



*First-in-Class Small Molecule Dual HIF-1 and HIF-2
Inhibitors for Treatment of Advanced Solid Cancers*

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Chief Executive Officer

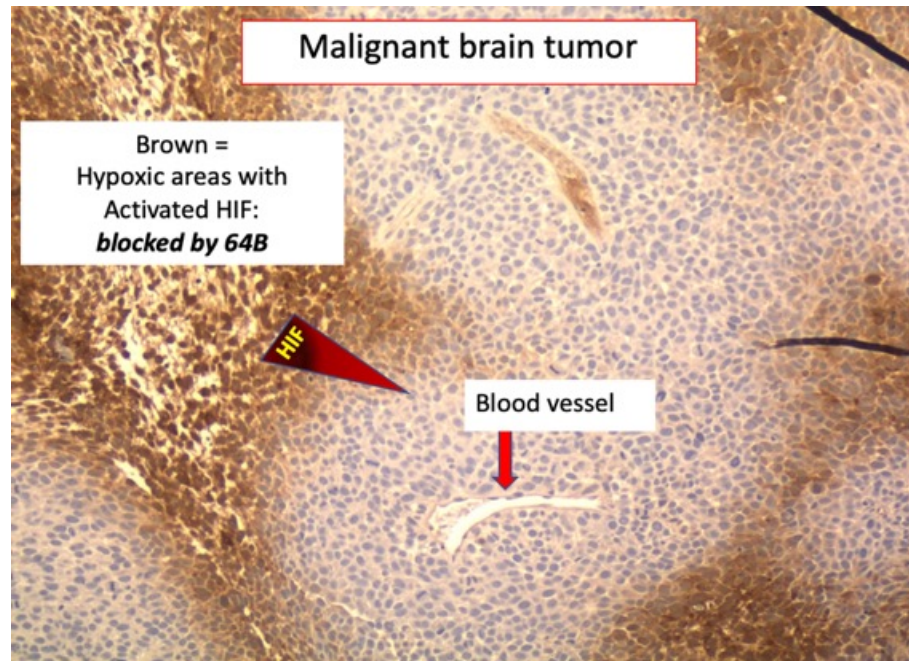
OncoSpherix: Improving Quality of Life and Survival of Patients with Advanced and Aggressive Cancers

- **Our Approach:**
 - Develop proprietary HIF inhibitors
 - *Combination therapies* for advanced cancers
- **Combinations are based on:**
 - Preclinical data
 - Medical need
 - Market opportunity
 - Co-development opportunities
- **Our Advantage:**
 - First-in-class compounds
 - Disrupt the function of *both* HIF-1 and HIF-2

Indications

- **Probable Lead indication:**
 - Relapsed glioblastoma multiforme
- **Additional indications:**
 - Metastatic triple negative breast cancer
 - Unresectable pancreatic cancer
 - High risk and metastatic uveal melanoma
 - Unresectable adenocarcinoma of the lung
 - Other solid tumors based on preclinical data
- **Multi Billion-Dollar Potential**
- **Multiple Potential Co-Development Opportunities**

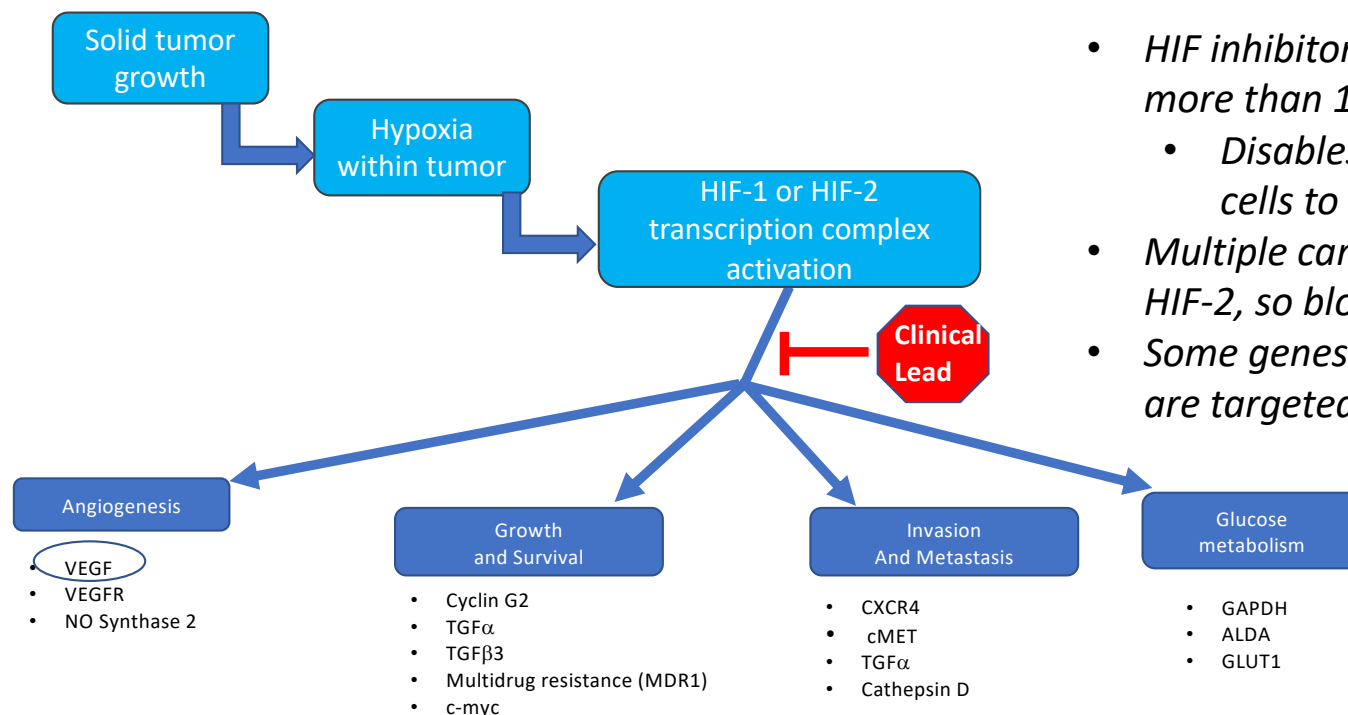
HIFs are Attractive Therapeutic Targets: Activated in Most Cancers and Contribute to Tumor Survival and Spread



Note: Well-oxygenated regions of cancers also need to be attacked

- Tumors grow faster than their blood supplies, resulting in hypoxia
- HIF-1 and/or HIF-2 become activated during hypoxia, enabling tumor cells to survive and spread

Lead Compounds Block the Function of *Both* HIF-1 and HIF-2: Block Expression of Genes that Help Cancer Cells Survive and Spread



- *HIF inhibitors block the transcription of more than 100 genes*
 - *Disables ability of hypoxic cancer cells to survive and spread*
- *Multiple cancers express both HIF-1 and HIF-2, so blocking both is advantageous*
- *Some genes blocked by HIF inhibitors are targeted by FDA-approved drugs*

OncoSpherix's Lead Compounds Inhibit Primary Tumor Growth and Metastasis in Multiple Types of Solid Tumors in Mice

Broad Efficacy Profile:

- Primary tumor growth inhibited:
 - Glioblastoma, ocular melanoma, breast cancer, lung cancer, pancreatic cancer
- Metastasis inhibited:
 - Ocular melanoma, breast cancer, lung cancer (others not tested)

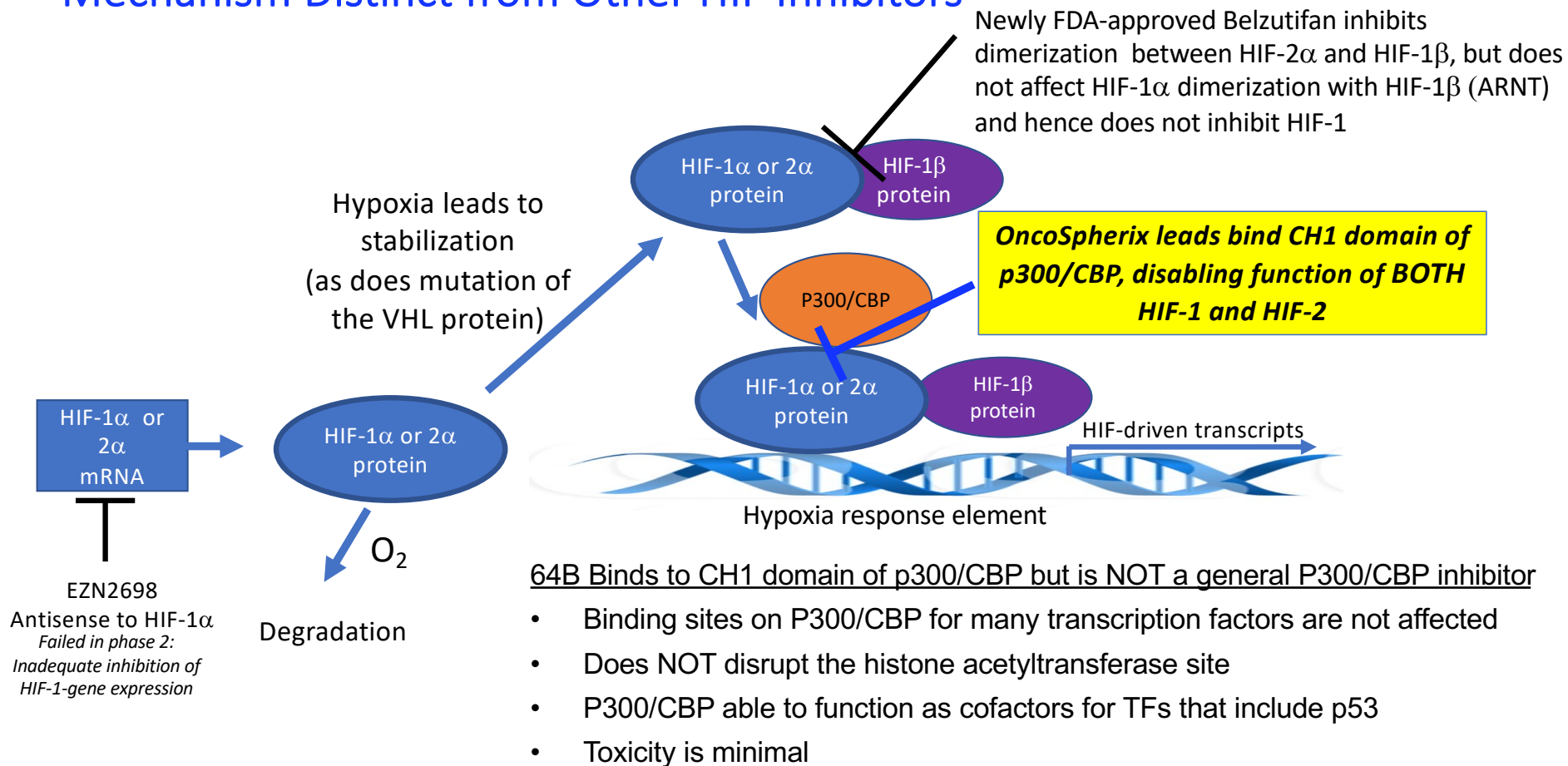
Excellent Safety Profile:

- Maximum tolerated dose not yet reached
- No behavioral changes/organ toxicity at 60 days (daily dose)

Well-tolerated with synergistic efficacy with some combinations:

- Docetaxel and 64B: Adenocarcinoma of the lung
- Sorafenib and 64B: Uveal melanoma
- Other combinations in testing phase

Lead Compounds Block Function of Both HIF-1 and HIF-2: Mechanism Distinct from Other HIF Inhibitors



64B Selected as Clinical Lead: Significant Advantages Over Other HIF Inhibitors and Agents that Target HIF-Regulated Processes

- **Dual inhibition** of HIF-1 *and* HIF-2 allows more complete disruption of hypoxic response in broader range of tumors than disruption of single HIF
 - Peloton's HIF-2 inhibitors *bought by Merck in 2019 for \$1.05 billion with an additional \$1.15 billion possible based on milestones*
 - Approved by FDA on August 13, 2021, for cancers in patients with von Hippel Lindau disease
 - In Phase 3 testing for renal cell carcinoma with VHL mutations (most RCC) in non-VHL patients
 - Named Belzutifan (Welireg)
 - Price per month is \$26,400. Benchmark price for 64B
- **Enhanced therapeutic efficacy of 64B** when part of combination therapy
- **64B blocks multiple cellular processes**, offering advantages over approved angiogenesis inhibitors
 - Bevacizumab (FDA-approved for glioblastoma, ovarian cancer, non-squamous lung cancer and colorectal cancer) is a multi-billion dollar drug that only blocks VEGF-induced angiogenesis, whereas 64B blocks VEGF, VEGFR expression and much more
 - Currently comparing and combining with tyrosine kinase inhibitors that have distinct mechanisms but some overlap in targets

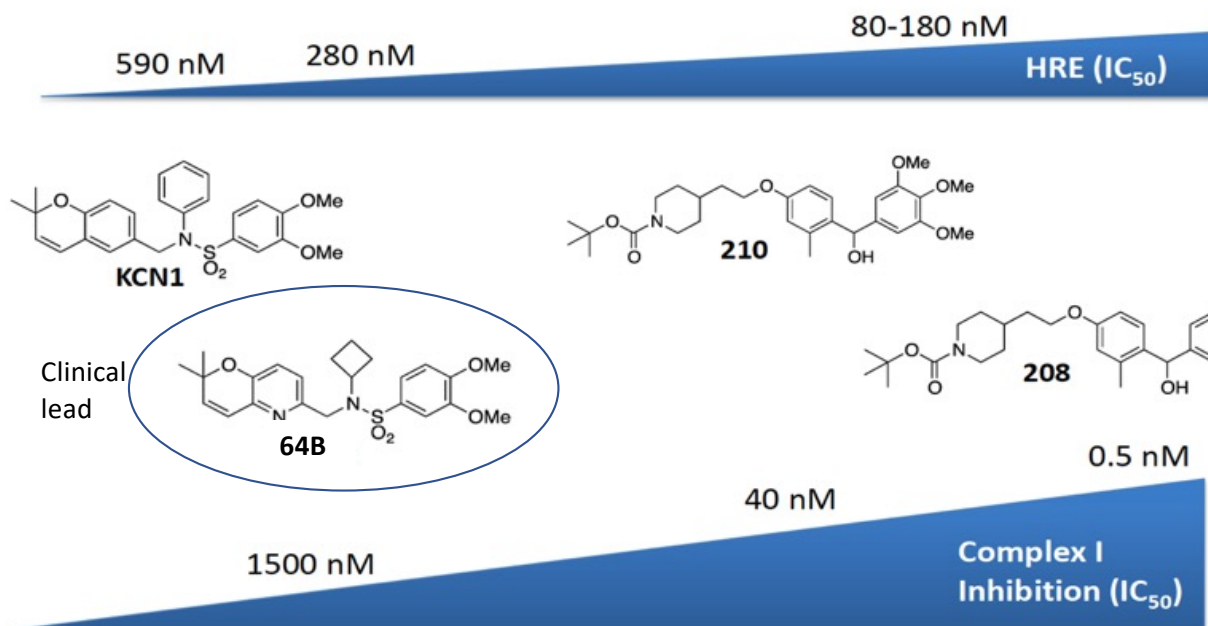
Patent Position

Technology licensed: Emory/GA State Universities on 7/14/19

- **United States Patent 9,062,072:** Inhibitors of HIF and angiogenesis; Filed 4-20-11; issued 06-23-2015; active through 2032 (36-month extension)
- **United States Patent 10,772,858:** Benzhydrol Derivatives for the Management of Conditions Related to Hypoxia Inducible Factors: Filed 5-02-16; issued 09-15-2020; Active through 2036; being prosecuted in China and Europe
- **New IP filings expected as studies progress**

Multiple Classes of HIF Inhibitors, Some with Additional Functionality

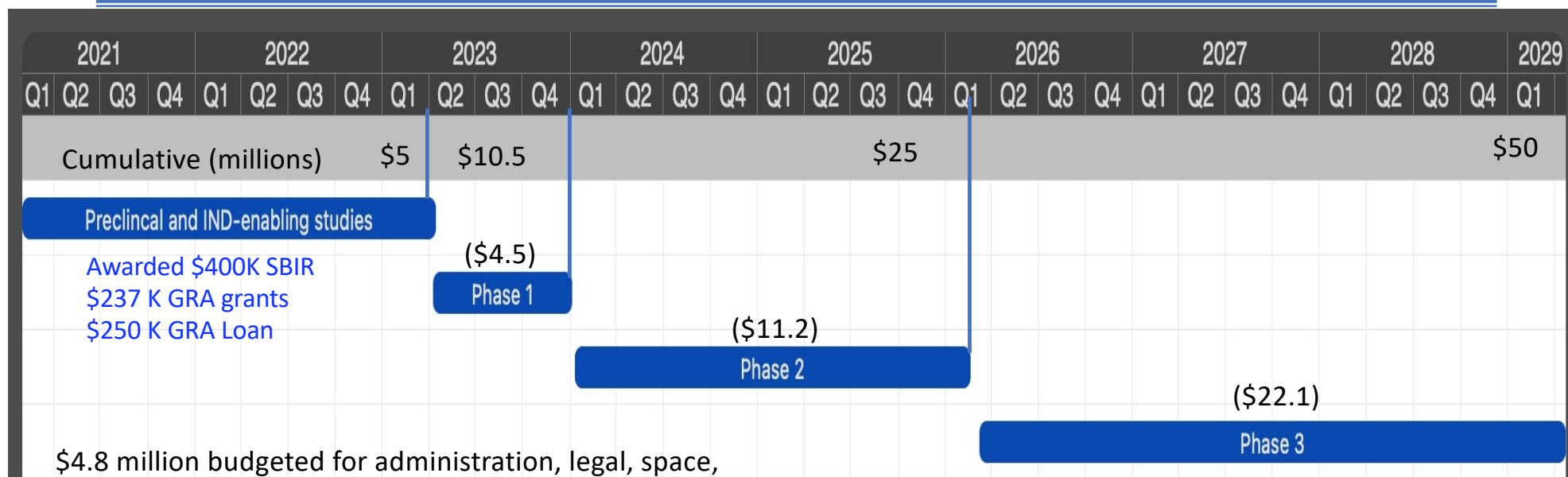
Arylsulfonamides -> benzhydrols



Mitochondrial complex I

- Essential role in biosynthesis and redox control
- Proliferation
- Resistance to cell death
- Metastasis

Seeking \$25 Million Series A: Funding Through Completion of Phase 2

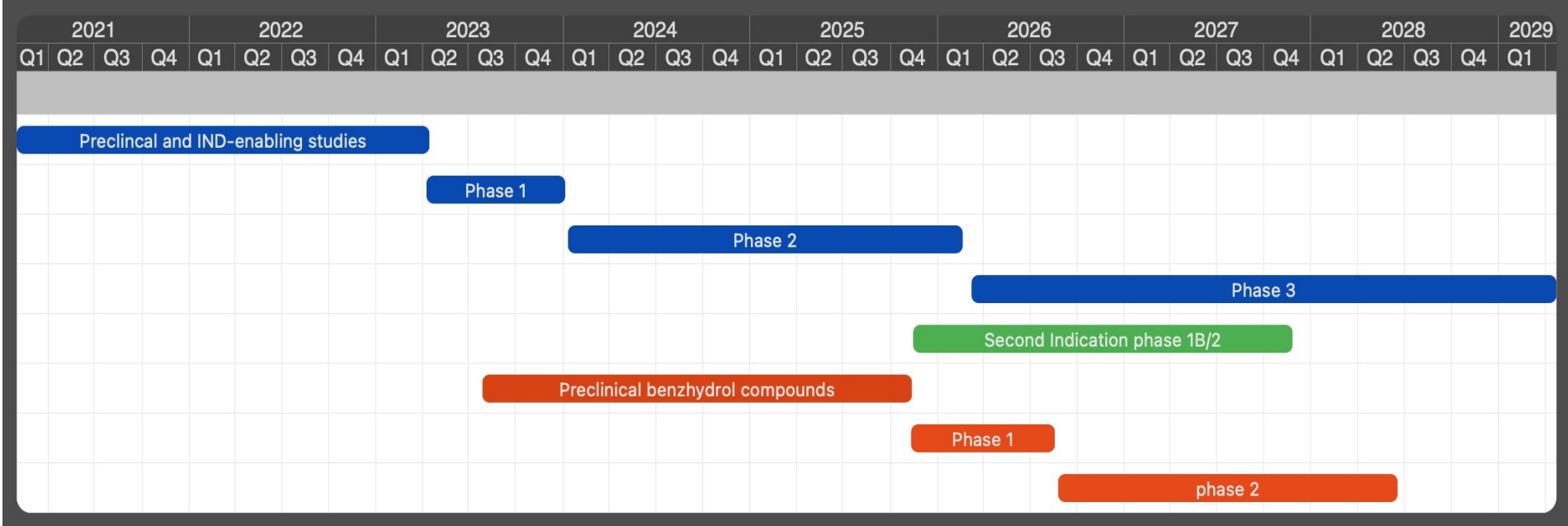


\$4.8 million budgeted for administration, legal, space, regulatory, research through completion of first Phase 2

Note: Based on Phase 2 data, Merck bought Peloton Therapeutics' HIF-2 inhibitors in 2019 for \$1.05 billion cash with the potential for \$1.15 in milestone payments



Additional Indications for 64B and Additional Compounds Will Be Advanced in a Staged Fashion



Team: Leaders in Tumor Biology, Oncology, Medicinal Chemistry, Drug Development, Biotechnology Company Value Creation and Financing

Founding Team

- **Margaret K. Offermann, MD, PhD, Chief Executive Officer, BOD:** Served as President of FASEB, Deputy National Vice President for Research at the American Cancer Society, Professor of Hematology and Oncology at Emory University.
- **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.
- **Erwin G. Van Meir, PhD, Chief Scientific Officer, Scientific founder, BOD.** Was Professor of Neurosurgery at Emory; Now Professor of Neurosurgery and Associate Director at the NCI-designated O'Neal Comprehensive Cancer Center at University of Alabama at Birmingham. Expertise in molecular basis of tumorigenesis and drug discovery.
- **Binghe Wang, PhD. Scientific founder and BOD:** Regents' Professor of Chemistry at Georgia State University and Georgia Research Alliance Eminent Scholar in Drug Discovery. Synthetic medicinal chemist with experience in drug design and delivery, and molecular recognition.

Joined in 2021

- **Kenneth I. Moch, MBA, Special Advisor to the CEO:** Skilled chief executive, board leader and strategist with more than 35 years of experience in managing and financing private and public life science companies from start-up through commercialization. He most recently served as CEO of Cognition Therapeutics through March 2020.
- **Robert Scott, MD, BOD:** Leadership positions in global Pharma for over thirty years. Recently retired as the Chief Medical Officer at Abbvie where he had responsibility for around 40 new molecular entities, four thousand people and a budget of close to two billion dollars.
- **Kendyle Woodard, MBA, Chief Operating Officer:** Business operations management executive with experience co-founding a biotech company and taking it public on Nasdaq.





OncoSpherix

Advanced Drugs for Advanced Cancer

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