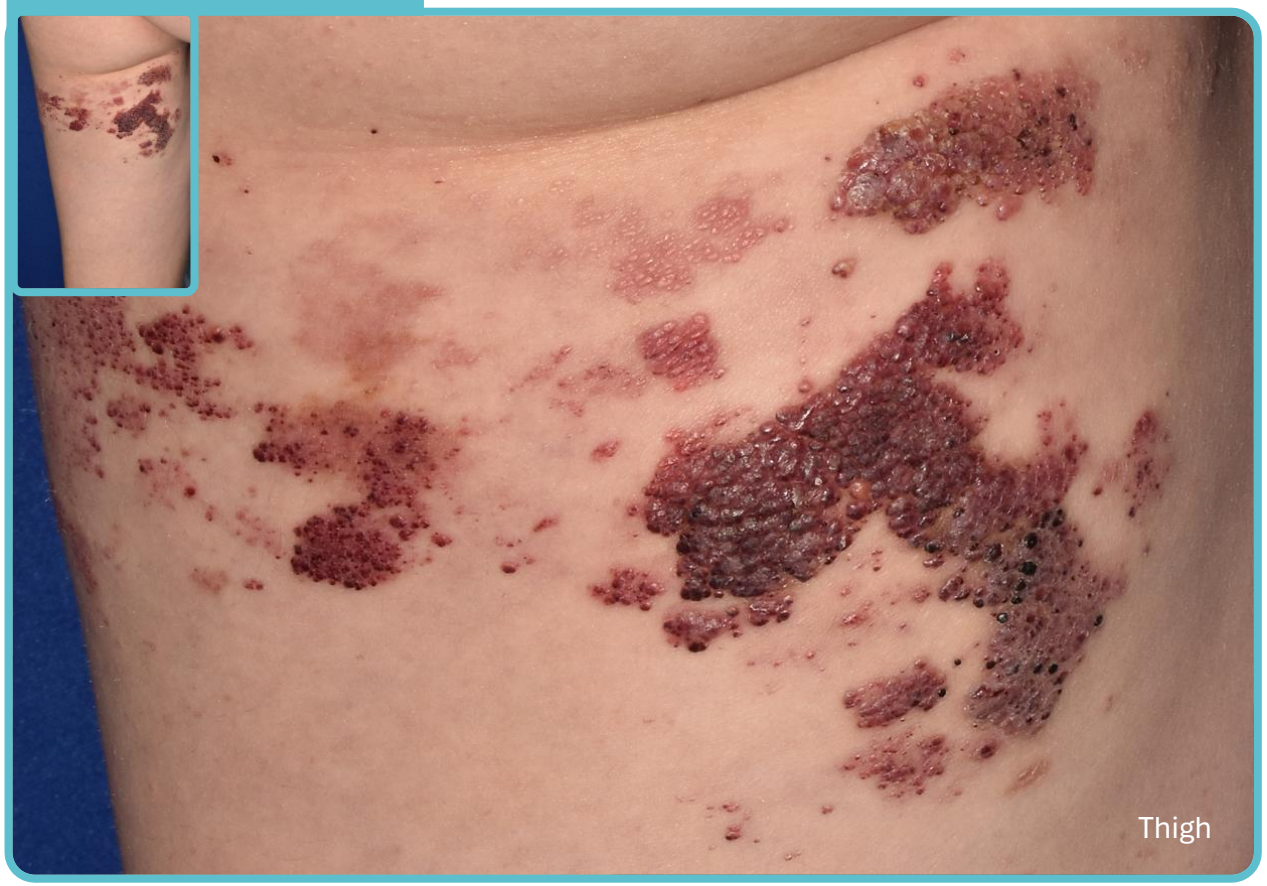
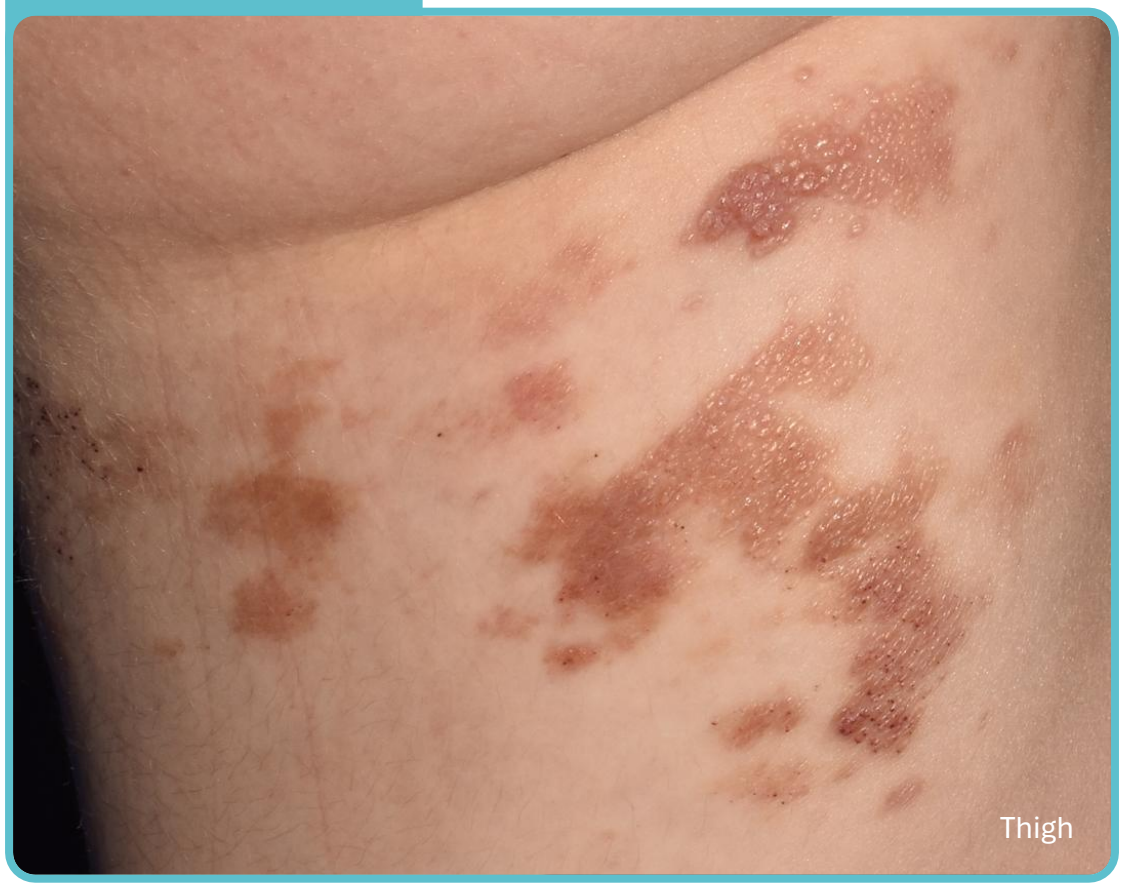
Phase 3 Results: Age 10, Male, mLM-IGA: +2 “Much Improved”

Baseline



Week 24



Note: Selective photos.

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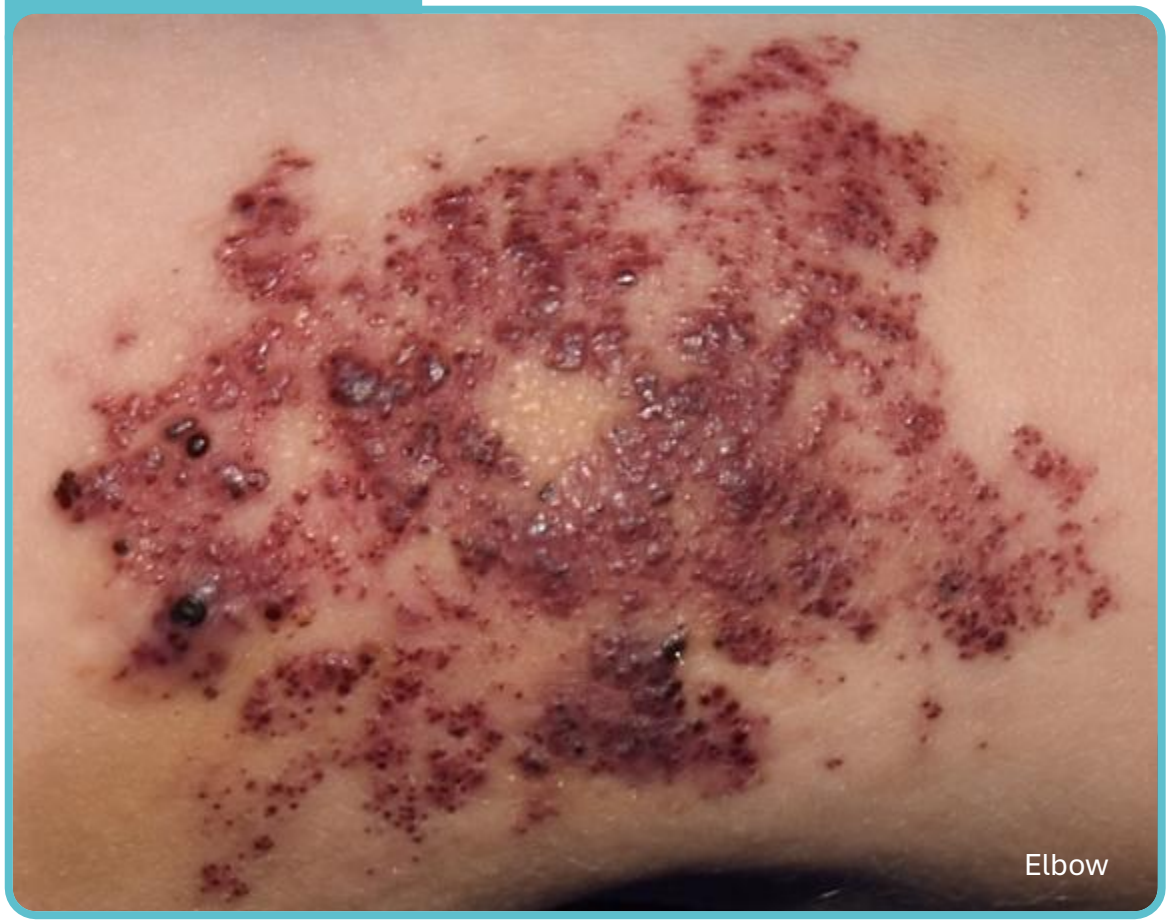
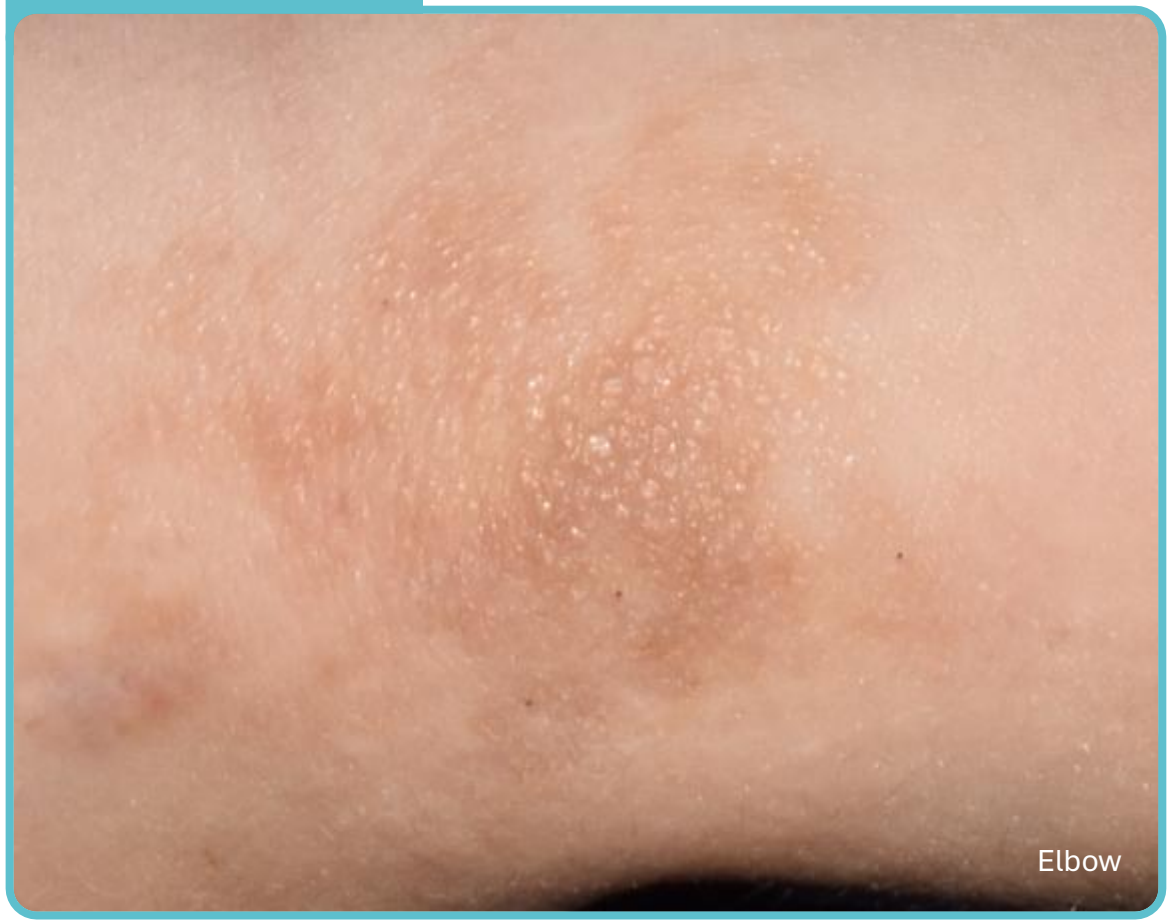
Phase 3 Results: Age 7, Female, mLM-IGA: +3 “Very Much Improved”

Baseline



Week 24



Note: Selective photos.

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Regulatory: NDA Submission On Track for 2H 2026

Breakthrough, Fast Track, and Orphan Designations granted

Pre-NDA meeting *granted* by FDA

1. Phase 3 SELVA data highly statistically significant and clinically meaningful, confirming positive Phase 2 results
2. Seeking **traditional approval** (not accelerated) **based on clinical endpoints**; intent to seek broad label age 3 and above
3. Previously granted Breakthrough, Fast Track, and Orphan Designations; 505(b)(2) submission
4. Collaborating with FDA Office of Orphan Products Development, which is providing non-dilutive funding, to participate in Pre-NDA meeting

Since April 2025, there have been at least 10 drug approvals based on one or more single-arm studies, of which 8 were orphan-designated[1]

1. Hyman Phelps & McNamara analysis.

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Strong Barriers Through Multi-Layered Exclusivity Strategy

IP portfolio, trade secrets, and regulatory exclusivities through at least 2038

Granted U.S. Patents	**6 issued U.S. patents with claims through at least 2038** Including protection against 0.1% to 20% anhydrous gel compositions of rapamycin and other mTOR inhibitors
Trade Secrets	**Multiple trade secrets related to proprietary formulation processes and manufacturing know-how**
Regulatory	**Orphan drug designation and 7-year data exclusivity from anticipated FDA approval**

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U.S. Commercial Launch Planning

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Microcystic LMs: Multi-billion Dollar, Uncontested U.S. Market Opportunity with Commercial Build-Out Underway

1. **Large orphan market:** Claims analysis presented at 2025 Society for Investigative Dermatology (SID) Meeting verified > 30k estimated diagnosed U.S. patients, with >1,500 incident patients annually

2. Positioned to be **first and only FDA-approved therapy;** market research indicates **strong intent to prescribe, including in pediatric population**

3. Payor testing and orphan analogues validate **expected orphan pricing corridor above $100k per patient per year**

4. **Concentrated prescriber base** in vascular anomaly centers (VACs) & other clinics

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QTORIN™ Rapamycin: >$1bn U.S. Peak Sales Potential in Microcystic LMs

Microcystic Lymphatic Malformations

>30k diagnosed U.S. patients, with concentration in vascular anomaly centers	**Recent field checks, annual incidence estimates,** published claims analysis
Annual ~$100k-$200k pricing range per patient	**Supported by Phase 3 SELVA data,** payor testing, analogues

QTORIN™ Rapamycin Potential to Achieve >$1bn Peak Sales

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QTORIN™ Rapamycin Physician Market Research:
Potential to be First Line, Standard of Care Therapy for Microcystic LMs

Product X: Topical 3.9% rapamycin gel, including results from Phase 2 study of QTORIN™ rapamycin

Core Intent to Prescribe Insights

Would consider Product X as a **first-line** therapy

98% of physicians

Percent of my microcystic LM patients I would prescribe Product X:

75% of patients

"[Product X] would be an excellent safe option that I would readily prescribe"

Additional Insights into Pediatric Population

96% of physicians

See **advantages to targeted, localized delivery of Product X for pediatric patients** compared to oral mTOR or PI3K inhibitor

"Most parents would not like a young child treated with a systemic drug with so many potential long-term and serious side effects"

Physician Segmentation Insights

VAC* Physicians (n=21) — **73%** of patients

Non-VAC Physicians (n=31) — **77%** of patients

*Vascular Anomaly Centers

17 of 52 physicians stated they would **prescribe to 100% of patients**

Source: Medacorp Research, 2024. n=52 microcystic LM treaters.

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QTORIN™ Rapamycin Pricing: Prior First-in-Disease Launches and Recent Topical Orphan Launches Support Potential Orphan Drug Pricing

Rare Disease Medications	ARIKAYCE® (amikacin liposome inhalation suspension)	oxervate® (cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL)	TEPEZZA® teprotumumab-trbw
U.S. Annual List Price at Launch	~$135k[1]	~$190k[2]	~$200k-350k[3]
Indication	Refractory non-tuberculous mycobacterial (NTM) lung infections	Neurotrophic keratitis	Thyroid eye disease
Market Size	~12K-17K prevalent U.S. patients[4]	~50K prevalent U.S. patients[5]	~65K-100K prevalent U.S. patients[6]

1. Medscape Medical News interview with Mandy Fahey, Insmed Director of Corporate Communications (2018). 2. Assumes one course of 8-week therapy for both eyes. 3. Horizon Therapeutics Management guidance and Wall Street research. Price dependent on weight-based dosing. 4. Insmed corporate presentation (2025). 5. Sacchetti et al., *Clin Opth* (2014). 6. Stan et al., *Clin Endocrinol (Oxf)* (2024), Horizon Therapeutics investor presentation (2023).

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Highly Concentrated Patient Population: ~400 Established High Volume Centers for Treating Vascular Malformations Comprise ~50% of Market

CLAIMS ANALYSIS SUPPORTS THREE SEGMENTS

Highly Concentrated Patients: ~50% of market at ~400 centers

- **Already established** Centers of Excellence for mLM
- **~96% of VACs today prescribe oral mTOR inhibitors**[1]: familiarity with class & mechanism of drug

Secondary Targets at Launch

Omni-channel approach

Inside sales can provide a high ROI

Long-tail Targets

Apply additional learnings from Oxervate and other orphan launches

All three market segments to be covered by orphan sales force of ~30-40 reps

Source: Palvella and ZS Associates claims analysis (2025). 1. Cohen-Cutler et al., *The Journal of Pediatrics,* (2023).

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QTORIN™ 3.9% RAPAMYCIN

FOR

Cutaneous Venous Malformations

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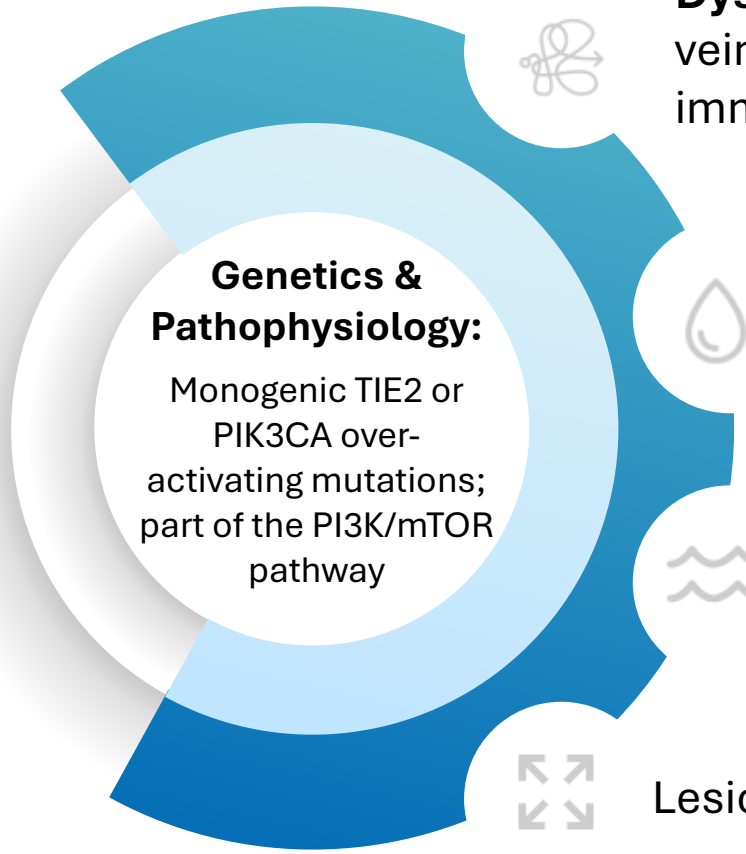
Cutaneous Venous Malformations:
Serious, High Unmet Need



Dysregulated growth of malformed veins and **hyperproliferation** of immature venous endothelial cells

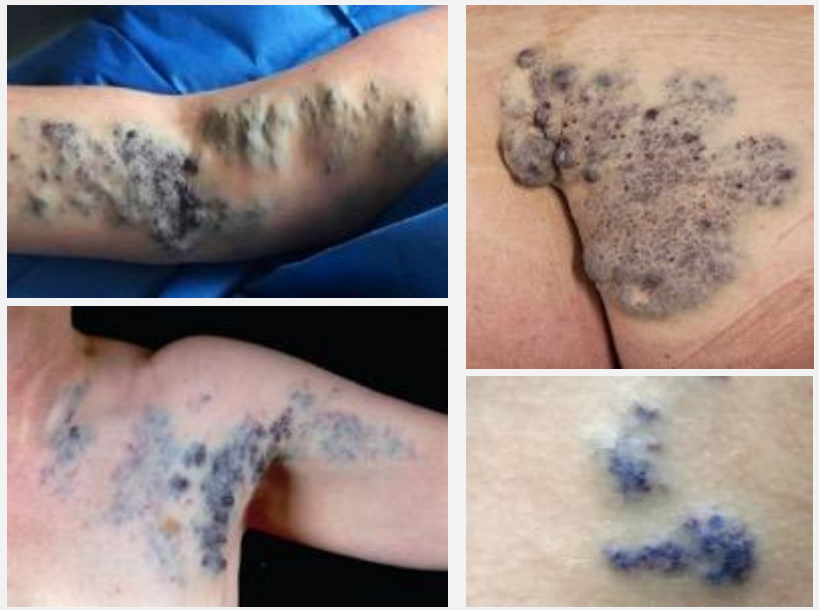
Dysfunctional venous architecture leads to bleeding, thrombosis, ulceration

Skin involvement in ~50-80% of venous malformations patients[2]

Lesions **do not resolve spontaneously**[3]

> 75k patients

ESTIMATED DIAGNOSED IN THE U.S.[1]



Leads to physical & functional impairment, psychological distress, with no FDA-approved therapies

Pipeline-in-a-product: sNDA planned

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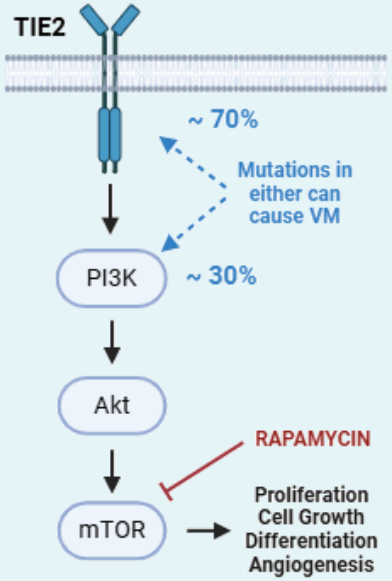
1. Primary prospective research conducted by Clarity Pharma. 2. Rikihisa et al., *Journal of Vascular Surgery, (*2019); Boon et al., *Arch Dermatol, (*2004); Mazoyer et al., *Arch Dermatol, (*2008). 3. Fujino et al., *Lymphatic Research and Biology*, (2024).

Venous Malformations: Progress Towards the Potential First Targeted Therapy for Unaddressed Cutaneous Disease

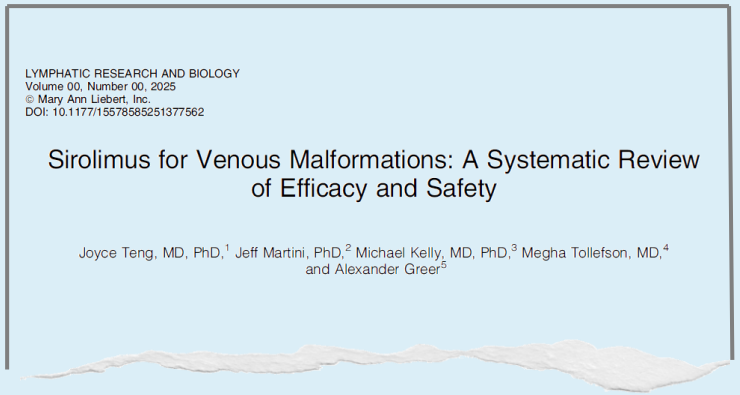
Known Genetics / Clear Biology



Plausible mechanism

Limaye et al (2009, 2015)

Real-world Evidence



Real-world evidence supports rapamycin's off-label use in primarily internal manifestations of VMs…

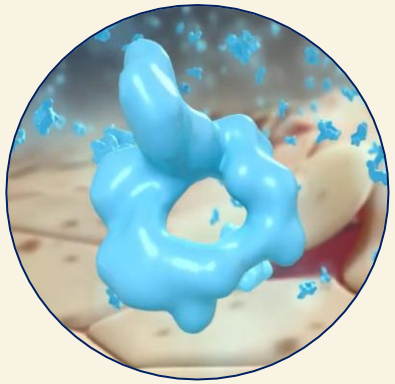
…however, poor patient outcomes persist in cutaneous disease

Teng et al (2025)

On Target, In Tissue

QTORIN™

RAPAMYCIN



3.9% concentration
Dermal penetration
Extensive CMC package

Phase 2 TOIVA Data (2025)

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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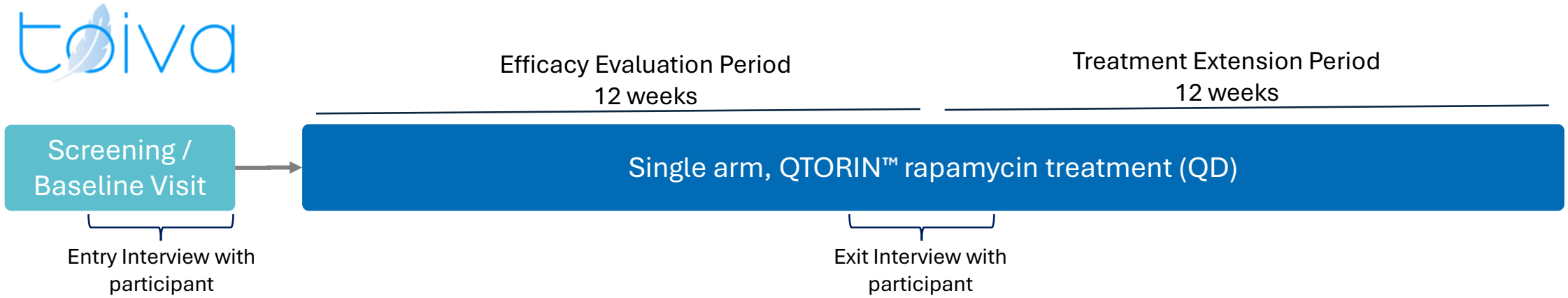
Phase 2 TOIVA Study in cVMs: 24-Week Study

Single-arm, baseline-controlled, QD dose, age 6+



Safety and Tolerability

Efficacy (no pre-specified primary endpoint): cVM-IGA (7-point clinician change scale), cutaneous VM multi-component static scale (cVM-MCSS), other clinician- and patient-reported outcomes

Statistics: Intent-to-Treat (ITT) population, based on available data at each time point and analyzed per statistical analysis plan

Key Entry Criteria: Enriched for patients with cutaneous disease and confirmed by third party eligibility consult team; genetics not required

Enrollment: 16 participants enrolled and dosed

Sites: Mayo Clinic; Cleveland Clinic; Children's Hospital of Philadelphia; Stanford Medicine; UCI; Children's Hospital Colorado; Children's Healthcare of Atlanta; Johns Hopkins Medicine; University of Utah Health; UNC Health; Minnesota Clinical Study Center

Note: Statistical significance ($p<0.05$) is nominal as there was no adjustment for multiplicity amongst efficacy endpoints. Data analyzed per statistical analysis plan; ITT analyzed with no imputation of values for missing data.

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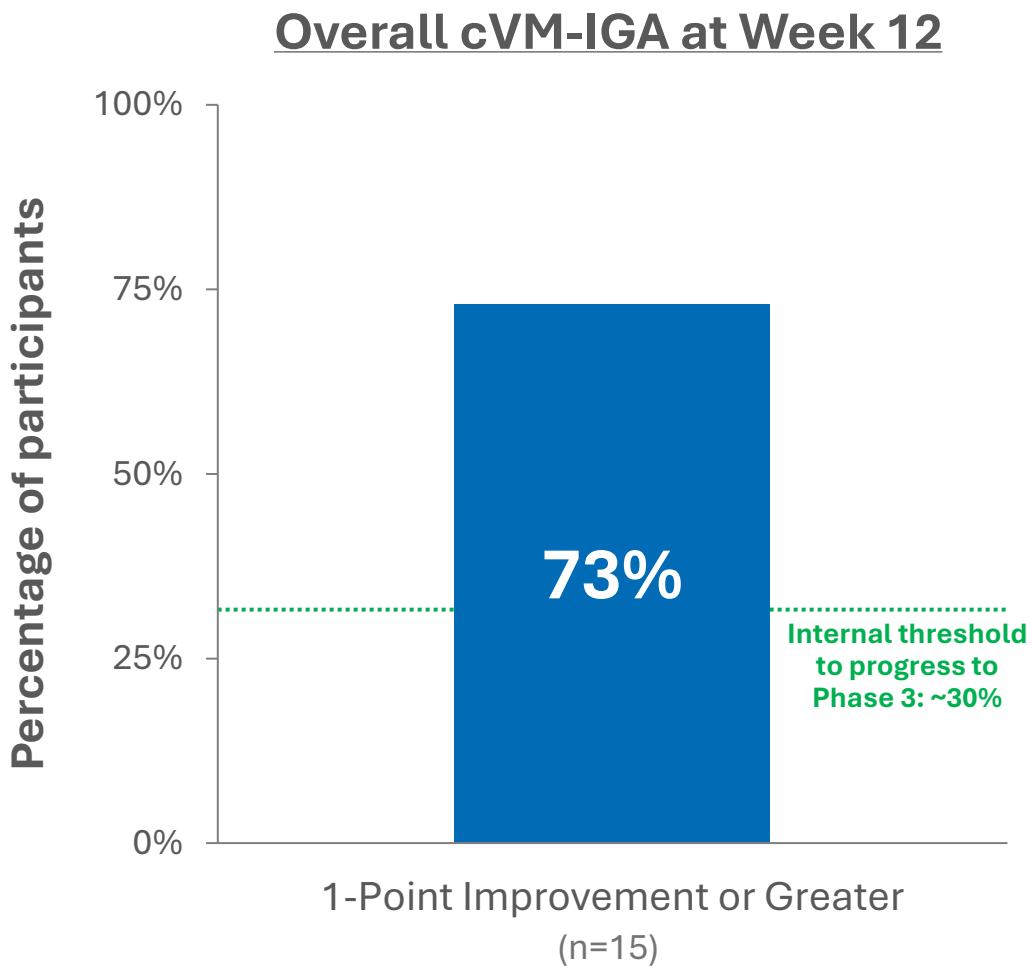
Overall cVM-IGA: 73% of Participants Demonstrated Improvement at Week 12

Single-arm, baseline-controlled, QD dose, age 6+



- **Overall cVM-IGA:** 7-point clinician-assessed dynamic change scale ranging from “Very Much Worse” (-3) to “Very Much Improved” (+3)
  - Mean effect size at week 12: **+1.5 (p<0.001)**
  - Median effect size at week 12: **+2.0**
- **73%** of participants (11/15 participants) demonstrated at least a 1-point improvement on the Overall cVM-IGA at Week 12
- **67%** of participants (10/15 participants) were rated as either “Much Improved” (+2) or “Very Much Improved” (+3) on the Overall cVM-IGA at Week 12

Note: Statistical significance (p<0.05) is nominal as there was no adjustment for multiplicity amongst efficacy endpoints. Data analyzed per statistical analysis plan; ITT analyzed with no imputation of values for missing data.
1. Genetic testing was not required as part of the protocol; Palvella is continuing efforts to collect genetic data on trial participants.

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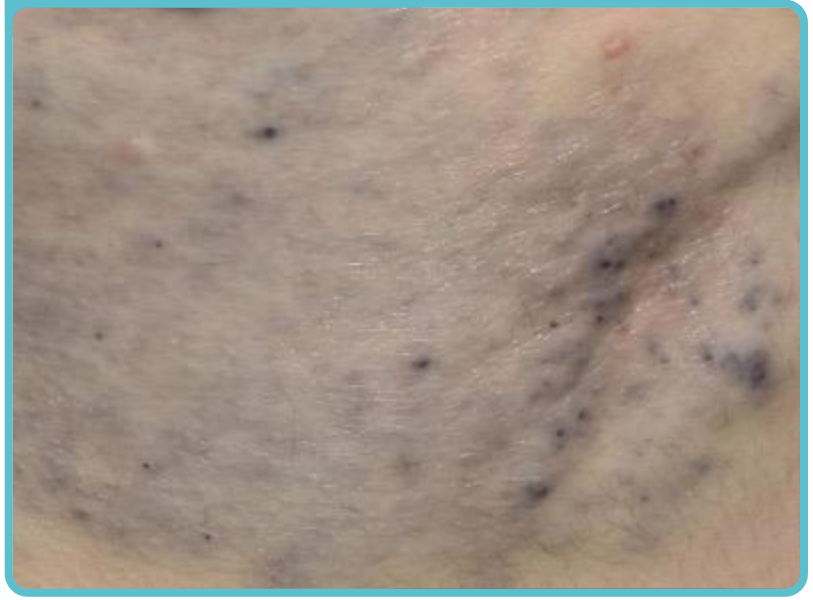
Phase 2 Results: Meaningful Improvement in Patient QoL

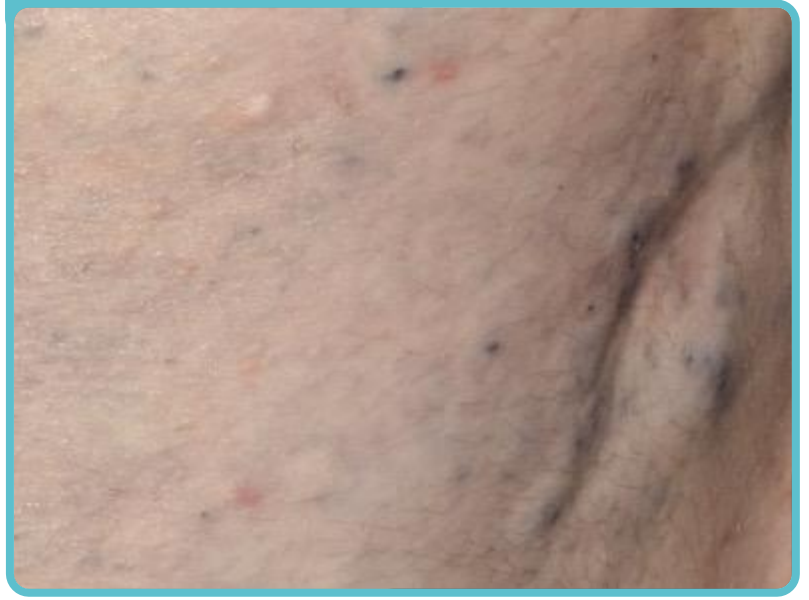
Site: CHOP
Investigator: Dr. Denise Adams

Participant Age: 17
Mutation: TEK
cVM-IGA at Week 12:
Very Much Improved (+3)

Baseline



Week 12



Participant Qualitative Interview: *"I've definitely noticed some improvements…it's definitely had a positive effect…It's more comfortable to wear a bra now…I've had less pain in that specific area"*

Note: Selective photos.

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Phase 2 Results: Safety and Tolerability

- QTORIN™ rapamycin was generally well-tolerated, similar to previous clinical trials
- Most common Treatment-Emergent Adverse Events were application site reactions (erythema, 25%)
- All Treatment-Related Adverse Events were moderate or mild (no severe events)
  - Majority of AEs were mild
  - No SAEs related to study drug
  - No unexpected AEs

Rapamycin levels were below the lower limit of quantification (2 ng/mL) in systemic circulation on a standard lab assay for all participants at all timepoints in the study

Significantly below 5 ng/mL which is the lower boundary where rapamycin begins to exert immunosuppressive effects

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QTORIN™ 3.9% RAPAMYCIN

FOR

Clinically Significant Angiokeratomas

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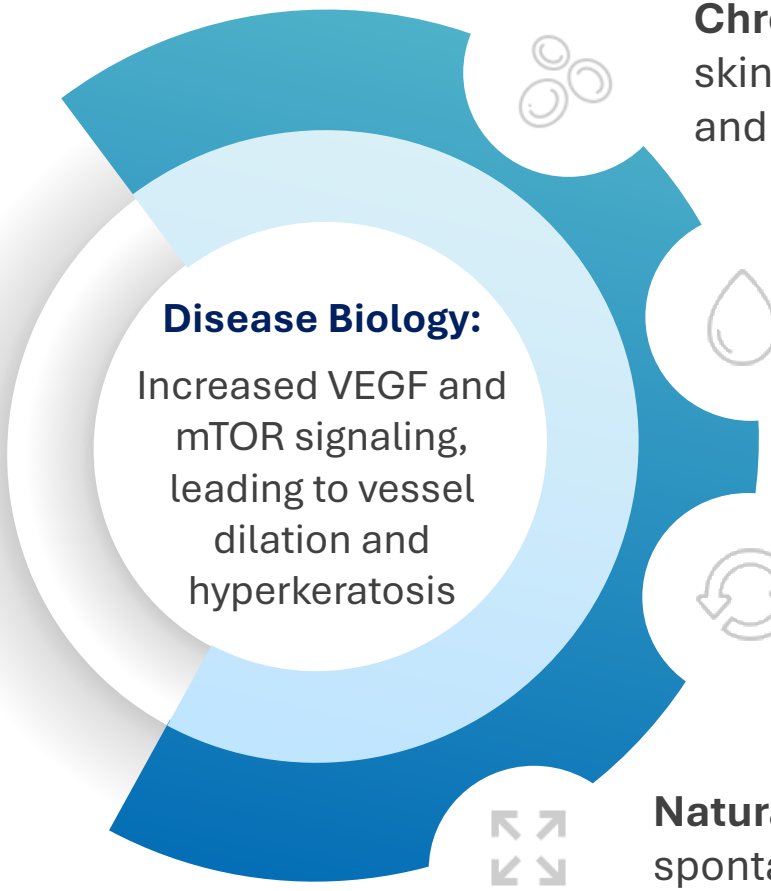
Clinically Significant Angiokeratomas:
Superficial Lymphatic Malformations

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



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

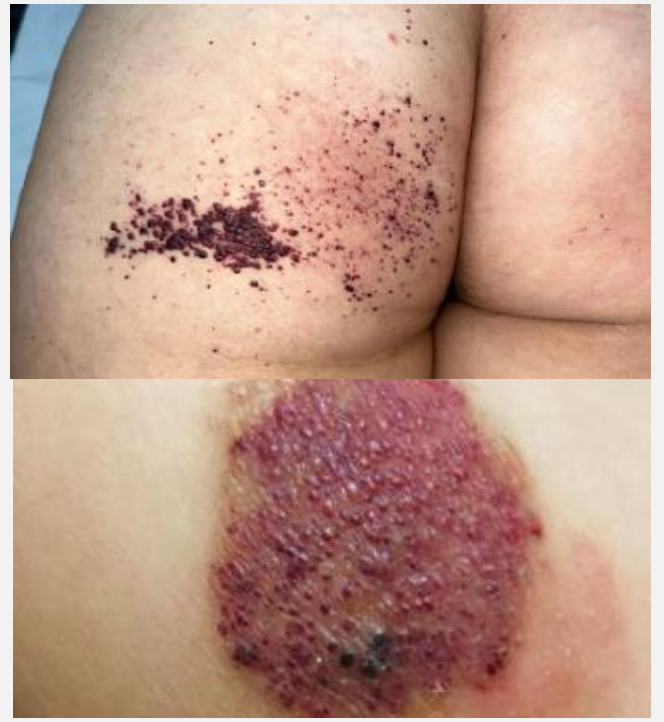
Recurrent bleeding: Friction can cause fragile lesions to frequently bleed

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 DIAGNOSED IN THE U.S.[1]



No FDA-approved therapies

Pipeline-in-a-product: sNDA planned

Phase 2 trial initiated May 2026 ahead of schedule

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

QTORIN™ PITAVASTATIN

FOR

Disseminated Superficial Actinic Porokeratosis

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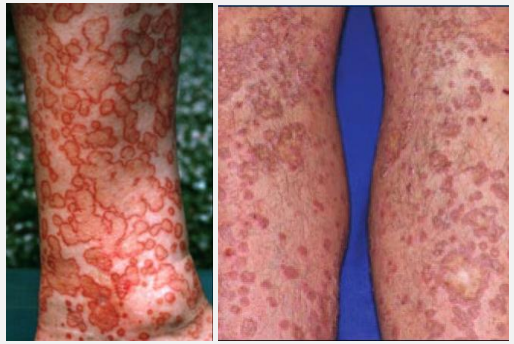
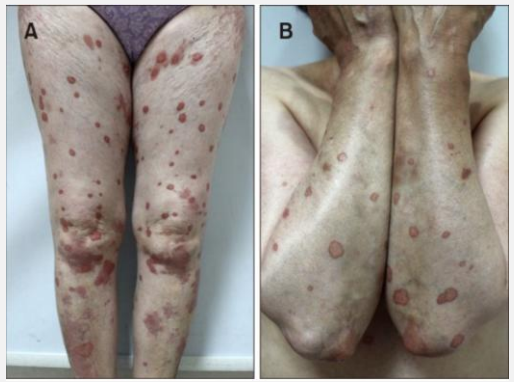
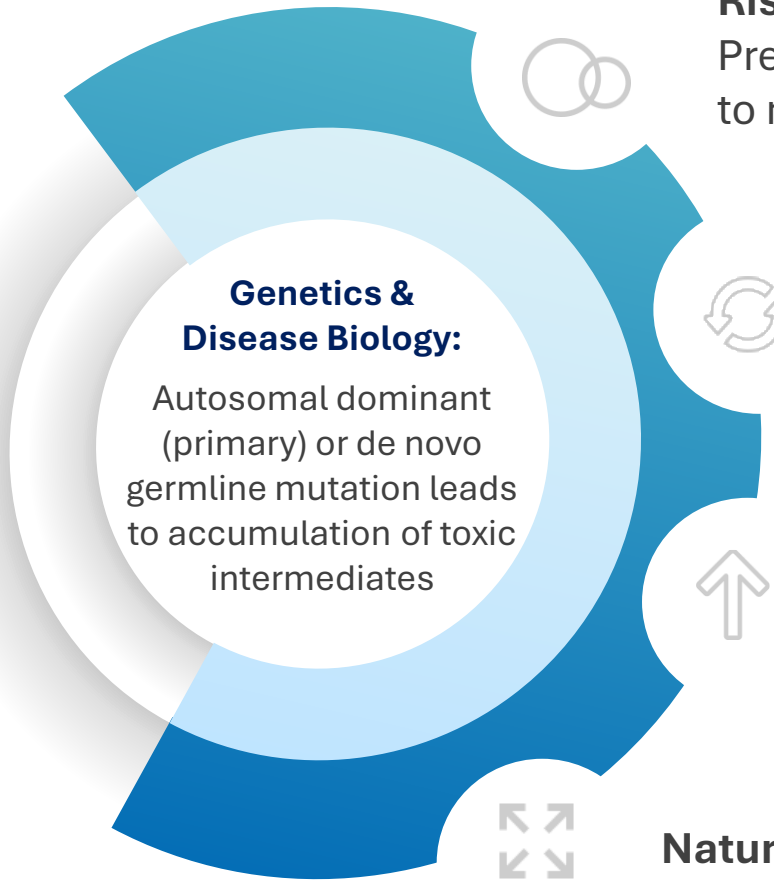
Disseminated Superficial Actinic Porokeratosis (DSAP):
Chronic, Pre-Cancerous, and Progressive

> 50k patients
ESTIMATED DIAGNOSED 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

Phase 2 trial initiation expected 2H 2026

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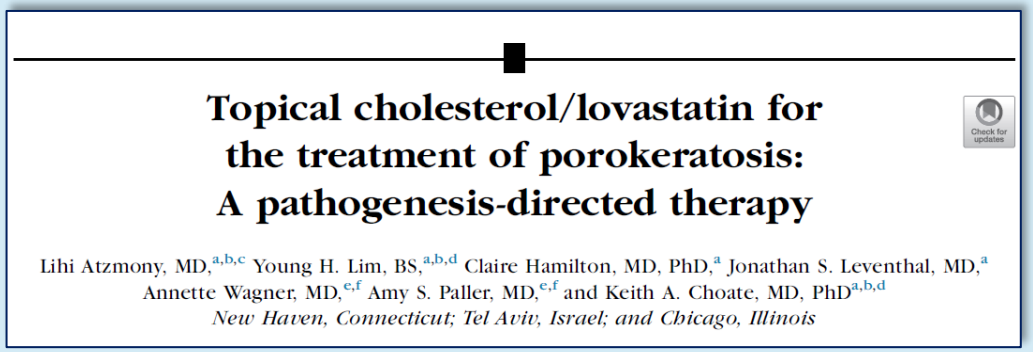
1. Clarity Pharma research (April 2025), n=277 physicians surveyed. 2. Williams, Grant M., et al. “Porokeratosis.” StatPearls Publishing, 2024.

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

Recently published systematic review in *Clinical and Experimental Dermatology* (Martini et al, 2026) included **24 case 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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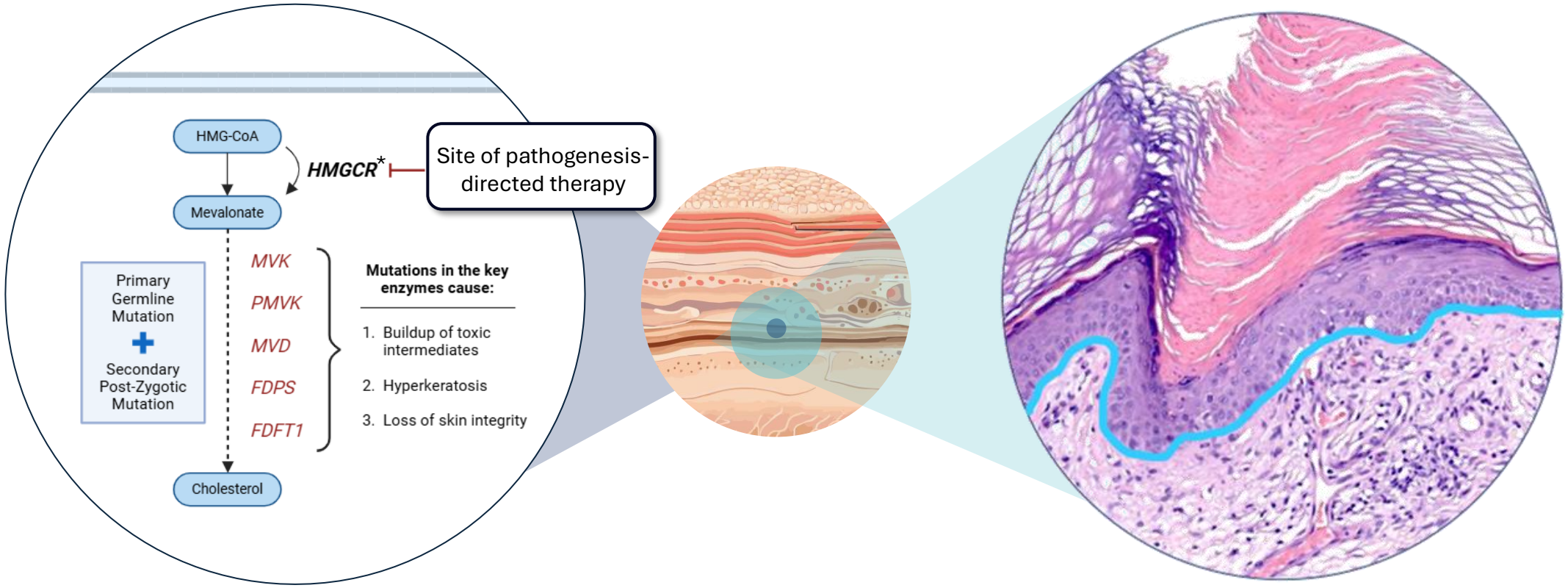
Clear Biology: Targeting the Causal Mevalonate Pathway

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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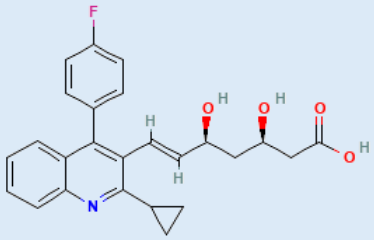
QTORIN™ Pitavastatin: On Target, In Tissue

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™

Platform

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QTORIN™: New Product Development Engine

DAVID OSBORNE, PhD

Chief Innovation Officer

- **VALIDATION OF QTORIN™ PLATFORM**

  Two positive clinical study readouts (Phase 3 SELVA trial and Phase 2 TOIVA trial results)

- **SCALING OF PIPELINE WITH NEW QTORIN™ PROGRAMS**

  Rapidly advancing and testing multiple molecules through QTORIN™ platform in capital- and time-efficient manner

- **PLANNING TO PURSUE PLATFORM DESIGNATION**

  We expect to apply for FDA's Platform Technology Designation Program following QTORIN™ rapamycin's targeted approval in 2027

We plan to announce one new QTORIN™ program and one new QTORIN™ rapamycin indication later this year

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Finance

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Well-Capitalized with High-Quality Investor Participation in $230mm Oversubscribed Feb. 2026 Financing Following Positive SELVA Data

$262 million

3/31/26 cash

Potential to Fund Through:

- NDA filing, FDA approval, and, if approved, U.S. launch for QTORIN™ rapamycin in microcystic LMs
- NDA filing for QTORIN™ rapamycin in cutaneous VMs
- Multiple Phase 2 data readouts from pipeline programs

QTORIN™ + 505(b)(2) + rare disease focus offers potential for attractive ROI

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What Sets Palvella Apart: Building The Leader in Rare Skin Diseases and Vascular Malformations

Positive Phase 3 data in microcystic lymphatic malformations, focused on NDA submission and potential U.S. commercial launch

QTORIN™ rapamycin: potential to be first approved therapy and SOC in U.S. for microcystic LMs, cutaneous VMs, and angiokeratomas

U.S. commercial opportunity: multi-billion dollar TAM in mLMs, with potential to expand addressable pool of patients by 10x

Deep pipeline of rare disease therapies: six diseases anticipated by year end 2026

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Striving to be first for rare disease patients

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Thank You

Striving to be first for rare disease patients

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No Spontaneous Regression Well-Established in Microcystic LMs

OPEN

PRS GLOBAL OPEN ORIGINAL ARTICLE
Reconstructive

Spontaneous Regression of Lymphangiomas in a Single Center Over 34 Years

Motoi Kato, MD*
Shoji Watanabe, MD, PhD*
Reiko Kato, MD†
Hiroshi Kawashima, MD, PhD†
Takuya Iida, MD, PhD‡
Azusa Watanabe, MD, PhD*

Background: A lymphangioma, also called a lymphatic malformation, is a congenital condition that frequently occurs in young children. It is classified into 3 groups depending on the size of the cysts (macrocystic, microcystic, and mixed). Spontaneous regression occurs in some cases; however, the characteristics of patients who show regression have not been studied previously. Furthermore, the types and the timing of the initial treatment are still controversial. Therefore, we statistically analyzed the occurrence of short-term spontaneous regression, patient age at original occurrence, cyst types, cyst sizes, and cyst locations in patients diagnosed with peripheral localized lymphangiomas in a single children center over 34 years.
Methods: We retrospectively collected the data of 153 patients and reviewed the medical charts.
Results: Spontaneous regression occurred only in macrocystic or mixed type; regression was most frequent in patients who, at the time of onset, were more than 2 years old.
Conclusions: We concluded that elderly patients with macrocystic or mixed type lymphangioma may have to wait for treatment for over 3 months from the initial onset. Conversely, microcystic type could not be expected to show regression in a short period, and prompt initiation of the treatments may be required. The difference of the regression or not may depend on the characteristics of the lymph flow. *(Plast Reconstr Surg Glob Open 2017;5:e1501; doi: 10.1097/GOX.0000000000001501; Published online 25 September 2017.)*

MATERIALS AND METHODS

We retrospectively reviewed the medical charts of 501 patients who were diagnosed with lymphangiomas or lymphatic malformations in our hospital over 34 years (April 1983 to December 2016). Lymphangioma cases that showed peripheral localization and were observed for more than 3 months without medical or surgical intervention were included. The diagnosis was reconfirmed on the basis of radiological findings and the clinical course according to the vascular anomalies classification of the International Society for the Study of Vascular Anomalies.[1]

Patients diagnosed with lymphangiomatosis, Gorham disease, combined vascular anomalies (Klippel–Trenaunay syndrome, Proteus syndrome, and Maffucci syndrome), intraabdominal lesions, and/or intrathoracic lymphangiomas were excluded from this study. Additionally, patients who were misdiagnosed, those who did not undergo radiological assessments (ultrasound, computed tomography, or magnetic resonance imaging), those who were not followed for 6 months after onset, and those who were administered treatments for the lesions (medication, aspiration, sclerotherapy, and/or surgery) within 3 months after the original onset were excluded (Table 1; Fig. 1). Patients who were prescribed acetaminophen and/or antibiotics for pain and/or infection and those with peripheral lesions that connected to the intrapleural region were included.

Spontaneous regression was considered as an over 20% decrease in the lesion size over 3 months when compared with the size at the original onset. We analyzed the patient age at the original onset, original lesion size, and lesion location retrospectively. Congenital lesions were considered as having an onset at 0 years of age, even when diagnosed prenatally.

Statistical analyses involved the 2-sided *t* test for normally distributed data and the F-test for assessment of less than 5 patients. A receiver operating characteristic (ROC) curve was drawn using the SPSS software (IBM Corp., Ar-

*From the *Department of Plastic and Reconstructive Surgery, Lymph Clinic, Saitama Children's Medical Center, Saitma, Japan; †Department of Pediatric Surgery, Saitama Children's Medical Center, Saitma, Japan; and ‡Department of Plastic and Reconstructive Surgery, The University of Tokyo, Tokyo, Japan.*
Received for publication March 29, 2017; accepted July 26, 2017.

DOI: 10.1097/GOX.0000000000001501

Disclosure: *The authors have no financial interest to declare in relation to the content of this article. The Article Processing Charge was paid for by the authors.*

A 34-year, 28-subject study confirmed no spontaneous regression

Types	Microcystic
Subtotal	28
Sex (F:M)	14:14
Age (y), mean ± SD	0.89 ± 1.4
Maximum diameter (cm), mean ± SD	—
Spontaneous regression	
Positive	0
Negative	28

** Consistent with well-established history of PI3K Related Overgrowth Spectrum, which includes microcystic LM*
***Kato M et al., Plast Reconstr Surg Glob Open. 2017 Sep 25;5(9):e1501.*

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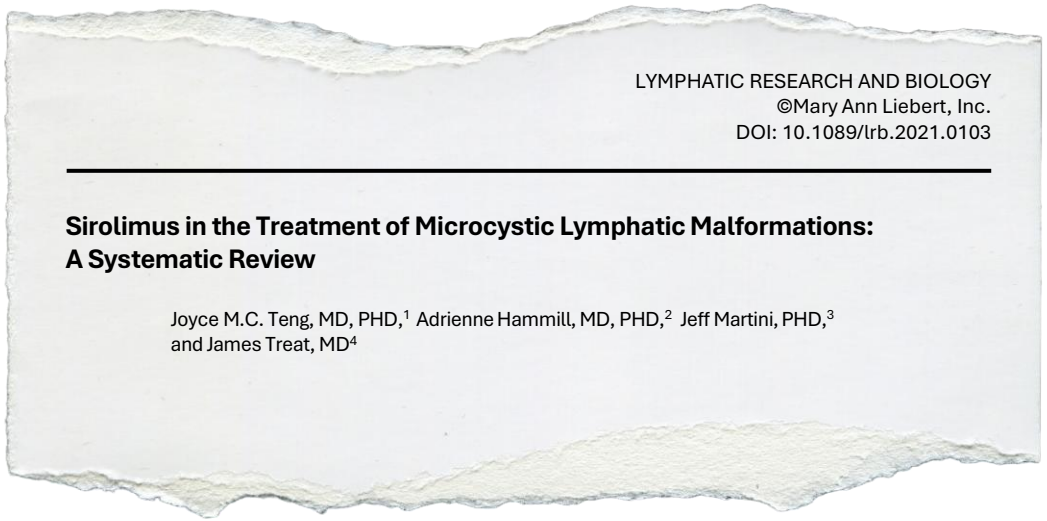
Regulatory: Real-world Evidence to Support NDA Submission



LYMPHATIC RESEARCH AND BIOLOGY
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DOI: 10.1089/lrb.2021.0103

Sirolimus in the Treatment of Microcystic Lymphatic Malformations: A Systematic Review

Joyce M.C. Teng, MD, PHD,[1] Adrienne Hammill, MD, PHD,[2] Jeff Martini, PHD,[3] and James Treat, MD[4]

"Micro LMs represent therapeutically challenging congenital vascular lesions. There is no universally accepted gold standard of care and there are no FDA approved therapies…this review examines clinical data over the last 10 years on the role of sirolimus [rapamycin]…a total of 16 studies were identified…clinically meaningful, long-term improvement (up to 3 years) was noted…however, developing a commercial topical sirolimus formulation faces important challenges."

Leboulanger *et al.*
Orphanet Journal of Rare Diseases (2023) 18:10
https://doi.org/10.1186/s13023-022-02608-y

French national diagnosis and care protocol (PNDS, protocole national de diagnostic et de soins): cystic lymphatic malformations

Nicolas Leboulanger[1,2*], Annouk Bisdorff[3], Olivia Boccara[4], Anne Dompmartin[5], Laurent Guibaud[6], Christine Labreze[7], Jacques Lagier[8], Bénédicte Lebrun-Vignes[9], Denis Herbreteau[10], Aline Joly[11], Julie Malloizel-Delaunay[12], Arnaud Martel[8], Stéphane Munck[13], Frédérique Saint-Aubin[14] and Annabel Maruani[15,16]

"Sirolimus [rapamycin] is the disease-modifying treatment of choice. It should be started early in life (early childhood) to prevent the increase in volume of the LM."

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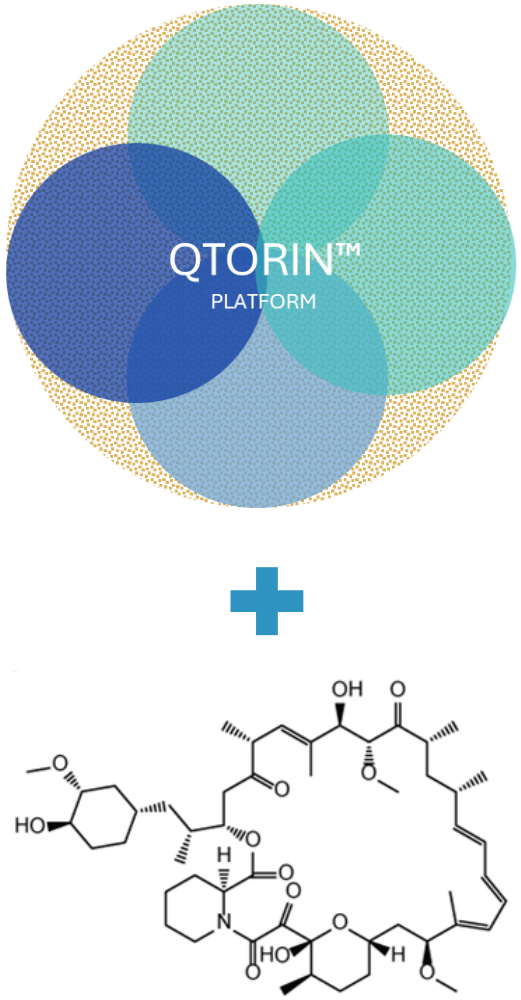
QTORIN™: Targeted mTOR Inhibition with Dermal Target Engagement



QTORIN™ 3.9% Rapamycin Anhydrous Gel

3.9% concentration enabled through synergistic multi-excipient anhydrous solubilization system

Single-phase gel maintaining dissolved rapamycin without crystallization or suspension

Elevated thermodynamic activity drives rapamycin vehicle release and skin bioavailability

Deep dermal penetration & sustained dermal retention for prolonged inhibition of hyperactivated mTOR signaling

Adherence-optimized vehicle designed for chronic dosing in pediatric and adult populations

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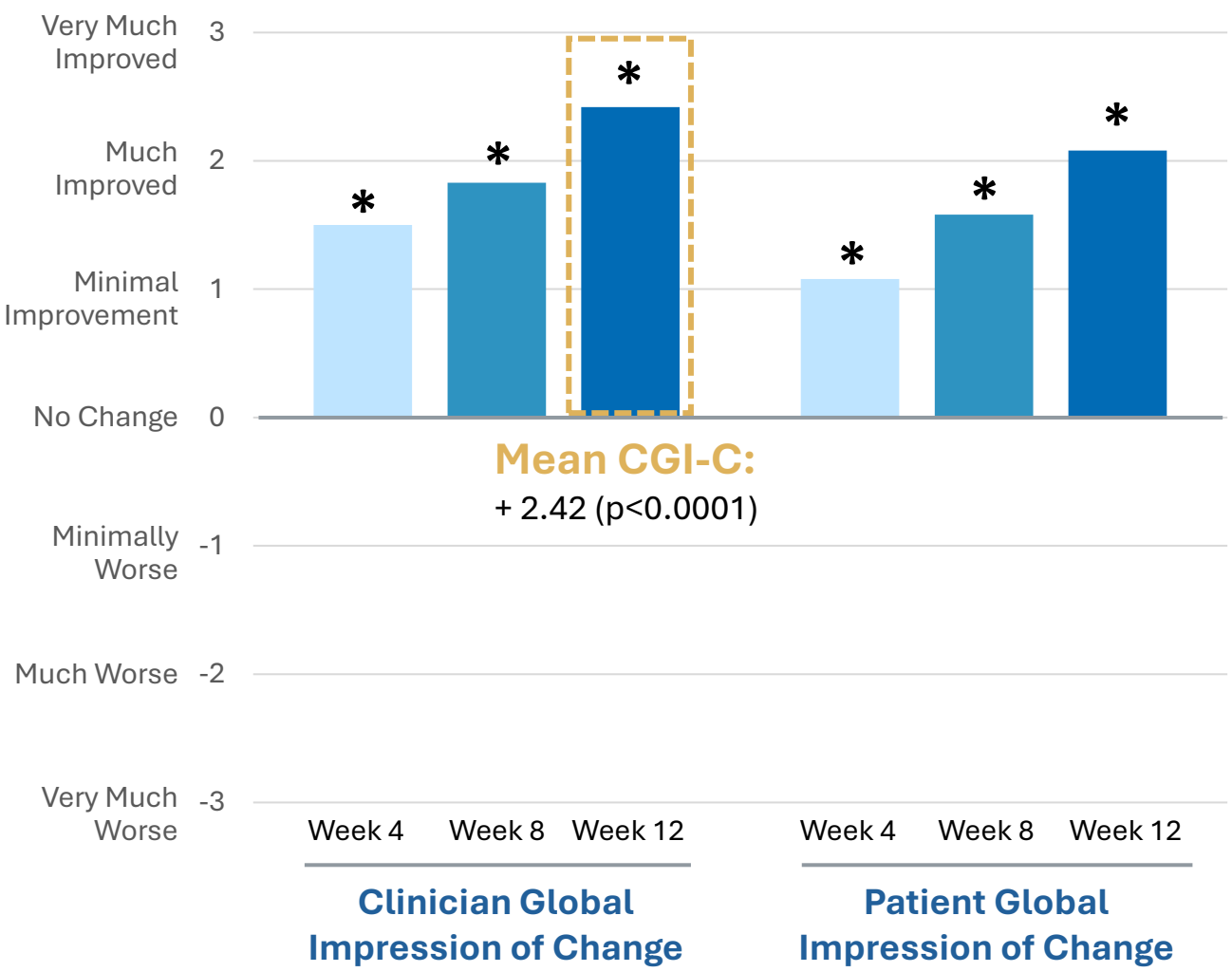
Phase 2: Clinically Meaningful, Statistically Significant Improvements

n=12; QD dose



Statistically significant across key clinician-assessed individual signs of microcystic LM at week 12

- Height (p<0.0001)
- Leaking (p<0.005)
- Bleeding (p<0.05)
- Erythema (p<0.005)
- Hyperkeratosis (p<0.005)

→ **100% of participants were either "Much Improved" or "Very Much Improved"** on CGI-C after 12 weeks of treatment

→ **Palvella was subsequently granted FDA Breakthrough Therapy Designation** based on this data

* = p-value <0.0001

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Phase 3 SELVA: Baseline Characteristics

	ITT Population (n=49)[1]
Age, Mean [Range]	19.4 [6-57]
Sex M:F	24:25
Prior Medical Interventions for mLM[2]	34 (69%)
Laser	17 (35%)
Sclerotherapy	14 (29%)
Surgery	13 (27%)
Topical Sirolimus [Rapamycin]	13 (27%)
Oral Sirolimus [Rapamycin]	2 (4%)

1. 51 participants entered Baseline period; 50 dosed with QTORIN™ rapamycin (49 participants ≥6 years old = ITT population; 1 participant 3-5 years old included in safety database). 2. Percentages may not sum to 100% due to some patients having more than one intervention.

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SELVA: All Additional Secondary Endpoints Achieved

	Mean Change at Week 24 (95% CI)	**p-value**
Patient Global Impression of Change*	**+1.9** (1.66, 2.16)	p<0.001
Live mLM-MCSS**	**-4.6** (-5.20, -3.92)	p<0.001
Clinician Global Impression of Severity***	**-1.7** (-1.91, -1.39)	p<0.001
Patient Global Impression of Severity***	**-1.0** (-1.26, -0.74)	p<0.001

*Dynamic change scales (7-point scales ranging from "Very Much Worse" (-3) to "Very Much Improved" (+3); positive values indicate improvements from baseline)
**mLM-MCSS (Sum of three static severity scales: Height, Leaking/Bleeding, Vesicle Appearance: Each scale rated "Clear or Almost Clear" (1) to "Very Severe" (5); total score 3-15. Test baseline to Week 24 change; negative values indicate improvements from baseline)
***Static severity scales (5-point scales ranging from 1 to 5; negative values indicate improvements from baseline)

Note: Data analyzed per statistical analysis plan; non-completer data imputed per statistical analysis plan for primary endpoint; endpoints tested according to pre-specified hierarchical testing procedure; statistical significance (p<0.05).

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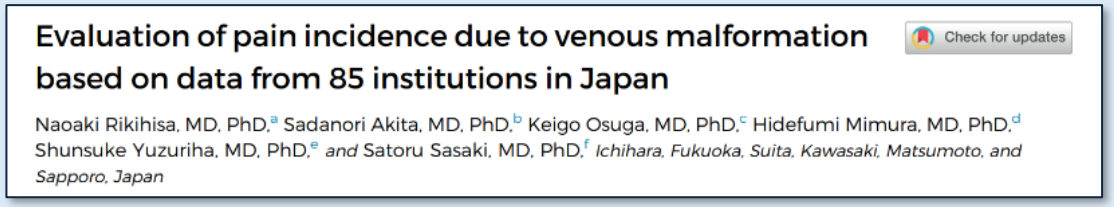
Multiple Studies Indicate At Least Half of Venous Malformation Cases Have Cutaneous Involvement

Percentage of venous malformation cases with cutaneous involvement

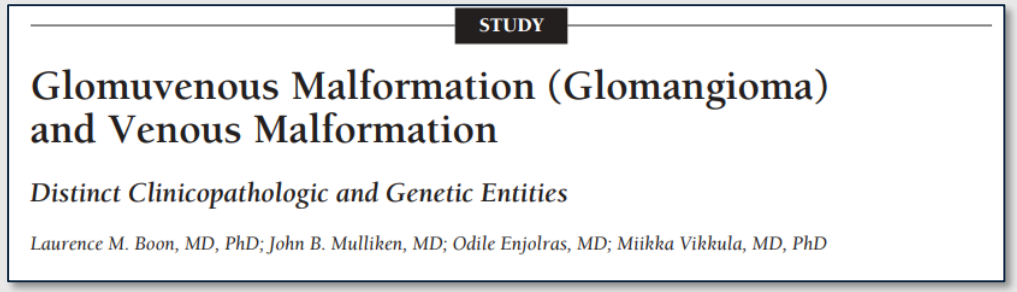


Evaluation of pain incidence due to venous malformation based on data from 85 institutions in Japan

Check for updates

Naoaki Rikihisa, MD, PhD,[a] Sadanori Akita, MD, PhD,[b] Keigo Osuga, MD, PhD,[c] Hidefumi Mimura, MD, PhD,[d] Shunsuke Yuzuriha, MD, PhD,[e] *and* Satoru Sasaki, MD, PhD,[f] *Ichihara, Fukuoka, Suita, Kawasaki, Matsumoto, and Sapporo, Japan*

~47% of 2,075 cases



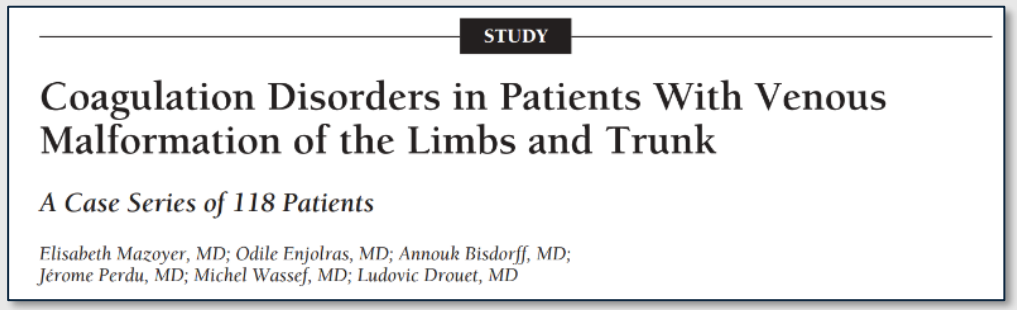
STUDY

Glomuvenous Malformation (Glomangioma) and Venous Malformation

Distinct Clinicopathologic and Genetic Entities

Laurence M. Boon, MD, PhD; John B. Mulliken, MD; Odile Enjolras, MD; Miikka Vikkula, MD, PhD

~80% of 1,517 cases



STUDY

Coagulation Disorders in Patients With Venous Malformation of the Limbs and Trunk

A Case Series of 118 Patients

Elisabeth Mazoyer, MD; Odile Enjolras, MD; Annouk Bisdorff, MD; Jérome Perdu, MD; Michel Wassef, MD; Ludovic Drouet, MD

~65% of 118 cases

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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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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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