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*Emerging Company Profile*

# Intensity: More with less

**By Jennifer Rhodes**
**Staff Writer**

**Intensity Therapeutics Inc.** is developing what could become the first intratumoral chemotherapeutics to achieve better efficacy than systemic chemo by using a formulation technology that enables passive diffusion into tumor cells.

Early preclinical data show the formulations produce more complete responses and longer survival than IV chemo in models the company believes are both more robust and more representative of human pathology than those typically used.

Traditional chemotherapeutics must be actively transported across the cell membrane, which poses challenges for both systemic and intratumoral delivery.

According to CEO Lewis Bender, the number of membrane receptors is a rate-limiting step, while other factors such as mutations can affect uptake.

IV delivery is further hampered by irregular tumor vasculature that unevenly distributes the chemotherapy, and by low concentrations of drug in the tumor, he added.

Intensity is reformulating existing chemotherapeutics with amphiphilic "enhancer molecules" that improve solubility in both lipids and water.

## Intensity Therapeutics Inc.

Norwalk, Conn.
Technology: Intratumoral delivery of chemotherapeutics formulated with amphiphilic molecules
Disease focus: Cancer
Clinical status: Preclinical
Founded: 2012 by Lewis Bender
University collaborators: National Cancer Institute
Corporate partners: None
Number of employees: 2
Funds raised: More than $1 million
Investors: Company management; angels
CEO: Lewis Bender
Patents: None issued

Improved lipid solubility enables receptor-independent passive diffusion into tumor cells.

Better water solubility improves drug distribution throughout the mass. After the tumor degrades, water solubility also could enable the drug to travel through the bloodstream to treat micrometastases, though Intensity has not studied this possibility.

Bender spent several months structurally analyzing thousands of enhancer molecules for their physical and chemical properties using computer modeling. He then used an *in vitro* assay to select five enhancers.

"You have to find the right enhancer structure for each drug and the right conditions for where it will work," he said. For instance, "the different morphology in cancers may play a role in the choice of the enhancer formulations."

The set includes enhancers discovered and designed by Intensity that Bender said are "completely novel molecules." He declined to disclose details.

Intensity has tested intratumoral delivery of INT223-8, a formulation of cisplatin with an enhancer, vs. systemic cisplatin in immunocompetent mouse models with tumors of 300-400 $mm^3$.

Bender noted most mouse cancer models use tumors 50-150 $mm^3$ in size, which do not reflect late-stage disease in humans. Companies also use large drug doses that are effective in mice but cause toxicity when scaled up for humans, he added.

In one study in CT-26 colon carcinomas and baseline tumors of about 350 $mm^3$, INT223-8 given once daily for five

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days produced complete responses in two of 10 mice. There were no CRs in 10 mice receiving systemic cisplatin.

Mean survival was 46.8 days for mice treated with INT223-8, 35.8 days for mice treated with systemic cisplatin ($p=0.05$) and 12 days in 10 untreated mice ($p< 0.000009$).

In a separate study, there were seven CRs among 40 mice treated with INT223-8; cisplatin with vinca alkaloid and an enhancer; or a formulation of cisplatin with a different enhancer. There were no CRs in 30 mice that were untreated or treated with systemic cisplatin with and without vinca alkaloid.

Bender said mice treated with INT223-8 also showed an adaptive immune response, though the cause is not clear.

The company tested this by administering CT-26 cells to 10 mice that had achieved CRs after prior treatment with INT223-8, and to 10 naïve mice. No further treatment was given.

By day 28, the control animals started dying, and only one of the 10 previously treated mice had tumors.

Although INT223-8 has been able to demonstrate proof of concept, Bender said Intensity is unlikely to move the compound into the clinic. Within the next month or two, the company will instead choose a candidate for clinical development that includes two chemotherapeutics with different MOAs and an enhancer.

Bender said Intensity is positioning its formulations for use in patients with metastatic, inoperable tumors who have failed chemotherapy.

Bender plans to meet with FDA this half to discuss the design of a Phase I/IIa trial in about 30 patients with solid tumors. He expects to test Intensity's product both alone and with concomitant, low-dose systemic chemotherapy to treat micrometastases.

Systemic chemotherapy may not be needed if Intensity's formulations "can stimulate an immune response to target the micrometastases," Bender noted. But if systemic chemotherapy is needed in addition to intratumoral chemotherapy, he expects patients will be able to receive a lower dose and fewer cycles than those used today, reducing systemic side effects.

Intensity is looking to raise about $7.5 million and is aiming to start the trial in 1H15.

The products would be delivered using standard small gauge syringe-needle systems guided to the tumor site by conventional imaging technologies.

Bender expects an oncologist and radiologist will work together to use CT scans to locate tumors and ultrasound imaging to deliver the chemotherapeutics to the tumor, similar to how biopsies are done. In some cases, he said interventional radiologists also may deliver the chemotherapeutics.

The company has filed U.S. and international patent applications with composition of matter, use and method claims for products with the enhancers.

COMPANIES & INSTITUTIONS MENTIONED

**Intensity Therapeutics Inc.**, Norwalk, Conn.