

Modifi Bio

Investor Deck

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



Ranjit Bindra, MD, PhD

Co-Founder and Chief Executive Advisor
Harvey and Kate Cushing Professor, Yale



Mike Dillon, PhD

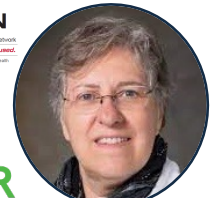
Senior Scientific Advisor
Founding CSO of IDEAYA

Scientific Advisory Board



Roger Stupp, MD

Chief of Neuro-Oncology at Northwestern University



Pat LoRusso, DO

Chief, Exp. Therapeutics
Yale Medical School



Kingson Lin, PhD, MD ('24)

Yale Medical School



Joseph Park, PharmD

Vice President, Corporate Development & Clinical Affairs



Bruce Ruggeri, PhD

Vice President, Pharmacology



Manmeet Ahluwalia, MD

Deputy Director and CSO
Miami Cancer Institute



Joseph Costello, PhD

Professor
UCSF



Kevin Rakin

Partner HighCape Capital



Kyle Tarantino, PhD

Director, Chemistry



Ashish Juvekar, PhD

Director, Biology



Jann Sarkaria, MD

Professor Mayo Clinic

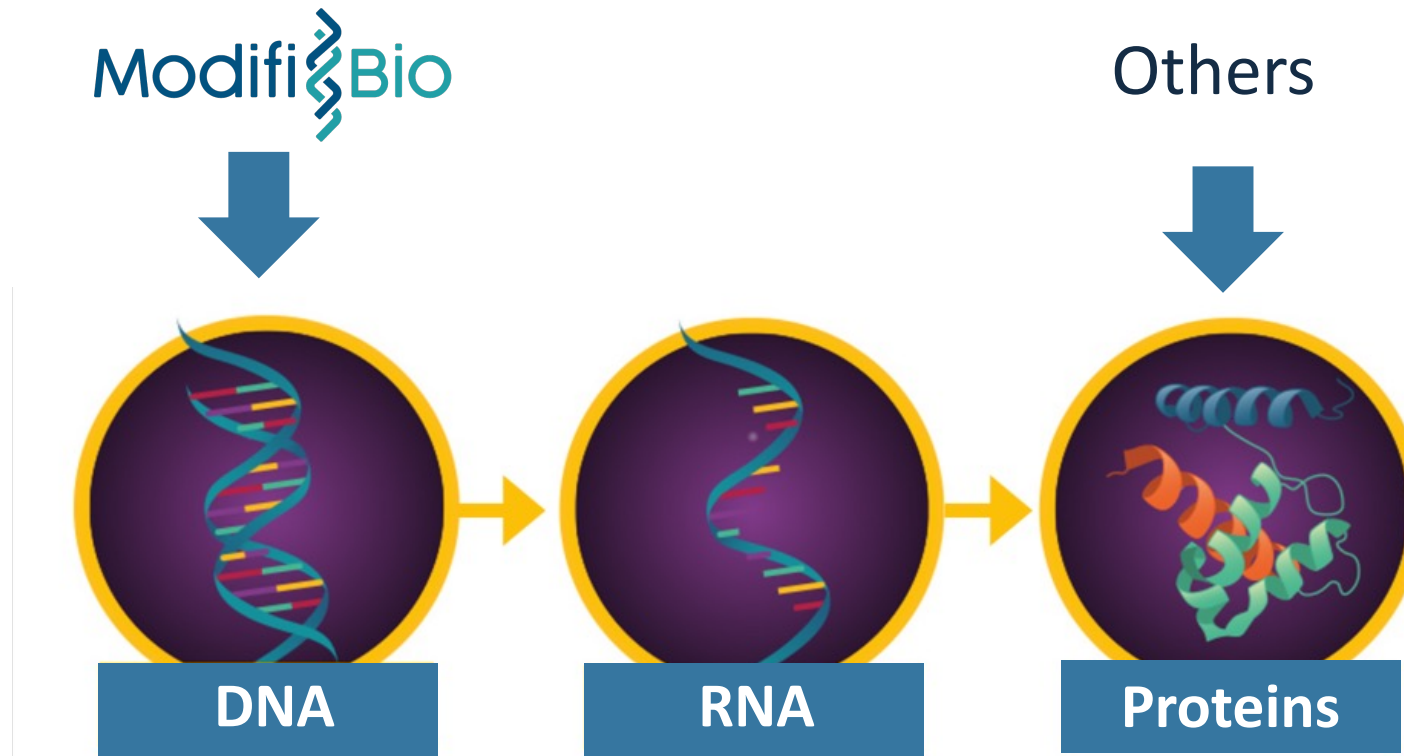


Peter Glazer, MD, PhD

Chair, Yale RadOnc



Drug discovery focused on direct tumor DNA modification



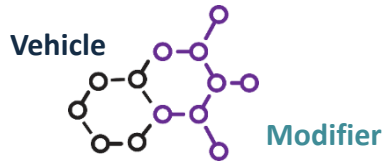
Disruption of DNA integrity is a proven approach to eradicate cancer

Modifi is exploiting cancer cell defects at the DNA level

Modifi Bio's Core Technology

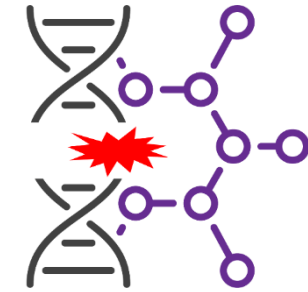


DNA **Modifiers**
(DMs)



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

Cancer Type	% MGMT Methylation
Glioma	40-80%
Lung Cancer	25-30%
Gastic Cancer	30%
Colorectal Cancer	30-40%
Cervical Cancer	30%
Pancreatic NENs	60-75%



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

CNS Cancers (Glioma)

1580 Neuro-Oncology
22(11), 1580–1590, 2020 | doi:10.1093/neuonc/noaa059 | Advance Access date 13 March 2020

MGMT promoter methylation level in newly diagnosed low-grade glioma is a predictor of hypermutation at recurrence

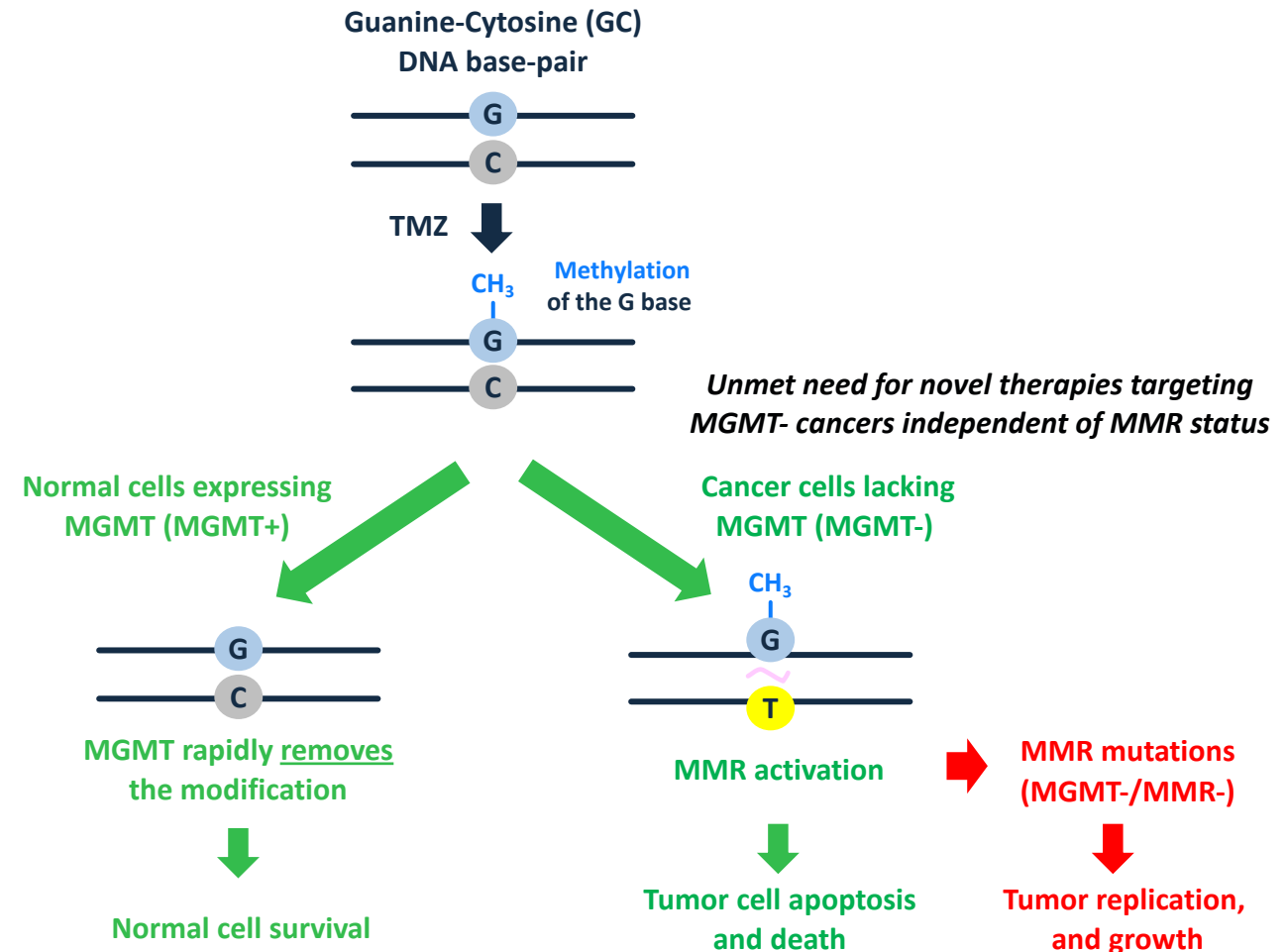
Non-CNS Cancers (Colon Cancer)

RESEARCH ARTICLE CANCER DISCOVERY

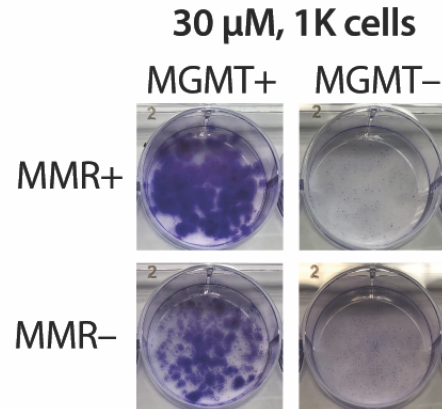
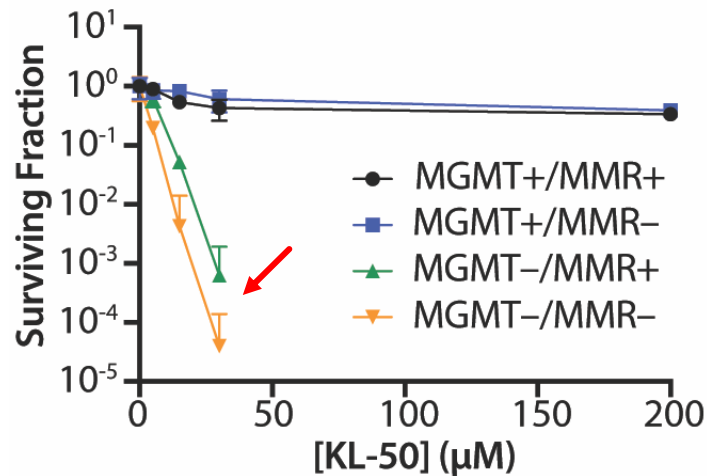
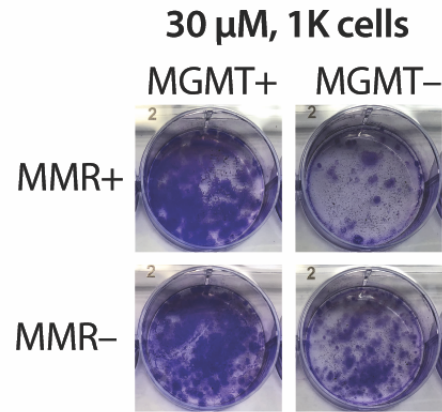
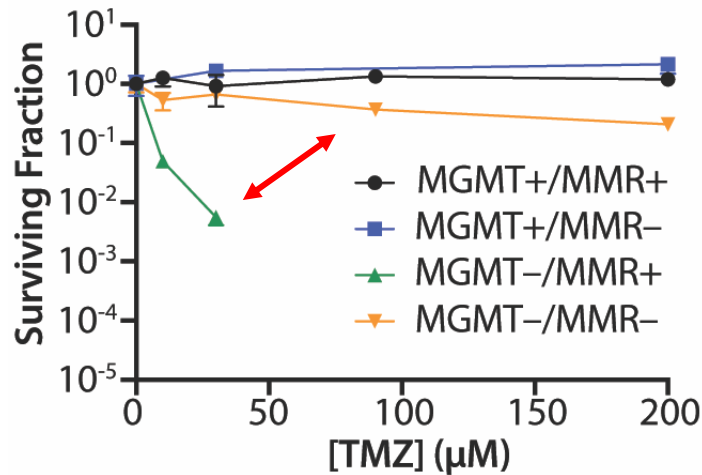
Temozolomide Treatment Alters Mismatch Repair and Boosts Mutational Burden in Tumor and Blood of Colorectal Cancer Patients

Giovanni Crisafulli^{1,2}, Andrea Sartore-Bianchi^{3,4}, Luca Lazzari⁵, Filippo Pietrantonio⁶, Alessio Amatu³, Marco Macagno⁷, Ludovic Barault^{1,2}, Andrea Cassingena³, Alice Bartolini⁸, Paolo Luraghi⁹, Gianluca Mauri^{4,5}, Paolo Battuello¹, Nicola Personeni^{7,8}, Maria Giulia Zampino⁹, Valeria Pessei⁷, Pietro Paolo Vitiello^{1,2}, Federica Tosi¹, Laura Idotta³, Federica Morano³, Emanuele Valtorta³, Emanuela Bonoldi³, Giovanni Germano^{1,2}, Federica Di Nicolantonio^{1,2}, Silvia Marsoni¹⁰, Salvatore Siena^{4,5}, and Alberto Bardelli^{1,2}

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



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



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

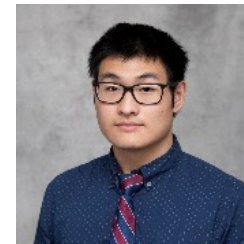
Science

RESEARCH

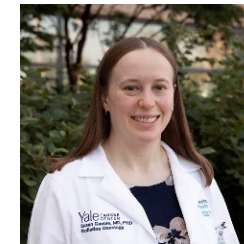
CANCER

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

Kingson Lin^{1,2,3†}, Susan E. Gueble^{2†}, Ranjini K. Sundaram², Eric D. Huseman¹,
Ranjit S. Bindra^{2,3*}, Seth B. Herzon^{1,4*}



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



S. Gueble, MD/PhD
Bindra Lab Alumni
RadOnc Attending ('23)



Yale SCHOOL OF MEDICINE

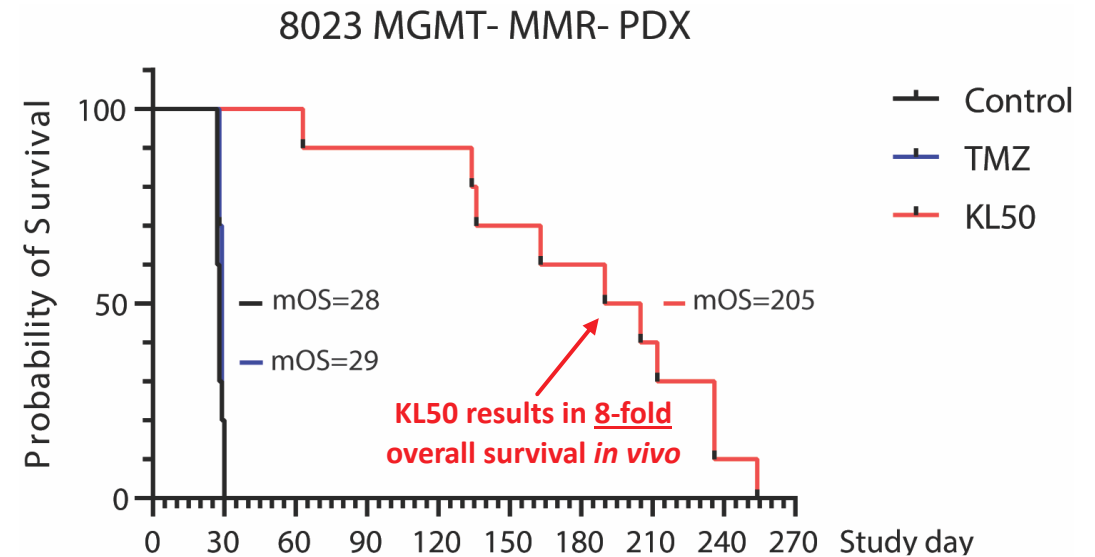
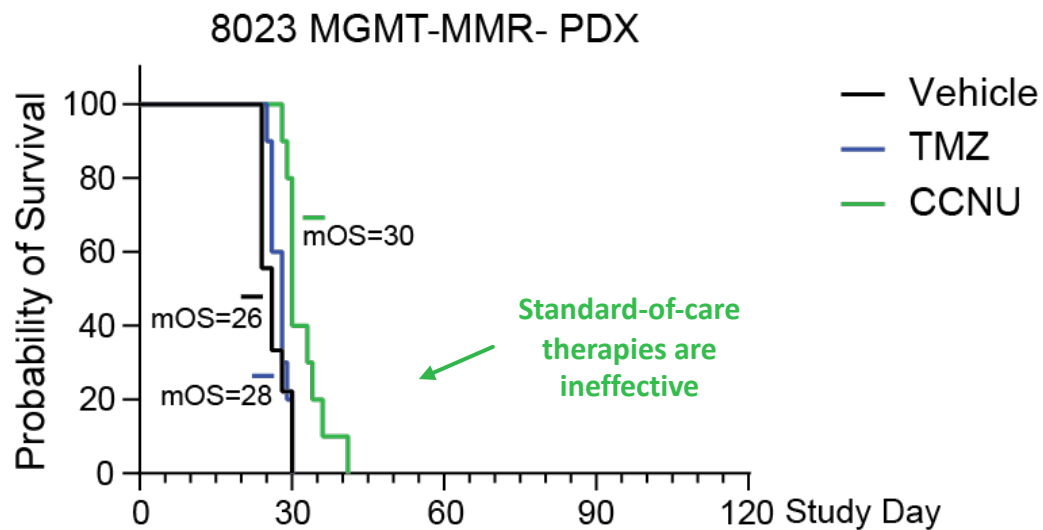


Robust KL50 efficacy in intracranial MGMT-/MMR- PDX glioma models with distinct profile from known alkylating agents

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

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

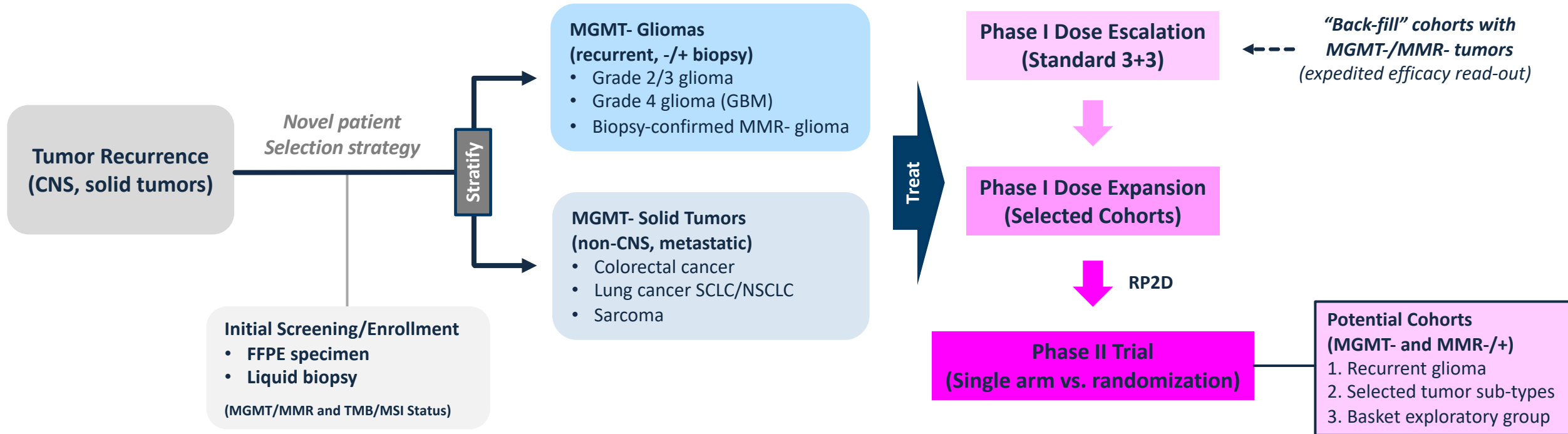
25mpk QDx5 PO every 28 days x 3 cycles



Sarkaria Laboratory – Mayo Clinic
(in collaboration with Modifi Bio)



Patient selection strategy in the Modifi O⁶ trial



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

Yale



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

N



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

Miami Cancer Institute

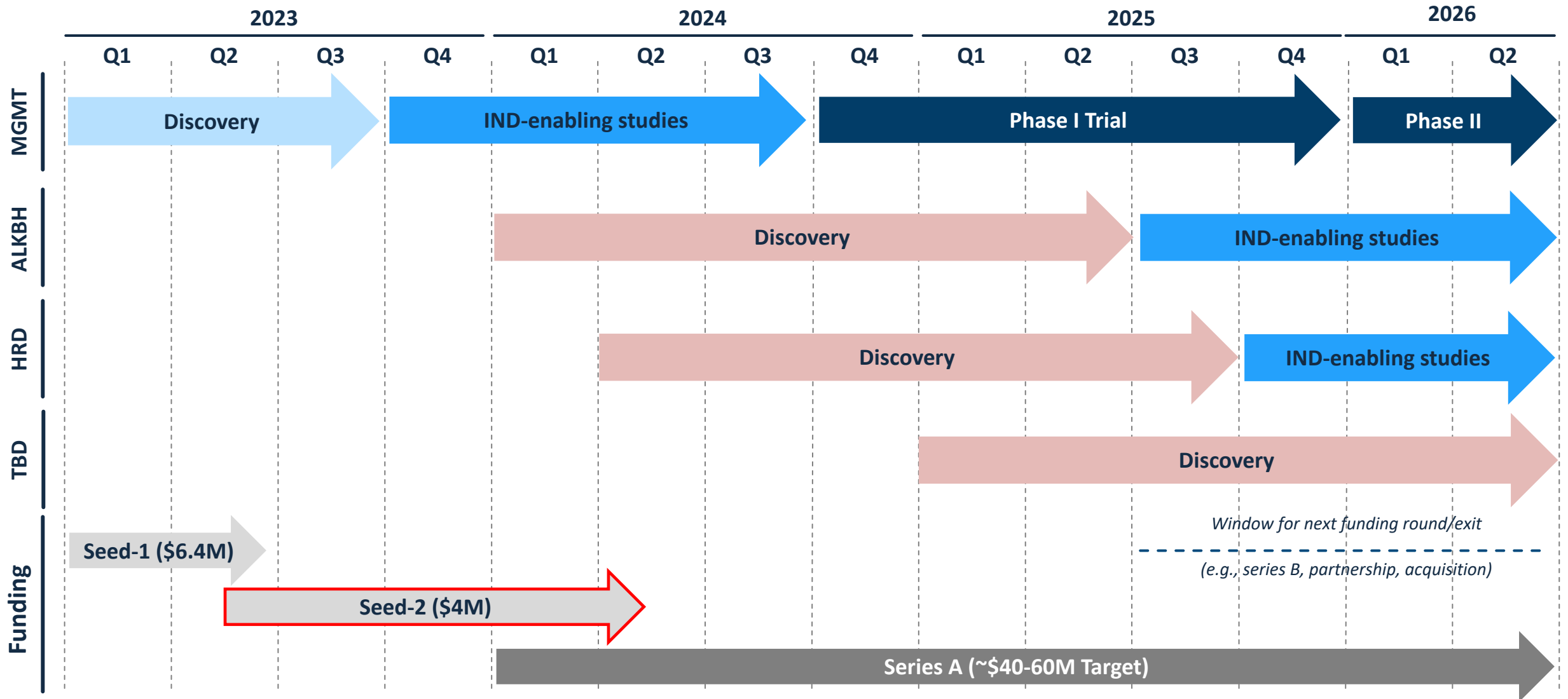


Manmeet Ahluwalia, MD
Deputy Director and CSO
Miami Cancer Institute



Drug development strategy

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



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

ModifiBio

Modifying DNA to Eradicate Cancer



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