Palvella Therapeutics Announces Pipeline Update on QTORIN™ 3.9% Rapamycin Anhydrous Gel (QTORIN™ Rapamycin) for Serious, Rare Genetic Skin Diseases with No FDA-approved Therapies

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- Pivotal Phase 3 data for the treatment of Pachyonychia Congenita anticipated mid-2023 -

- Phase 2 data for the treatment of Microcystic Lymphatic Malformations anticipated March 2023 -

- Phase 2b data for the prevention of Basal Cell Carcinomas in patients with Gorlin Syndrome anticipated 2Q 2023 -

WAYNE, Pa., Feb. 21, 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 patients suffering from serious, rare genetic skin diseases in indications for which there are no FDA-approved therapies, today reported progress on its three lead development programs for QTORIN™ rapamycin. The company announced that it has completed enrollment in clinical studies that are investigating QTORIN™ rapamycin for the treatment of individuals with Pachyonychia Congenita (PC) and Microcystic Lymphatic Malformations (Microcystic LM), as well as for the prevention of Basal Cell Carcinomas (BCCs) in individuals with Gorlin Syndrome (GS). There are currently no FDA-approved therapies indicated for the treatment of PC, Microcystic LM, or for the prevention of BCCs in GS.

Palvella also announced preliminary timelines for release of top-line results from each of those studies. For the pivotal Phase 3 VAPAUS study in patients with PC, the company anticipates reporting top-line results in mid-2023; for the Phase 2 Microcystic LM study, the approximate top-line release date is

March 2023; and for the Phase 2b GS study, Palvella expects top-line data in the second quarter of 2023.

“Individuals living with serious, functionally debilitating, rare genetic skin diseases deserve access to targeted therapies,” said Wes Kaupinen, Founder and Chief Executive Officer of Palvella. “The rapid enrollment of our three ongoing clinical studies reflects the urgent unmet need in each of these diseases. We are grateful to the investigators and study participants for advancing our understanding of these diseases, and we look forward to reporting top-line clinical results.”

Palvella’s research team, led by Dr. Braham Shroot, developed QTORIN™, a patented and versatile platform designed to generate new therapies that penetrate the deep layers of the skin to locally treat a broad spectrum of serious, rare genetic skin diseases. QTORIN™ rapamycin is the lead product candidate from Palvella’s QTORIN™ platform and is initially under evaluation for three diseases: the treatment of PC and Microcystic LM, and for the prevention of BCCs in GS. These three initial clinical indications for QTORIN™ rapamycin share similarities in the underlying disease pathology whereby the mammalian target of rapamycin, or mTOR, pathway is overactivated leading to chronically debilitating disease burdens for affected individuals.

QTORIN™ Rapamycin for the Treatment of PC: Data expected mid-2023

- PC is a serious, rare, and chronically debilitating disease caused by genetic mutations in any of the inducible keratin genes 6A, 6B, 6C, 16, and 17 which are regulated by the mTOR pathway; individuals with PC experience extreme pain and difficulty with ambulation, frequently necessitating the use of either ambulatory aids or alternative forms of mobility such as crawling on hands and knees.
- There are currently no FDA-approved therapies for the estimated 9,300 diagnosed PC patients currently under the management of dermatologists in the U.S.[1] QTORIN™ rapamycin has the potential to become the first approved therapy and standard of care for PC.
- In partnership with Pachyonychia Congenita Project, Palvella completed enrollment of VAPAUS, a pivotal Phase 3 randomized, double-blind, vehicle-controlled study of QTORIN™ rapamycin in approximately 80 patients with PC; the study design incorporates key data and learnings from the completed VALO Phase 2/3 and Phase 3b studies.
- Orphan Drug and Fast Track Designations from the U.S. FDA have been granted to QTORIN™ rapamycin for the treatment of PC. Orphan Drug

Designation has also been granted by the European Medicines Agency (EMA).

QTORIN™ Rapamycin for the Treatment of Microcystic LM: Data expected March 2023

- Microcystic LM is a chronically debilitating rare genetic disease with overgrowth of lymphatic vessels via the PI3K/mTOR pathway, causing the development of vesicles on the skin that leak lymph fluid (lymphorrhea) and blood, often leading to recurrent serious infections and cellulitis.
- There are no FDA-approved treatments for the estimated more than 30,000 individuals in the U.S. with Microcystic LM.[2] QTORIN™ rapamycin has the potential to become the first approved therapy and standard of care for Microcystic LM.
- Palvella completed enrollment in an open-label, twelve-week Phase 2 study of QTORIN™ rapamycin in 12 patients with Microcystic LM designed to evaluate safety, pharmacokinetics, and clinician and patient reported efficacy outcomes.
- Palvella supported a systematic review that identified 16 published studies of off-label use of rapamycin (sirolimus) in the treatment of Microcystic LM; rapamycin yielded improvements in key clinical manifestations, including lymphatic leakage, bleeding, and vesicle bulk, and the preliminary findings are sufficiently compelling to provide an impetus for prospective, controlled trials to elucidate the safety and efficacy of rapamycin for these patients.[3]
- Orphan Drug and Fast Track Designations from the U.S. FDA have been granted to QTORIN™ rapamycin for the treatment of Microcystic LM. Orphan Drug Designation has also been granted by EMA.

QTORIN™ Rapamycin for the Prevention of BCCs in GS: Data expected 2Q 2023

- GS is a serious, rare, and lifelong genetic cancer which can lead to the development of hundreds to thousands of BCCs, which are cancers of the skin, most commonly appearing on the face; GS requires continual lifetime management, including repeated invasive surgical intervention, to avoid progression of BCCs to advanced, locally destructive, and possibly fatal metastatic BCCs.
- There are no FDA-approved therapies indicated for the prevention of BCCs for the estimated approximately 11,000 individuals in the U.S. with

GS.[4] QTORIN™ rapamycin has the potential to become the first approved therapy and standard of care for the prevention of BCCs in GS.

- Foundational research at Yale University and Columbia University has identified mTOR as a key driver of BCC tumorigenesis in GS, and preclinical studies demonstrated that rapamycin significantly reduced total BCC tumor burden when compared to vehicle treatment in a mouse model that closely mimics the accelerated BCC growth pattern of patients with GS;[5] targeting inhibition of mTOR may overcome limitations associated with smoothened inhibitors which have been documented to be associated with clinical resistance and substantial tumor recurrence.
- In partnership with The Gorlin Syndrome Alliance, Palvella has completed enrollment of a randomized, double-blind, vehicle-controlled Phase 2b study to evaluate the safety and efficacy of once daily QTORIN™ rapamycin for the prevention of BCCs in approximately 60 patients with GS.
- Fast Track Designation from the U.S. FDA has been granted to QTORIN™ rapamycin for the prevention of BCCs in patients with GS.

Recent Corporate Updates

- Palvella recently announced the closing of its Series D Financing of up to $37.7 million to accelerate the development and support commercialization of QTORIN™ rapamycin. The financing was led by Petrichor and included new investor Gore Range Capital. Existing investors Samsara BioCapital, BVF Partners L.P., Agent Capital, Nolan Capital, and BioAdvance also participated in the financing.

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.

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.

References

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