Company overview

- Exploiting cancer-associated DNA repair defects via direct DNA modification
- World class team of Yale founders; SAB members and core scientific team established
- Lead program: first generation candidate decision in Q3 ’23, second generation candidate decision in Q3/4 ’23; IND filing planned in 2H ’24
- MOD016 is being profiled extensively *in vivo* to explore dose, regimen, and therapeutic index (TI)
- Differentiated second generation molecules with potential for enhanced TI in early profiling
- Innovative biomarker plan for patient selection, including non-invasive liquid biopsies, for first-in-human studies
- Second program: early, positive *in vitro* proof of concept data supports further exploration
- Line-of-sight targeting HR-defective (HRD+) cancers utilizing DNA modifiers
- Foundational IP exclusively licensed from Yale, NCE and method-of-use filings ongoing at Modifi
- $6.4M seed round closed 4/22, $2.4M SBIR Fast-Track Phase I/II awarded 8/22
- Raising Series Seed 2 round to support first program candidate declaration and initiation of IND-enabling studies
Our Founders, Team and Scientific Advisory Board

Founders
- Seth Herzon, PhD
  Milton Harris ’29 Professor of Chemistry, Yale University
- Kingson Lin, PhD, MD (‘24)
  Yale Medical School
- Kevin Rakin
  Partner HighCape Capital

Team
- Ranjit Bindra, MD, PhD
  Co-Founder and Chief Executive Advisor
  Harvey and Kate Cushing Professor, Yale
- Joseph Park, PharmD
  Vice President, Corporate Development & Clinical Affairs
- Kyle Tarantino, PhD
  Director, Chemistry
- Bruce Ruggeri, PhD
  Vice President, Pharmacology
- Ashish Juvekar, PhD
  Director, Biology

Scientific Advisory Board
- Roger Stupp, MD
  Chief of Neuro-Oncology at Northwestern University
- Pat LoRusso, DO
  Chief, Exp. Therapeutics Yale Medical School
- Joseph Costello, PhD
  Professor UCSF
- Peter Glazer, MD, PhD
  Chair, Yale RadOnc
- Manmeet Ahluwalia, MD
  Deputy Director and CSO Miami Cancer Institute
- Mike Dillon, PhD
  Senior Scientific Advisor
  Founding CSO of IDEAYA
- Jann Sarkaria, MD
  Professor Mayo Clinic
- Joseph Park, PharmD
  Chief, Exp. Therapeutics Yale Medical School
- Kyle Tarantino, PhD
  Director, Chemistry

 ACS RSG Awardees
- Seth Herzon, PhD
  Milton Harris ’29 Professor of Chemistry, Yale University
- Kingson Lin, PhD, MD (‘24)
  Yale Medical School
- Kevin Rakin
  Partner HighCape Capital
Drug discovery focused on direct tumor DNA modification

Disruption of DNA integrity is a proven approach to eradicate cancer
Modifi is exploiting cancer cell defects at the DNA level

**Modifi Bio’s Core Technology**

Fragmentation of the molecule releases the modifier, which rapidly and selectively binds to DNA.

**Cancer Cell**
Defective DNA Repair

Modifier further reacts with DNA over time, causing irreversible DNA damage and tumor cell death.

**Healthy Cell**
Intact DNA Repair

Modifier is rapidly eliminated from DNA, preventing DNA damage and resulting in normal cell survival.
MGMT loss drives alkylator sensitivity but requires intact MMR

1. MGMT loss is common across many cancers and confers exquisite alkylator sensitivity

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>% MGMT Methylation</th>
</tr>
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<tbody>
<tr>
<td>Glioma</td>
<td>40-80%</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>25-30%</td>
</tr>
<tr>
<td>Gastic Cancer</td>
<td>30%</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>30-40%</td>
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<tr>
<td>Cervical Cancer</td>
<td>30%</td>
</tr>
<tr>
<td>Pancreatic NENs</td>
<td>60-75%</td>
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</tbody>
</table>

2. Mismatch repair (MMR) mutations are a common alkylator resistance mechanism in MGMT- tumors

3. Mechanistic basis for MGMT/MMR-dependent sensitivity and resistance

- Guanine-Cytosine (GC) DNA base-pair
  - TMZ
  - Methylation of the G base

CNS Cancers (Glioma)

Non-CNS Cancers (Colon Cancer)

MGMT rapidly removes the modification

Normal cell survival

Tumor cell apoptosis and death

Unmet need for novel therapies targeting MGMT- cancers independent of MMR status

MMR mutations (MGMT-/MMR-)

Tumor replication, and growth

Normal cells expressing MGMT (MGMT+)

Cancer cells lacking MGMT (MGMT-)

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KL50: The first MGMT-dependent MMR-independent DNA modifier

Exquisite anti-cancer efficacy, even in highly resistant tumor models...

RESEARCH

Mechanism-based design of agents that selectively target drug-resistant glioma

K. Lin MD/PhD (’21)
Bindra/Herzon Lab
Modifi Co-Founder

S. Gueble, MD/PhD
Bindra Lab Alumni
RadOnc Attending (’23)
Robust KL50 efficacy in intracranial MGMT-/MMR- PDX glioma models with distinct profile from known alkylating agents

**MGMT-/MMR- patient-derived GBM xenografts, *in vivo* survival**

5 mg/kg QDx1 PO every 7 days x 3 cycles

25mpk QDx5 PO every 28 days x 3 cycles

Sarkaria Laboratory – Mayo Clinic
(in collaboration with Modifi Bio)
Patient selection strategy in the Modifi O\textsuperscript{6} trial

**Tumor Recurrence (CNS, solid tumors)**

**Stratify**

Initial Screening/Enrollment
- FFPE specimen
- Liquid biopsy
  (MGMT/MMR and TMB/MSI Status)

**Novel patient Selection strategy**

**MGMT- Gliomas (recurrent, +/- biopsy)**
- Grade 2/3 glioma
- Grade 4 glioma (GBM)
- Biopsy-confirmed MMR- glioma

**MGMT- Solid Tumors (non-CNS, metastatic)**
- Colorectal cancer
- Lung cancer SCLC/NSCLC
- Sarcoma

**Stratify**

**Phase I Dose Escalation**
(Standard 3+3)

**Phase I Dose Expansion**
(Selected Cohorts)

**RP2D**

**Phase II Trial**
(Single arm vs. randomization)

**Potential Cohorts (MGMT- and MMR-/+)**
1. Recurrent glioma
2. Selected tumor sub-types
3. Basket exploratory group

“Back-fill” cohorts with MGMT-/MMR- tumors
(expedited efficacy read-out)

Leverage experience of the SAB and CEO for our initial trial designs...

**Yale**
Ranjit Bindra, MD, PhD
Professor, YBTC Co-Director
Yale Medical School

Roger Stupp, MD
Chief of Neuro-Oncology at Northwestern University

**Miami Cancer Institute**
Manmeet Ahluwalia, MD
Deputy Director and CSO

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Drug development strategy

On track for first-in-human (FIH) studies in Fall 2024 for our lead series targeting MGMT loss in cancer

<table>
<thead>
<tr>
<th>Year</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
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<tbody>
<tr>
<td>2023</td>
<td>MGMT Discovery</td>
<td>IND-enabling studies</td>
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<tr>
<td>2024</td>
<td></td>
<td>Phase I Trial</td>
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<td>Phase II</td>
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<td>2026</td>
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**Funding**

- **Seed-1 ($6.4M)**
- **Seed-2 ($4M)**

**Series A (~$40-60M Target)**

**Window for next funding round/exit**

(e.g., series B, partnership, acquisition)
Key milestones and deliverables supported by the Seed 2 round

- Declare first development candidate (DC) for the MGMT program
- Initiate IND-enabling studies and complete non-GLP toxicology studies
- Recruit VP of Drug Discovery (committed, contingent on Seed 2 closing)
- Initiate series A fund-raising with projects close by 4Q23-1Q24 (target $40-60M)
- Validation of efficacy in combination therapies for GBM (e.g., radiotherapy)
- Expand data set to support efficacy in non-CNS cancers (PDX and CDX in vivo studies)
- Establish key biomarkers for patient enrollment, dose selection, safety, and response