Palvella Therapeutics Announces Planned Pivotal Phase 3 Study Design of QTORIN™ 3.9% Rapamycin Anhydrous Gel (QTORIN™ rapamycin) for the Treatment of Microcystic Lymphatic Malformations and Topline Results from Phase 2b CODY Study in Gorlin Syndrome

July 20, 2023 08:55 ET| Source: **Palvella Therapeutics**

QTORIN™ rapamycin has potential to become first approved therapy and standard of care for Microcystic Lymphatic Malformations in U.S.; significant commercial opportunity based on an estimated more than 30,000 individuals in the U.S. with Microcystic Lymphatic Malformations

Phase 3 SELVA pivotal study to enroll approximately 50 subjects with Microcystic Lymphatic Malformations; productive FDA end-of-phase 2 meeting completed in Q1 2023

Phase 2 study of QTORIN™ rapamycin demonstrated 100% of participants with Microcystic Lymphatic Malformations were either "Much Improved" or "Very Much Improved" as rated by the Clinician Global Impression of Change following 12-weeks of QTORIN™ rapamycin

Phase 2b CODY study of QTORIN™ rapamycin for Basal Cell Carcinomas in Gorlin Syndrome did not meet primary endpoint of new Basal Cell Carcinoma prevention at 24-weeks; pre-specified secondary endpoint demonstrated nominally statistically significant reduction in existing Clinically Suspicious and Biopsy Confirmed Basal Cell Carcinoma lesion size compared to placebo

WAYNE, Pa., July 20, 2023 (GLOBE NEWSWIRE) -- Palvella Therapeutics, Inc., a clinical-stage biopharmaceutical company developing and commercializing novel therapies to treat patients suffering from serious, rare genetic skin diseases for which there are no FDA-approved therapies, today announced the planned pivotal Phase 3 study design of QTORIN™ 3.9% rapamycin anhydrous gel (QTORIN™ rapamycin), a topical mTOR inhibitor and the lead product candidate from the QTORIN™ platform, in Microcystic Lymphatic Malformations (Microcystic LMs). Microcystic LMs are a serious, rare, chronically debilitating genetic disease for which there are no FDA-approved therapies. The company also announced topline results from the Phase 2b CODY study that evaluated QTORIN rapamycin in individuals with Basal Cell Carcinomas (BCCs) in Gorlin Syndrome (GS).

"We're accelerating towards a Phase 3 pivotal study in Microcystic LMs based on the positive Phase 2 results in which study investigators reported that all twelve subjects dosed with QTORIN rapamycin for 12-weeks were 'much improved' or 'very much improved' which was further supported by objective photographic evidence displaying lesion improvement," said Wes Kaupinen, Founder and Chief Executive Officer. "With more than 30,000 individuals in

the U.S. suffering from Microcystic LMs, we see a very significant and attractive commercial opportunity to potentially introduce QTORIN rapamycin as the first FDA-approved therapy for this disease."

Mr. Kaupinen continued, "Regarding our Gorlin Syndrome program, while QTORIN rapamycin did not achieve statistical significance on the primary endpoint in the Phase 2b CODY study, we are pleased with the nominally statistically significant reduction in lesion size that QTORIN rapamycin demonstrated on existing Clinically Suspicious and Biopsy Confirmed BCCs, a pre-specified secondary endpoint. We look forward to regulatory interactions in the U.S. and Europe that will guide our path forward on this program. Our team remains relentlessly focused on advancing the development and realizing the full commercial potential of a QTORIN-enabled targeted therapy for Microcystic Lymphatic Malformations, BCCs, and other mTOR-driven diseases."

QTORIN™ Rapamycin for the Treatment of Microcystic LM

Palvella initiated research on QTORIN rapamycin as a targeted therapy for Microcystic LMs in 2017 based on scientific insights implicating abnormal activation of the mTOR pathway in this disease. The company previously announced positive topline Phase 2 results from the multi-center, open-label study of 12 subjects receiving QTORIN rapamycin once-daily for 12-weeks in which all participants in the study demonstrated improvements on the Clinician Global Impression of Change scale, with all rated as either "Much Improved" or "Very Much Improved" after 12-weeks of treatment compared to the pre-treatment baseline period. In February 2023, the company had a productive end-of-Phase 2 meeting with the FDA in which a Phase 3 study design and efficacy endpoints were discussed.

Key findings from the Phase 2 study included:

Efficacy Endpoints	Week 12 Mean (n=12)	Nominal, Two-sided p-value
Clinician Global Impression of Change (CGI-C)	2.42	*<0.0001*
Clinician Global Impression of Severity (CGI-S) – Overall	-1.33	*<0.0001*
· CGI-S Height	-1.67	*<0.0001*
· CGI-S Leaking	-0.92	*0.0047*
· CGI-S Bleeding	-0.92	*0.0197*
· CGI-S Erythema	-1.08	*0.0016*
· CGI-S Crusting/Hyperkeratosis	-1.17	*0.0012*
Patient Global Impression of Change (PGI-C)	2.08	*<0.0001*
CGI-C and PGI-C improvements are represented by increases; CGI-S improvements are represented by reductions CGI-C and PGI-C are 7-points scales ranging from "Very Much Worse" (-3) to "Very Much Improved" (+3) 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		

Additionally, 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 (SAE), and no unexpected adverse events occurred.

“Microcystic Lymphatic Malformations is a serious, rare genetic skin disorder with significant unmet medical needs due to its infiltrative, progressive nature and lifetime morbidity,” stated Joyce M. Teng, M.D., Ph.D., professor of dermatology and pediatrics at Stanford University School of Medicine. “Patients are looking forward to an FDA-approved topical therapy that targets the underlying pathogenesis via direct inhibition of the mTOR pathway. QTORIN™ rapamycin demonstrated compelling preliminary clinical evidence in the Phase 2 study, and has potential to be first line, standard of care therapy for patients of all ages with Microcystic LMs.”

The Phase 3 SELVA pivotal study will be a 24-week, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of QTORIN rapamycin in patients with Microcystic LMs. The Phase 3 study will enroll approximately 50 subjects, with an interim analysis and potential sample size adjustment after 26 subjects have completed at least 12 weeks of treatment. The primary and key secondary endpoints will be clinician-reported outcomes. The company anticipates enrolling subjects at sites in the U.S. and U.K., including leading vascular anomaly centers.

The FDA has granted Orphan Drug and Fast Track Designations to QTORIN rapamycin for the treatment of Microcystic LMs. The European Medicines Agency has also granted Orphan Drug Designation to QTORIN rapamycin for the treatment of Microcystic LMs.

QTORIN™ Rapamycin for BCCs in GS

Conducted in partnership with The Gorlin Syndrome Alliance, the Phase 2b CODY study was a 24-week, randomized, double-blind, placebo-controlled clinical trial of QTORIN rapamycin in 73 subjects with GS.

In the Intent to Treat population (n=73), while QTORIN rapamycin demonstrated numerical improvement compared to placebo on the primary endpoint of prevention of new BCCs based on the cumulative number of new biopsy-confirmed BCCs on the face through Week 24, the results were not statistically significant. Noteworthy findings from among the prespecified secondary efficacy endpoints included QTORIN™ rapamycin demonstrating a nominally statistically significant reduction in existing Clinically Suspicious and Biopsy Confirmed BCC lesion size compared to placebo.

“The Phase 2 results demonstrate QTORIN™ rapamycin’s promise as a targeted therapy for BCCs and longer-term as a potential new treatment option for other cutaneous oncology populations,” stated Vishal A. Patel, M.D., Associate Professor of Dermatology & Hematology/Oncology and Director of Cutaneous Oncology at George Washington University School of Medicine & Health Sciences. “BCCs are highly disfiguring cancers, with many patients with Gorlin Syndrome enduring hundreds to thousands of BCCs in their lifetime. Treatment approaches have been limited to invasive surgical intervention and topical treatments which are associated with significant toxicities, both of which are especially suboptimal in the pediatric and adolescent populations. The availability of a targeted, topical mTOR inhibitor such as QTORIN™ rapamycin to reduce BCCs would be transformative for this population – and potentially for all skin cancer patients.”

QTORIN rapamycin was generally well-tolerated in the Phase 2b study. No drug-related SAEs were reported, and all other adverse events were deemed mild or moderate in nature, with the most common (>10%) treatment-emergent adverse events reported in the category of skin and subcutaneous tissue disorders.

The company plans to incorporate these results into discussions with regulatory agencies in the U.S. and Europe. QTORIN rapamycin has received Fast Track Designation for the prevention of BCCs in Gorlin Syndrome from the FDA.

QTORIN rapamycin is protected by multiple composition patents in the U.S. and Japan, and pending applications in the U.S., Europe, and Japan broadly covering anhydrous gel formulations of rapamycin.

About Palvella Therapeutics

Founded and led by rare disease veterans, Palvella Therapeutics 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. 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 Microcystic Lymphatic Malformations (Microcystic LMs) and Basal Cell Carcinomas (BCCs) in Gorlin Syndrome (GS). QTORIN rapamycin has received FDA Fast Track Designation for Microcystic LMs and 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.

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.

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