



## **Palvella Therapeutics Announces Scientific Publication in Lymphatic Research and Biology Highlighting Recent Advances in the Pathogenesis of Venous Malformations and the Real-World Use of Rapamycin as an Emerging Targeted Therapy**

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*Recent advances in understanding venous malformation disease pathogenesis highlight the PI3K/AKT/mTOR pathway as a key driver of disease proliferation, spurring real-world off-label use of systemic rapamycin (sirolimus)*

*Publication includes a systematic review of 26 studies evaluating the use of rapamycin for the treatment of venous malformations*

*Study authors highlight unmet clinical need for venous malformations and lack of FDA-approved pharmacologic options while advocating for an FDA-approved targeted topical formulation of rapamycin for patients with cutaneous venous malformations*

WAYNE, Pa., Sept. 17, 2025 (GLOBE NEWSWIRE) -- (Nasdaq: PVLA) [Palvella Therapeutics, Inc.](#) (Palvella), a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapies to treat patients suffering from serious, rare genetic skin diseases for which there are no U.S. Food and Drug Administration (FDA)-approved therapies, today announced the publication of a manuscript in *Lymphatic Research and Biology* which summarizes a systematic literature review of rapamycin for the treatment of venous malformations (VMs). The manuscript supports the scientific rationale and clinical potential of Palvella's QTORIN™ 3.9% rapamycin anhydrous gel (QTORIN™ rapamycin) for the treatment of cutaneous VMs, currently under evaluation in the Phase 2 TOIVA trial with top-line data anticipated in mid-December 2025.

"This publication highlights the significant unmet need in the management of cutaneous venous malformations and the large, growing real-world experience that rapamycin as a therapy can benefit patients with this challenging disease," said Joyce Teng, M.D., Ph.D., Professor of Dermatology and Pediatrics at Stanford University. "Data summarized in this review further strengthen the scientific and clinical rationale for a targeted, non-systemic approach to treat cutaneous venous malformations which currently have no FDA-approved therapy."

*Lymphatic Research and Biology* is a peer-reviewed journal dedicated to delivering the most current advances and developments in the genetics, biology, pathology, and diseases and disorders of the lymphatic system. The publication, titled "Sirolimus for Venous Malformations: A Systematic Review of Efficacy and Safety," reviews 26 studies comprising 98 patients treated with rapamycin (also known as sirolimus) for VMs. In addition to Dr. Teng, leading clinicians in the field of vascular malformations, including Michael Kelly, M.D., Ph.D., pediatric hematologist and oncologist at Cleveland Clinic, and Megha Tollefson, M.D., pediatric dermatologist at Mayo Clinic, contributed to the publication. Key findings from the publication included:

- Recent advances in the pathogenesis of VMs have implicated abnormal activation of the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT)/mammalian target of rapamycin (mTOR) signaling pathway, a critical intercellular pathway that plays a central role in venous malformation expansion and proliferation.
- Interventional treatments, including surgery, sclerotherapy, and laser therapy, are highlighted as potentially inadequate for VMs patients with extensive, cutaneous, or invasive disease.
- The majority of patients showed evidence of treatment efficacy with off-label rapamycin, despite an inadequate response to previous standard treatment; improvements were noted in several areas, including bleeding, functional capacity, quality-of-life measurements, and other clinical signs.
- Across the studies, there was no difference in efficacy based on mutation subtype, although not all studies reported on mutation subtype.
- A targeted, topical formulation of rapamycin could provide clinical benefit for cutaneous VMs by achieving therapeutic levels in the dermis while minimizing the risk of off-target effects of oral rapamycin.

"There is a serious unmet need in cutaneous VMs, with no FDA-approved therapies and a high burden of disease leading to physical and functional impairment and psychological distress," said Jeff Martini, Ph.D., Chief Scientific Officer of Palvella. "This systematic review supports a potentially important role for rapamycin in venous malformations, and further validates Palvella's approach to potentially address cutaneous venous malformations with QTORIN™ rapamycin, our innovative 3.9% rapamycin anhydrous gel. We look forward to announcing top-line results from our fully enrolled Phase 2 TOIVA study later this year."

Palvella recently announced the completion of enrollment of the Phase 2 TOIVA trial with 16 patients enrolling in the study. The program is focused on evaluating QTORIN™ rapamycin for the treatment of cutaneous VMs, a disease for which there are

currently no FDA-approved therapies for the estimated more than 75,000 diagnosed patients in the U.S. In April 2024, the FDA granted Fast Track Designation to QTORIN™ rapamycin for the treatment of VMs.

### **About Cutaneous Venous Malformations**

Cutaneous VMs is a serious, rare genetic disease caused by mutations in genes that cause overactivation of the PI3K/mTOR signaling pathway, leading to dysregulated growth of malformed veins within the skin. These malformations can cause substantial morbidity and functional impairment, significantly impact quality of life, and are associated with bleeding, swelling, ulceration, thrombosis, and other potential complications. An urgent need exists for an FDA-approved, targeted, localized therapy to treat cutaneous VMs. While published case studies and real-world evidence have provided preliminary evidence of clinical benefit from the off-label use of systemic mTOR inhibitors for venous malformations, there are currently no FDA-approved therapies for the estimated more than 75,000 diagnosed patients with cutaneous VMs in the U.S.

### **About Palvella Therapeutics**

Founded and led by rare disease drug development veterans, Palvella Therapeutics, Inc. (Nasdaq: PVLA) is a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapies to treat patients suffering from serious, rare genetic skin diseases for which there are no FDA-approved therapies. Palvella is developing a broad pipeline of product candidates based on its patented QTORIN™ platform, with an initial focus on serious, rare genetic skin diseases, many of which are lifelong in nature. Palvella's lead product candidate, QTORIN™ 3.9% rapamycin anhydrous gel (QTORIN™ rapamycin), is currently being evaluated in the Phase 3 SELVA clinical trial in microcystic lymphatic malformations and the Phase 2 TOIVA clinical trial in cutaneous venous malformations. For more information, please visit [www.palvellatx.com](http://www.palvellatx.com) or follow Palvella on [LinkedIn](#) or [X](#) (formerly known as Twitter).

QTORIN™ rapamycin is for investigational use only and has not been approved or cleared by the FDA or by any other regulatory agency for any indication.

### **Forward-Looking Statements**

This press release contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended (Securities Act)). These statements may discuss goals, intentions, and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of the management of Palvella, as well as assumptions made by, and information currently available to, the management of Palvella. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as “may,” “will,” “should,” “would,” “expect,” “anticipate,” “plan,” “likely,” “believe,” “estimate,” “project,” “intend,” and other similar expressions or the negative or plural of these words, or other similar expressions that are predictions or indicate future events or prospects, although not all forward-looking statements contain these words. Statements that are not historical facts are forward-looking statements. Forward-looking statements include, but are not limited to, statements regarding the expected timing of the presentation of data from ongoing clinical trials, Palvella's clinical development plans and related anticipated development milestones, Palvella's cash and financial resources and expected cash runway, and the potential of, and expectations regarding, Palvella's programs, including QTORIN™ rapamycin, and its research-stage opportunities, including its expected therapeutic potential and market opportunity. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various factors, including, without limitation: the ability to raise additional capital to finance operations; the ability to advance product candidates through preclinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, Palvella's product candidates, including QTORIN™ rapamycin; the outcome of early clinical trials for Palvella's product candidates, including the ability of those trials to satisfy relevant governmental or regulatory requirements; the fact that data and results from clinical studies may not necessarily be indicative of future results; Palvella's limited experience in designing clinical trials and lack of experience in conducting clinical trials; the ability to identify and pivot to other programs, product candidates, or indications that may be more profitable or successful than Palvella's current product candidates; the substantial competition Palvella faces in discovering, developing, or commercializing products; the negative impacts of global events on operations, including ongoing and planned clinical trials and ongoing and planned preclinical studies; the ability to attract, hire, and retain skilled executive officers and employees; the ability of Palvella to protect its intellectual property and proprietary technologies; reliance on third parties, contract manufacturers, and contract research organizations; and the risks and uncertainties described in the filings made by Palvella with the Securities and Exchange Commission (SEC), including the annual report on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, filed with or furnished to the SEC and available at [www.sec.gov](http://www.sec.gov). The events and circumstances reflected in our forward-looking statements may not be achieved or occur, and actual results could differ materially from those projected in the forward-looking statements. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties that Palvella may face. Except as required by applicable law, Palvella does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. This press release contains hyperlinks to information that is not deemed to be incorporated by reference into this press release.

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