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ProLynx announces allowance of additional U.S. patent for PLX038, a novel DNA damage response enhancer

SAN FRANCISCO, April 10, 2018 (GLOBE NEWSWIRE) -- Prolynx LLC (San Francisco, CA) announced it received a Notice of Allowance for its DNA damage enhancer PLX038 (PEG~SN-38), currently in Phase 1 trials at MD Anderson. PLX038 is a prodrug of SN-38, the active metabolite of the anti-cancer agent Irinotecan, which inhibits Topoisomerase 1 (Topo 1) during DNA replication and causes replication stress and DNA damage. The new allowed claims expand ProLynx's broad patent coverage of PEG~SN-38 conjugates using ProLynx beta-eliminative linkers in US Patent 8,754,19.

DNA damaging agents, such as PLX038, have assumed a new importance in the context of the DNA damage response (DDR) and synthetic lethality. To combat threats posed by DNA damage, cells have mechanisms to signal the presence of DNA damage and promote its repair – collectively termed the DNA-damage response. Cells defective in DDR – as in many tumors – display heightened sensitivity towards DNA-damaging agents such as Topo 1 inhibitors. Such agents can increase DNA damage to a level that is tolerable to normal cells but lethal to cancer cells with DDR deficiencies. Hence, an effective Topo 1 inhibitor will enhance DNA damage and death of cells with DDR defects – such as cells deficient in DNA repair proteins BRCA, ATM or ATR – or in cells treated with inhibitors of DDR components – such as PARP, ATM or ATR inhibitors.

ProLynx's PLX038 slowly releases SN-38 such that tumors are exposed to the DNA-damaging agent SN-38 for long periods. In addition, the nanomolecule accumulates and remains in tumors for long periods, slowly releasing the drug at high intra-tumoral concentrations.

ProLynx's PEG~SN-38 conjugates show remarkable antitumor effects in mouse models of human tumors with DDR defects and those treated with DDR inhibitors. For example, in the BRCA1 human xenograft MX-1, a single, non-toxic dose completely inhibited tumor growth and resolved massive tumors. Likewise, a combination of low dose PEG~SN-38 with a PARP inhibitor completely inhibited tumor growth, and shrank large tumors. Moreover, a low dose of PEG~SN-38 followed by a period to allow tumor accumulation and systemic elimination sensitized the tumor such that treatment with a low dose of PARP inhibitor completely inhibited tumor growth.

Daniel Santi, cofounder and President of ProLynx, said, "PLX038 may provide a general agent for enhancing the selective killing of cancer cells with certain DDR defects. In addition, PLX038 seems to enhance the effects of other inhibitors that act on DDR components by synthetic lethality, suggesting that it may be used in combination with such agents."

About ProLynx: ProLynx LLC is a privately held biotechnology company located in San Francisco, CA, developing delivery systems for half-life extension of small molecules, peptides and proteins. The company applies its technology to extend half-lives of new drug candidates, and to improve properties of off-patent therapeutics. ProLynx has a monthly GLP-1 receptor agonist in its pre-clinical portfolio, and PLX038 in Phase 1 clinical trials. Further information about the company may be found at www.ProLynxllc.com.

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