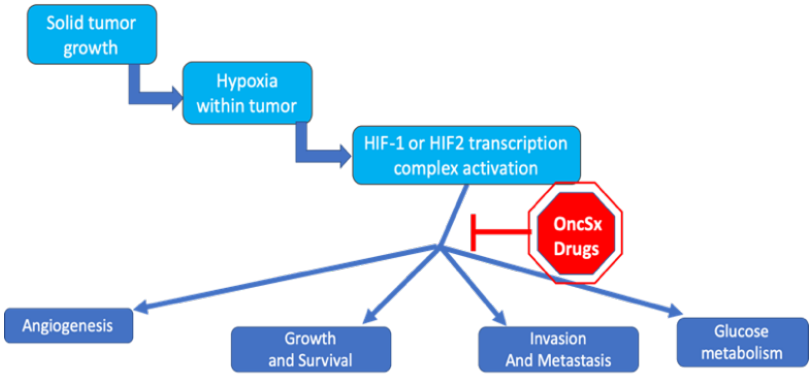
OncoSpherix
Advanced Drugs for Advanced Cancer

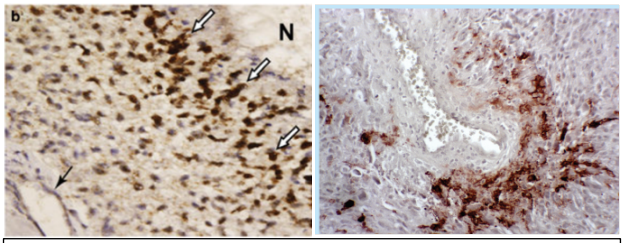
Executive Summary

Overview: OncoSpherix, a preclinical stage oncology drug development company, is developing proprietary first-in-class small molecules that disrupt the function of the transcription factors HIF-1 and HIF-2, thereby crippling the ability of cancer cells to survive and spread from regions of low oxygen (hypoxia).

Many types of cancer utilize both HIF-1 and HIF-2 for their adaptive response to hypoxia, so the dual inhibition of both forms of HIF is advantageous over agents that merely inhibit one form. Regions of hypoxia occur in most solid cancers due to tumor cells growing faster than their blood supplies. By blocking the function of HIFs, OncoSpherix compounds inhibit expression of more than 100 gene products that help tumors survive and spread, including proteins that bring in new blood vessels (angiogenesis), drive tumor invasion and metastasis, and alter tumor cell metabolism.



Lead Compounds, Clinical Indications and Development Strategy: OncoSpherix has a broad platform with different drug classes that have novel mechanisms of action. The clinical lead candidate, 64B, is a dual HIF-1 and HIF-2 inhibitor that functions by binding to the CH1 domain of coactivator paralogs p300/CBP, thereby preventing recruitment to the HIF transcriptional complex. The binding site for 64B does not inhibit p300/CBP's ability to function with some other important transcription factors. As a consequence, 64B is well tolerated, both alone and in combination with cytotoxic chemotherapy in preclinical models, unlike the toxicity that occurs when the function of p300/CBP is fully disabled. Efficacy studies in mice demonstrate that 64B and a related compound inhibit primary tumor growth and metastasis, leading to prolongation of survival with many types of cancer, including eye melanoma, breast cancer, pancreatic cancer, lung cancer and glioblastoma. Furthermore, 64B synergizes with some other chemotherapies, crosses the blood brain barrier (BBB), and does not cause discernable organ toxicity at doses that block tumor growth and metastasis.



HIF-1 (left) and HIF-2 (right) are expressed glioblastoma multiforme, as shown in surgical specimens from different patients.

Relapsed glioblastoma multiforme (GBM) is being considered as the first development target for 64B, but the final decision will depend on ongoing preclinical studies. HIF-1 and HIF-2 are both expressed, as shown by immunohistochemistry in GBM surgical specimens (figure). GBM is an orphan indication with approximately 12,000 cases diagnosed in the US each year. Most patients relapse within 1-2 years and die within 3-6 months post relapse despite the use of best available treatment. 64B is predicted to be superior to the VEGF-inhibitor, bevacizumab, that is FDA-approved for recurrent GBM. Bevacizumab does NOT prolong survival, in part because HIF is activated due to the hypoxia that results from inhibition of angiogenesis. 64B not only blocks VEGF and VEGF receptor expression but also other angiogenesis genes and genes involved in metastasis and invasion. 64B is estimated to be within 18 months of beginning Phase I clinical testing.

Intellectual property: Founding technologies were licensed from Emory University and Georgia State University and include novel composition of matter and use. The license includes two issued patents, and the company is working to expand its global patent estate.

Market: The market for the OncoSpherix small molecules includes most of the > 600,000 US cancer patients who die from unresectable solid tumors each year. The market for the probable lead indication, GBM, is projected to reach nearly $1.4 billion by 2025. Additional indications will follow, including non-small cell lung carcinoma (NSCLC) which had a $6.45 billion market in the US in 2018, and the global market for NSCLC is forecast to reach $10.53 billion by 2026.

Competition: Merck has a selective HIF-2 inhibitor called belzutifan that was approved for Von Hippel Lindau-associated tumors in August, 2021. Merck acquired belzutifan by purchasing Peloton Therapeutics for upfront $1.05 billion in 2019. OncoSpherix molecules have an advantage in that they inhibit both HIF-1 and HIF-2, and both HIFs play an important role in tumor survival and spread. OncoSpherix drugs are designed to be given in combination with other agents, so targeted therapies, immunotherapies and cytotoxic drugs represent opportunities for combinations rather than competitors.

Series A Goal: OncoSpherix is seeking $25 M in investment to advance its clinical lead, 64B, through completion of Phase 2 clinical testing for its first indication ($5M and 18 months to complete preclinical and IND-enabling studies and file an IND). Proceeds will be used to grow the leadership team, file additional IP, execute additional preclinical efficacy studies, complete IND-enabling studies, file an IND, and complete phase 1 and 2 clinical trials for the initial indication. OncoSpherix's operations are currently supported by $400,000 in non-dilutive funding from the National Cancer Institute (SBIR) and an additional $487,000 from the Georgia Research Alliance.

Team: OncoSpherix's leadership team has deep experience in tumor biology, medicinal chemistry, oncology, pharmaceutical drug development, biotechnology company value creation and financing.

Margaret K. Offermann, MD, PhD, President and Chief Executive Officer, BOD was Deputy National Vice President for Research at the American Cancer Society, Professor of Hematology and Oncology at Emory University, and President of the Federation of American Societies for Experimental Biology (FASEB). She has extensive leadership experience in academic, non-profit and commercial organizations. She has multiple publications and awards and is board certified in Internal Medicine and Medical Oncology.

Russell M. Medford, MD, PhD, Chair, BOD. CEO of Covanos, Inc, a cardiovascular diagnostic company. Previously CEO of Atherogenics Inc. and a founding Board member of Inhibitex, Inc., both NASDAQ traded biotechnology companies. Serves on boards of additional public and private companies.

Kenneth Moch, MBA, *Advisor to the CEO*: Skilled chief executive, board leader and strategist with proven experience building, managing and financing private and public life science companies from start-up through commercialization. Former CEO of Chimerix, Cognition Therapeutics, and other companies.

Robert Scott, MD, *BOD*: Biotechnolgy and Pharmaceutical executive who served as Chief Medical Officer at Abbvie (retired in April, 2020) where he had responsibility for around 40 new molecular entities, four thousand people and a budget of close to two billion dollars. He created the Development Design Center, a Center of Excellence focused on using predictive analytics and big data to design and implement better clinical trials.

Erwin G. Van Meir, PhD, Chief Scientific Officer and Scientific founder of OncoSpherix (biology), BOD. Professor of Neurosurgery and Associate Director at the NCI-designated O'Neal Comprehensive Cancer Center at University of Alabama at Birmingham. Extensive expertise in molecular basis of tumorigenesis, experimental therapeutics and drug discovery. Author of over 200 peer-reviewed scientific articles in translational oncology and co-inventor on over 30 U.S. and international patent applications.

Binghe Wang, PhD, BOD. Scientific founder of OncoSpherix (chemistry). Regents' Professor of Chemistry at Georgia State University and Georgia Research Alliance Eminent Scholar in Drug Discovery. Synthetic medicinal chemist with extensive experience in drug design and delivery, and molecular recognition.

Kendyle Woodard, MBA, COO. Business operations management executive with an MBA and experience co-founding a biotech company and taking it public on Nasdaq.