

TARGETED GENE THERAPY FOR TREATMENT OF CANCERS

TransGenex Nanobiotech, Inc., Tampa, FL

Business Opportunity:

TransGenex Nanobiotech, Inc. (TGN), an early stage biotechnology R&D company located in Tampa, Florida, has developed platform technologies for drug delivery and drug discovery for a broad range of diseases. The U.S. demand for drug delivery systems is expected to expand to \$132 billion in 2012, according to a Freedonia industry study – “**Drug Delivery Systems.**”

Strategically, TGN208 is the first product being developed under its novel platform, aimed specifically at metastatic ovarian cancer, with products for other organ systems and disease therapies to follow. The global cancer drug market is projected to be \$53 billion in 2009 of which the innovative cancer drug market is nearly \$13 billion. TGN’s initial target market segment, ovarian cancer, is the most common cause of death from gynecological tumors. 160,000 women in the 7 major global markets were diagnosed with ovarian cancer in 2007. The company is looking for investment, or alliance to advance the core platform IP, disease-specific partnering strategy for drug development, and or/ licensing strategy with pharmaceutical companies.

Company Background:

The company, founded in 2004, has a staff of 6. Its mission is to develop novel nanoparticle platform technologies for drug delivery and compatible drug discovery leading to collaboration and licensing with pharmaceutical companies for disease-specific products. TGN has a 1200 ft² wet lab and access to a 2000 ft² shared lab in the University of South Florida Incubator. In 2005 and 2006 the company was recognized for its innovative R&D by Tampa Bay Technology Forum.

Industry Problem:

The current technologies including chemotherapy (taxol and paraplalin) and radiotherapy are painful, have many side effects and not always successful. Many patients resort to surgery which is risky and affects quality of life. A drug delivery system, which places therapy on target tissue without impacting healthy tissue, would be ideal. Industry goals for drug delivery are to make the experience easy, pain-free, and safe; also, reducing risks of toxicity and drug rejection.

Technology:

TGN’s drug delivery technology involves nanoparticle platforms that use natural polymer(s), which readily lend themselves for multi-functionalization and permit target cell-specific delivery (*TARGET*TM) of drugs, DNAs and siRNAs (*SiPLEX*TM). These platforms are safe and have an in-built mechanism for mucosal delivery and slow, sustained release. Among TGN’s candidate drug targets, the most advanced is the atrial natriuretic peptide receptor A (NPRA), which has been found to possess anti-inflammatory and anti-cancer activities. NPRA signaling pathway was shown to play a dominant role in cancer pathogenesis and was selected by experts as “lead discovery” as an anti-cancer drug in 2008.

TGN 208 combines TGN's *TARGET*TM technology with a proprietary expression cassette that encodes peptide inhibitors of NPRA signaling, and has been shown to decrease tumor volume and tumor burdens in preclinical studies. The technology includes proprietary chemical modification of the polymer to attach the targeting moiety so that once engineered, these polymers can be used to load drugs and administered to the patient. The engineered polymers, once in the circulation go to the destination target tissue and cells.

Advantages

Drug Delivery System:

- Nanoparticles are natural, biocompatible, biodegradable, cationic polysaccharides.
- Safe, non-toxic, non-hemolytic, non-immunogenic, GRAS, no side effect.
- Can be tailored to conjugate with a variety of drug molecules, genes and siRNAs.
- Allow slow, sustained, controlled release of drug.
- Can be lyophilized for storage without loss of bioactivity.
- Mucosal administration (intranasal, oral or intraperitoneal) or intravaginal.

Anti-Cancer Drug

- Combines anti-inflammatory and anti-cancer activities.
- Can be used as a target for a variety of inflammatory diseases.

Distinctive Feature

The distinctive feature for TGN's bi-polar platform, with tissue attachment and drug release is its ability to carry different therapeutic drugs and its ability to adjust delivery technology for target-specific tissue, including hard-to-get-to locations.

Stage of Development:

- Delivery System – Proof of concept, feasibility, biochemistry design, and initial prototyping have been completed for both nasal drop and oral feeding methods; followed by pre-clinical validation tests to lungs for asthma and respiratory viruses.
- Anti-Cancer Drug – Pre-clinical tests on mice have been completed for lung, prostate, melanomas, and ovarian cancer. TGN 208 has been advanced to non-human primates in ovarian cancer model.
- Combination Delivery System with Anti-Cancer Drug – Proof of concept, feasibility, biochemistry design for drug attachment/release, and initial prototyping have been completed. TGN has done significant innovation in prototyping particles for large scale production and testing, without any adverse effects in different routes including, oral, intranasal, topical routes. Also completed are pre-clinicals with mice and rhesus monkeys including prototype modification and partial safety and efficacy studies in ovarian cancer model. Next phase includes fast-track (on compassionate ground) application to FDA for advanced ovarian cancer patients and pre-IND studies leading to IND filing by 2011.

Competing Technologies:

TGN's tissue targeting platform can be engineered for attachment to each of a variety of organ tissues as well as specific cells such as cancerous tumor cells. No current technology does both.

Tissue-targeting technologies are currently under development in the pharma industry. Some examples are antibody fragment conjugates, peptide-induced release, and magnetically-targeted delivery.

Current non tissue-targeting modalities include the following:

- Oral delivery: most frequently used method
- Parenteral: ease of administration and infection prevention
- Polymer-encapsulation: reduced toxicity
- Liposome-encapsulation: reduced toxicity
- Inhalation therapy: more efficacious
- Transdermal: ease of administration
- Injection with nano crystal technology:
- Implantables:

Currently only chemotherapeutics are approved for ovarian cancer. TGN's first application targets ovarian cancer with TGN208 which consists of tissue-targeting platform and NPRA inhibiting gene(s). To date, no gene therapy drugs have been approved for ovarian cancer therapy.

Applications:

- Drug Delivery System – TGN's tissue-targeting design has been validated for lung, prostate, ovary, and colon tissue. This nanoparticle platform is capable of delivering drugs or genes against cancers, asthma, viral infections and other diseases.
- Anti-Cancer Drug, TGN208 – This NPRA inhibiting gene therapy drug is efficacious for ovarian cancer with possible extension to lung, prostate, and other types of cancer.

Benefits:

- Patients – Slow, sustained release of the drug would reduce the frequency of use, cost, and side effects; and increase quality of life.
- Physicians – Therapeutic for hard to get to locations, such as the pancreas.
- Insurance Companies – The system may replace or supplement chemotherapies, radiation therapies, and surgery, in the latter case decreasing their adverse effects.

Intellectual Property:

TransGenex has filed an application for patent on the drug target and the nanoformulation for ovarian cancer induction and treatment. Additionally, several key IP rights are currently under negotiation from the University of South Florida for delivery technology and anti-cancer drug. USF has in principle agreed to license these required additional patents.