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ProLynx announces initiation of Phase I/II clinical trial of its DNA-damaging agent PLX038 in patients with rare CNS tumors at the National Cancer Institute (NCI)

SAN FRANCISCO, Feb. 05, 2024 (GLOBE NEWSWIRE) -- ProLynx Inc. announced today that the first patient was treated with PLX038 (PEGylated SN-38) in a Phase I/II clinical trial for primary CNS tumors driven by *MYC* or *MYCN* amplifications. National Institutes of Health's NCI investigators Dr. Marta Penas-Prado and Dr. Mark Gilbert are conducting the trial.

MYC genes regulate expression of genes involved in cell division. High levels of MYC drive oncogenesis in many cancers and induce DNA changes leading to the formation of "topoisome complexes". *MYC* and *MYCN* amplifications are seen in multiple primary tumors of the central nervous system (CNS). This includes 30% of relapsed medulloblastomas, and *MYCN*-amplified ependymoma, characterized by aggressive clinical behavior and treatment resistance. The MYC or MYCN-induced topoisome contains high levels of topoisomerases that should be susceptible to topoisomerase inhibitors.

PLX038 is a long-acting prodrug of the topoisomerase 1 inhibitor, SN-38 – the active metabolite of irinotecan and sacituzumab govitecan. PLX038 is unique as the SN-38 is covalently bound to a circulating nanomolecule and is slowly released to provide free SN-38 with a long half-life, low C_{max} and very high exposure – important for optimal safety and efficacy. Importantly, in preclinical studies, PLX038 was shown to accumulate in CNS tumors, where it slowly releases SN-38.

The NCI trial will assess whether PLX038 is safe and efficacious in primary CNS tumors driven by *MYC* or *MYCN* amplifications. The Phase I trial will confirm the recommended Phase II dose. The Phase II trial will test PLX038 in 3 independent cohorts: 1) newly diagnosed *MYCN*-amplified ependymoma, 2) recurrent ependymoma or medulloblastoma with *MYCN* or *MYC* amplification, and 3) other recurrent primary CNS tumors with *MYC* or *MYCN* amplifications.

Notably, the Phase II trial will incorporate on-treatment tumor biopsies to investigate biomarkers of response and resistance, including SLFN11, MYC, MYCN and Top1, 2a, and 2b expression. This data could prospectively identify patients most responsive to the drug. Additionally, working collaboratively with The Office of Patient-Centered Outcomes (OPCORe), researchers will collect patient-reported outcomes (PROs) to measure the impact of therapy, including toxicity, symptom severity and interference with daily activities, and physical functioning.

ProLynx co-founder, Daniel V. Santi, stated, "We are excited to work with NCI investigators to bring novel treatments to patients with rare CNS cancers, in hope of improving their outcomes." He added, "Conventional short-acting topoisomerase 1 inhibitors have clinical activity in certain CNS tumors. Accordingly, we are optimistic that a long-acting SN-38 will result in increased efficacy and safety."

Additional information on this clinical trial is available at clinicaltrials.gov, through identifier number NCT06161519. For patients interested in enrolling in this clinical trial, please call NCI's toll-free number: 1-800-4-Cancer (1-800-422-6237) (TTY: 1-800-332-8615); visit the website: https://trials.cancer.gov; and/or email: NCIMO_referrals@mail.nih.gov.

ProLynx is a San Francisco biotechnology company developing proprietary systems to improve the pharmacokinetics/efficacy of important drugs (www.Prolynxinc.com).