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

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QTORIN™ rapamycin generally well-tolerated; no drug related severe adverse events and no observed rapamycin in systemic circulation

100% of participants were either "Much Improved" or "Very Much Improved" as rated by the Clinician Global Impression of Change following 12-weeks of QTORIN™ rapamycin

End of Phase 2 meeting completed with U.S. Food and Drug Administration in February 2023; pending additional interactions with FDA, anticipate potential initiation of pivotal Phase 3 study in second half of 2023

FDA previously granted Fast Track Designation and Orphan Drug Designation to QTORIN™ rapamycin for Microcystic Lymphatic Malformations

QTORIN™ rapamycin has potential to become first therapy and standard of care for the estimated more than 30,000 individuals with Microcystic Lymphatic Malformations in U.S., if approved

WAYNE, Pa., March 09, 2023 (GLOBE NEWSWIRE) -- Palvella Therapeutics, Inc., a late clinical-stage biopharmaceutical company whose vision is to become the leading rare disease company focused on developing and

commercializing novel therapies to treat individuals suffering from serious, rare genetic skin diseases for which there are no FDA-approved therapies, today announced positive topline results from the Company's Phase 2 study of QTORIN™ rapamycin in Microcystic Lymphatic Malformations (Microcystic LM). Microcystic LM is a rare, chronically debilitating genetic disease caused by dysregulation of the PI3K/mTOR pathway. The disease is characterized by localized masses of malformed lymphatic vessels that protrude through the skin barrier and persistently leak lymph fluid (lymphorrhea) and bleed, often leading to recurrent serious infections and cellulitis. There are no FDA-approved treatments for the estimated more than 30,000 individuals living with Microcystic LM in the U.S.

"People living with Microcystic LMs face daily challenges and frequent, sometimes life-threatening hospitalizations due to cellulitis. Current treatments are inadequate, invasive, and do not address the underlying mechanisms of this debilitating disease," said James Treat, MD, a pediatric dermatologist at Children's Hospital of Philadelphia and study investigator. "The encouraging results from the Phase 2 study of QTORIN™ rapamycin build upon the large, growing evidence base supporting targeted therapeutic intervention of Microcystic LMs via the mTOR pathway. We look forward to potentially initiating a pivotal Phase 3 study of QTORIN™ rapamycin in the second half of 2023, and to sharing the results from that study when they are available."

The proof-of-concept Phase 2, multi-center, open-label study featured multiple efficacy assessments, including clinician and patient global impression assessments as well as assessments of individual clinical manifestations that are important disease burdens for individuals living with Microcystic LM (lesion height, leaking, bleeding, erythema, and crusting/hyperkeratosis). Twelve individuals (n=12) with Microcystic LMs received QTORIN™ rapamycin once-daily for 12 weeks. Key findings from among the prespecified efficacy endpoints comparing end of treatment (Week 12) to the pre-treatment baseline period demonstrated improvements in several clinician and patient-reported outcomes:

Efficacy Endpoints	**Week 12** Mean (n=12)
Clinician Global Impression of Change (CGI-C)	2.42
Clinician Global Impression of Severity (CGI-S) – Overall	-1.33
• CGI-S Height	-1.67
• CGI-S Leaking	-0.92
• CGI-S Bleeding	-0.92

• CGI-S Erythema	-1.08
• CGI-S Crusting/Hyperkeratosis	-1.17
Patient Global Impression of Change (PGI-C)	2.08
CGI-C and PGI-C improvements are represented by increases; CGI-S improvements are represented by CGI-C and PGI-C are 7-points scales ranging from “Very Much Worse” (-3) to “Very Much Improved” (+ CGI-S is a 5-point lesion severity scale p-values are nominal as there was no adjustment for multiplicity amongst efficacy endpoints All p-values from paired t-tests vs mean change of 0 as compared to baseline	

All twelve participants in the study demonstrated improvements on the PGI-C and CGI-C scales with all rated as either “Much Improved” or “Very Much Improved” by the clinicians after twelve weeks of treatment with QTORIN™ rapamycin. 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.

In the study, QTORIN™ rapamycin was generally well-tolerated with the most common adverse events being application site pain and pruritus. No participants experienced drug related serious adverse events, and no unexpected adverse events occurred. No rapamycin was detected in the systemic circulation for all participants at all timepoints in the study. Palvella plans to present additional results of the Phase 2 study, including the results of the qualitative exit interviews, at an upcoming scientific meeting.

Palvella completed an End of Phase 2 Meeting with the FDA in February 2023. Pending additional interactions with FDA, Palvella anticipates potentially initiating a pivotal Phase 3 study of QTORIN™ rapamycin in the second half of 2023. The FDA has granted Orphan Drug and Fast Track Designations to QTORIN™ rapamycin for the treatment of Microcystic LM. The European Medicines Agency (EMA) has also granted Orphan Drug Designation to QTORIN™ rapamycin for the treatment of microcystic LMs.

About Palvella Therapeutics

Founded and led by rare disease veterans, Palvella Therapeutics is a late clinical-stage biopharmaceutical company whose vision is to become the leading rare disease company focused on developing and commercializing novel therapies to treat patients suffering from serious, rare genetic skin diseases in indications for which there are no FDA-approved therapies. Palvella’s development model involves partnering with patient advocacy organizations and their patient registries to design accelerated development programs aimed at expediting the introduction of targeted therapies to patients who currently lack any approved treatment options. We are

developing a broad pipeline of product candidates based on our patented QTORIN™ platform, with an initial focus on serious, rare genetic skin diseases, many of which are lifelong in nature. Our lead product candidate, QTORIN™ 3.9% rapamycin anhydrous gel (QTORIN™ rapamycin) is currently in late-stage clinical development for Pachyonychia Congenita (PC), Microcystic Lymphatic Malformations (Microcystic LM), and the prevention of Basal Cell Carcinomas (BCCs) in Gorlin Syndrome (GS). QTORIN™ rapamycin has received FDA Fast Track Designation for PC, Microcystic LM, and for the prevention of BCCs in GS.

QTORIN™ rapamycin 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.

James Treat, MD is a consultant for Palvella Therapeutics and a study investigator for the Phase 2 trial.

Forward-Looking Statements

This press release contains forward-looking statements concerning the development and commercialization of Palvella's products, the potential benefits and attributes of such products, and the company's expectations regarding its prospects. Forward-looking statements are subject to risks, assumptions and uncertainties that could cause actual future events or results to differ materially from such statements. These statements are made as of the date of this press release. Actual results may vary. Palvella undertakes no obligation to update any forward-looking statements for any reason.

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