November 2021

NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicines

Safe Harbor Statement

Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future financial performance of IDEAYA Biosciences, Inc. (the “Company”) and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “potential” or other comparable terminology. All statements other than statements of historical fact could be deemed forward-looking, including any expectations regarding the Company’s target discovery platform or new target validation efforts as creating opportunities for research and development initiatives; any projections of financial information, market opportunities, cash runway or profitability; any statements about historical results that may suggest trends for the Company's business; any statements of the plans, strategies, and objectives of management for development programs or future operations; any statements about the timing of preclinical research, clinical development, regulatory filings, manufacturing or release of data; any statements of expectation or belief regarding future events, potential markets or market size, technology developments, or receipt of cash milestones, option exercise fees or royalties; and any statements of assumptions underlying any of the items mentioned. The Company has based these forward-looking statements on its current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company's control. These and other important factors may cause actual results, performance or achievements to differ materially from those expressed or implied by these forward-looking statements. The forward-looking statements in this presentation are made only as of the date hereof. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see the Company's periodic filings with the Securities and Exchange Commission (the "SEC"), including its Quarterly Report on Form 10Q for the quarter ended September 30, 2021 and any current and periodic reports filed thereafter. Except as required by law, the Company assumes no obligation and does not intend to update these forward-looking statements or to conform these statements to actual results or to changes in the Company's expectations.

This presentation concerns anticipated products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). It is currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

IDEAYA Biosciences Highlights

Leading Synthetic Lethality (SL) focused biotechnology company advancing transformative precision medicine therapies for cancer patients

- **Broad Pipeline for Key Emerging Targets** including clinical stage IDE397 (MAT2A) and darovasertib (PKC), and development candidate selection for PARG and Pol Theta
- **Pharma Collaborations** with GSK (over ~$3 billion in potential milestones) and Pfizer
- **Strong Balance Sheet** with ~$386 M in cash anticipated to fund operations into 2025 [1, 2]
- **NASDAQ**: IDYA

- **Target Catalysts**
  - IDE397 Phase 1
    - Cohort Expansions (H1 2022)
    - GSK Option Package & Clinical Data Update (H1 2022)
  - PARG Development Candidate Lead Nominated
  - Pol Theta Development Candidate (December 2021)
  - Darovasertib (IDE196) Phase 1/2
    - Clinical Data Update for IDE196 + Crizotinib (Q4 2021)
    - Regulatory Guidance for IDE196 + Crizotinib (H1 2022)

(1) IDEAYA Form 10Q and Q2 2021 Financials filed with the U.S. Securities and Exchange Commission on November 15, 2021
(2) Includes cash, cash equivalents and marketable securities as of September 30, 2021

Synthetic Lethality

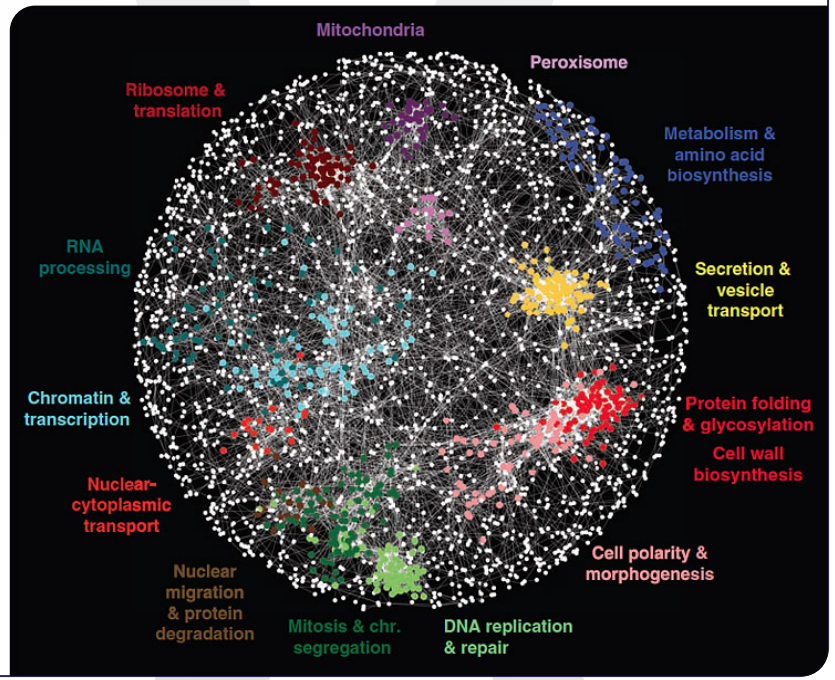
The Next Frontier in Precision Medicine Oncology

Synthetic Lethality provides a powerful approach to discover novel precision medicine therapies with patient biomarkers, including MTAP-deletion (~15% of solid tumors), BRCA/HRD (Breast, Prostate, Ovarian), and high-MSI (15% GI Cancers)

nature REVIEWS GENETICS

- **Synthetic lethality** occurs when the simultaneous perturbation of two genes results in cell death
- Synthetic lethality provides a novel approach to target several historically undruggable loss of function mutations
- Large-scale screening for synthetic lethal targets has progressed through advances in molecular biology (e.g., RNA interference, CRISPR-Cas9 editing) and bioinformatics

Nature Reviews Genetics, Vol. 18, 2017, Hieter, et al. , as edited by IDEAYA



Reference: Charles Boone

IDEAYA BIOSCIENCES

IDEAYA's Precision Medicine Oncology Pipeline

Building the Industry Leading Synthetic Lethality Focused Biotechnology Company

Precision Medicine Pipeline

	Modality/Indication	Biomarker	Preclinical	IND Enabling	Phase 1	Phase 2	Program Goals	Collaborations	Commercial (IDEAYA)
IDE397 *MAT2A*	Monotherapy Solid Tumors	MTAP					Cohort Expansion H1 2022 Option Package & Clin Data Update H1 2022	gsk (1)	US 50/50 Profit Share Ex-US Royalties
	Combinations Solid Tumors	MTAP					Preclinical Data to enable Combos (Taxanes, PRMTi, Others)		
PARG	Ovarian, Gastric, Breast Cancers	HRD					Development Candidate Lead Selected	CANCER RESEARCH UK (2)	WW Commercial Rights
Pol Theta	Small Molecule Protein Degraders	HRD					Select Small Molecule Helicase Inhibitor Development Candidate December 2021	gsk (1)	Global Royalties
WRN	GI Cancers	High-MSI					Chemistry Lead Optimization	gsk (1)	US 50/50 Profit Share Ex-US Royalties
MTAP-SL	Solid Tumors	MTAP					Lead Series		WW Commercial Rights
SL Platform	Solid Tumors	Defined Biomarker					Lead Series New Target / Biomarker Validation		WW Commercial Rights
Darovasertib *PKC*	Monotherapy MUM, UM Adjuvant	GNAQ/11					Expand to UM Adjuvant - IST H1 2022		WW Commercial Rights
	+MEK, +cMET Combos MUM	GNAQ/11					Clinical Data – IDE196 + Crizotinib Q4 2021 Regulatory Guidance H1 2022	Pfizer (3)	
	GNAQ/11 Basket Skin, Mucosal	GNAQ/11					Enhance enrollment of GNAQ/11 Basket		

(1) Pursuant to GSK Collaboration, Option and License Agreement: MAT2A and WRN: 50/50 US Profits + ex-US Royalties; Polθ: Global Royalties
(2) Pursuant to CRUK Evaluation, Option and License Agreement, with ongoing Collaborative Research; IDEAYA controls all Commercial Rights
(3) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreement for MEK and cMET Combinations; IDEAYA retains all IDE196 Commercial Rights

= Target Program Milestone

MAT2A=methionine adenosyltransferase 2a, MTAP=methylthioadenosine phosphorylase, PARG= poly (ADP-ribose) glycohydrolase, DDT = DNA Damage Target, WRN = Werner Helicase, Polθ = DNA Polymerase Theta, HRD = homologous recombination deficiency, MSI = microsatellite instability, PKC = protein kinase C, MUM = metastatic uveal melanoma, MEK = binimetinib, cMET = crizotinib, SWS = Sturge Weber Syndrome, PWS = Port Wine Stain, WW = worldwide

IDEAYA Leadership Team and Scientific Advisory Board

Experienced Team & Scientific Thought Leaders in Precision Medicine Oncology

IDEAYA Executives & R&D Leadership

Yujiro Hata, M.B.A.
President, Chief Executive Officer, Director
FLEXUS BIOSCIENCES · Bristol-Myers Squibb · ONYX PHARMACEUTICALS · ENANTA Pharmaceuticals · AMGEN

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SVP, Chief Scientific Officer, Head of Research
Pfizer · UT Southwestern Medical Center

Paul Stone, J.D.
SVP, Chief Financial Officer
5AM VENTURES · ILYPSA · AMGEN

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Genentech · AMGEN

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SVP, Head of Drug Discovery
5AM VENTURES · nurix · NOVARTIS · CHIRON

Jason Throne, J.D.
SVP, General Counsel
neotract · THORATEC CORPORATION

IDEAYA Scientific Advisory Board

William Sellers, M.D.
Broad Institute, Dana Farber, and Harvard, Professor
Novartis, Former Head Oncology Research,
SL Project Drive initiative

Frank McCormick, Ph.D.
UCSF, Professor and former Director,
Helen Diller Cancer Center
Former President AACR; Founder and CSO, Onyx

Trey Ideker, Ph.D.
UCSD, Professor, Co-Director Cancer Genomes & Networks Program, Research in Dual-CRISPR and SL interaction maps

Brian Daniels, M.D.
Bristol Myers Squibb, Former SVP Global Development & Medical Affairs

Elizabeth Swisher, M.D.
University of Washington, Professor; Co-Leader, Breast and Ovarian Cancer Research Program, Seattle Cancer Care Alliance
Principal Investigator on multiple PARP inhibitor trials

Jeffrey Hager, Ph.D.
Former Chief Technology Officer, IDEAYA

IDEAYA BIOSCIENCES

IDEAYA and GSK Strategic Partnership

Landmark Partnership in Synthetic Lethality

Transformative Strategic Partnership

- Validates IDEAYA Synthetic Lethality platform
- Creates strategic combination opportunities
- Advancing small molecules and protein degraders

Key Partnership Terms

- $100M cash upfront
- $20M equity investment as direct private placement
- $50M option exercise fee for MAT2A
- Over $3 billion in potential Milestone Payments, including approximately $1 billion per program
- 50/50 US profit share for MAT2A and Werner Helicase
- 20% cost share allocated to IDEAYA for MAT2A, Werner
- Royalties tiered high single-digit to sub-teen double digit %

MAT2A (MTAP Deletion)

- $50M Option Fee, 50/50 US Profit Share & ex-US Royalties
- Option Data Package based on Clinical Dose Escalation Data
- ~$1B potential Milestone Payments
- Evaluating multiple clinical combination opportunities

Werner Helicase (MSI High)

- 50/50 US Profit Share and ex-US Royalties
- ~$1B potential Milestone Payments
- Potential Combination with GSK's Dostarlimab, a PD-1 IO Agent

Pol Theta (BRCA/HRD)

- GSK covers all Costs
- Global Royalties and ~$1B potential Milestone Payments
- Potential Combination with GSK's Zejula™, a PARP Inhibitor

IDEAYA Form 8-K filed with the U.S. Securities and Exchange Commission on June 16, 2020; GlaxoSmithKline Q2 2020 Earnings Presentation

IDEAYA Synthetic Lethality Platform

Fully-Integrated Target, Biomarker, Drug Discovery and Translational Capabilities

SL Target & Biomarker Discovery and Validation

Bioinformatics, including AI Algorithms

Dual CRISPR, CRISPR, siRNA

Genetically Engineered Models

- Key emerging SL targets identified, such as Werner Helicase, Pol Theta and PARG
- DECIPHER™ - Dual CRISPR SL Library in DDR in collaboration with UCSD
- PAGEO™ - Paralogous Gene Evaluation in Ovarian in collaboration with Broad Institute

Drug Discovery and Pharmacological Validation

Structure Based Drug Design

Small Molecule Chemistry

Protein Degrader Capabilities

- Crystal structures for five SL programs obtained to enable structure-based design
- Differentiated candidate compounds discovered, including IDE397
- Protein degraders advancing for selected targets, including Pol Theta

Translational Research and Opportunity Expansion

Genomics – DNA and RNA Analysis

Proteomics – Protein Expression Profiling

Tissue (IHC, IF) and Liquid Biopsies Analysis

- Translational research to define clinical biomarkers
- Opportunity expansion through broad cell panel screening
- Pharmacodynamic biomarker analysis to confirm target modulation and correlation with clinical activity

IDEAYA Synthetic Lethality Platform

Synthetic Lethality Target and Biomarker Discovery and Validation

Synthetic Lethality Target Discovery & Validation Platform

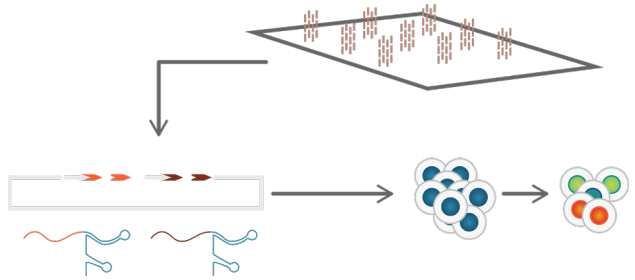
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

Bioinformatic analysis enables identification and validation of synthetic lethal target / biomarker interactions across vast datasets

Robust SL interactions validated genetically (Dual CRISPR, paralogues, isogenic pairs, CRISPR/siRNA), pharmacologically, & *in vivo*

DECIPHER™

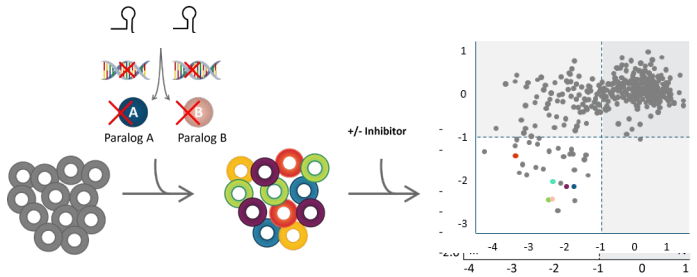
Dual CRISPR SL Library in DNA Damage Repair [2]



Evaluation of DNA Damage Targets synthetic lethal with tumor suppressor or oncogenes

PAGEO™

Paralogous Gene Evaluation in Ovarian Cancer [1]



Evaluation of SL targets in context of functionally redundant paralogous genes in ovarian cancer

Partnership Datasets

Cancer Dependency Map – Broad Institute

Foundation Insights™ – Foundation Medicine

depmap portal FOUNDATIONINSIGHTS™

Public Databases

IDEAYA data mining and analysis across data sets

PROJECTGENIE TCGA MSK-IMPACT™ Project Achilles BioPortal CCLE

>20 Novel Drug Targets Identified
Target Validation Ongoing

[1, 2] IDEAYA Proprietary Libraries and Datasets – Strategic Collaborations with Broad Institute[1] and UC San Diego[2]

IDEAYA's Synthetic Lethality Pipeline Strategy

Building the Industry Leading Synthetic Lethality Focused Biotechnology Company

Focus on Potential *First-in-Class* Synthetic Lethality Programs to Deliver Patient Breakthroughs

Patient Impact: Potential First-in-Class / Best-in-Class

Significant Opportunities: Large Target Patient Populations

Precision Medicine: Compelling Patient Selection and Pharmacodynamic Biomarkers

Synthetic Lethality Platform: Deep and rich Target Pipeline with ongoing Target Identification and Validation

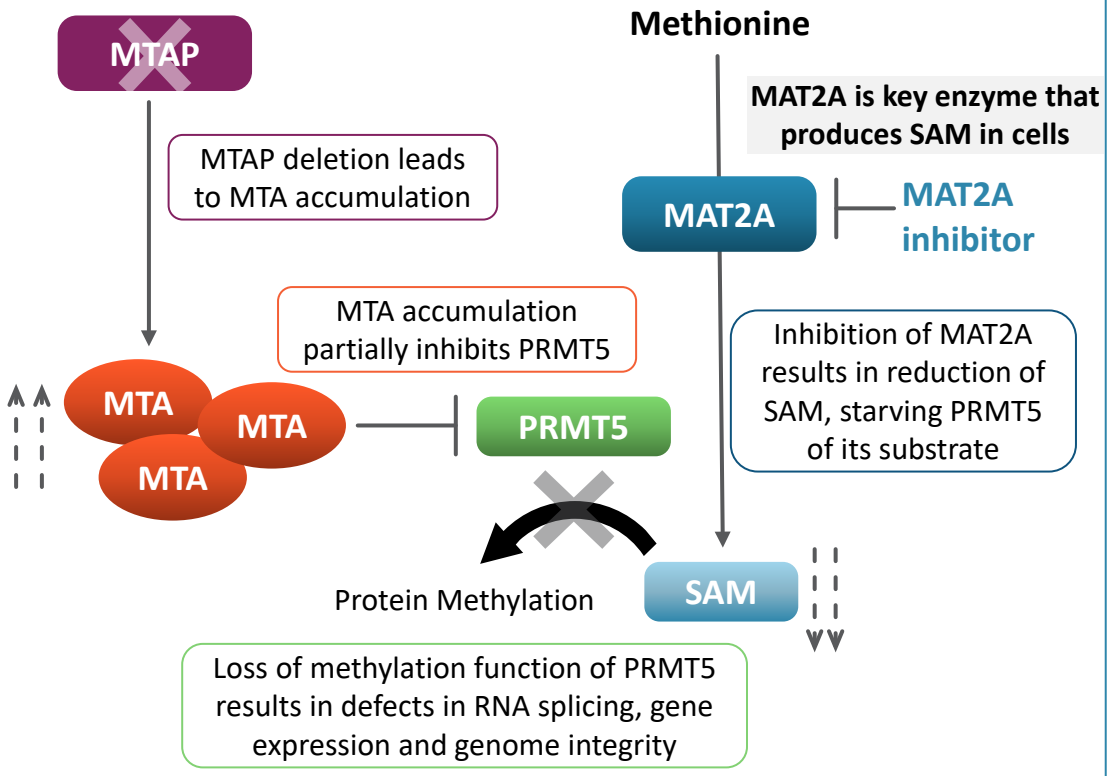
MTAP Deletion	HRD / BRCA	MSI-High	GNAQ/11	SL Platform
IDE397 (Ph1) MTAP-SL (PC)	PARG (DC) Pol Theta (Late PC) Pol Theta Degrader (PC)	Werner (PC)	Darovasertib (Ph2) Daro + cMET (Ph2) (SL Combination)	Novel Targets

PC = Preclinical Stage, DC = Development Candidate Stage, Ph2 = Phase 2

MAT2A Inhibition is Synthetic Lethal with MTAP Deletion

MTAP Deletion Prevalence ~15% of all Solid Tumors

MTAP-MAT2A Synthetic Lethality Biology



MTAP Deletion Prevalence

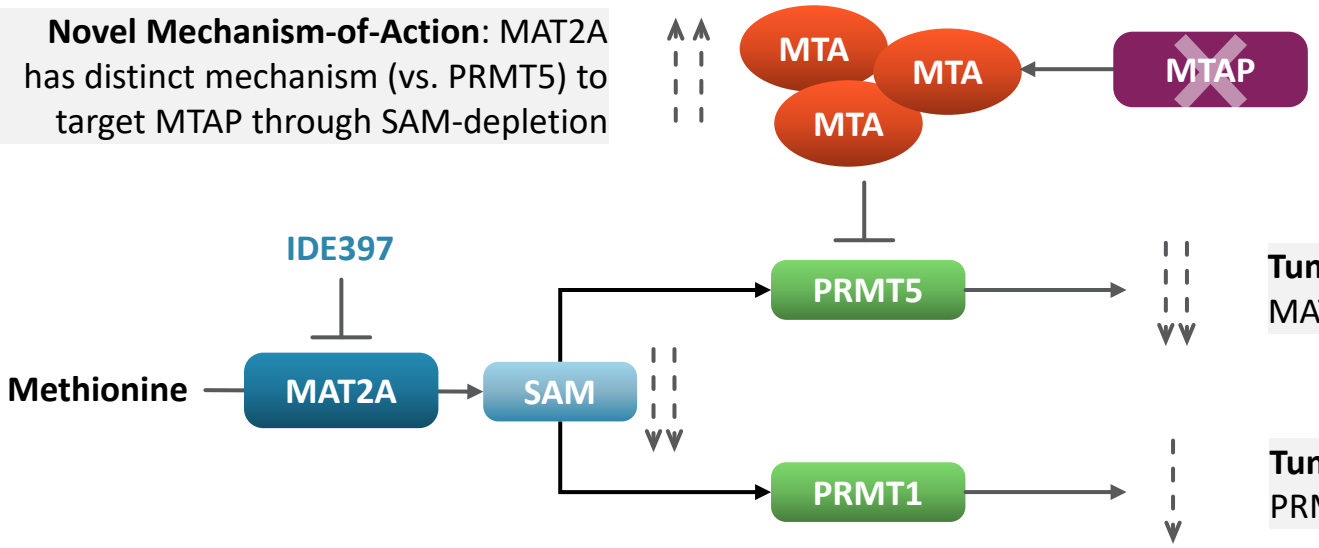
Cancer Type	N	MTAP Deletions (%)
Glioblastoma	592	41
Mesothelioma	87	32
Esophageal	95	28
Bladder	411	26
Pancreatic	184	22
Melanoma	448	16
Lung Cancer (NSCLC)	1053	15
Head and Neck	523	14
Sarcoma	255	10
Esophagogastric	514	10
Diffuse Glioma	513	9
Breast	1084	3
Ovarian	585	3
Adrenocortical	92	3
Thymic	123	3
Hepatocellular	369	3
Renal non-clear cell	348	2

Data from The Cancer Genome Atlas in cBioPortal

MAT2A Has Novel Mechanism vs PRMT5 to Target MTAP Deletion Through SAM Depletion and Inhibition of a Selective-Essential Gene

MAT2A Mechanism and Biology

Novel Mechanism-of-Action: MAT2A has distinct mechanism (vs. PRMT5) to target MTAP through SAM-depletion

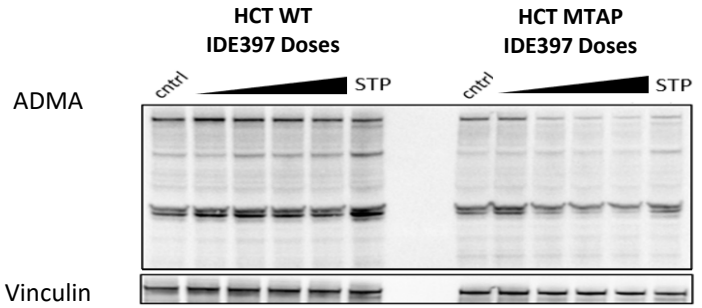


MTAP Biomarker: MAT2A is a Selective Essential Gene in presence of MTAP (vs PRMT5 = Pan Essential Gene), which may enhance Therapeutic Index and Combination Potential vs. PRMT5

Tumor SDMA: PD biomarkers preclinically correlate with efficacy; MAT2A inhibition shows robust modulation of specific SDMA substrates

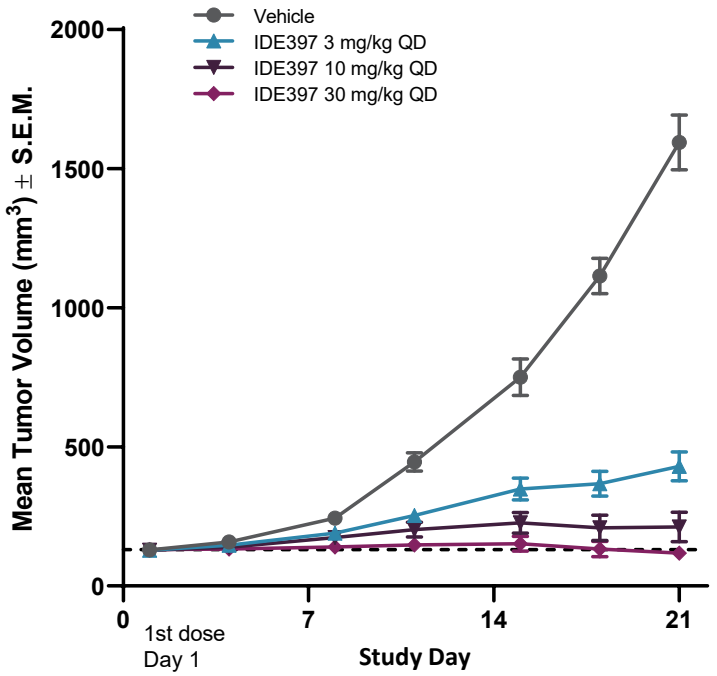
Tumor ADMA: downstream PD biomarker reduced in preclinical studies PRMT5 mechanistically not anticipated to reduce ADMA-levels

Pharmacodynamic Biomarkers: IDE397 reduction of proximal plasma and tumor SAM demonstrates robust target engagement preclinically



IDE397 Monotherapy Demonstrates Tumor Regressions and Robust SAM and SDMA Tumor PD Modulation in CDX Xenograft models

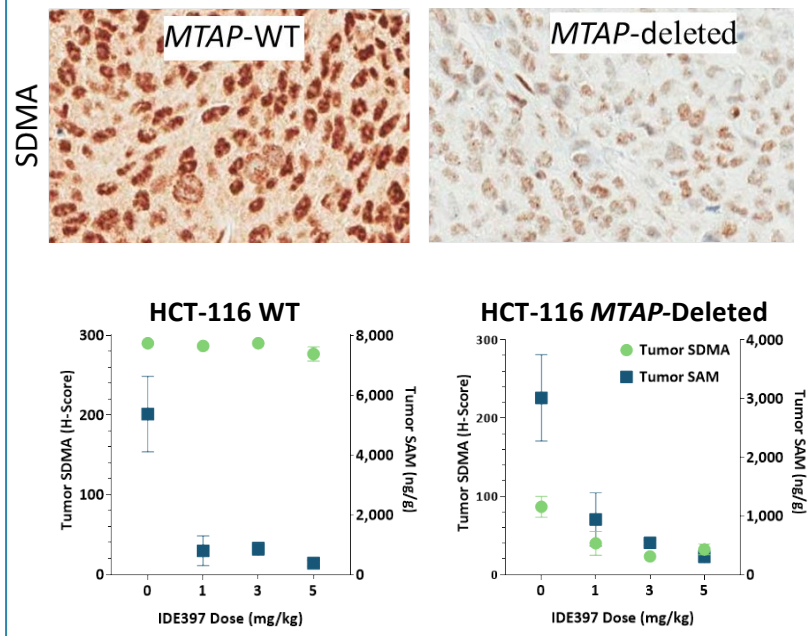
NSCLC Endogenous MTAP-/- CDX Model



IDEAYA Data

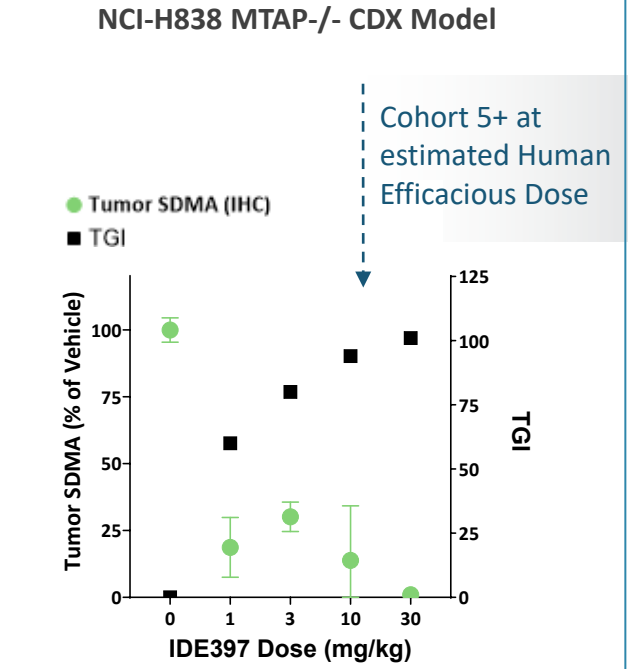
SDMA and SAM are Proximal PD Biomarkers of MAT2A inhibition

IDE397 modulates SDMA and SAM



IDEAYA Data: Fischer et. al., AACR 2021

SDMA modulation correlates to TGI



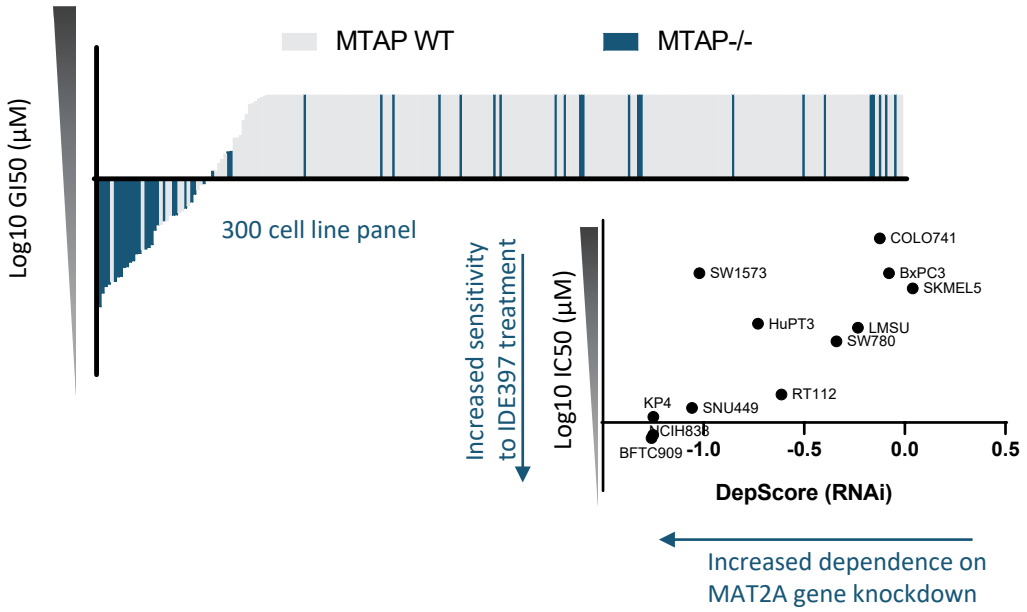
IDEAYA Data

Robust dose-dependent efficacy and PD modulation observed in NSCLC CDX Model

IDE397: MAT2A Development Candidate *in vitro* Profile

IDE397 is selective for MTAP-/- Cell Lines

IDE397 is Selective for MTAP-/- Cell Lines

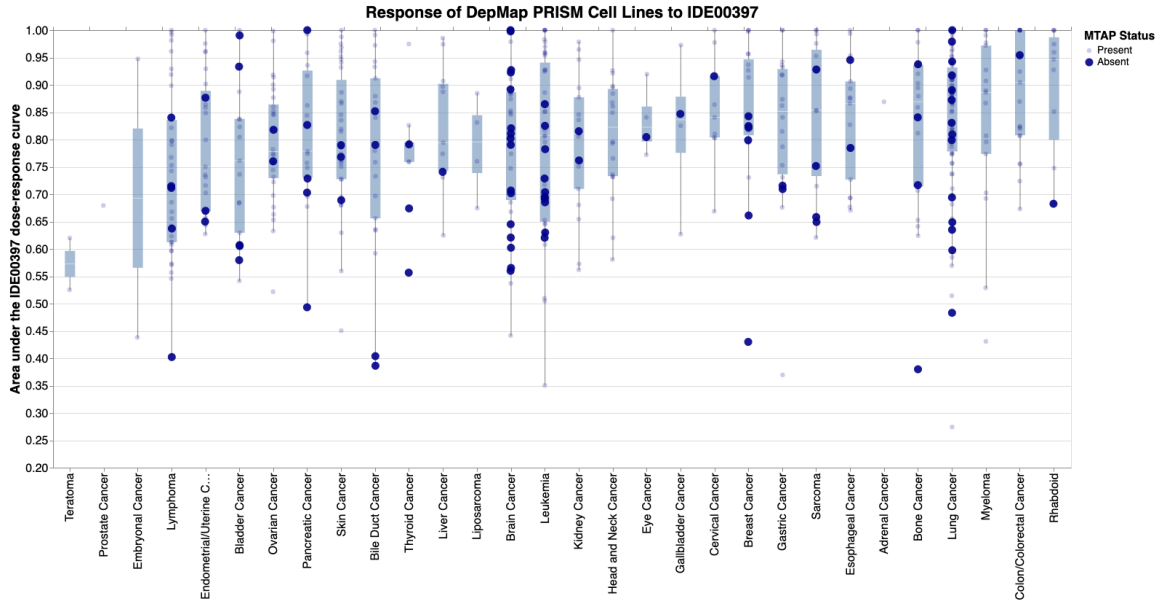


MTAP-/- cell lines are sensitive to IDE397

MTAP WT cell lines are generally insensitive

Pharmacological inhibition correlates with MAT2A genetic knockdown

IDE397 has Broad Activity across Tumor Types



~800 cell line panel

Differential sensitivity across tumor types; potential for discovery of additional predictive biomarkers

MTAP gene expression and copy number loss emerge as top predictors of sensitivity across cell lines

IDEAYA Data

IDEAYA Analysis / PRISM Screen - Broad DepMAP Consortium

IDE397: MAT2A Inhibitor

Preclinical Evaluation of IDE397 – Differentiated Profile and Selective for MTAP-/- Cell Lines

IDE397 Target Product Profile

IDE397 demonstrates superior cellular potency and selectivity compared to AG-270

IDE397 has not caused preclinical liver injury or increased bilirubin

- Not an inhibitor of UGT1A1 (AG-270 noted to inhibit UGT1A1)[1] or BSEP transporters at relevant concentrations
- Liver injury not observed in preclinical tox studies

IDE397 has favorable physical properties, including solubility

- AG-270 observed non-linear exposure >200mg QD (GI absorption)

IDE397 demonstrates *in vivo* efficacy and PD modulation at 5 to 30mg/kg

- AG-270 published preclinical dose typically 200mg/kg QD [1]

Biochemical and *in vitro* Potency and Selectivity

	IDE397	AG-270
MAT2A biochemical IC_{50} (nM)	7	12
KP4 EC_{50} cellular (nM) MAT2A dependent	15	731
BXPC3 cellular EC_{50} (nM) MAT2A independent	13200	1630
HuCCT1 cellular EC_{50} (nM) MAT2A independent	>20000	**1400**

Differentiating ADME/Physicochemical Properties

	IDE397	AG-270
BSEP inhibition @10µM (%)	1	**25.2**
UGT1A1 inhibition (%)	34	83
PXR Emax @30 µM (%)	9	**35**
Solubility @pH 7.4 (µM)	>100µM	**BLOQ***

IDEAYA Data

*BLOQ = below limit of quantitation

(1) Agios, AACR 2019, Keystone 2019, Triple Meeting 2019 (Webcast Call Q&A), J Med Chem 2021

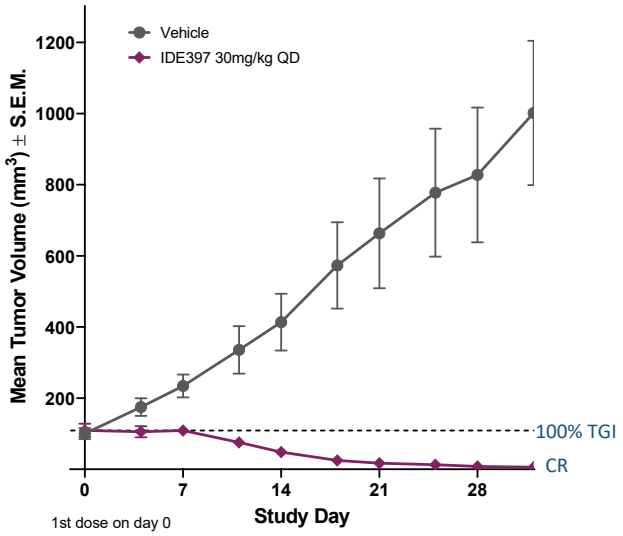
IDEAYA BIOSCIENCES

IDE397: PDX Study of >40 MTAP-/- Models in Multiple Indications

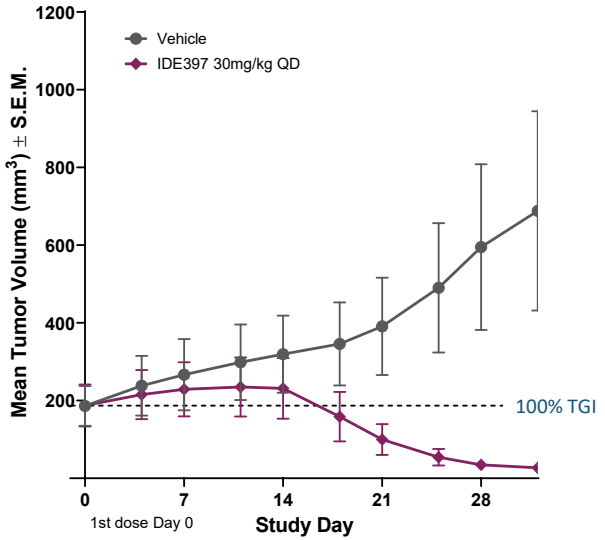
Monotherapy Tumor Regressions & Significant TGI Across Multiple Solid Tumor Types

NSCLC and Bladder Cancer MTAP-/- PDX Models

NSCLC PDX Model

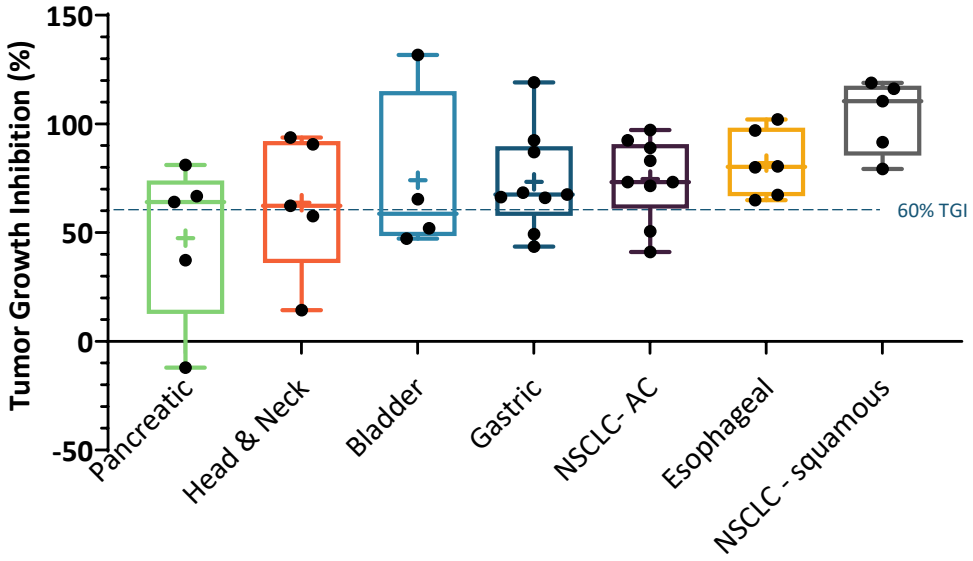


Bladder PDX Model



IDEAYA Data

Panel Study of >40 MTAP-/- PDX Models



IDEAYA Data: Fischer et. al., AACR 2021

IDE397 evaluation in Patient Derived Xenograft (PDX) models with homozygous MTAP deletions in Solid Tumors

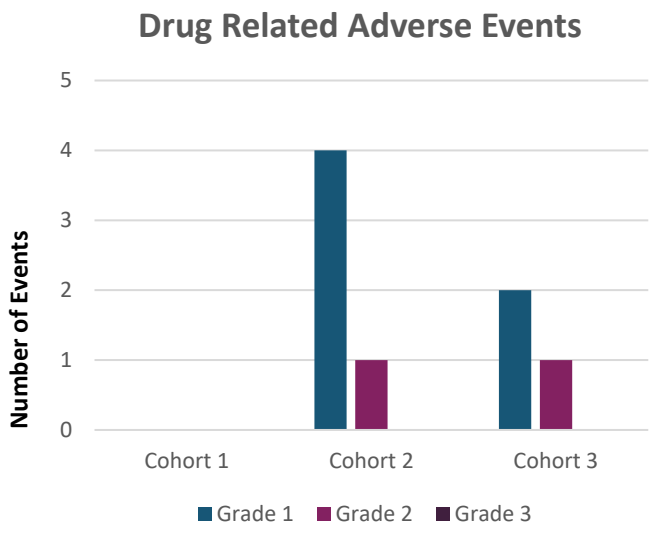
- Tumor Regressions (≥ 100% TGI) observed in multiple PDX models / indications, including in 3 of 5 NSCLC squamous models, with 1 CR
- Observed > 60% TGI in 12 of 14 NSCLC PDX models, including in 7 of 9 adenocarcinoma and in 5 of 5 squamous carcinoma PDX models

TGI = Tumor Growth Inhibition, CR = Complete Response

Observed Preliminary IDE397 Clinical Activity and Tolerability

Plasma PD Reduction and Tumor Shrinkage in MTAP Deletion Patients

IDE397 Safety / Tolerability

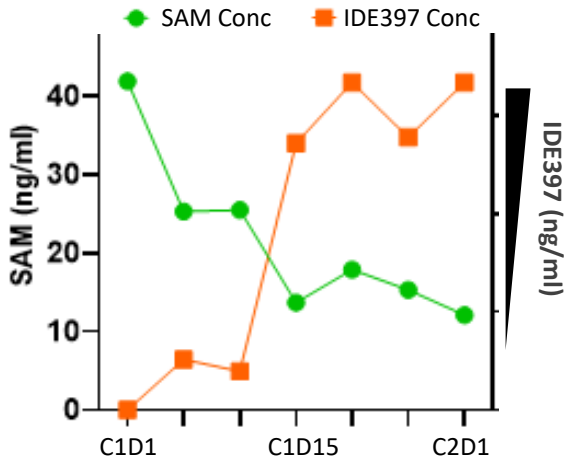


Cohorts 1 thru 3

IDE397 Plasma SAM PD

PK / PD Analysis

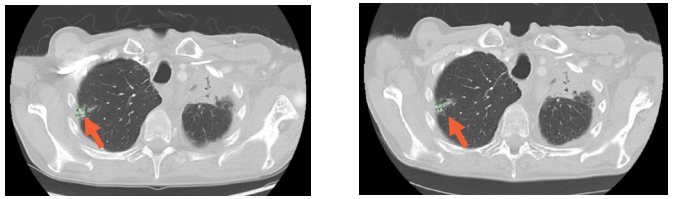
Plasma SAM vs IDE397 Concentration



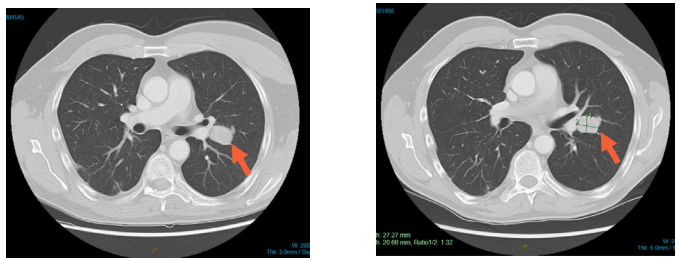
Cohort 3 Patient

Observed Tumor Shrinkage

Baseline CT Scan | Early Treatment Scan



Cohort 2 NSCLC: 15% Reduction*



Cohort 3 ACC with Lung Mets: 11% Reduction*

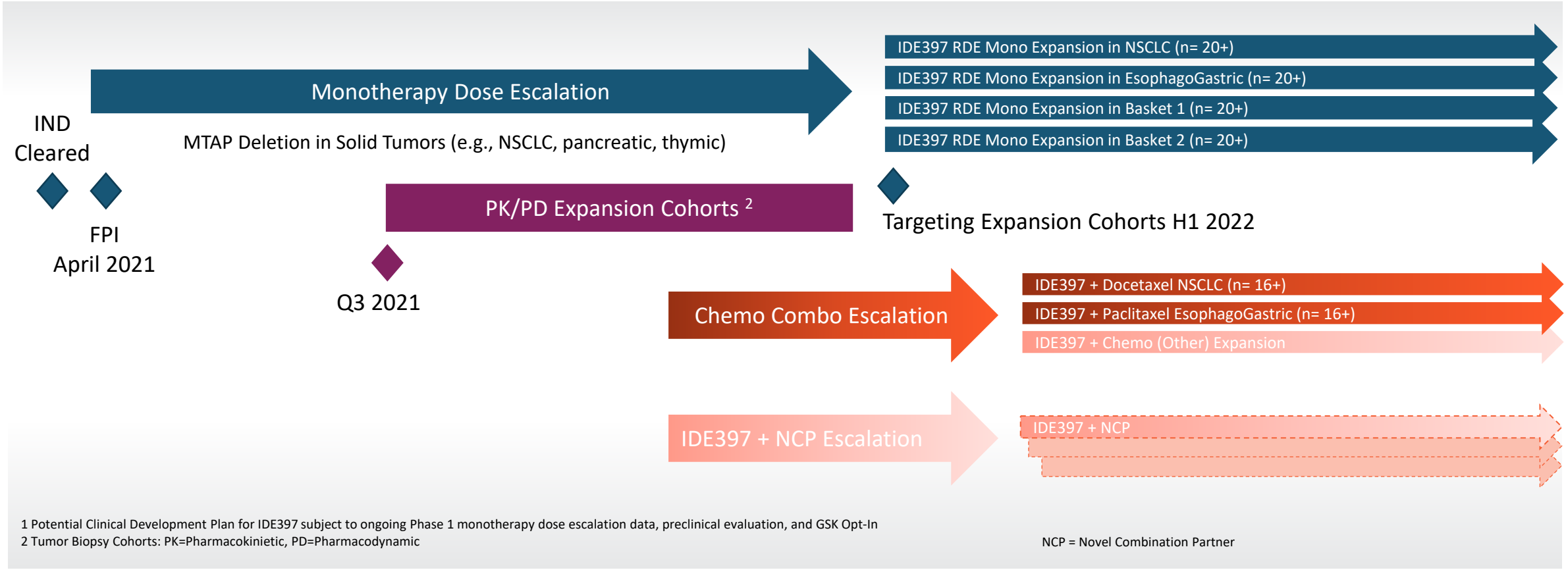
- No drug-related Serious Adverse Events: drug-related adverse events have been Grade 1/2, with no reported myelosuppression or liver toxicity
- Observed plasma SAM PD reduction in early dose escalation Cohorts 1 thru 3, achieving predefined target ≥ 60% plasma SAM suppression
- Observed tumor shrinkage in MTAP-deletion patients in early dose escalation Cohorts 2 and 3
- 80+ year-old Cohort 2 patient with large thymic carcinoma mediastinal remains on treatment after almost 6 months
- Enrolling Cohort 5; Maximum Tolerated Dose (MTD) has not yet been established

IDEAYA Data: drug related adverse events as of November 5, 2021; plasma SAM reduction as of September 29, 2021; NSCLC Non-small cell lung cancer; ACC Adenoid Cystic Carcinoma; *reported reduction in target lesions

IDE397 Phase 1 Clinical Trial

Comprehensive Approach for Concurrent Evaluation of Monotherapy and Combinations

Phase 1 Dose Escalation and Expansion Strategy [1]



1 Potential Clinical Development Plan for IDE397 subject to ongoing Phase 1 monotherapy dose escalation data, preclinical evaluation, and GSK Opt-In
2 Tumor Biopsy Cohorts: PK=Pharmacokinetic, PD=Pharmacodynamic

NCP = Novel Combination Partner

Addressable Patient Population of ~75,000 estimated in US, EU5 and JP across six indications, including NSCLC, head and neck, bladder, gastric, pancreatic and esophageal cancers

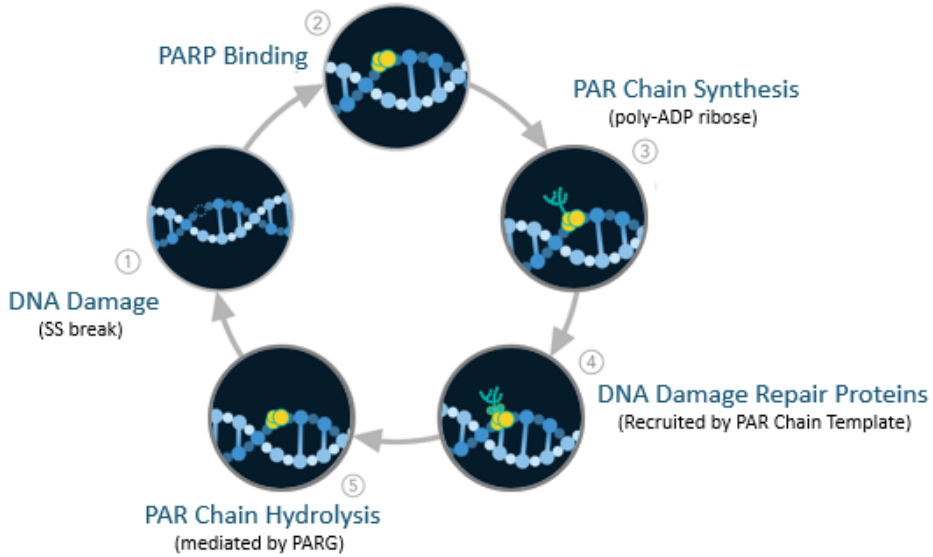
PARG Synthetic Lethality Program

Development Candidate Lead Selected

PARG Biology

Novel target in Clinically Validated Pathway

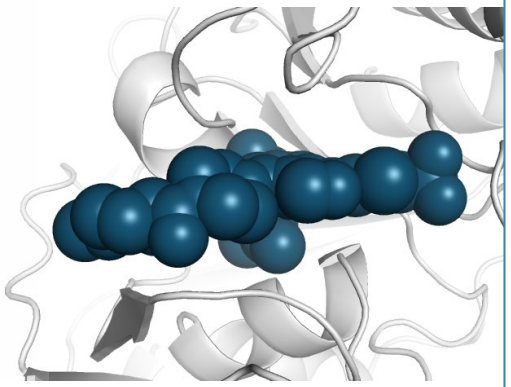
Poly(ADP-ribose) glycohydrolase (PARG) regulates DNA repair by hydrolyzing PAR chains in final step of DDR cycle



Cancer Research (Aug 2019), Cancer Research (Jul 2019), Cancer Cell (Mar 2019)

PARG Drug Discovery Program

Key Emerging Target with lead optimization program guided by structure-based drug design to identify potent, selective candidates



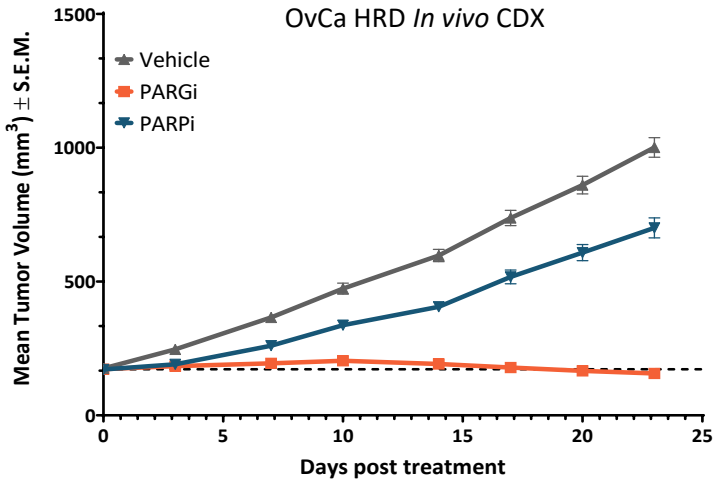
- Multiple potent cellularly active compounds demonstrate *in vitro* and *in vivo* PAR accumulation (PD) and *in vivo* efficacy in defined biomarker setting
- Collaboration with Bill Sellers lab (Broad) established to identify additional genetic sensitizers to PARGi

IDEAYA Data

Biomarker Selected *in vitro & in vivo* Models are Sensitive to IDEAYA PARGi

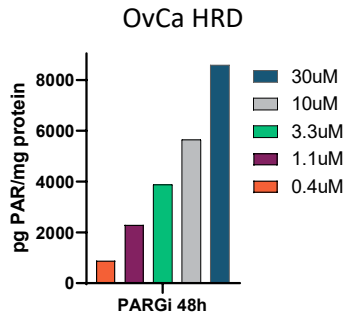
Differentiated Activity to PARP inhibition in Ovarian, Gastric and Breast Cancer Models

Ovarian Cancer HRD Cell Line Models

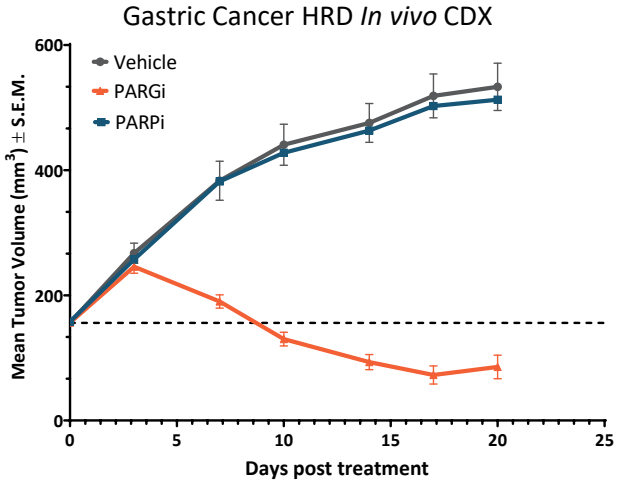


PARGi Tumor Regression and enhanced TGI relative to PARPi

Dose-dependent poly-PAR (PD) accumulation

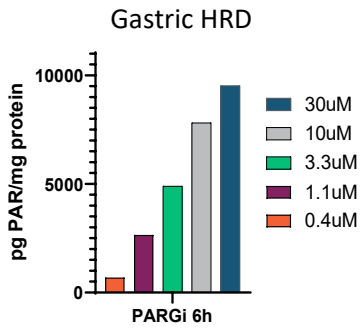


Gastric Cancer HRD Cell Line Models

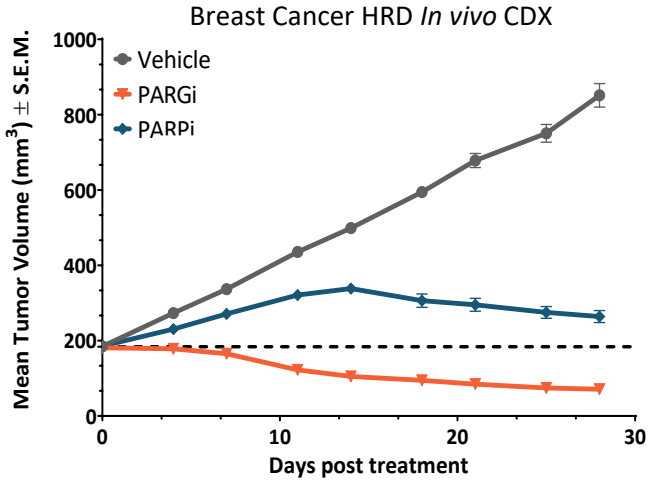


PARGi Tumor Regression in PARPi Refactory Setting

Dose-dependent poly-PAR (PD) accumulation

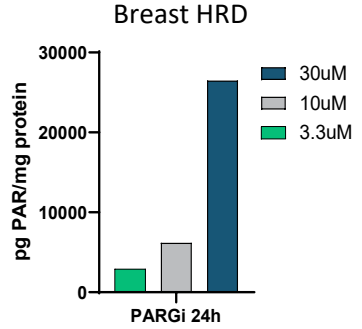


Breast Cancer HRD Cell Line Models



PARGi Tumor Regression and enhanced TGI relative to PARPi

Dose-dependent poly-PAR (PD) accumulation



IDEAYA Data: PARPi dosed at MTD ; PARGi dosed at <MTD

Pol Theta Synthetic Lethality Program

Targeting Development Candidate in December 2021

Pol Theta Synthetic Lethality with BRCA/HRD

DNA polymerase theta (Pol Theta) promotes DNA repair by Microhomology-Mediated End-Joining (MMEJ) an error-prone mutagenic DNA repair pathway

MMEJ is active, and Pol Theta is overexpressed, in HRD cancer cells (e.g. BRCA1/2) making Pol Theta a SL target in HRD cancers

PARP1 & Pol Theta are both involved in MMEJ mediated DNA repair supporting a synergistic effect

IDEAYA Pol Theta inhibitors show selective cell viability effects in DLD1 BRCA2-/- vs. wildtype cell lines

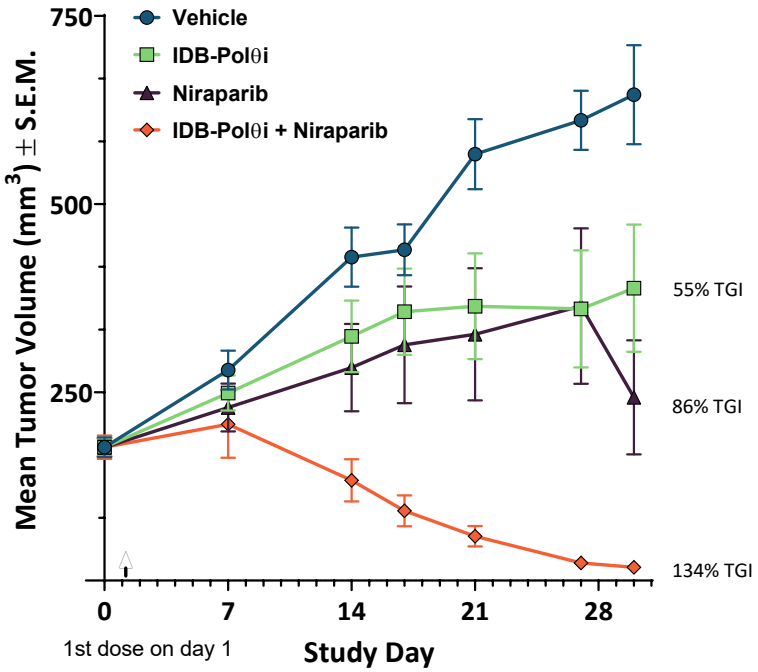
Advancing both small molecule inhibitors and protein degraders

IDEAYA Data

Pol Theta ATPase inhibitor *In Vivo* Activity

Pol Theta inhibitor in combination with niraparib demonstrates significant tumor regression in DLD1 BRCA2-/- xenograft model

Regressions observed for all animals dosed within combination study



IDEAYA Data

Werner Helicase Synthetic Lethality Program

Candidate Biomarker: High-MSI (15% GI Cancers and 16% CRC) [1]

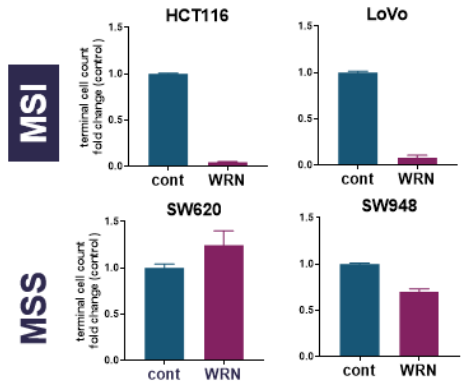
Werner Helicase Synthetic Lethal with High-MSI

CellPress

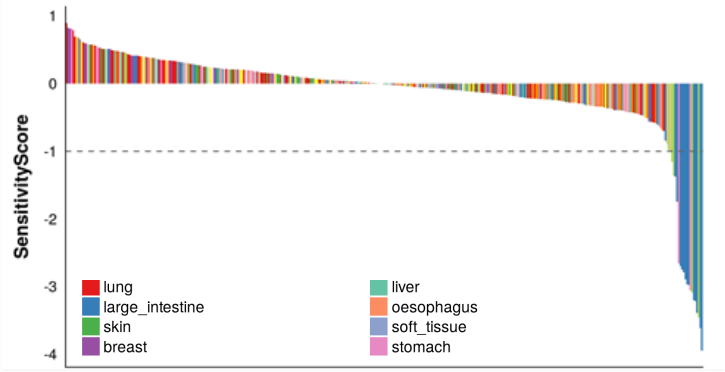
Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al



Project Drive: WRN is essential in MSI-High cancer cell lines



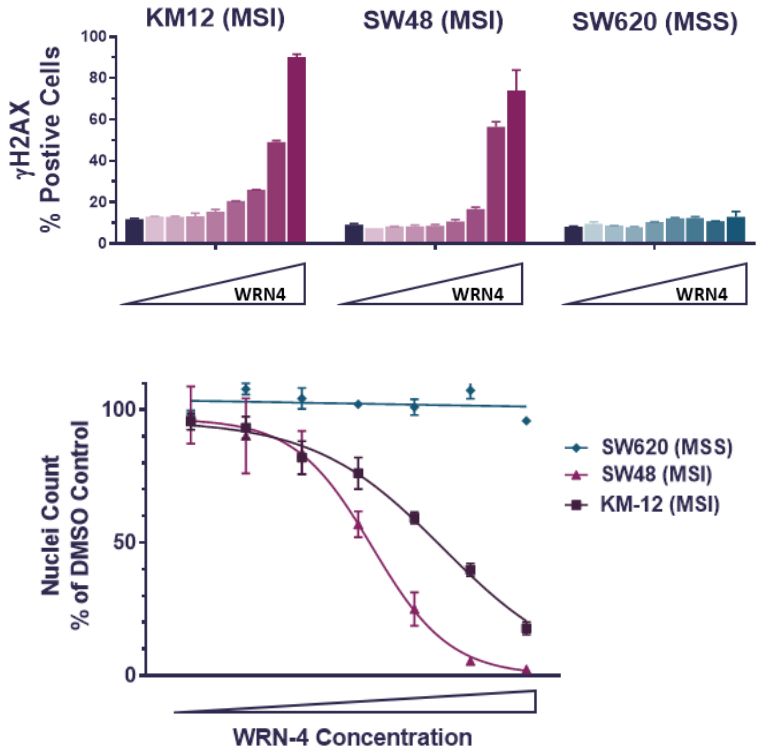
Project Drive

Werner Inhibitor Cellular PD and Viability

PD-marker: dose dependent increase of DNA damage marker γH2AX

Cell viability: MSI-high specific cell viability effect; no effect in MSS cell lines

***In vivo* efficacy**: Preliminary WRN inhibitor *in vivo* PD and efficacy



IDEAYA Data

[1] Cancer Res., November 1998

Darovasertib Phase 1/2 Clinical Trial in GNAQ/11 Patients

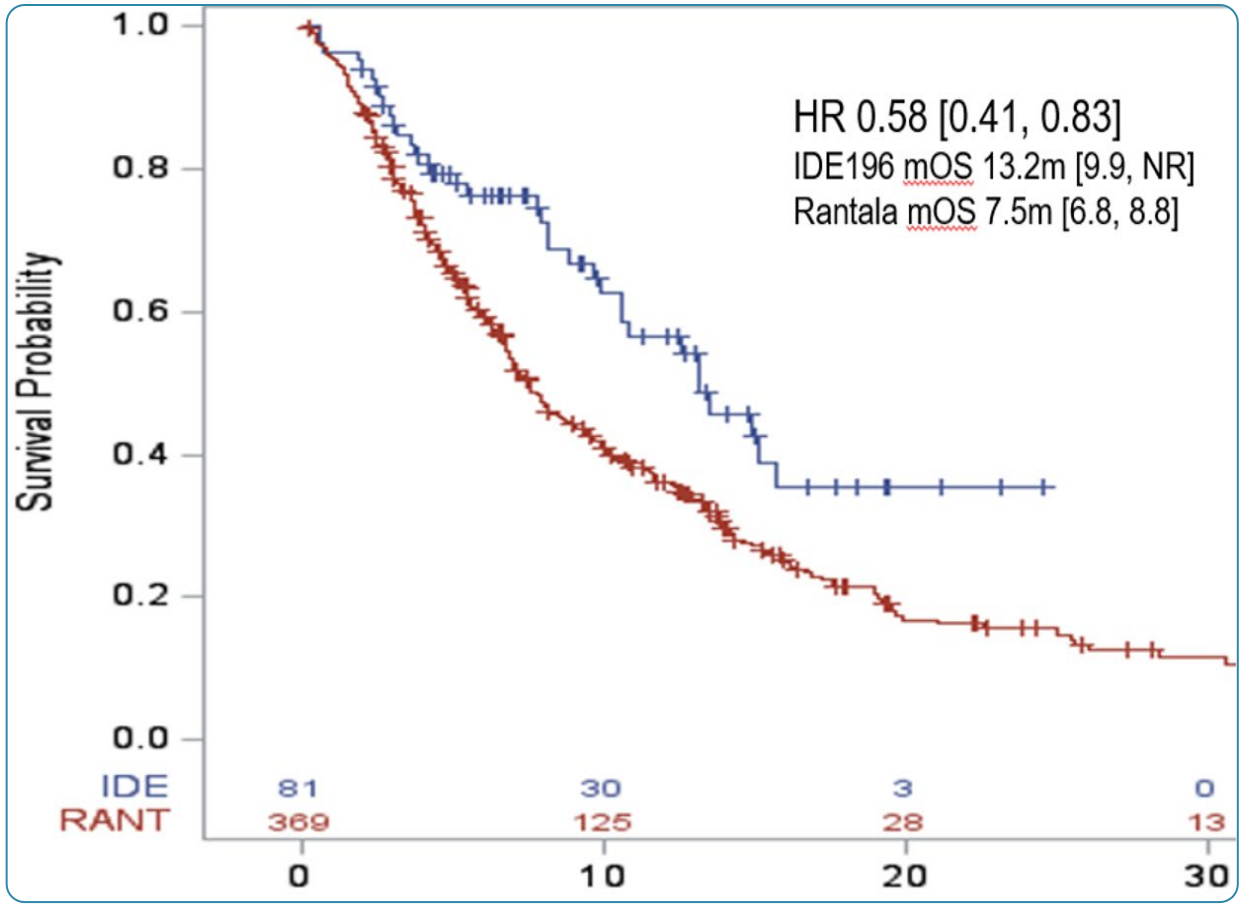
Monotherapy 1-Year % OS and Median Overall Survival Data in MUM

Darovasertib Monotherapy Overall Survival in MUM [1, 2]

Monotherapy

n=81 (predominantly 2L/3L and heavily pre-treated to 7L/8L, with elevated baseline LDH in 66.7% of patients)

- 57% 1-Year Overall Survival with 95% CI (44%, 69%); 13.2 mo Median OS with 95% CI (10.7 mo, Not Reached)
- Historical 1-Year OS = 37% and Median OS = 7.5 mo[2] in similar predominantly 2L/3L+ patient population



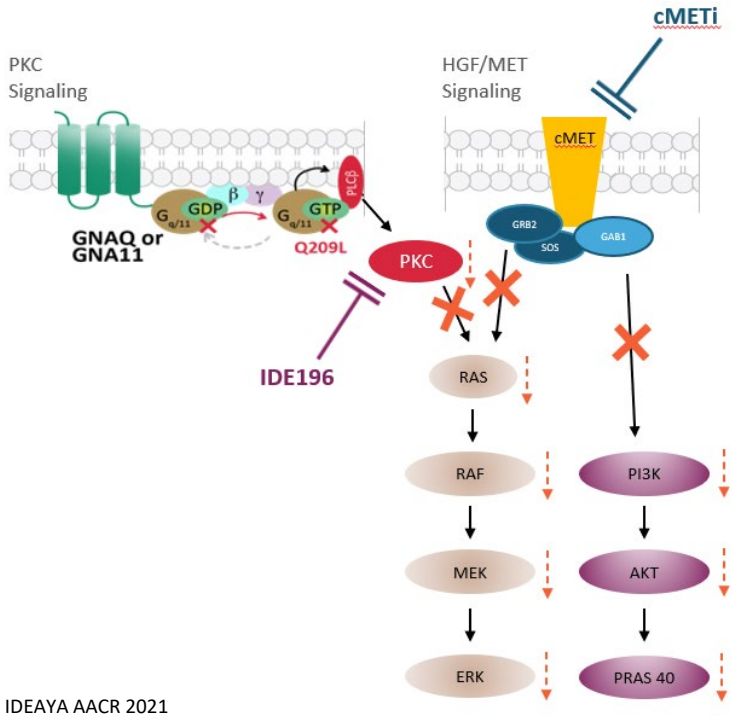
[1] IDEAYA Data (based on preliminary analysis of unlocked database, including: pooled IDEAYA and Novartis BID monotherapy clinical data as of Apr 13, 2021)
[2] Synthetic Control Arm based on Rantala 2019 (meta-analysis of overall survival of patients with metastatic uveal melanoma over 1980 to 2017 evaluated by treatment modality and lines of treatment)

Synthetic Lethal Combination: Darovasertib (PKC) + Crizotinib (cMET)

Crizotinib reduces HGF activation of cMET, MAPK, PI3K signaling to Synergize with IDE196

PKC + cMET Synthetic Lethal Combo

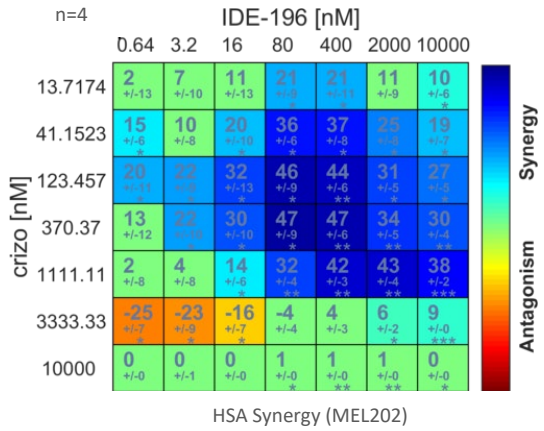
Progression to MUM is associated with high MET receptor expression in UM



IDEAYA AACR 2021

Preclinical Synergy

Darovasertib + Crizotinib synergy exhibited in Mel202 (MUM) cell line

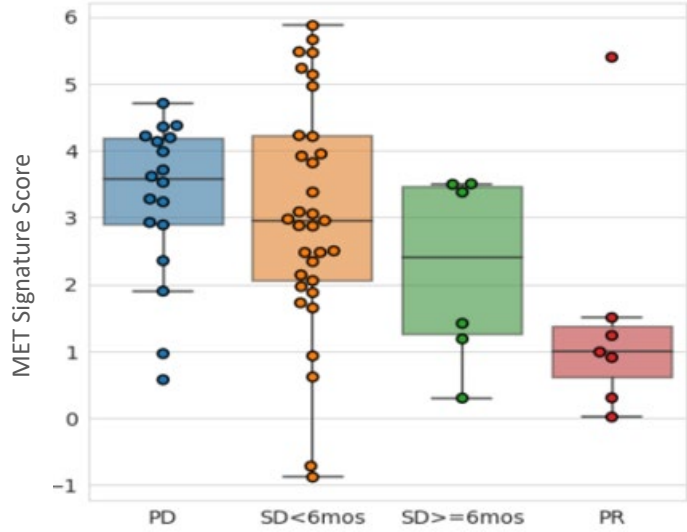


IDEAYA Data AACR 2021

Clinical Phase 1 Data Correlation

High c-MET expression correlates to poorer responses in IDE196 Phase 1 Clinical Trial

Darovasertib Monotherapy Ph 1



Ph 1 Clinical Outcomes
PD=Progressive Disease, SD=Stable Disease, PR=Partial Response

IDEAYA Data

Darovasertib Phase 1/2 Clinical Trial in GNAQ/11 Patients

Early Combo Partial Responses & Prioritization of Darovasertib/Crizotinib Combination

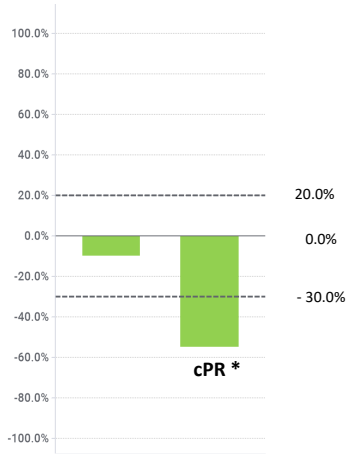
Darovasertib Combination Activity in MUM [1]

Daro/Bini: tumor reduction observed in 11 of 14 (79%) evaluable patients, with 2 partial responses out of nine patients with >2 post-baseline scans (22%)

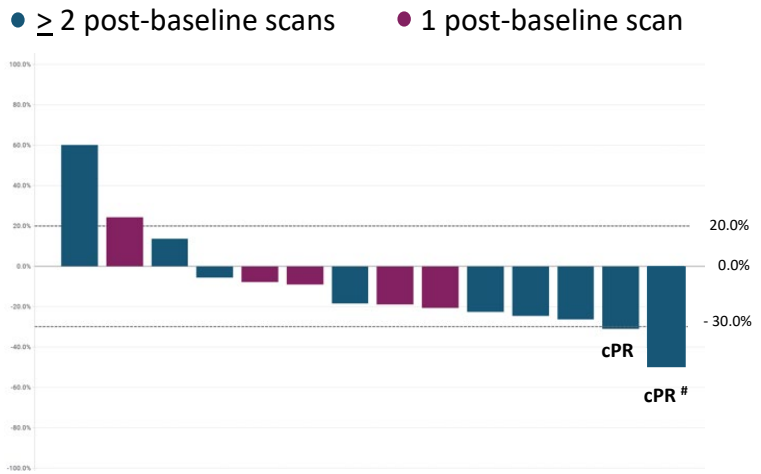
Daro/Crizo: one partial response observed in first cohort; Targeting clinical data update in December 2021

Historical response in MUM = zero to low/mid-single-digit %

Darovasertib + Crizotinib
n=4 with 2 evaluable patients



Darovasertib + Binimetinib
n=24 with 14 evaluable patients



* prior uPR confirmed at subsequent scan (-56.5%)

prior uPR confirmed at subsequent scan (-51.7%)

[1] IDEAYA Data (based on preliminary analysis of unlocked database, including: IDEAYA darovasertib + binimetinib as of Apr 13, 2021 and darovasertib + crizotinib as of May 5, 2021

Darovasertib (IDE196) Phase 1/2 Clinical Development Plans

Evaluating Potential Registrational Strategies

Metastatic Uveal Melanoma [1, 2]

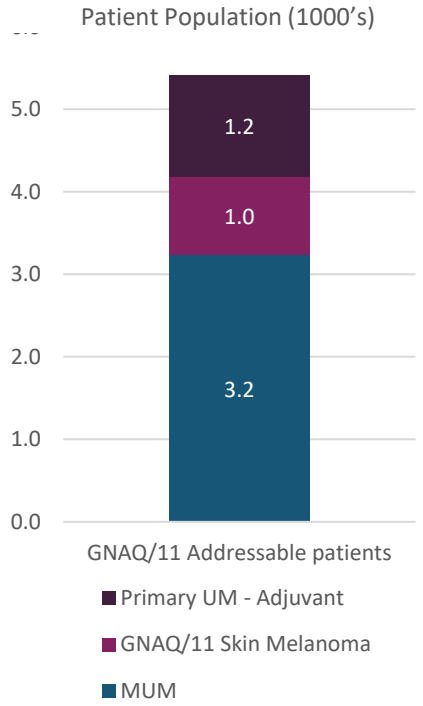
Clinical and Regulatory Strategy to Define Registrational Path

- Plan to obtain regulatory guidance in MUM – targeting feedback on potential registrational path (H1 2022) with focus on darovasertib + crizotinib combination
- Evaluate optionality for 1L or 2L/3L+, e.g., considering HLA status and ORR and PFS endpoints with potential fast-track and accelerated approval path

GNAQ/11 Indication Expansion Efforts beyond MUM

- Enhance GNAQ/11 basket enrollment: Skin Melanoma, Mucosal Melanoma
- Uveal Melanoma Adjuvant setting: IST to initiate in H1 2022
- GNAQ rare diseases: Sturge Weber and Severe Port Wine Stains [1,2]
  - Pending FDA feedback, targeting clinical trial initiation in 2022

Addressable GNAQ/11 Patients (US/EU5)



GNAQ/11 Oncology Market:

- No FDA Approved Therapies for MUM or other GNAQ/11-Mutation Tumors
- Evaluating population expansion opportunities in GNAQ/11 basket (skin and mucosal), and adjuvant uveal melanoma
- Total Addressable Patient Population = ~5.4K patients/yr

[1] Singh, et al, Sturge-weber syndrome. 2019; Sturge Weber Foundation

[2] Tallman, et al, Location of Port Wine Stains and the likelihood of Ophthalmic of Central Nervous System Complications, Pediatrics, 1991; Nguyen et al, The Pathogenesis of Port Wine Stain and Sturge Weber Syndrome: Complex Interactions between Genetic Alterations and Aberrant MAPK and PI3K Activation, Int J of Mol Sci, 2019

Building a Premier Synthetic Lethality Focused Precision Medicine Oncology Biotech in 2021 and Beyond

Focus on Potential *First-in-Class* Synthetic Lethality Programs to Deliver Patient Breakthroughs

Patient Impact: Large addressable patient populations in major solid tumor types

Potential First-in-Class / Best-in-Class: Optimized small molecule and protein degrader development candidates

Precision Medicine: Compelling patient selection and pharmacodynamic biomarkers

Synthetic Lethality Platform: Deep and rich target pipeline with ongoing target identification and validation

SL Degraders: Pol Theta Protein Degraders demonstrate degradation in cell models; additional SL degrader opportunities

MTAP-Deletion

IDE397 (MAT2A)
Cohort Expansions - H1'22
GSK Option Package - H1'22
Clinical Data Update - H1'22

MTAP-SL Target
Lead Series ID

HRD/BRCA

PARG
DC Lead Nominated

Pol Theta
DC Nomination - Dec'21
Advance Protein Degraders

MSI-High

Werner Helicase
Lead Optimization

GNAQ/11

SL Combo: PKC + cMET
Crizo Combo Data - Q4'21
Registration Trial - H1'22

SL Platform

Novel Targets
Chemistry Optimization

Target Milestones to Advance Industry Leading Synthetic Lethality Pipeline

IDEAYA BIOSCIENCES