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Zacharon Pharma Targets Glycans with Small Molecules

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Zacharon Pharmaceuticals Inc. is on a quest to make glycans druggable.

The San Diego-based start-up developed a high-throughput screening platform to identify small-molecule glycan inhibitors. And with the recent close of its $3.5 million Series A financing, Zacharon is prepared to advance its lead program toward preclinical proof of concept.

Glycans are large, complex molecules involved in cell signaling and other cellular functions. Like proteins, they are critical to regulating cell behavior. But while there's no shortage of biotech products targeting proteins, glycans have proven less druggable due to their low-affinity for receptors and their tendency to cluster.

Companies such as Cytel Corp. (which merged with Epimmune Inc.), Glycomed Inc. (which was acquired by Ligand Pharmaceuticals Inc.) and GlycoMimetics Inc. have attempted to target glycans with glycomimetics – small molecules designed to mimic glycans.

Yet Charles Glass, Zacharon's co-founder and senior vice president of research, said glycomimetics are "very expensive" and involve "complicated chemistry."

Rather than targeting the glycans directly, Zacharon uses "classic small molecules to inhibit the enzymes that make the glycans," Glass explained.

The inhibition of enzymes rather than glycans is Zacharon's "special sauce" and allows the company to access a "whole new universe" of druggable targets, President and CEO Jay Lichter told *BioWorld Today*.

Zacharon's technology originated in the lab of Jeffery Esko, a professor in the department of cellular and molecular medicine at the University of California, San Diego. Esko co-founded Zacharon with Glass in 2004, and the two attracted enough angel funding and grant support to spend the next few years developing and refining their high-throughput screening platform.

In August, the founders closed their first venture round: a $3.5 million Series A financing from Avalon Ventures LLC. Lichter, a managing member at Avalon, took the reins at Zacharon, bringing on Doug Downs as chief financial officer and Court Turner as chief operating officer.

Zacharon's most advanced program is for mucopolysaccharidosis (MPS), a progressive, often life-threatening genetic disorder that causes a toxic buildup of the glycan heparin sulfate. Zacharon has identified and validated more than 15 small molecules that target various enzymes needed to make the glycan, and the company expects to establish preclinical proof of concept and select a lead candidate in 18 to 24 months.

Approved treatments for MPS include enzyme replacement therapies such as Genzyme Corp.'s Aldurazyme (laronidase). While they can replace the enzyme needed to break down the dangerously high glycan buildup, Glass said the drugs cannot cross the blood-brain barrier to address neurological symptoms of the disease, as a small molecule would be able to do.

Behind the MPS program, Zacharon is developing small-molecule inhibitors of enzymes involved in making gangliosides, a glycan associated with cancer. A significant portion of the company's $2.2 million in NIH funding raised to date is being used to support that program.

Zacharon is further filling its pipeline by running about 100,000 assays per week on its platform. By initially focusing on four classes of glycans that play a role in cell signaling and adhesion, the company has identified hundreds of small-molecule inhibitors of various glycan-associated enzymes. The compounds are being validated in secondary screening, Glass said, and may be applicable in treating genetic disorders, cancer, inflammation, Alzheimer's disease and other conditions.

Lichter said Zacharon's plan is to hold on to the cancer programs through Phase II and out-license other indications earlier in development. But he added that Zacharon "is a biotech company – we're always looking for partners; we're always looking for investors." ■