Palvella Therapeutics Announces Positive Topline Results from Phase 2 TOIVA Clinical Trial of QTORIN™ 3.9% Rapamycin Anhydrous Gel (QTORIN™ rapamycin) for the Treatment of Cutaneous Venous Malformations, a Serious, Rare Genetic Disease with No FDA-approved Therapies

December 15, 2025

73% of trial participants (11/15 participants) improved on the Overall Cutaneous Venous Malformations Investigator Global Assessment (Overall cVM-IGA) at Week 12; 67% of trial participants (10/15 participants) rated as "Much Improved" (+2) or "Very Much Improved" (+3) on the Overall cVM-IGA at Week 12

Achieved statistical significance on multiple pre-specified clinician-reported and patient-reported efficacy endpoints, including dynamic change endpoints and static severity endpoints

QTORIN™ rapamycin was generally well-tolerated, with no drug-related serious adverse events reported

Based on Phase 2 results, Palvella to pursue near-term discussions with FDA regarding the potential for Breakthrough Therapy Designation and a Phase 3 pivotal study; FDA previously granted Fast Track Designation to QTORIN™ rapamycin for venous malformations

QTORIN™ rapamycin has the potential to become the first FDA-approved therapy and standard of care for the estimated more than 75,000 individuals with cutaneous venous malformations in the U.S.

Company to host conference call at 8:30am ET today

WAYNE, Pa., Dec. 15, 2025 (GLOBE NEWSWIRE) -- (Nasdaq: PVLA) Palvella Therapeutics, Inc. (Palvella or "the Company"), a clinical-stage biopharmaceutical company focused on developing and commercializing novel therapies to treat patients suffering from serious, rare skin diseases for which there are no U.S. Food and Drug Administration (FDA)-approved therapies, today announced positive topline results from the Company's Phase 2 TOIVA study of QTORIN™ 3.9% rapamycin anhydrous gel (QTORIN™ rapamycin) for the treatment of cutaneous venous malformations (cutaneous VMs).

"Based on the large magnitude of the treatment effect observed in the majority of patients in the Phase 2 TOIVA study, QTORIN™ rapamycin has potential to become first-line therapy and to establish a much-needed standard of care for individuals living with cutaneous venous malformations," said Megha Tollefson, M.D., pediatric dermatologist at Mayo Clinic and Principal Investigator of the Phase 2 TOIVA study. "Cutaneous venous malformations are congenital, chronic, progressive lesions that persist throughout life and can have a profound impact on patients' quality of life. They may affect functionally critical areas of the body, often leading to daily discomfort, limitations in activities, and substantial burden for patients and their families. Current procedure-based approaches can be painful, ineffective, or both, and result in high rates of recurrence. Taken together, we believe the Phase 2 data represent a milestone day for individuals living with cutaneous venous malformations, and we look forward to working with Palvella to advance development of this therapy for patients as quickly as possible."

TOIVA is a Phase 2, single-arm, open-label, baseline-controlled clinical trial of QTORIN™ rapamycin administered topically once daily for a 12-week efficacy evaluation period followed by a 12-week treatment extension period, for cutaneous VMs. The study enrolled 16 participants, ages six and older, at leading vascular anomaly centers across the U.S. Multiple measures of efficacy, including change in clinician and patient global impression assessments, as well as assessments of specific individual clinical manifestations which contribute to disease burden, were evaluated. To help contextualize changes on efficacy endpoints and, specifically, better understand any patient quality of life impact resulting from QTORIN™ rapamycin, qualitative exit interviews were conducted by a third-party interviewer with a subset of participants from the Phase 2 study.

Key findings from among the study's pre-specified efficacy endpoints at Week 12 demonstrated improvements in both clinician- and patient-reported outcomes:

Efficacy Endpoints at Week 12 (ITT Population)	Mean Change from Baseline (n=15)	Nominal, Two-sided p-value
Dynamic Change Scales *(7-point scales ranging from -3 to +3; positive values indicate improvements from baseline)*		
Overall Cutaneous VM Investigator Global Assessment (Overall cVM-IGA)	1.5	<0.001

cVM-IGA Height/Engorgement	1.3	<0.001
cVM-IGA Appearance (visualization/color of affected veins)	1.5	<0.001
cVM-IGA Bleeding	0.7	0.045
Overall Patient Global Impression of Change (PGI-C)	1.1	<0.001
Static Severity Scales *(5-point scales ranging from 1 to 5; negative values indicate improvements from baseline)*		
Overall Clinician Global Impression of Severity (CGI-S)	-1.0	<0.001
cVM-MCSS (Cutaneous VM Multi-Component Static Scale) Severity of Height/Engorgement	-1.3	<0.001
cVM-MCSS Severity of Appearance (visualization/color of affected veins)	-1.1	<0.001
Overall Patient Global Impression of Severity (PGI-S)	-0.5	0.027

- p-values are nominal as there was no adjustment for multiplicity amongst efficacy endpoints; change scores and changes from baseline in static scores were compared vs. mean 0 using a 1-sample t-test.
- n=15 subjects completed treatment period (one additional dosed participant lost to follow up); data analyzed per statistical analysis plan; analysis conducted per available data at each timepoint; ITT analyzed with no imputation of values for missing data.
- Ulceration was also assessed with no disease present at baseline. CGI-S Bleeding assessed with limited disease present at baseline.

The Overall Cutaneous Venous Malformations Investigator Global Assessment (Overall cVM-IGA) is a 7-point, clinician-assessed, single-item efficacy endpoint measuring change in severity from baseline, with the numeric rating scale ranging from “Very Much Worse” (-3) to “Very Much Improved” (+3).

On the Overall cVM-IGA at Week 12:

- 73% of trial participants (11/15 participants) improved
- 67% of trial participants (10/15 participants) were either “Much Improved” (+2) or “Very Much Improved” (+3)
- No trial participants (0/15 participants) were “Minimally Worse” (-1), “Much Worse” (-2), or “Very Much Worse” (-3)

Represented in the ten (10) participants who were rated either “Much Improved” (+2) or “Very Much Improved” (+3) on the Overall cVM-IGA at Week 12 were participants with (i) genetically confirmed TEK mutations, (ii) genetically confirmed PIK3CA mutations, and (iii) a non-TEK/PIK3CA mutation or unconfirmed genotype.

Genetic mutation confirmation was not required for entry into the Phase 2 TOIVA study. Additional data from trial participants, including mutation confirmation, continue to be collected, with genotype-stratified results planned for presentation at future medical meetings. Based on analysis of data at Week 12, the Company does not anticipate requiring confirmed genotypes or genetic testing in future studies.

Similar to previous clinical trials of QTORIN™ rapamycin, in the Phase 2 TOIVA study QTORIN™ rapamycin was generally well-tolerated, with the most common treatment-emergent adverse events being application site reactions (erythema, 25%). All treatment-related adverse events were moderate or mild, with no unexpected adverse events reported. 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.

“Based on the strength of the Phase 2 TOIVA results, including the 73% of participants who improved on the Overall cVM-IGA at Week 12, Palvella is planning for near-term discussions with FDA regarding the potential for Breakthrough Therapy Designation and a Phase 3 pivotal study, as well as the newly announced Plausible Mechanism Pathway,” said Wes Kaupinen, Founder and Chief Executive Officer of Palvella. “We are deeply grateful to the patients and families who participated in this trial, as well as the investigators and clinical centers whose partnership made this study possible. These data reinforce our conviction in the therapeutic potential of QTORIN™ rapamycin, the strength of the QTORIN™ platform, and our long-term vision to become the leading rare disease company focused on developing and commercializing novel therapies for patients with serious, rare skin diseases.”

FDA has previously granted Fast Track Designation to QTORIN™ rapamycin for the treatment of venous malformations.

Conference Call Details

Palvella will host a conference call and live audiovisual webcast to discuss the Phase 2 TOIVA topline results at 8:30 a.m. ET today. To access the live webcast of the call with slides, please click here or visit the "Events & Presentations" section of Palvella’s website. To access the call by phone, please use this registration link, and you will be provided with dial in details. A replay of the webcast will be available approximately 2 hours after the conclusion of the call and archived for 90 days under the "Events & Presentations" section of the Company's website at www.palvellatx.com.

About Cutaneous Venous Malformations

Cutaneous VMs are a rare genetic disease caused by mutations in genes that cause overactivation of the PI3K/mTOR signaling pathway, leading to dysfunctional veins within the skin. These malformations can cause substantial morbidity and functional impairment, significantly impact quality of life, and are associated with severe bleeding, 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 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 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 developed for the treatment of microcystic lymphatic malformations, cutaneous venous malformations, and clinically significant angiokeratomas. Palvella's second product candidate, QTORIN™ pitavastatin, is currently being developed for the topical treatment of disseminated superficial actinic porokeratosis. For more information, please visit www.palvellatx.com or follow Palvella on LinkedIn or X (formerly known as Twitter).

QTORIN™ rapamycin and QTORIN™ pitavastatin are for investigational use only and neither has been approved by the FDA o 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, including the TOIVA study, Palvella's clinical development plans and related anticipated development milestones, Palvella's plans to pursue Breakthrough Therapy Designation, Palvella's plans to meet with regulatory authorities, Palvella's cash, financial resources and expected runway, Palvella's expectations regarding its programs, including QTORIN™ rapamycin and QTORIN™ pitavastatin, 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 and QTORIN™ pitavastatin; 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. 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.

Contact Information

Investors

Wesley H. Kaupinen
Founder and CEO, Palvella Therapeutics
wes.kaupinen@palvellatx.com

Media
Marcy Nanus
Managing Partner, Trilon Advisors LLC
mnanus@trilonadvisors.com