***Source:*** *ProLynx LLC*

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# ProLynx announces initiation of the Phase II Topology clinical trial of its DNA-damaging agent PLX038 in triple-negative breast cancer at the Institut Curie

SAN FRANCISCO, March 25, 2024 (GLOBE NEWSWIRE) -- ProLynx Inc. announced that the first patient was included in TOPOLOGY by investigator Dr. Delphine Loirat, with a Phase II clinical trial investigating PLX038 (PEG~SN-38) for locally-advanced or metastatic triple-negative breast cancer (TNBC). Patients will have been previously treated with at least two therapies, including the antibody-drug conjugate (ADC) sacituzumab govitecan (SG; Trodelvy). The TOPOLOGY trial is run by Institut Curie (Paris and Saint Cloud, France), with principal investigator Prof. Francois-Clement Bidard .

PLX038 is a long-acting prodrug of the topoisomerase 1 (Top1) inhibitor, SN-38, which is also the active component of anti-cancer agents irinotecan and the ADC SC. Top1 inhibitors cause DNA breaks and kill tumors that are unable to repair the damage. Previously, Curie researchers showed that about one-third of TNBC patients have defects in DNA damage repair, and should respond to an effective SN-38-based therapy (Coussy et al., 2020). In PLX038, SN-38 is covalently bound to a circulating nanoparticle and is slowly released to provide free SN-38 with a long half-life, low $C_{max}$, and high exposure – important facets for optimal safety and efficacy. Importantly, in preclinical studies PLX038 was shown to accumulate and be retained in solid tumors, where it slowly releases its SN-38.

SG is an anti-TROP2 ADC with an SN-38 payload that was recently approved for use in advanced TNBC. However, the rapid spontaneous linker hydrolysis in SG releases a large amount of SN-38 cargo systemically, which may in part contribute to its efficacy and also in part be responsible for systemic side effects. Unfortunately, the median progression-free survival after SG therapy is only ~6 months due to resistance, and there are limited rescue therapies available.

ProLynx co-founder and President Daniel V. Santi commented, “Although the active SN-38 payload of PLX038 and SG is the same, the anti-tumor mechanisms of the prodrugs are quite different; and, some mechanisms of resistance may also quite be different (Santi et al., Biodrugs,2024). Taken together, it is reasonable to believe that PLX038 may be effective in SG-resistant tumors.”

Curie investigator Francois-Clement Bidard added, “As with our earlier preclinical study of the correlation of efficacy of irinotecan with BRCAness and SFLN11 biomarkers, TOPOLOGY will assess association of PLX038 efficacy with homologous recombination defects, and biomarkers such as SFLN11 expression and RB1 loss. If confirmed in TOPOLOGY, these biomarkers will allow pre-selection of patients most likely to respond to the drug.”

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

Institut Curie, France’s leading cancer center, combines a renowned research center and hospital which treats all types of cancer. Institut Curie has 3 sites (Paris, Saint-Cloud and Orsay) with over 3,700 health professionals working on treatment, research and teaching (www@curie.fr) Information on this clinical trial is available at clinicaltrials.gov, NCT06162351.

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