ProLynx Publishes Results of Ultralong Half-Life PEG-SN38 Pro-Drug With Lower Intestinal Toxicity

Japanese Partner Advances ProLynx PEG-SN38 Conjugate Toward Phase I Clinical Trials

SAN FRANCISCO, March 27, 2014 (GLOBE NEWSWIRE) -- ProLynx LLC today announced a publication in the Journal of Medicinal Chemistry on macromolecular pro-drugs that provide the irinotecan active-metabolite SN-38 with ultralong half-life, low Cmax, and low glucuronide formation. These macromolecular pro-drugs have unique pharmacokinetic profiles that may translate to less intestinal toxicity and interpatient variability than the SN-38 pro-drugs thus far studied.

Irinotecan is converted to SN-38 in the liver, which is then detoxified by conversion to its inactive glucuronide, SN-38G; the latter is transported to the intestinal tract, where resident bacteria convert it back to the active agent SN-38. In addition to its anti-tumor effects, SN-38 is toxic to the intestine. In fact, the dose-limiting toxicity of irinotecan is a late, life-threatening diarrhea that occurs in 20-30% of patients taking the drug, and requires cessation of treatment. A marker that traces the liver/bile/intestine history of irinotecan metabolism is the high SN-38G/SN-38 AUC ratio in plasma which is usually 5 to 10.

The ProLynx PEG-SN-38 conjugate continuously releases low levels of SN-38 with an effective half-life of about two weeks. In addition to greatly increasing the half-life, the authors anticipated that the conjugate might reduce the toxicity by redirecting exposure to the drug away from the intestine. Indeed, the SN-38G/SN-38 ratio in plasma is only 0.1 – some 100-fold lower than when irinotecan is the pro-drug. The Cmax of SN-38 is also greatly decreased, so Cmax-associated toxicities such as neutropenia, might also be reduced.

ProLynx founder and President Daniel V. Santi, M.D., Ph.D, stated, "We rationalized that the simplest way to avoid the intestinal-toxicity of SN-38, would be to keep it away from the intestine. The reason for the low SN-38G/SN-38 ratio of our conjugate is that unlike irinotecan, SN-38 does not require activation in the liver, and only enters the liver via the concentration-dependent OATP1B1 transporter. When delivered with our technology, plasma SN-38 levels are kept low by very slow release, so hardly any gets in the liver or, as a consequence, in the intestine. Since it isn't present, it doesn't cause the intestinal toxicity seen with irinotecan."

ProLynx has granted limited territorial rights to a Japanese pharmaceutical company. The partner has produced GMP material, will begin IND-enabling studies shortly, and expects to initiate Phase I trials in late 2014, early 2015. Dr. Santi noted, "We are very encouraged by the findings reported in this paper and more importantly, by the confirmation of these findings in our partner's animal studies. If these findings translate to humans, we will have a very attractive anticancer agent." ProLynx retained all rights to the drug outside the licensed Asian territories. These retained rights are available for partnering.

About ProLynx LLC

ProLynx LLC is a privately held biotechnology company developing proprietary drug delivery systems (DDS) for half-life extension of proteins, peptides and small molecules. The company is seeking to apply its DDS to extend half-lives of drugs and drug candidates of pharmaceutical and biotechnology companies. ProLynx is also seeking to out-license the long lasting drug conjugates in its pre-clinical product portfolio. The company is located in San Francisco, CA. Further information about the company and its capabilities may be found online at http://www.prolynxllc.com.

CONTACT: Peg Horn, COO
ProLynx LLC
415-552-5306