REPRINT FROM JUNE 16, 2014

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*Emerging Company Profile*

# OncoSynergy: Detoxing its target

**By Michael J. Haas**
**Senior Writer**

While integrin beta(1) is involved in tumor growth and metastasis, cancer researchers have long assumed that targeting the protein would be prohibitively toxic because of its essential role in normal cellular signaling processes. **OncoSynergy Inc.** is developing a first-in-class antibody that is designed to safely block a subset of integrin beta(1) interactions to treat solid tumors.

The company also thinks its product's ability to tamp down multiple cancer-related processes will have an advantage over competing compounds that only block one or two mechanisms.

"Up-regulation of the integrin occurs in virtually all cancers at all stages and usually correlates with aggressiveness and resistance to treatment," said President and CEO W. Shawn Carbonell. "Integrin beta(1) is an untapped critical target that we think is an Achilles' heel of solid cancers."

According to Carbonell, the target is untapped because key opinion leaders have hypothesized that inhibiting integrin beta(1) (CD29) would have severe toxicities — such as loss of skin and gastrointestinal bleeding — because of its role in normal intercellular signaling processes.

## OncoSynergy Inc.

San Francisco, Calif.

Technology: Humanized mAb that blocks interactions between integrin beta(1) and a subset of its ligands

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2011 by W. Shawn Carbonell and Catherine Park

University collaborators: Baylor University; Ohio State University; University of California, San Francisco; University of Chicago; University of Geneva; University of Strasbourg

Corporate partners: None

Number of employees: 6

Funds raised: $3.8 million

Investors: Undisclosed private individuals

CEO: W. Shawn Carbonell

Patents: 5 issued covering OS2966, OS47720 and OS342 and their therapeutic uses

OncoSynergy's OS2966 is a humanized mAb that inhibits interactions between the integrin and an undisclosed subset of its ligands to simultaneously block multiple cancer processes such as mechanisms of drug resistance.

"It's akin to combination therapy in a single compound," said Carbonell.

Carbonell developed the antibody while a postdoctoral fellow in neurological surgery at the **University of California, San Francisco**, and spun out the technology into OncoSynergy in 2011.

In a study published in *Cancer Research* last year, OncoSynergy and collaborators at UCSF reported that primary glioblastoma multiforme (GBM) tumors from patients treated with Avastin bevacizumab from **Roche** and its **Genentech Inc.** unit showed high expression of CD29. In addition, levels of the integrin were associated with resistance to Avastin.

In mice with Avastin-resistant xenograft GBM tumors, OS2966 decreased tumor growth compared with an inactive control antibody. In mice with Avastin-sensitive tumors, Avastin plus OS2966 decreased growth compared with Avastin plus control antibody.

Avastin, a humanized mAb against vascular endothelial growth factor (VEGF), is marketed to treat brain, breast and colorectal cancers.

The team could not evaluate the safety

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of OS2966 because the antibody does not react with mouse CD29. However, OncoSynergy said unpublished studies showed no toxicity in normal mice receiving systemic injections of a rodent mAb that inhibited the same CD29 interactions as OS2966 or in macaques receiving intracranial injections of OS2966.

Carbonell said additional unpublished studies in xenograft models have shown the mAb is effective in triple-negative breast cancer, metastatic ovarian cancer, drug-resistant pancreatic cancer and GBM tumors that are resistant to other undisclosed therapies.

OncoSynergy chose recurrent GBM as the lead indication for OS2966 because there are few effective therapies. Only 3-5% of GBM patients survive more than three years after standard treatment that includes surgical resection coupled with radiotherapy, chemotherapy and possibly Avastin.

Initially the company will develop OS2966 as a first-line monotherapy in the indication. "We also envision using it in combination therapy for glioma patients at all treatment stages" because of the mAb's potential to have synergistic effects with radiation and other drug therapies, Carbonell said.

Five companies co-market a chemotherapy and a sixth markets a nanoparticle-based thermotherapy to treat recurrent GBM. At least 18 therapies are in the clinic for the indication, including four vaccines, four anti-angiogenics, three kinase receptor antagonists, two chemotherapies and two oncolytic viruses.

Carbonell said a key advantage OS2966 has over other therapies approved or in development to treat recurrent GBM or other solid tumors is its ability to inhibit a protein that drives multiple features of cancer — including proliferation, resistance to apoptosis, angiogenesis, invasion and metastasis. Competing molecules, he said, inhibit just one or two of those features.

OncoSynergy is aiming to complete a series A round in October that would fund the clinical development of OS2966.

The company also has two small molecule therapies in preclinical development. OS47720 is an inhibitor of heat shock protein (Hsp90) to treat gastric cancer, and OS342 is an undisclosed molecule being repurposing for intratumoral injection to treat neurofibromatosis.

COMPANIES AND INSTITUTIONS MENTIONED

**Genentech Inc.**, South San Francisco, Calif.
**OncoSynergy Inc.**, San Francisco, Calif.
**Roche** (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
**University of California**, **San Francisco**, San Francisco, Calif.