• Founded in 2016 to develop life-changing therapies against debilitating aggressive cancers that have limited treatment options

• Integrated platform technology for discovery of novel molecular targets and therapeutics for glioblastoma and melanoma

• We focus on targeting stem cell-like, invasive subpopulations of glioblastoma and melanoma with a new generation of highly selective small-molecule kinase drugs

• Our team brings together world-class experts and recognized pioneers in clinical oncology, synthetic biology, and medical technologies

• We are building a robust pipeline to bring our most promising drugs to the market

www.sideramedicine.com
Core Team

Farren Isaacs, PhD
Professor @ Yale
Bioengineering & Synthetic Biology

Jesse Rinehart, PhD
Professor @ Yale
Cell Signaling & Human Disease

Onur Kilic, PhD
Biotech Entrepreneur
Stanford/Johns Hopkins, >50 licensed patents

Alfredo Quiñones-Hinojosa (Dr. Q), MD
Chair of Neurosurgery @ Mayo Clinic
Glioblastoma Clinical Research

Andre Levchenko, PhD
Professor & Director of Systems Biology Institute @ Yale
Glioblastoma & Melanoma Signaling

Hiring plan: Experienced CEO
Our current focus is on Glioblastoma

- Median survival of 14.6 months with treatment (American Brain Tumor Association)
- Brain cancer now the leading childhood cancer killer (CDC)
- Combined glioblastoma market for the US, UK, Spain, France, Germany, Italy and Japan is expected to rise from $659 million in 2014 to $3.3 billion in 2024 according to GlobalData
- High levels of unmet need in the market have created ample opportunities for players with effective therapies

The Problem
- There are no effective therapeutics for glioblastoma

The Opportunity
- Kinase-S pathway in glioma cells is well-studied
- Kinase-S plays a critical role in migration of invasive tumors
Novel kinase targets discovered

- Generated a library of novel potential targets for glioblastoma and melanoma
- One of these targets is **Kinase-S**, shown to affect both slow and fast subpopulations
Proprietary technology 2: A novel & rapid drug discovery platform

Genomically Recoded Organism + Phosphoserine Technology
- Synthesis of custom phosphorylated proteins to activate human kinase drug targets in engineered bacteria

Functionalized mammalian signaling in engineered bacteria
- Kinase-S network that drives glioma migration is active only in proprietary platform technology

Inhibitor screen with small molecule library
- Platform produced lead kinase inhibitors YU252 & YU566

Validation in malignant glioblastoma
- YU252 & YU566 show on target activity in vivo and in cultured glioma cells
Results

Platform accurately identifies aggressive phenotypes and predicts patient prognosis

60 nM inhibitor active in both biochemical and cell-based assays

YU566: IC50 ~60 nM

YU252 inhibits proliferation in 5 patient-derived GBMs

YU566 inhibits migration in primary GBMs but not in normal human brain cells

Ongoing in vivo YU252/566 experiments with intracranial injection of patient GBM cells
Commercial Activity & Financing

- **Strong Intellectual Property Portfolio**
  - 7 patents/pending patents

- **Commercial Activity**
  - **Pfizer:** OCR6049, sold phosphorylated kinase (Dec 2012)
  - **Biogen Idec:** OCR3015, licensed SepOTS for drug discovery (Dec 2014)
  - **Agios Inc.:** Novel Phosphoproteins for Structural Analysis (June 2016)
  - **Agilent:** OCR6602, CDA for development of Human Phosphoproteome Platform

- **Financing** (Non-dilutive capital)
  - $80,945 awarded, 2013-2015, YCMD Pilot program
  - $5,000 awarded, 2014, SBI pilot project
  - ~$500,000 awarded from PITCH program for lead-compound development
  - $30,000 awarded, 2017, CT Biopipeline for platform development
  - Pending SBIR
  - Current support for R&D
    - $10M awarded to Levchenko, Isaacs, Rinehart for NIH-funded U54 Cancer Research Center grant
    - >$20 M to Isaacs, Rinehart, Levchenko, & Dr. Q
Why Invest Now?

- High unmet need (no effective therapeutics for glioblastoma) and large market (expected to reach 3.3 billion by 2024 for glioblastoma)
- Novel kinase target
- Proprietary phosphoprotein expression technology enabling programmable activation of signaling pathways for drug development
- 60 nM inhibitor active in both biochemical and cell-based assays
- Availability of high resolution Kinase-S crystal structure and excellent structure-guided medicinal chemistry potential
- Unique animal model and a large collection of primary patient-derived glioblastoma cells for *in vivo* efficacy studies
- Ongoing pipeline expansion