Amunix Operating Inc.

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Amunix expands its XTEN half-life extension technology

Amunix, a private biotech company, has developed a versatile platform based on recombinant polypeptides that safely increases the half-lives of pharmaceuticals for a broad range of diseases.

Many human proteins are rapidly cleared from circulation, making their potential use as pharmaceuticals impractical because they would require frequent dosing. One common strategy for increasing the half-life of therapeutic molecules involves the chemical attachment of a compound called polyethylene glycol (PEG), which increases the effective size of drugs and thereby slows their clearance from the bloodstream via kidney filtration. Due to the polydisperse nature of PEG, attachment of PEG results in complex product mixtures that are difficult to purify and characterize. Moreover, PEG is not biodegradable and can accumulate in the kidneys and other tissues.

"There's a huge need out there for safer and more effective half-life extension technologies," said Volker Schellenberger, a biochemist by training and CEO of Amunix Operating Inc. "Our company is positioned to become the premier provider of best-in-class molecules whose half-lives can be customized for many therapeutic applications, including endocrinology, metabolic disorders, oncology and cardiovascular diseases."

Amunix is a private, collaboration-financed biotech company that was cofounded by Schellenberger and Willem 'Pim' Stemmer in 2006. To overcome the limitations associated with PEG and related approaches, Amunix has developed a half-life extension technology based on XTEN—a polymer comprised of natural amino acids that can be attached to therapeutic peptides, proteins or small molecules through either chemical conjugation or genetic fusion (**Fig. 1**). Similar to PEG, XTEN greatly increases the size of therapeutic molecules and prolongs their presence in the bloodstream. But compared with other half-life extension technologies, XTENylated products offer numerous advantages. For one, the biodegradable XTEN polymer does not accumulate in tissues, and it does not produce toxic metabolites. In addition, because XTEN is very hydrophilic, it minimizes immunogenicity risks, increases the solubility of therapeutics to which it is attached and is suitable for liquid drug formulations.

By adjusting the length of the XTEN polymer, it is possible to generate customized therapeutic molecules that have ideal half-lives. "Human growth hormone–XTEN, developed by our partner company Versartis, has by far the longest reported half-life of any competing growth hormone product in development," Schellenberger said. "This will significantly reduce the frequency of drug injections and should have a huge impact on the quality of life for patients, the majority of whom are children."

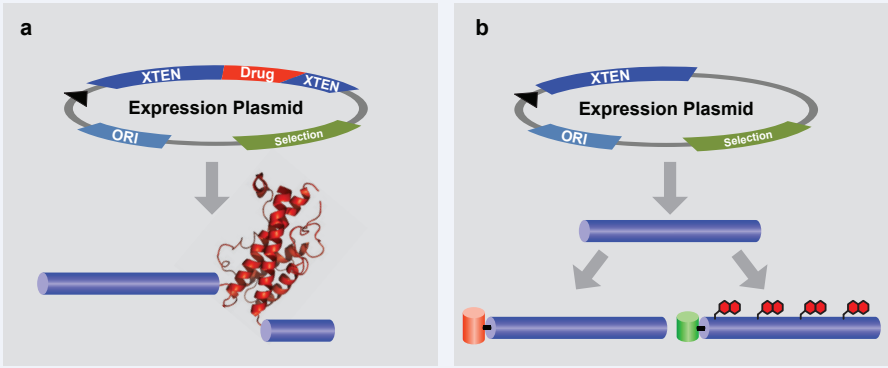

Figure 1. The XTEN platform. The proprietary recombinant half-life extension polymer, XTEN can be (a) genetically fused to peptides and proteins, or (b) chemically conjugated to peptides, proteins, peptidomimetics and cytotoxic drugs.

Because XTEN products are homogenous, they do not require extensive purification steps. "One major benefit of XTEN is that it has a clearly defined chemical composition," Schellenberger said. "This greatly facilitates process development as well as the characterization of drug product to ensure removal of any drug-related contaminants."

XTEN also offers flexibility during product design, especially through the chemical conjugation route. XTENylated pharmaceuticals can be multivalent and/or multispecific, may combine different classes of active moieties and/or contain different XTEN segments to maximize *in vivo* time action. Amunix further expanded the reach of its technology by offering XTEN-drug conjugates that can be linked to a variety of tumor-specific binding domains—such as antibody fragments, peptides and metabolites—while maintaining perfect product homogeneity.

Pipeline and partnerships

To advance the clinical development of XTEN products for the treatment of metabolic and endocrine disorders, Amunix created two spin-off companies: Diartis Pharmaceuticals and Versartis. Diartis Pharmaceuticals' VRS-859 is a small peptide called exenatide genetically fused to XTEN. VRS-859, which stimulates insulin production in response to glucose, has successfully completed a phase 1 clinical trial in patients with type 2 diabetes. Meanwhile, Versartis has focused its efforts on VRS-317, a long-acting human growth hormone genetically fused to XTEN. VRS-317 has completed a phase 1 studies in adult and pediatric patients with growth hormone deficiency, and is currently being evaluated in a phase 2 trial for pediatric patients.

Amunix is also conducting preclinical studies to investigate XTEN's potential for treating diseases ranging from cancer to gastrointestinal conditions such as short bowel syndrome and Crohn's disease. Moreover, Amunix has formed partnerships with Janssen Biotech to develop products in a wide range of therapeutic areas and is collaborating with Biogen Idec to develop new, long-acting blood factors for the treatment of hemophilia. Additional collaborations with a number of other large pharmaceutical companies to apply XTEN to undisclosed targets are also ongoing.

Having established a broad patent portfolio for XTEN technology, Amunix is actively seeking new partnerships to pursue additional therapeutic applications for its polymer. Under a simple material transfer agreement, Amunix provides access to the XTEN technology and XTENylation reagents to organizations so that they can quickly assess the utility of the polymer for their products prior to obtaining licenses.

CONTACT DETAILS

Volker Schellenberger, PhD
President and CEO
Amunix Operating Inc.
California, USA
Tel: +1 650 889 5095
Email: vschellenberger@amunix.com