September 26, 2024

Pasithea Therapeutics Announces Positive Initial Safety, Tolerability, Pharmacokinetic (PK), and Preliminary Efficacy Data from its Phase 1 Clinical Trial of PAS-004 in Advanced Cancer

-- Single patient in 2mg cohort with stage 3 colon cancer who received 4 prior lines of therapy achieves prolonged stable disease and remains on drug into 6th dosing cycle --

-- No treatment-related adverse events (TRAEs) or dose-limiting toxicities (DLTs) observed to date, including no rash or gastrointestinal (GI) AEs --

-- Systemic exposure at steady-state enables constant target inhibition while avoiding peak plasma toxicities --

-- Half-life of approximately 70 hours supports once-daily or less frequent oral dosing --

-- Distinctive MEK inhibitor profile for the treatment of both NF1-related plexiform and cutaneous neurofibromas, cancer, and other opportunities --

MIAMI, Sept. 26, 2024 (GLOBE NEWSWIRE) -- Pasithea Therapeutics Corp. (NASDAQ: KTTA) ("Pasithea" or the "Company"), a clinical-stage biotechnology company developing PAS-004, a next-generation macrocyclic MEK inhibitor, for the treatment of neurofibromatosis type 1 (NF1) and other cancer indications, today announced safety, tolerability, pharmacokinetic (PK) and preliminary efficacy data from the first 2 cohorts of patients (n=6) in its Phase 1 clinical trial of PAS-004, being conducted at four clinical sites in the United States.

The Phase 1 clinical trial is a multi-center, open-label, dose escalation 3+3 study design to evaluate the safety, tolerability, pharmacokinetic (PK), pharmacodynamic (PD), and preliminary efficacy of PAS-004 in patients with MAPK pathway driven advanced solid tumors with a documented RAS, NF1 or RAF mutation or patients who have failed BRAF/MEK inhibition (NCT06299839).

"We are very pleased to share the PK, safety, and preliminary efficacy data from the 2 mg and 4 mg cohorts in our first-in-human Phase 1 clinical trial of PAS-004. We believe these data demonstrate a PK and safety profile that differentiates PAS-004 as a next-generation MEK inhibitor. We have already achieved significant PAS-004 exposures with a favorable safety profile and have not seen adverse side effects such as rash or GI toxicity, which are typical for MEK inhibitors even at low doses. The long half-life at approximately 70 hours, and the ability to achieve a flat PK curve at steady-state, aim to provide a constant target inhibition while avoiding peak plasma toxicities, which is a unique PK profile among MEK

inhibitors used for the treatment of Neurofibromatosis type 1 (NF1)," stated Dr. Tiago Reis Marques, Chief Executive Officer of Pasithea.

"In addition, we are encouraged to see early potential signs of efficacy, with a heavily pre-treated patient with colorectal cancer showing prolonged stable disease. Colorectal cancer is known to not provide a RECIST response when treated with single-agent MEK inhibitors. This patient has a BRAF K601E mutation, a mutational status with no approved therapies. We are encouraged that this patient has been treated continuously into the 6th 28-day dosing cycle with no toxicities or AEs observed. While still early in clinical development, we believe PAS-004 is showing early signs of differentiation, indicating PAS-004 has the potential to outperform current MEK inhibitors in terms of safety, reduced administration frequency, and potentially efficacy. Our goal is to provide a once-daily or less frequent dosing treatment with broader application, not only for NF1 but also for other indications."

Interim Phase 1 Results

Pharmacokinetics (PK) data for cohort 1 (2mg) and cohort 2 (4mg) at day 1 and day 22 (steady state)

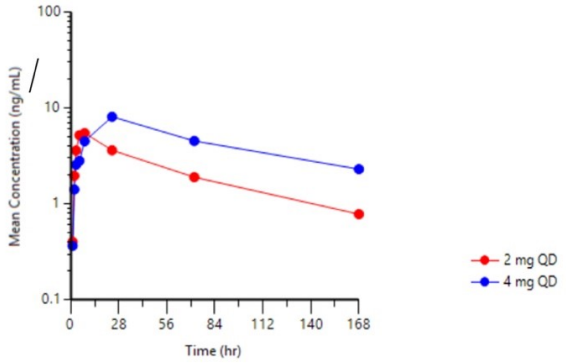
Dose Cohort	Cmax (ng/mL)*	Cmin (ng/mL)*	AUC_{0-24} (ng*h/mL)*
2 mg Day 1	4.91 (101.3)	N/A	86.3 (89.2)
2 mg Day 22	16.2 (89.7)	10.2 (119.4)	354 (95.2)
4 mg Day 1	6.36 (135.6)	N/A	100 (97.1)
4 mg Day 22	61.3 (10.3)	51.5 (20.8)	1,390 (12.8)

* Data are Geometric Mean (Geometric coefficient of variation (CV)%), Cmax - highest concentration of a drug after a dose is given; Cmin - Lowest concentration of a drug after a dose is given; AUC - area under the concentration-time curve and measures the total drug exposure (the extent) across time

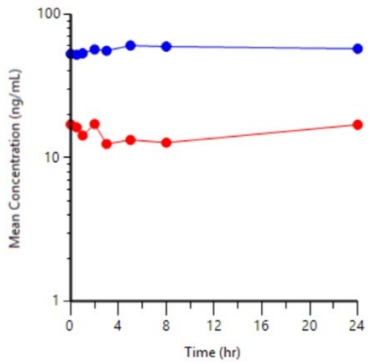
Pharmacokinetics (PK)

- Plasma exposure increased with an increase in dose and linear PK is observed
- Long half-life of approximately 70 hours will allow for once daily dosing or longer intervals
- Prolonged systemic exposure with minimal fluctuation in PAS-004 plasma concentration at steady state (Cmax/Cmin ratio of 1.2) indicates a potential to achieve constant target inhibition

PK plasma curve at day 1



PK plasma curve at day 22 (steady-state)



At steady-state, drug levels peaked at about 5 hours with a geometric mean maximum concentration (C_{max}) of 16.2 and 61.3 ng/mL for the 2 mg and 4 mg dose groups, respectively. The mean elimination half-life was 67.9 hours supporting once-daily or less frequent oral dosing.

“PAS-004 has demonstrated distinct properties that we believe are significant advantages for an oral MEK inhibitor. PAS-004 has a significantly longer half-life compared to early-generation MEK inhibitors, particularly those used for the treatment of NF1, which have half-lives of less than 8 hours. The ability to achieve prolonged plasma exposures, as reflected in stable plasma concentrations at steady state, may potentially allow PAS-004 to achieve efficacious doses with a favorable safety profile,” stated Dr. Tiago Reis Marques, Chief Executive Officer of Pasithea.

Safety & Tolerability

- No treatment-related adverse events (TRAEs) or dose limiting toxicities (DLTs) observed to date

In the first 2 dosing cohorts (n=6), PAS-004 was shown to be well-tolerated with a favorable safety profile with no drug-related dose interruptions, reductions or discontinuations. There were no drug-related serious AEs (SAE) in any dose arm and no protocol-defined stopping criteria were met. Importantly, at the 2 and 4 mg dose levels no rash or skin toxicity, gastro-intestinal (GI) toxicity, or ocular toxicity have been observed to date.

The study independent Safety Review Committee has completed its safety review of data from the second dose cohort of 4 mg and the Company has initiated cohort 3 dosing at an increased dose of 8 mg in capsules and has filed a protocol amendment to increase dosing schedule.

PAS-004 Demonstrates a Differentiated MEK Inhibitor Profile

Unlike first-generation MEK inhibitors for the treatment of NF1 that require twice-daily dosing (BID) and exhibit short half-lives (<8 hours), PAS-004 has the potential to achieve prolonged target inhibition due to its long half-life of approximately 70 hours with once-daily dosing (QD). The PK profile shows consistent plasma levels at steady-state, as reflected by a low Cmax to Cmin ratio, potentially reducing the risks for Cmax-related toxicity. These findings provide a compelling rationale for the advancement of PAS-004 into clinical trials for both the treatment of cutaneous and plexiform neurofibromas in NF1, cancer and other MAPK-driven opportunities. The company expects to provide additional trial updates on a periodic basis as the trial progresses.

About Pasithea Therapeutics Corp.

Pasithea is a biotechnology company focused on the discovery, research and development of innovative treatments for central nervous system (CNS) disorders and RASopathies. With an experienced team of experts in the fields of neuroscience, translational medicine, and drug development, Pasithea is developing new molecular entities for the treatment of neurological disorders, including Neurofibromatosis type 1 (NF1), Solid Tumors, and Amyotrophic Lateral Sclerosis (ALS).

Forward Looking Statements

This press release contains statements that constitute “forward-looking statements” made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include statements regarding the Company’s ongoing Phase 1 clinical trial and the safety, tolerability, pharmacokinetic (PK) and preliminary efficacy of PAS-004, as well as all other statements, other than statements of historical fact, regarding the Company’s current views and assumptions with respect to future events regarding its business, as well as other statements with respect to the Company’s plans, assumptions, expectations, beliefs and objectives, the success of the Company’s current and future business strategies, product development, preclinical studies clinical studies, clinical and regulatory timelines, market opportunity, competitive position, business strategies, potential growth opportunities and other statements that are predictive in nature. Forward-looking statements are subject to numerous conditions, many of which are beyond the control of the Company. While the Company believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to the Company on the date of this release. These forward-looking statements are based upon current estimates and assumptions and are subject to various risks and uncertainties, including risks that future clinical trial results may not match results observed to date, may be negative or ambiguous, or may not reach the level of statistical significance required for regulatory approval, as well as other factors set forth in the Company’s most recent Annual Report on Form 10-K, Quarterly Report on Form 10-Q and other filings made with the U.S. Securities and Exchange Commission (SEC). Thus, actual results could be materially different. The Company undertakes no obligation to update these statements whether as a result of new information, future events or otherwise, after the date of this release, except as required by law.

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Photos accompanying this announcement are available at

https://www.globenewswire.com/NewsRoom/AttachmentNg/4765238d-9961-438e-b459-509a5c917974

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Source: Pasithea

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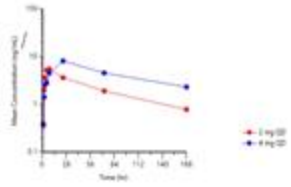
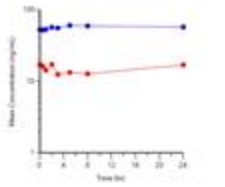
Interim Phase 1 Results

PK plasma curve

PK plasma curve at day 1



PK plasma curve at day 22 (steady-state)



PK plasma curve