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Financings Roundup

NormOxys Gets \$17.5M Series B to Fund Cardio, Cancer Studies

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After gathering encouraging preclinical data on its oxygen-boosting small molecules, NormOxys Inc. raised \$17.5 million in a Series B-1 financing to push its programs to proof of concept in chronic heart failure and cancer.

Founded in 2004, Wellesley, Mass.-based NormOxys previously raised an \$8 million Series A round and a \$4.5 million Series B round from Index Ventures. Joining Index in the new round was Care Capital LLC, which NormOxys CEO Martin Tolar said the company chose for its extensive big pharma experience.

The Care Capital partners formerly served as CEOs for Novartis AG, Squibb Corp. (now Bristol-Myers Squibb Corp.), SmithKline Beecham plc (now GlaxoSmithKline plc), Aventis Pharma (now Sanofi-Aventis Group) and Hoechst Marion Roussel (now Sanofi-Aventis Group).

That pedigree should come in handy when NormOxys completes its Phase II proof-of-concept trials and is ready to partner, likely around the end of 2011. Tolar noted that the biotech has "had significant interest from large pharma already."

And while many preclinical-stage biotechs are finding it difficult to raise funds in the current economic environment, Tolar said NormOxys "did not have much trouble.

"We usually get the comment, 'I've been in this business 30 or 40 years, and I've never seen anything like this,'" Tolar said.

Those comments have come in response to NormOxys' oxygen-release enhancers, or oxyrens, small-molecule allosteric modulators of the affinity of oxygen to hemoglobin.

Oxyrens allow hemoglobin to release twice as much oxygen as normal, facilitating oxygenation of hypoxic tissues. But unlike hyperbaric chambers and existing oxygen treatments, the effect is selective for diseased tissues, avoiding side effects.

In cardiovascular disease, the concept is straightforward, Tolar explained.

The heart muscle can't pump enough blood to maintain normal oxygen levels, so oxyrens make oxygen delivery more effective. Standard cardiovascular drugs like ACE inhibitors and beta-blockers only increase exercise capacity by about 5 percent to 10 percent, Tolar said, while pre-clinical studies published in the *Proceedings of the National Academy of Sciences* showed that oxyrens increased exercise capacity by 60 percent. (See *BioWorld Today*, Feb. 11, 2009.)

NormOxys also announced Monday the initiation of a Phase I trial of lead oxyren OXY111A. The randomized, single-blind, ascending-dose design will evaluate the safety, tolerability and pharmacokinetics of single intravenous doses of OXY111A in healthy volunteers. The trial also will evaluate P50, a biomarker aimed at establishing proof of pharmacology by quantifying changes in oxygen affinity, as well as cardiopulmonary exercise testing.

The Phase I trial should lay the foundation for Phase I/II trials first in chronic heart failure and later in cancer.

The concept in cancer is that solid tumors are often hypoxic, with that hypoxia leading to high levels of hypoxia-inducible factor, vascular endothelial growth factor and other tumor promoters.

Using OXY111A to boost oxygenation resulted in complete preclinical tumor clearance within eight weeks, with no recurrence, Tolar said, noting that those data soon will be published.

Also looking at hypoxia in cancer is Threshold Pharmaceuticals Inc., which is aiming to start a Phase II trial with its hypoxia-activated prodrug, TH-302.

But TH-302 is designed to target and kill hypoxic cancer cells rather than stimulating repair. Colby Pharmaceutical Co. also is developing small-molecule oxidative stress inhibitors for cancer, which are designed to block pathways by which tumors become hypoxic.

Beyond heart failure and cancer, NormOxys believes its platform could be applicable in anemia, obesity, Alzheimer's disease, macular degeneration and a host of other indications.

The biotech also has a number of backup molecules in its pipeline. But for now, the main goal is to "prove the impact" in the first two indications, Tolar said.