palvella THERAPEUTICS

QTORIN™ 3.9% Rapamycin Anhydrous Gel: Statistically Significant, Clinically Meaningful Improvement in Microcystic Lymphatic Malformations (Phase 3 SELVA Study) and Cutaneous Venous Malformations (Phase 2 TOIVA Study)

Presentation at ISSVA World Congress 2026

Dr. James Treat, Children's Hospital of Philadelphia

May 20, 2026

Conflict Statement

- Royalties: UpToDate (Tinea Capitis and Pityriasis Lichenoides et Varioliformis Acuta) and Andrews Diseases of the Skin
- Advisory Board: Incyte, Arcutis
- I provide consulting services for Arcutis and Palvella and Nektar.
- Many therapies in Pediatric dermatology are off label

Agenda

Phase 3 SELVA Study: QTORIN™ rapamycin for treatment of microcystic lymphatic malformations (mLMs)

1. SELVA Phase 3 Topline Results: Statistically Significant Improvement Across All Pre-specified Endpoints
2. Early Intervention and Chronic Disease Management: Results from Pediatric Patients Aged 6-11 Years ★
3. Rapid Onset and Large Treatment Effect in Leaking and Bleeding – Two of the Most Burdensome Signs of Microcystic LMs ★
4. Treatment Satisfaction Questionnaire for Medication (TSQM) and Patient Qualitative Interviews Support the Clinical Meaningfulness of QTORIN™ Rapamycin's Treatment Effect ★
5. Blinded Independent Review Demonstrated Stability During Run-In and Marked Improvement on Treatment ★

James R. Treat, MD

Professor of Clinical Pediatrics and Dermatology
Perelman School of Medicine at the University of Pennsylvania
Children's Hospital of Philadelphia

★ **= New data to be presented today**

Agenda (*cont.*)

Phase 2 TOIVA Study: QTORIN™ rapamycin for treatment of cutaneous venous malformations (cVMs)

1. TOIVA Phase 2 Topline Results: Statistically Significant Improvement
2. cVM Clinical Signs: Height/Engorgement and Appearance Results Through 24 Weeks ★

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Background

- QTORIN™ rapamycin 3.9% anhydrous gel (QTORIN™ rapamycin) is an investigational therapy in development for **microcystic LMs, cutaneous VMs, clinically significant angiokeratomas**, and other skin diseases driven by the mammalian target of rapamycin (mTOR) pathway
  - Microcystic LMs typically driven by PIK3CA mutations
  - Cutaneous VMs typically driven by TEK or PIK3CA mutations

- QTORIN™ rapamycin received **FDA Breakthrough Therapy Designation, Fast Track Designation**, and **Orphan Drug Designation** for microcystic LM and **Fast Track Designation** for cutaneous VMs

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Recent Epidemiology Findings

- Microcystic LMs: Estimated U.S. diagnosed prevalence of **~45k-90k** as presented at Society for Investigative Dermatology 2025 based on claims analysis[1]
- Cutaneous VMs: Estimated U.S. diagnosed prevalence of **~135k** as published in *Orphanet Journal of Rare Diseases*[2]

1. Palvella and ZS Associates claims analysis (2025). 2. Gallagher et al., *Orphanet Journal of Rare Diseases*, (2025).

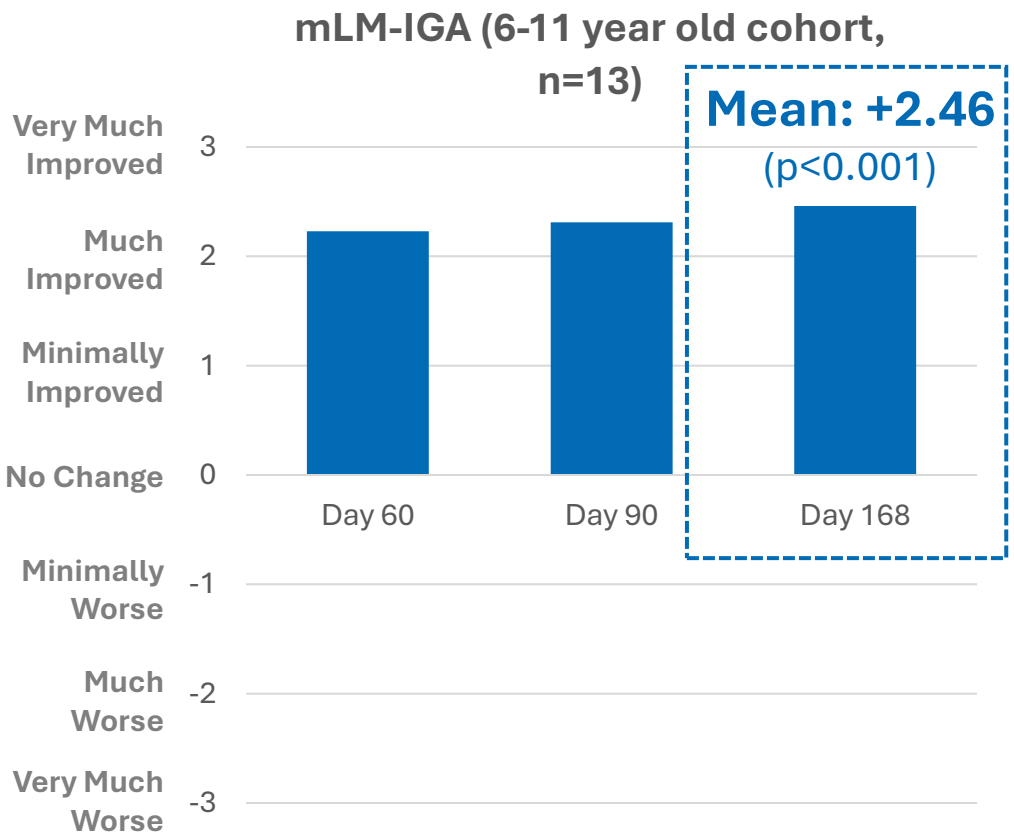
1 SELVA Phase 3 Topline Results: Statistically Significant Improvement Across All Prespecified Endpoints

	Mean Change at Week 24 (95% CI)	p-value
Primary Endpoint: mLM-IGA*	**+2.13** (1.88, 2.38)	p<0.001
Key Secondary Endpoint: Blinded mLM-MCSS***	**-3.4** (-4.34, -2.38)	p<0.001
Secondary Endpoint: Live mLM-MCSS***	**-4.6** (-5.20, -3.92)	p<0.001
Secondary Endpoint: PGI-Change*	**+1.9** (1.66, 2.16)	p<0.001
Secondary Endpoint: CGI-Severity**	**-1.7** (-1.91, -1.39)	p<0.001
Secondary Endpoint: PGI-Severity**	**-1.0** (-1.26, -0.74)	p<0.001

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

❷ Early Intervention and Chronic Disease Management: Results from Pediatric Patients Aged 6-11 Years



All pre-specified age cohorts in ITT were highly statistically significant

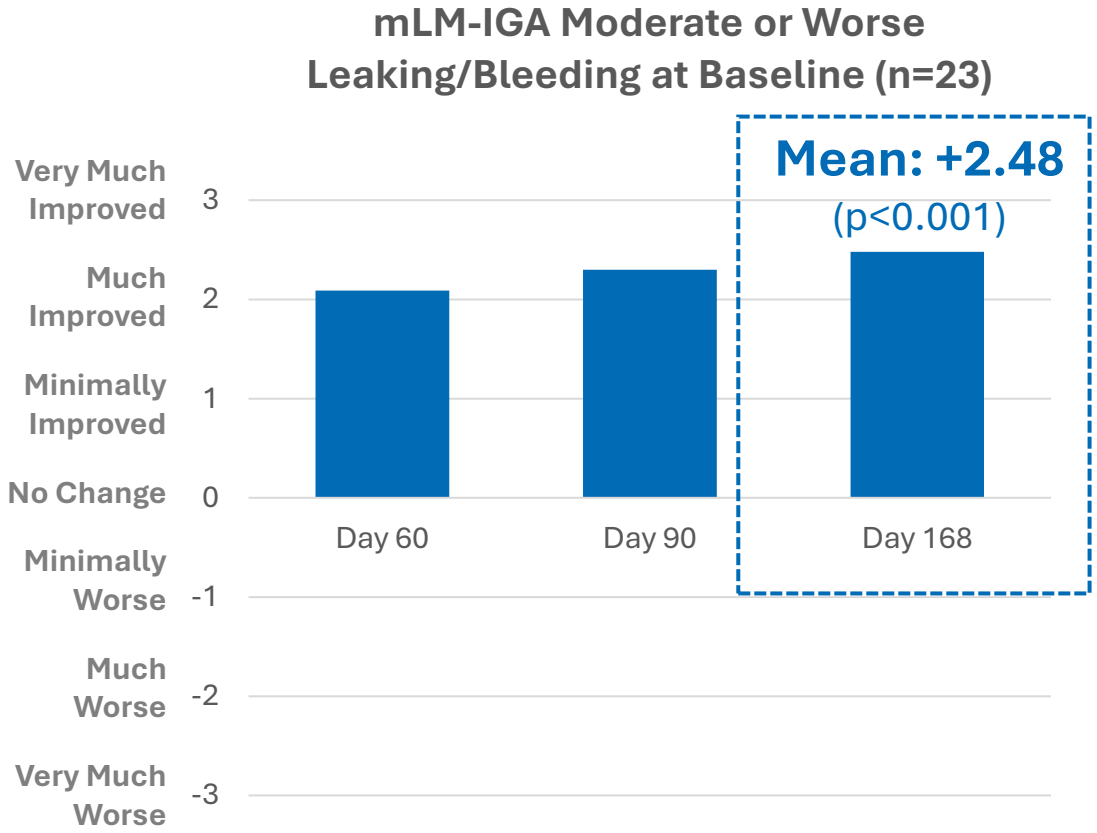
100% of the 6-11 y/o cohort at Day 168 were "***Much Improved***" (+2) or "***Very Much Improved***" (+3)

ALL rolled over into Treatment Extension, **supporting chronic disease management**

Age 7, Female

mLM-IGA: +3 "Very Much Improved"

3 Rapid Onset and Large Treatment Effect in Leaking and Bleeding – Two of the Most Burdensome Signs of Microcystic LMs



Among participants with moderate or worse leaking/bleeding at baseline,
87% (20/23) were either "Much Improved" or "Very Much Improved" at Day 168

4 Treatment Satisfaction Questionnaire for Medication (TSQM) and Patient Qualitative Interviews Support the Clinical Meaningfulness of QTORIN™ Rapamycin's Treatment Effect

Treatment Satisfaction Questionnaire for Medication (TSQM)

Validated patient-reported outcome measure that assesses satisfaction with medication

At Week 24, **100% of patients were at least somewhat satisfied with QTORIN™ rapamycin** on the TSQM-9 overall satisfaction item, with **84% reporting extremely satisfied, very satisfied, or satisfied**

Patient Qualitative Interviews

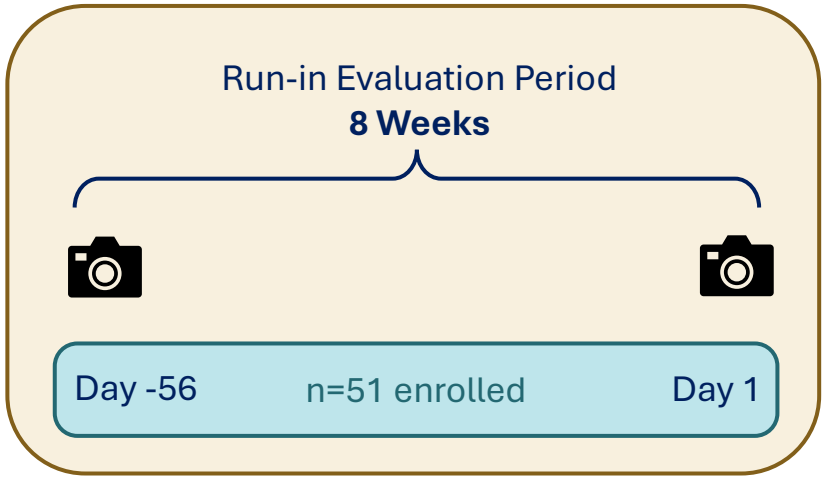
Pre-specified patient interview sub-study assessed treatment experience before and after QTORIN™ rapamycin

"…to go from something that I thought about every single day… ***it's not something that's on my mind anymore****, which is* ***incredibly meaningful after this many years****."*

- SELVA Patient

5 **Phase 3 SELVA Study for Treatment of Microcystic LMs:** Blinded Independent Review Demonstrated Stability During Run-In and Marked Improvement on Treatment

mLM-MCSS: Sum of 3 static severity scales: Height, Leaking/Bleeding, Vesicle Appearance: Each scale rated 1 to 5; total score 3-15; Negative values indicate improvements from baseline



Pre-Treatment:
Day -56 to Day 1

Blinded mLM-MCSS mean score:

Change: -0.1

- Finding consistent with microcystic LM natural history study from Kato et al.[1] which demonstrated no spontaneous regression

Efficacy Evaluation:
Following 24 weeks of QTORIN™ rapamycin

Blinded mLM-MCSS mean score:
Day 1 (9.9) → Day 168 (6.6)
Change: -3.4
(represents 48% of maximum potential improvement from Day 1)

Note: To preserve blinding, different raters were used to compare Day -56 vs Day 1 and Day 1 vs Day 168 photographs. 1. Kato M et al., *Plast Reconstr Surg Glob Open*. 2017 Sep 25;5(9):e1501.

Phase 3 SELVA Conclusion: Well-Tolerated and Favorable Safety and Efficacy Profile

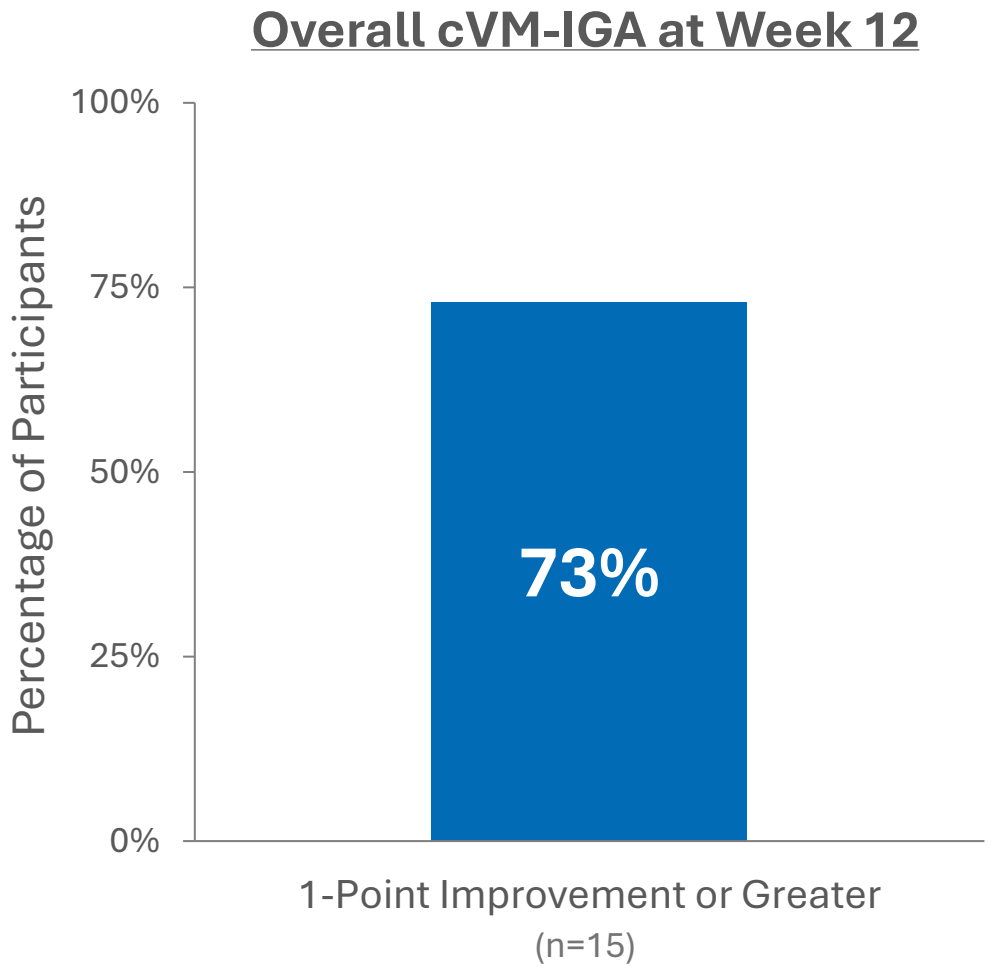
	Number of Participants (%)
Any Treatment-Emergent Adverse Event	35 (70%)
Severe (not related to study drug)	1 (2%)
Serious (not related to study drug)	4 (8%)
Any Treatment-Related[1] Adverse Event	17 (34%)
Severe	0 (0%)
Serious	0 (0%)
Treatment-Related AEs with ≥ 5% Incidence	
Application site acne	3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

- Overall, QTORIN™ rapamycin was well-tolerated
- All treatment-related AEs were mild to moderate in intensity
- Rapamycin levels were below 2 ng/mL in systemic circulation for all patients at all timepoints (0.18 ng/mL mean)
- High rollover to Treatment Extension (98%)

QTORIN™ rapamycin could provide physicians and patients with a targeted therapy that is an alternative to current interventional approaches

1 TOIVA Phase 2 Topline Results: Statistically Significant Improvement

Single-arm, baseline-controlled, daily 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.

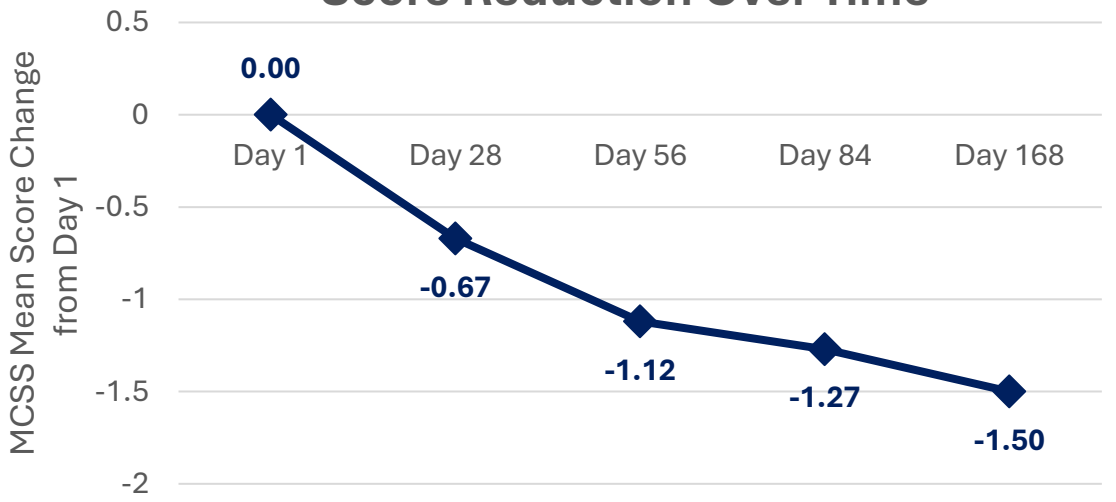
1. Genetic testing was not required as part of the protocol; Palvella is continuing efforts to collect genetic data on trial participants.

2 cVM Clinical Signs: Height/Engorgement and Appearance Results Through 24 Weeks

Today, presenting new 24-week data on two of the key clinical signs measured in the TOIVA trial: height/engorgement and appearance

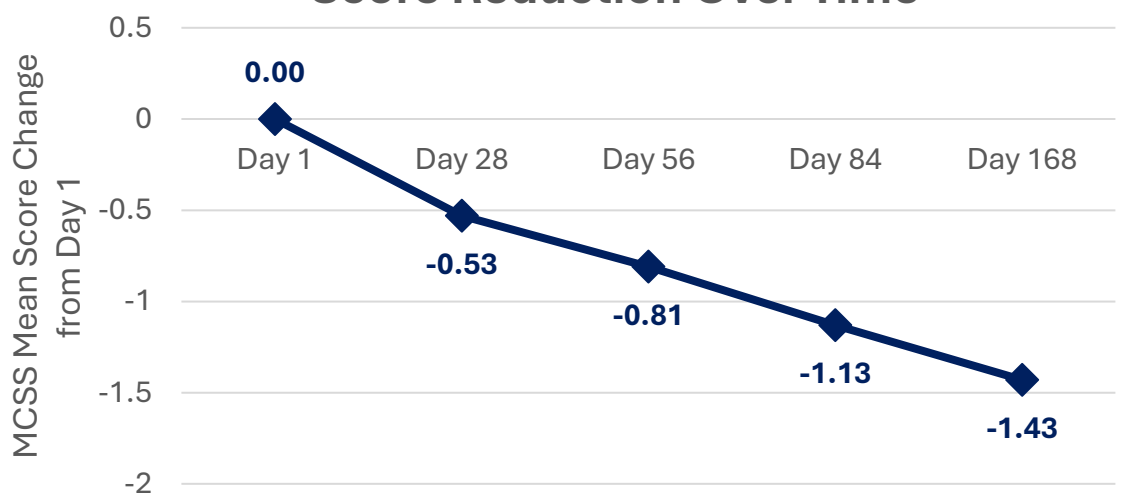
- Data on bleeding, another key clinical sign in cutaneous venous malformations, were recently presented at the 83rd Annual Meeting of the Society for Investigative Dermatology

cVM-MCSS Height Score Reduction Over Time



	Day 28	Day 56	Day 84	Day 168 (n=14)
p-value	0.027	0.001	<0.001	<0.001

cVM-MCSS Appearance Score Reduction Over Time



	Day 28	Day 56	Day 84	Day 168 (n=14)
p-value	0.001	0.001	<0.001	<0.001

cVM-MCSS (cutaneous VM multi-component static scale) Height and Appearance are rated on 5-point scales ranging from 1 to 5; negative values indicate improvements from Day 1

Note: Mean change and p-values collected on observed data only.

Thank You

Striving to be first for rare disease patients