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BioCentury

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Emerging Company Profile

VCN: Anti-tumor Ad-vantages

By Michael J. Haas
Senior Writer

Pancreatic cancer is highly resistant to drugs because about 80% of the tumor is stroma — normal fibrous and connective tissues that support cancer cell growth and invasion — that compounds cannot penetrate efficiently. To overcome this problem, **VCN Biosciences S.L.** is developing VCN-01, a genetically engineered adenovirus that selectively penetrates the tumor stroma and replicates in pancreatic tumor cells to kill them.

Pancreatic cancer is a large unmet medical need, with a five-year survival rate of less than 5%, according to the **American Association for Cancer Research** (AACR). The current standard of care is surgery, and Gemzar gemcitabine from **Eli Lilly and Co.** is the only drug approved as a first-line therapy to treat locally advanced or metastatic pancreatic cancer when surgery is not feasible.

VCN's solution is VCN-01, a modified adenovirus serotype 5 (Ad5) designed to replicate only in tumors and to degrade hyaluronan in tumor stroma but not in healthy tissue.

The viral capsid incorporates undisclosed modifications that allow the virus to preferentially infect tumor cells. Additional modifications enable replication of the virus only in cells lacking retinoblastoma protein — a deficiency found in many cancers.

After replication, VCN-01 expresses sperm adhesion molecule 1 (SPAM1; PH20). SPAM1 degrades hyaluronan. This extracellular matrix protein not only is produced at high levels by pancreatic and other tumor types, but also is present at high levels in tumor stroma compared with normal tissue. SPAM1 helps VCN-01 penetrate the stroma, clearing the way for the virus to reach malignant cells where the enzyme is also thought to have intrinsic anti-cancer activity.

Further modifications enhance viral release from cells after replication, thereby killing infected cells and spreading copies of VCN-01 to nearby tumor cells.

"We assume that the initial infection process is rather inefficient" because at that stage the virus lacks stroma-penetrating SPAM1, CEO Manel Cascallo told BioCentury. "But we only need to get a small amount of virus into the tumor to begin its self-amplifying cycle" of replication, SPAM1 expression and viral release.

In unpublished studies, IV or intratumoral administration of VCN-01 reduced tumor growth in mice bearing xenograft pancreatic tumors compared with Ad5 viruses that did not express SPAM1. IV administration of VCN-01 had no observable toxicities in the normal tissues of mice and hamsters, Cascallo said.

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VCN Biosciences S.L.

Barcelona, Spain

Technology: Genetically modified oncolytic adenoviruses to treat cancer

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2009 by Ramon Alemany, Manel Cascallo and Gabriel Capella

University collaborators: Institut Catala d'Oncologia (ICO), Institut d'Investigacio Biomedica de Bellvitge (IDIBELL), Instituto de Biologia Experimental e Tecnologica (IBET) and VU University

Corporate partners: None

Number of employees: 1

Funds raised: €200,000

Investors: BIOVCN Patrimonial S.L., BIO Cape Grup S.L., Ramon Alemany, Manel Cascallo and Gabriel Capella

CEO: Manel Cascallo

Patents: None issued

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VCN Bioscienes S.L.,
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He added that VCN has seen no preclinical evidence that immune responses to Ad5 compromise the efficacy VCN-01 — which contains no immune-stimulating or -suppressing factors. Nevertheless, the company would like to know whether modifying VCN-01 with either type of factor would make it more effective, and is testing both approaches in preclinical studies.

The company expects to begin a Phase I trial to treat pancreatic cancer in 2012. "In the Phase I trial we will deliver VCN-01 by intravenous and intratumoral routes" to determine which method of administration is more effective, Cascallo said.

VCN says it also has shown that VCN-01 is active against a panel of head and neck tumor cell lines. Cascallo said the company is validating those *in vitro* data in animal models and hopes to begin a Phase I trial to test intratumoral administration of the compound to treat head and neck cancer at an undisclosed date.

VCN has another engineered adenovirus, VCN-02, in preclinical development to treat undisclosed cancers.

The company has raised €200,000, which would allow it to run until 2Q11, Cascallo said. VCN has started to raise the funds needed to move VCN-01 into the clinic and has applied for public loans in Spain. By the time its existing cash runs out, the company hopes to have attracted investors that would keep the company running through the completion of Phase I trials in 2013, he said.

The company has submitted two patent applications: one covering the hyaluronan-targeting technology, and the other covering the genetic modifications that enhance viral release from infected tumor cells. VCN Biosciences has out-licensed the latter IP to **ORCA Therapeutics B.V.**, which has oncolytic adenoviruses in preclinical development to treat metastatic colorectal cancer.

At least eight companies have oncolytic viruses in the clinic to treat various cancers, but only **Oncolytics Biotech Inc.** is developing one for pancreatic cancer. The company's Reolysin, a formulation of human reovirus type 3, is in Phase II testing to treat the indication. Reolysin also is in Phase II and Phase III trials to treat head and neck cancer and multiple Phase II trials to treat other cancers.

COMPANIES AND INSTITUTIONS MENTIONED

American Association for Cancer Research, Philadelphia, Pa.
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Oncolytics Biotech Inc. (TSX:ONC; NASDAQ:ONCY), Calgary, Alberta
ORCA Therapeutics B.V., Amsterdam, the Netherlands
VCN Biosciences S.L., Barcelona, Spain