Therapeutic HIF-1 Pathway Inhibitors
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Opportunity

- Proven drug target pathway!
  - Avastin / Lucentis – Genentech, Oncology and Ophthalmology (AMD)
  - Macugen – Pfizer, Ophthalmology (AMD)

- Small molecule inhibitor to master regulatory transcription factor (HIF-1)

- HIF-1 is responsible for up-regulation of many cancer promoting pathways (e.g. VEGF, GLUT-1, and EGFR)
  - Angiogenesis
  - Metabolic adaptation

- Potential therapeutic markets
  - Oncology
  - Age related macular degeneration
Composition

- Small molecule inhibitor to Hypoxia Inducible Factor (HIF-1α)
- Belonging to the family of 2,2-dimethylibenzopyran compounds
  - Natural product-like compounds
  - Specific for HIF-1α

![Chemical structure](image)
R & D Status

- 10,000 compounds screened
- 5 structure families
- 300 compounds for SAR
- 22 active compounds

KCN1

- New compound family identified based on SAR work
- EmTechBio funding for PD/PK analysis
Competition

- Santaris
  - RNA based therapeutic

- FibroGen
  - HIF-PH antagonist

- EntreMed
  - Panzem – 2 methoxyestradiol analog
  - Phase II, microtubule destabilizer

- Others
  - Academic labs that are attempting to develop HIF-1 antagonists
PCT application nationalization
- US, Canada, EPO
- Filed 03/2003

Second provisional patent application pending
- Filed 08/2005

Claims address:
- Small molecules (i.e., compounds identified in primary screens)
- Methods of modulating HIF activity
- Methods of treating disease (i.e., cancer)