August 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 June 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 & Pol Theta
- **Pharma Collaborations** with GSK (over ~$3 billion in potential milestones) and Pfizer
- **Strong Balance Sheet** with ~$400 M in cash anticipated to fund operations into 2025 [1, 2]
- **NASDAQ**: IDYA

- **Target Catalysts – 2021**
  - IDE397 Phase 1 (Q4 2021)
    - Clinical Pharmacodynamic Data (Tumor PD)
  - PARG Development Candidate (Q4 2021)
  - Pol Theta Development Candidate (Q4 2021)
  - Darovasertib (IDE196) Phase 1/2
    - Clinical Data Update for Combination(s) (Q4 2021)
    - Regulatory Guidance Monotherapy (H2 2021) and/or
    - Regulatory Guidance Combinations (H1 2022)

(1) IDEAYA Form 10Q and Q2 2021 Financials filed with the U.S. Securities and Exchange Commission on August 10, 2021
(2) Includes cash, cash equivalents and marketable securities of $312.4M as of June 30, 2021, and subsequent $86.5M net proceeds, after deducting underwriting discounts and commissions but before deducting other offering expenses from issuance of shares under an underwritten public offering pursuant to IDEAYA Form 10Q and Q2 2021 Financials (August 10, 2021)

Synthetic Lethality

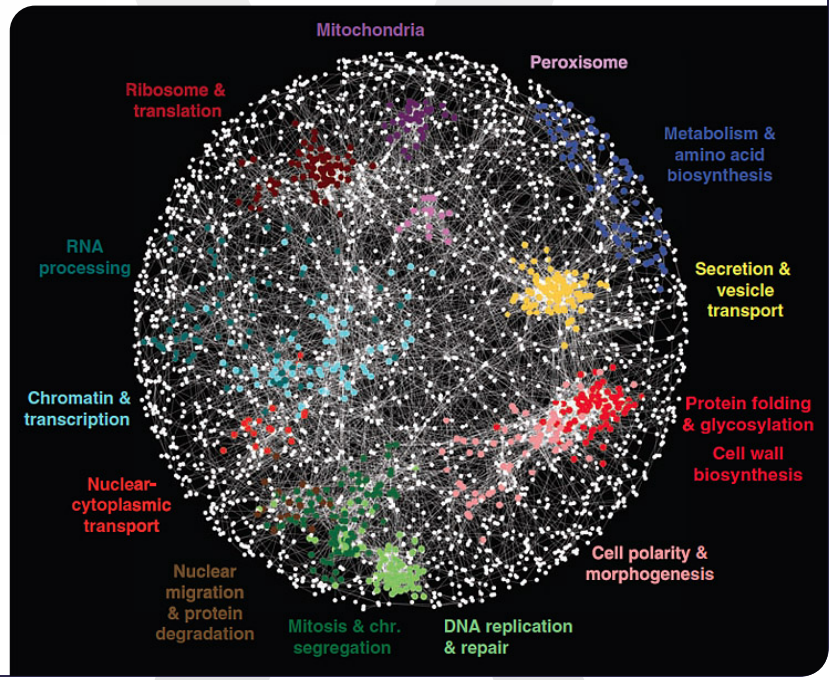
The Next Frontier in Precision Medicine Oncology

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 lethal interactions with tumor-specific mutations (biomarker) may be exploited to develop anticancer therapies
- 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



Reference: Charles Boone

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	2021 Goals	Collaborations	Commercial (IDEAYA)
Synthetic Lethality	**IDE397** *MAT2A*	Monotherapy Solid Tumors	MTAP	Phase 1	Clinical Pharmacodynamic Data (PD) Tumor PD Q4 2021	gsk (1)	US 50/50 Profit Share Ex-US Royalties
		Combinations Solid Tumors	MTAP	IND Enabling	Preclinical Data to enable Combos (Taxanes, PRMTi, Others)		
	PARG	Ovarian, Gastric, Breast Cancers	HRD	IND Enabling	Select Development Candidate Q4 2021	CANCER RESEARCH UK (2)	WW Commercial Rights
	Pol Theta	Small Molecule Protein Degraders	HRD	IND Enabling	Select Small Molecule Development Candidate Q4 2021	gsk (1)	Global Royalties
	WRN	GI Cancers	High-MSI	Preclinical	Chemistry Lead Optimization	gsk (1)	US 50/50 Profit Share Ex-US Royalties
	MTAP-SL	Solid Tumors	MTAP	Preclinical	Lead Series		WW Commercial Rights
	Platform	Solid Tumors	Defined Biomarker	Preclinical	Lead Series (DNA Damage Targets) New Target / Biomarker Validation		WW Commercial Rights
Kinase	**Darovasertib** *PKC*	Monotherapy MUM, Skin Melanoma	GNAQ/11	Phase 2	Regulatory Guidance - MUM Monotherapy (H2 2021) and/or Combination (H1 2022)		WW Commercial Rights
		+MEK, +cMET Combinations, MUM	GNAQ/11	Phase 2	Clinical Data Update - Combination(s) H2 2021	Pfizer (3)	
		Sturge Weber (SWS) Port Wine Stain (PWS)	GNAQ	IND Enabling / Phase 1	FDA Clearance to initiate Phase 1 in SWS / PWS (H1 2022)		

(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
NOVARTIS · Roche

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

Mark Lackner, Ph.D.
SVP, Head of Biology &
Translational Sciences
Genentech · EXELIXIS

Matthew Maurer, M.D.
VP, Head of Clinical Oncology &
Medical Affairs
Bristol-Myers Squibb · COLUMBIA

Mick O'Quigley, M.B.A.
VP, Development Operations
Genentech · AMGEN

Paul Barsanti, Ph.D.
SVP, Head of Drug Discovery
5AM VENTURES · nurix · NOVARTIS · CHIRON

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

IDEAYA Scientific Advisory Board

Alan D'Andrea, M.D.
IDEAYA SAB Chair
Harvard Medical School, Professor
Director, Center of DNA Damage and Repair, Dana Farber

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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

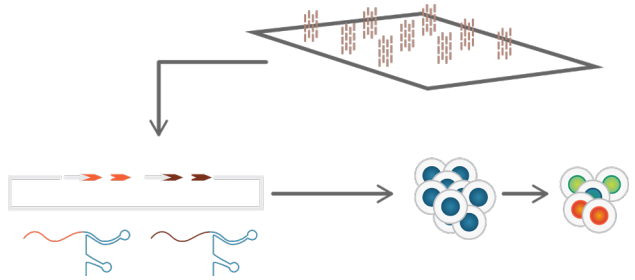
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

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™

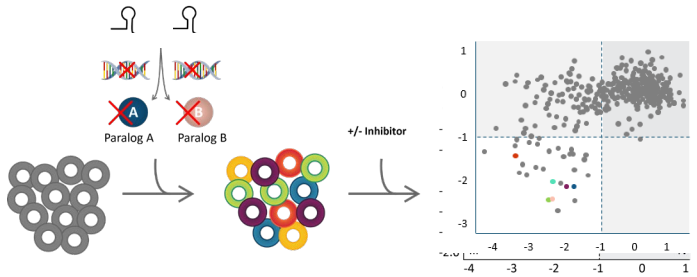
Dual CRISPR SL Library in DNA Damage Repair [2]



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 Genomics Evidence Neoplasia Information Exchange

TCGA

MSK-IMPACT™ Memorial Sloan Kettering Cancer Center

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 BIOSCIENCES

IDEAYA is Advancing the Next Generation of Synthetic Lethality Programs

IDEAYA Synthetic Lethality Pipeline

IDE397 (MAT2A/MTAP) in Phase 1 to treat MTAP-deletion Solid Tumors

Differentiated clinical candidate advancing in-clinic; observed early clinical PD modulation of plasma SAM

Potential to evaluate in major indications, including in NSCLC, Pancreatic, Gastric, Esophageal, Bladder, H&N

PARG and Pol Theta Development Candidates in Q4 2021

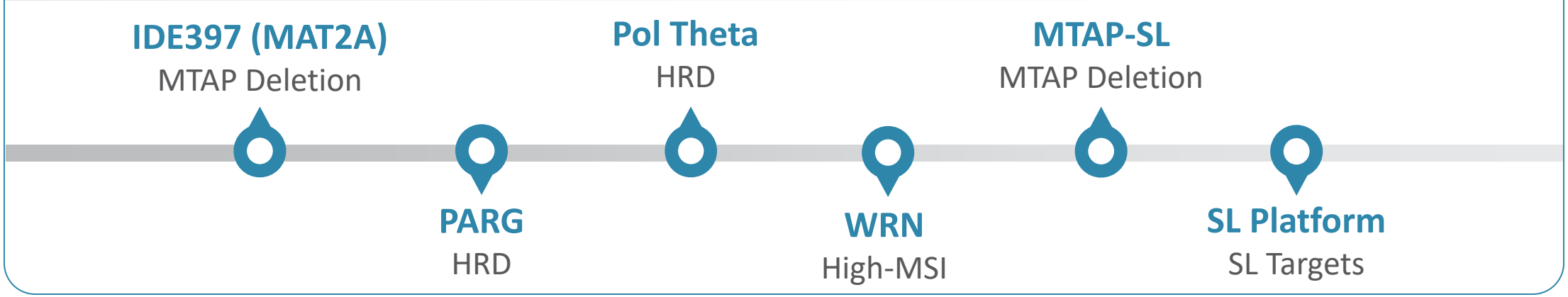
PARG monotherapy efficacy in multiple tumor types; Pol Theta + PARPi combination regressions in BRCA2-/- xenograft

Advancing Werner Helicase, MTAP-SL and Synthetic Lethality Platform Programs

Robust pipeline of next generation of synthetic lethality programs, including WRN, MTAP-SL and DDT Targets

Synthetic Lethality Protein Degraders

Pol Theta degrader program advancing; additional first-in-class SL degrader opportunities

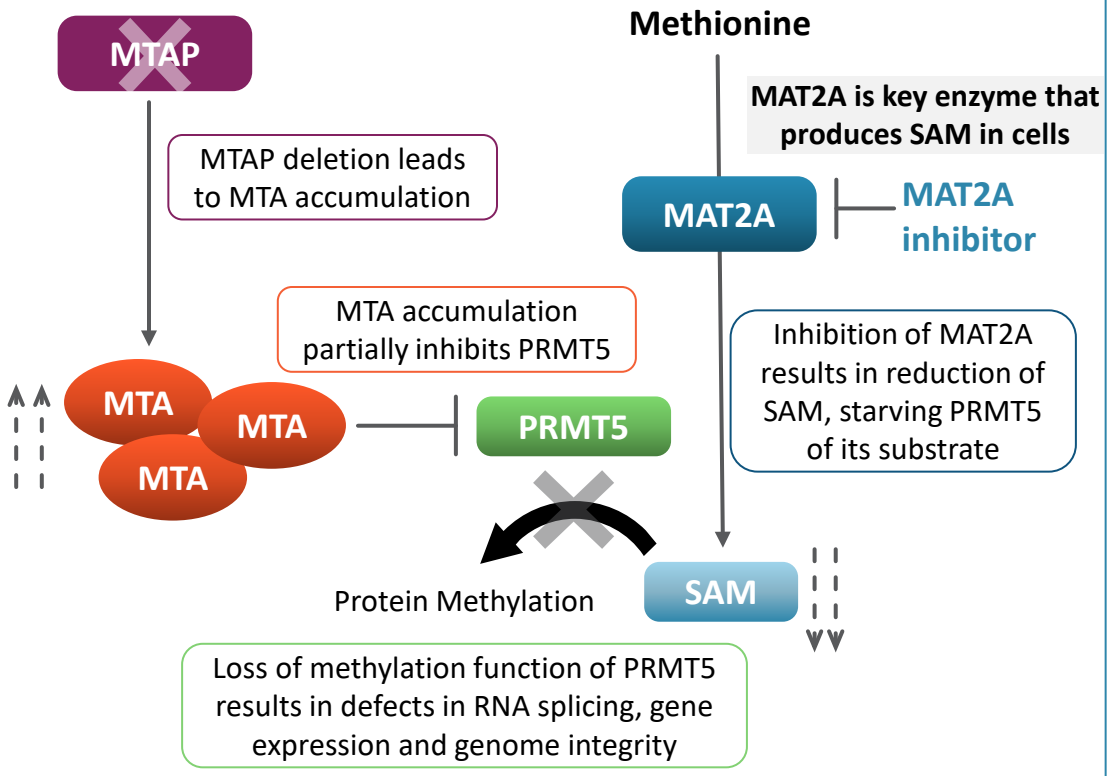


HRD = Homologous Recombination Deficiency, MSI = Microsatellite Instability

MAT2A Inhibition is Synthetic Lethal with MTAP Deletion

MTAP Deletion Prevalence ~15% of all Solid Tumors

MTAP-MAT2A Synthetic Lethality Biology



MTAP Deletion Prevalence

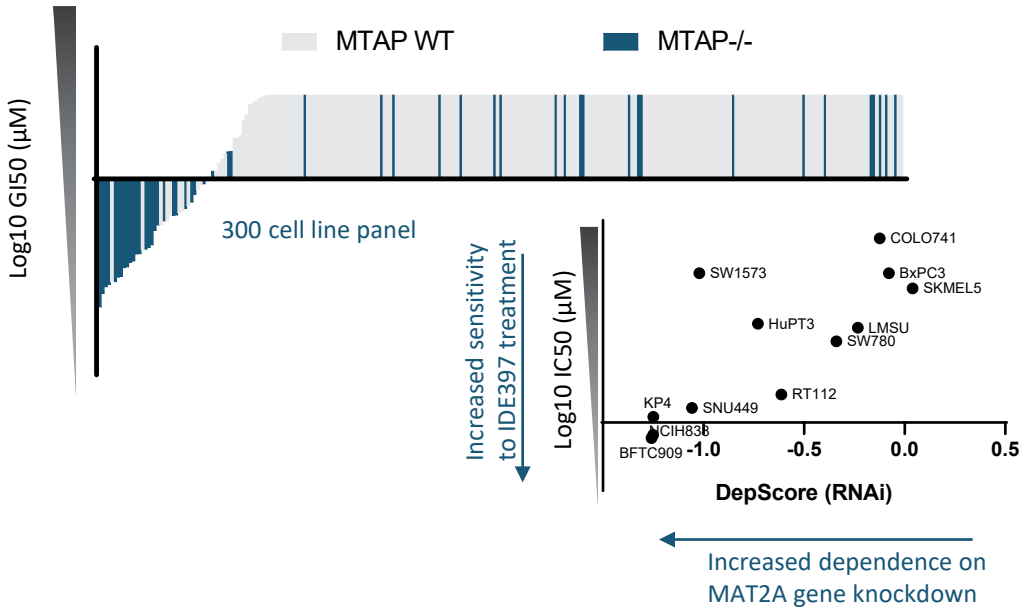
Cancer Type	N	MTAP Deletions (%)
Glioblastoma	592	41
Mesothelioma	87	32
Esophageal	95	28
Bladder	411	26
Pancreatic	184	22
Melanoma	448	16
Lung Cancer (NSCLC)	1053	15
Head and Neck	523	14
Sarcoma	255	10
Esophagogastric	514	10
Diffuse Glioma	513	9
Breast	1084	3
Ovarian	585	3
Adrenocortical	92	3
Thymic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

Data from The Cancer Genome Atlas in cBioPortal

IDE397: MAT2A Development Candidate *in vitro* Profile

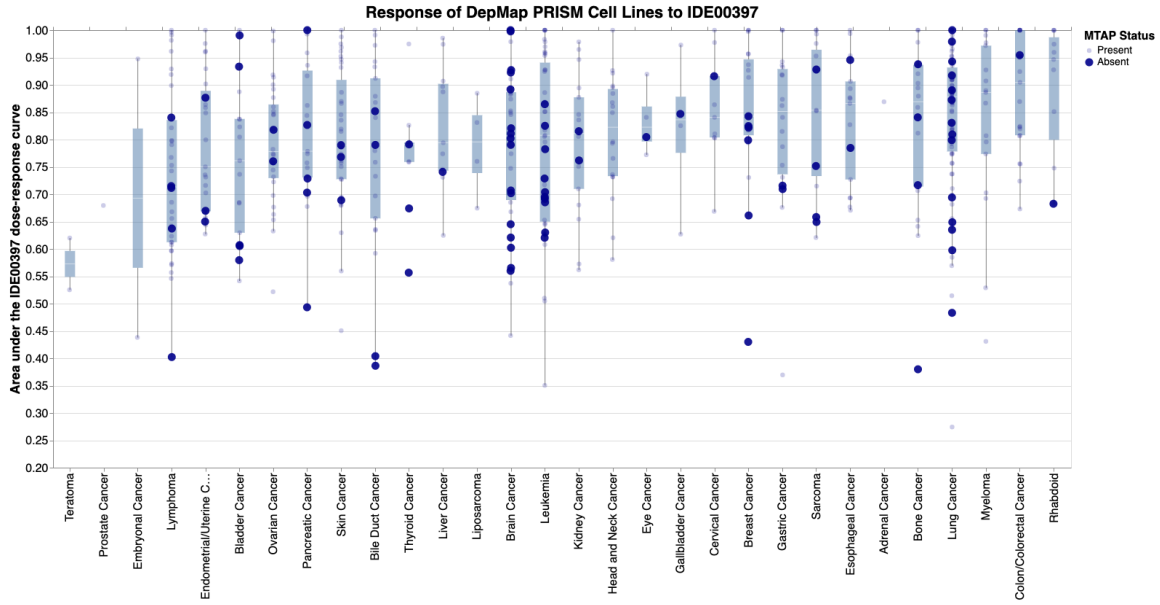
IDE397 is selective for MTAP-/- Cell Lines

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

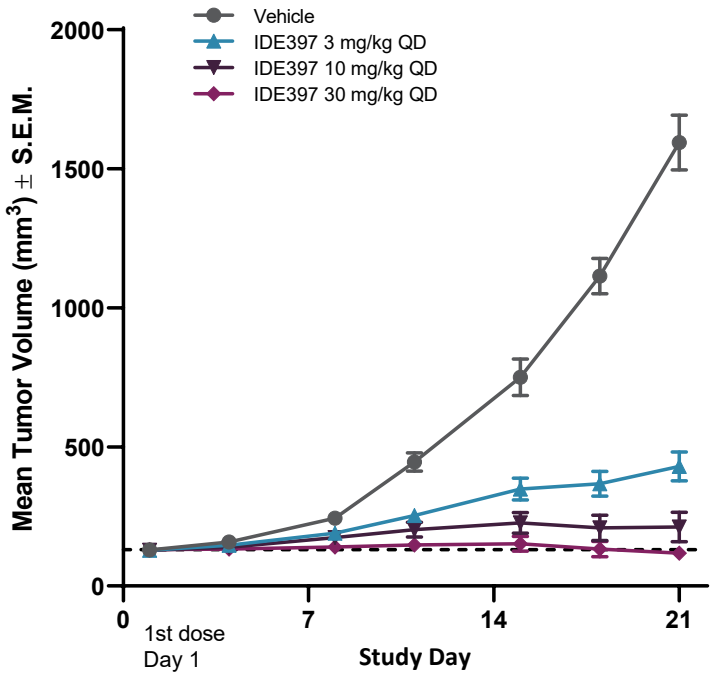
*BLOQ = below limit of quantitation

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

IDEAYA BIOSCIENCES

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

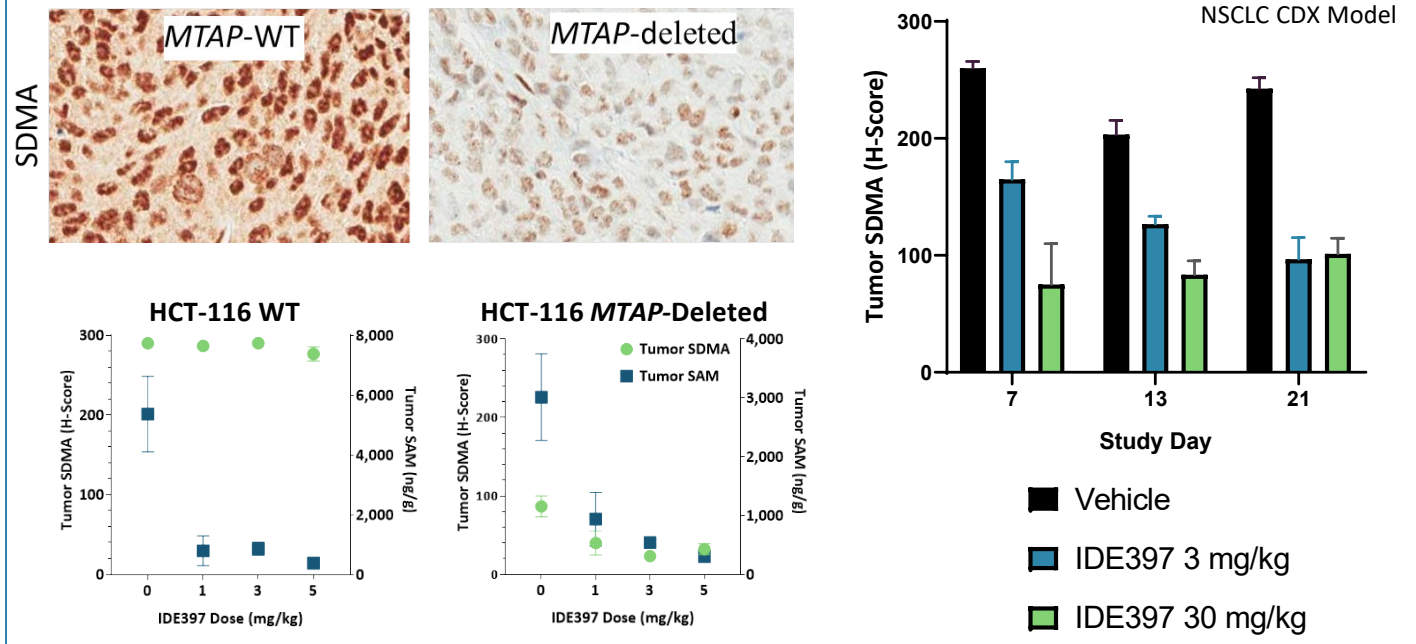
NSCLC Endogenous MTAP-/- CDX Model



IDEAYA Data

SDMA and SAM are Proximal PD Biomarkers of MAT2A inhibition

SDMA and SAM are modulated in a dose dependent manner



IDEAYA Data: Fischer et. al., AACR 2021

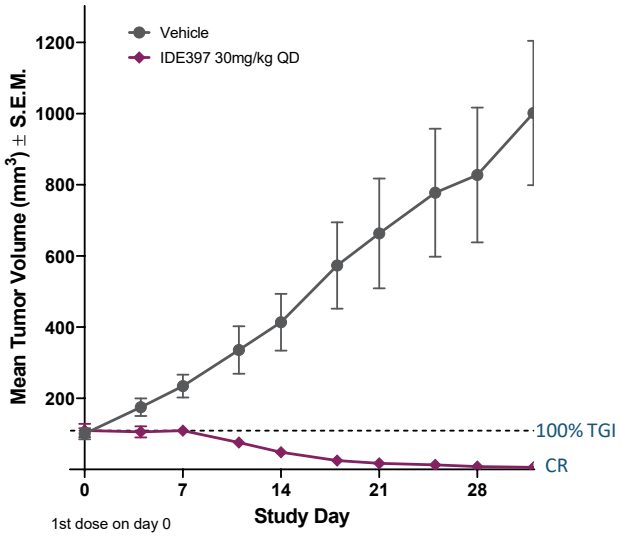
Robust dose-dependent efficacy and PD modulation observed in NSCLC CDX Model

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

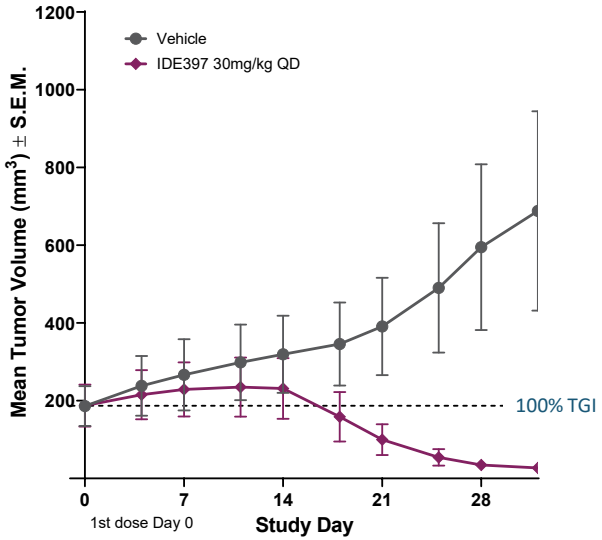
Monotherapy Tumor Regressions & Significant TGI Across Multiple Solid Tumor Types

NSCLC and Bladder Cancer MTAP-/- PDX Models

NSCLC PDX Model

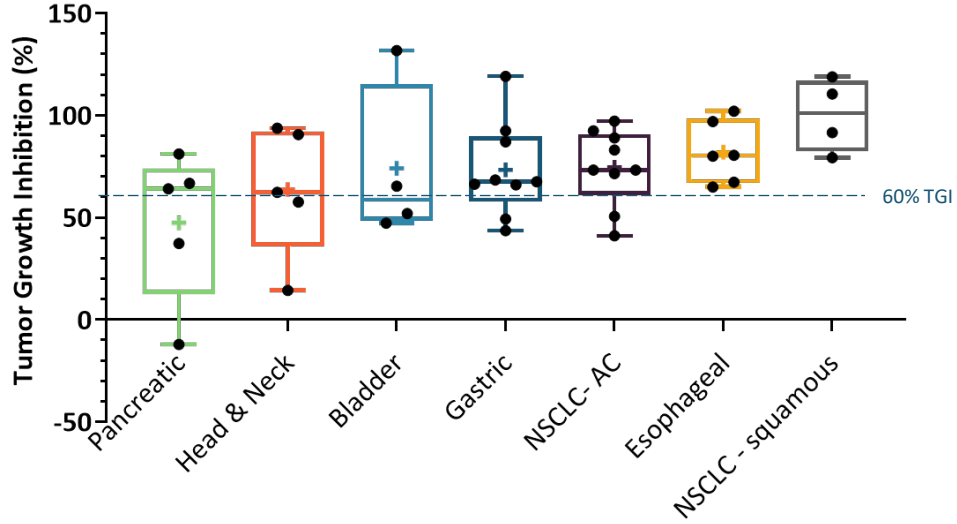


Bladder PDX Model



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

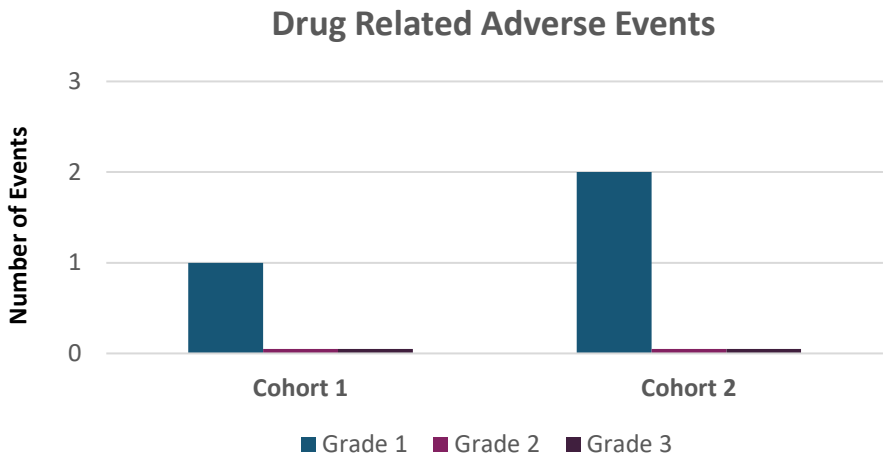
- Tumor Regressions (≥ 100% TGI) observed in multiple PDX models / indications, including in 2 of 4 NSCLC squamous models, with 1 CR
- Observed > 60% TGI in 11 of 13 NSCLC PDX models, including in 7 of 9 adenocarcinoma and in 4 of 4 squamous carcinoma PDX models

TGI = Tumor Growth Inhibition, CR = Complete Response

IDE397 Phase 1 Pharmacodynamic (PD) & Safety / Tolerability Data

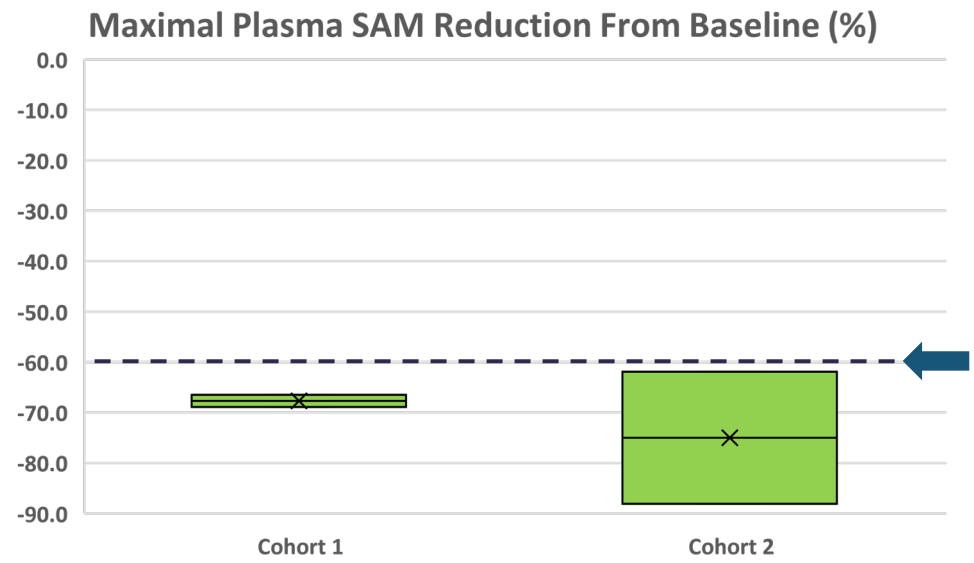
Observed Early Robust Plasma SAM PD Reduction with no Drug-Related SAEs

IDE397 Safety / Tolerability – Ph1 Cohorts 1 & 2



No Drug-Related Grade 2 or Grade 3 Adverse Events

IDE397 Plasma SAM PD – Ph1 Cohorts 1 & 2



Program Goal:
Targeting ≥~60% plasma SAM PD reduction, based on IDE397 preclinical *in vivo* efficacy data in MTAP-deletion

Preliminary Phase 1 Dose Escalation Data Shows early robust IDE397 Target Engagement in MTAP-deleted Patients with no related SAEs

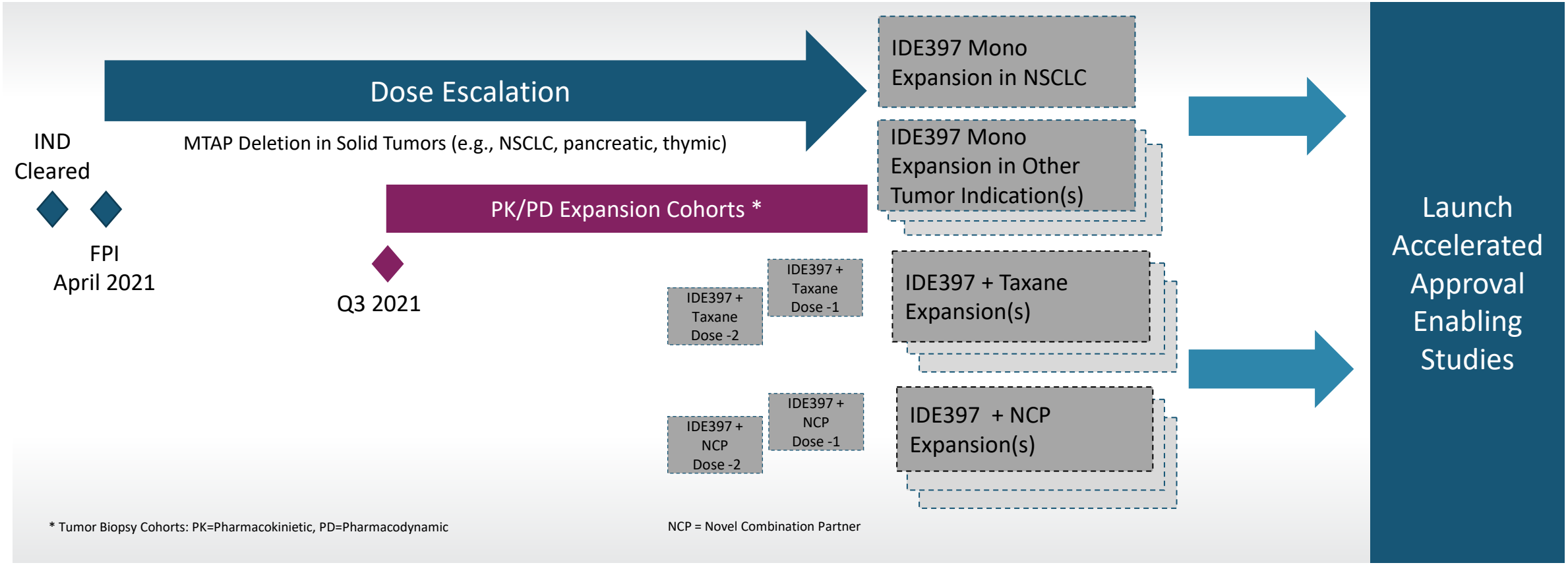
- Observed early and robust plasma SAM PD reduction in first two cohorts of Phase 1 dose escalation and achieved target clinical protocol threshold of ~60% or greater plasma SAM reduction to initiate tumor biopsy cohort for evaluating tumor PD markers, including SAM and SDMA
- All drug-related adverse events have been Grade 1 (no drug-related serious adverse events), including constipation, nausea and fatigue, and no reported myelosuppression, or changes to bilirubin or AST/ALT enzymes
- IDE397 demonstrates clinical protocol target of ~60% or greater plasma SAM PD reduction at a fraction of the clinical dose reported for AG270*

IDEAYA Data based on preliminary analysis of unlocked database as of June 25, 2021 (Cohort 1 n=2, Cohort 2 n=3)
* Agios, AACR-EORTC-NCI (Triple Meeting), 2019

IDE397 Phase 1 Clinical Trial

Comprehensive Approach for Concurrent Evaluation of Monotherapy and Combinations

Phase 1 Dose Escalation and Expansion Strategy



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

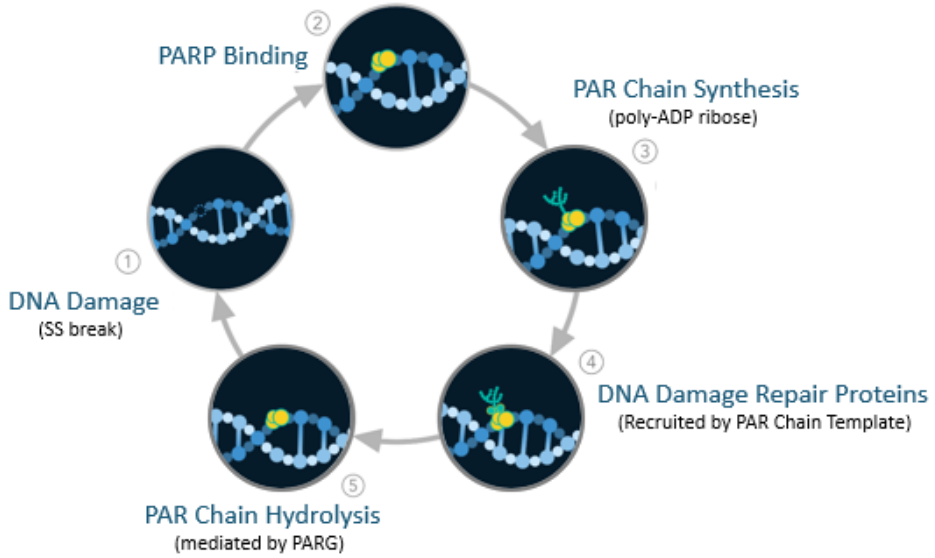
PARG Synthetic Lethality Program

Targeting Development Candidate in H2 2021

PARG Biology

Novel target in Clinically Validated Pathway

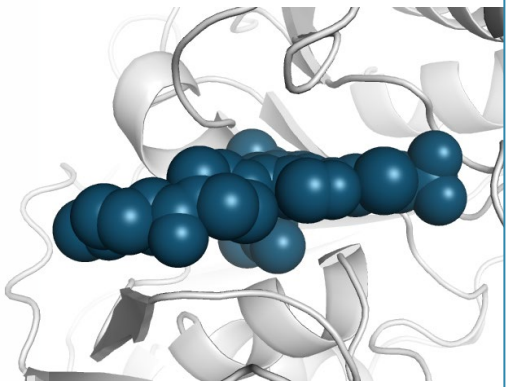
Poly(ADP-ribose) glycohydrolase (PARG) regulates DNA repair by hydrolyzing PAR chains in final step of DDR cycle



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



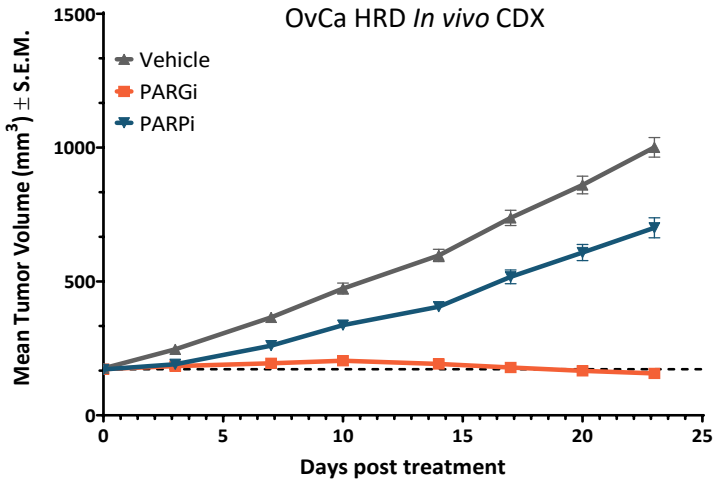
- Multiple potent cellularly active compounds demonstrate *in vitro* and *in vivo* PAR accumulation (PD) and *in vivo* efficacy in defined biomarker setting
- Collaboration with Bill Sellers lab (Broad) established to identify additional genetic sensitizers to PARGi

IDEAYA Data

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

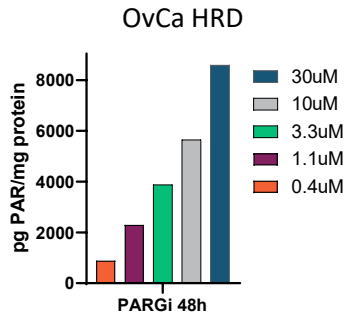
Differentiated Activity to PARP inhibition in Ovarian, Gastric and Breast Cancer Models

Ovarian Cancer HRD Cell Line Models

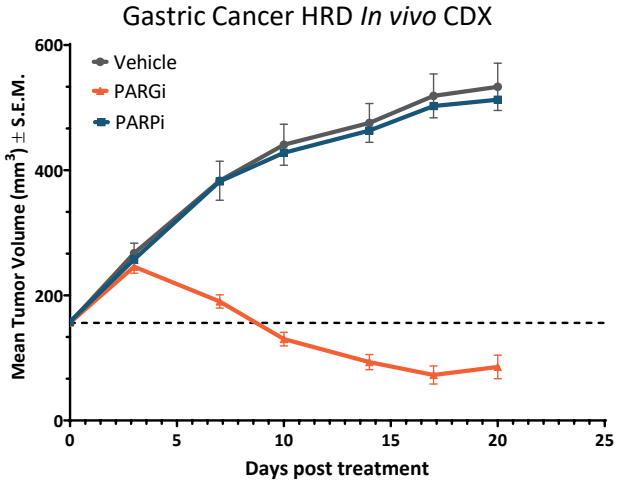


PARGi Tumor Regression and enhanced TGI relative to PARPi

Dose-dependent poly-PAR (PD) accumulation

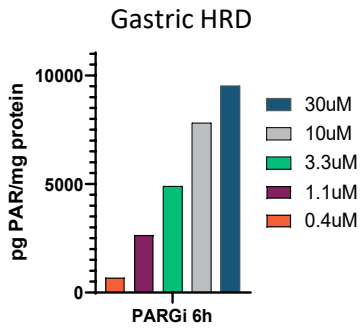


Gastric Cancer HRD Cell Line Models

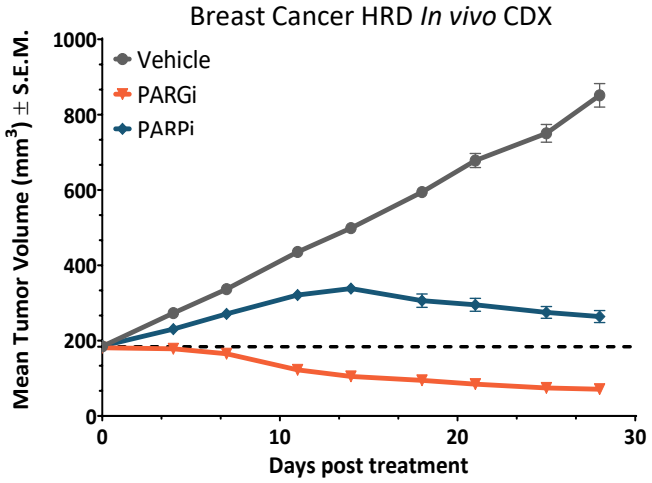


PARGi Tumor Regression in PARPi Refactory Setting

Dose-dependent poly-PAR (PD) accumulation

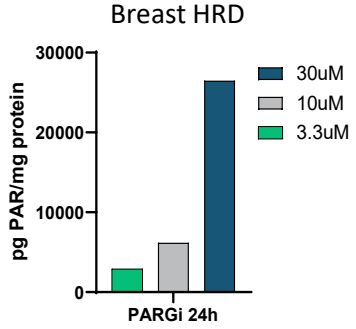


Breast Cancer HRD Cell Line Models



PARGi Tumor Regression and enhanced TGI relative to PARPi

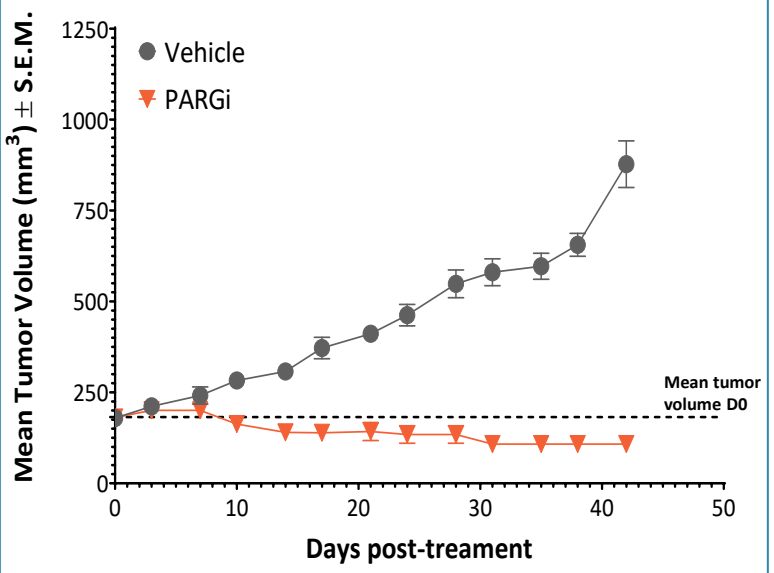
Dose-dependent poly-PAR (PD) accumulation



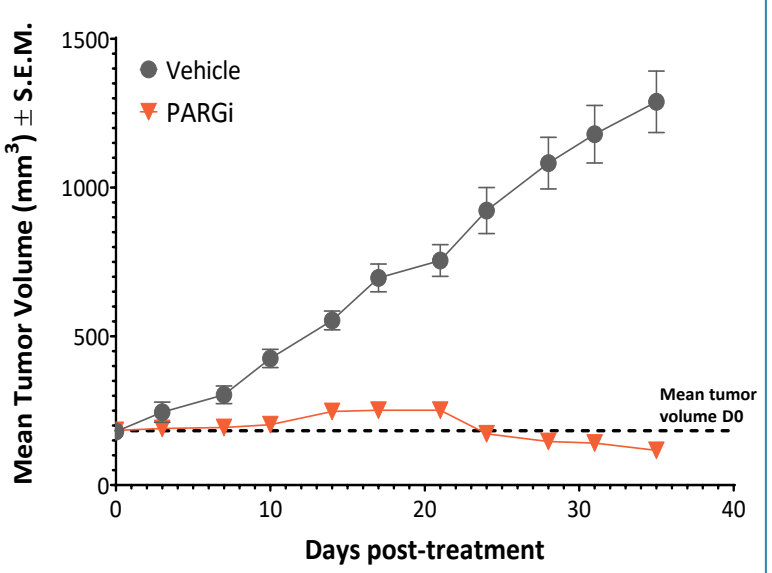
IDEAYA PARGi shows Robust TGI in Breast PDX Models

Monotherapy Tumor Regressions observed across Multiple Breast PDX Models

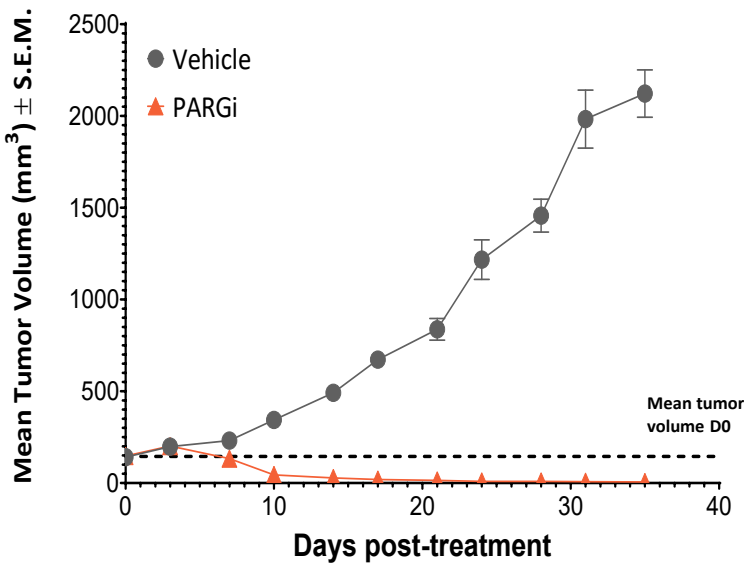
Breast Cancer PDX Model 1



Breast Cancer PDX Model 2



Breast Cancer PDX Model 3



Evaluation of IDB-PARG in Patient Derived Xenograft (PDX) models in Breast Cancer

- Tumor Regressions (≥ 100% TGI) observed in multiple PDX models with defined genetic and subtyping profiles
- Enhanced Tumor Growth Inhibition (TGI) relative to Niraparib (PARPi) observed in some models

Pol Theta Synthetic Lethality Program

Targeting Development Candidate in H2 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

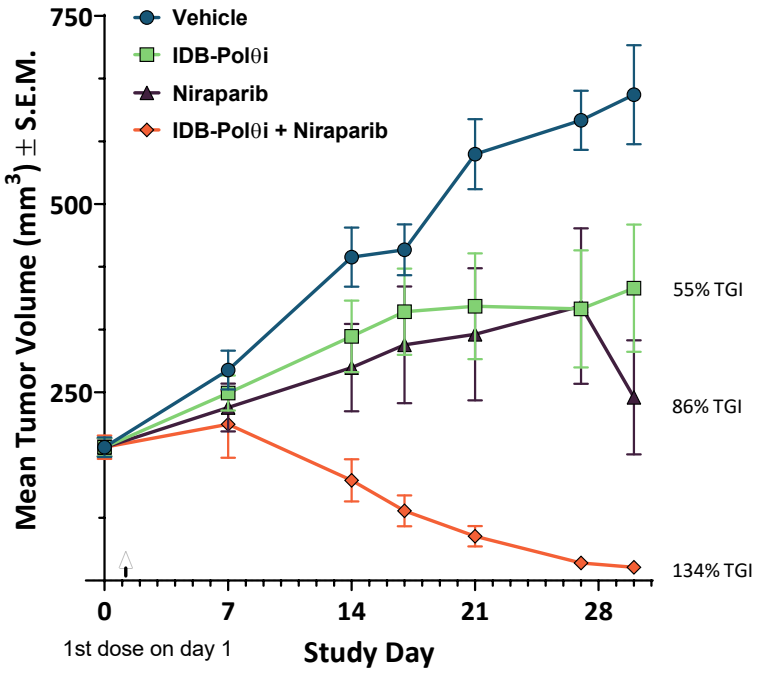
Advancing both small molecule inhibitors and protein degraders

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]

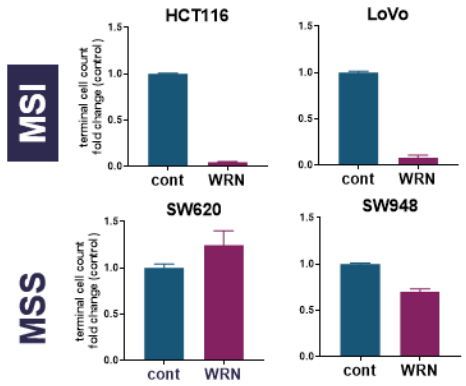
Werner Helicase Synthetic Lethal with High-MSI

CellPress

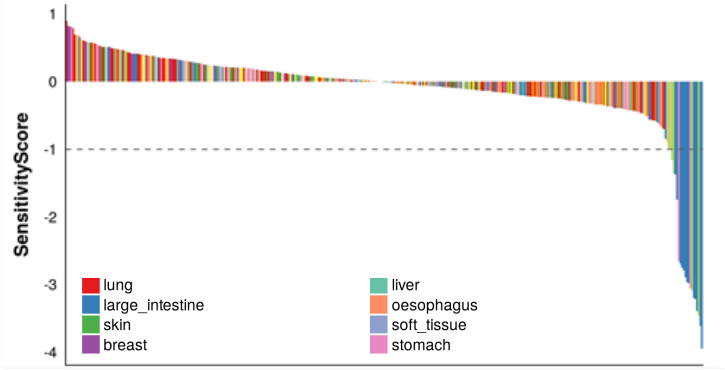
Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al



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



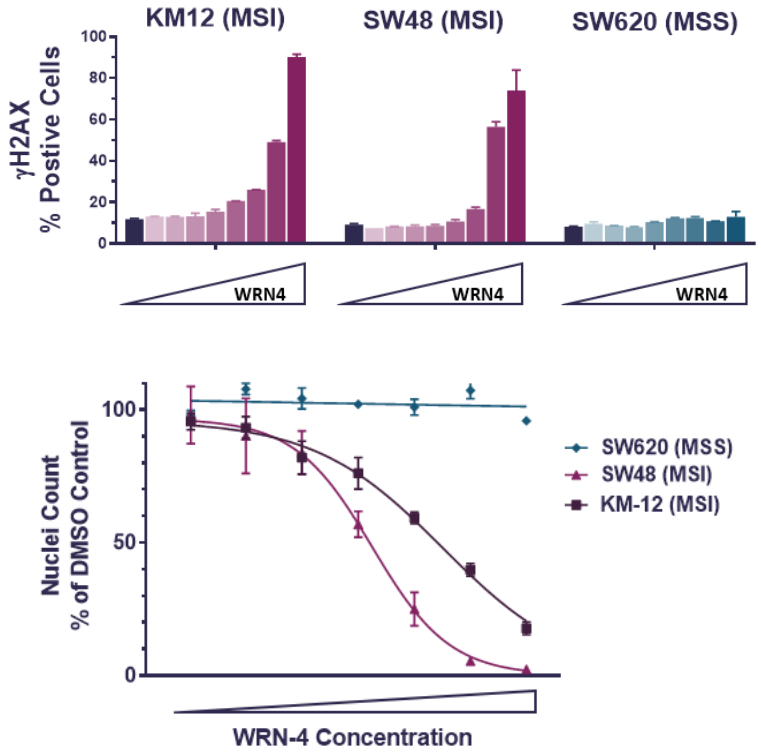
Project Drive

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

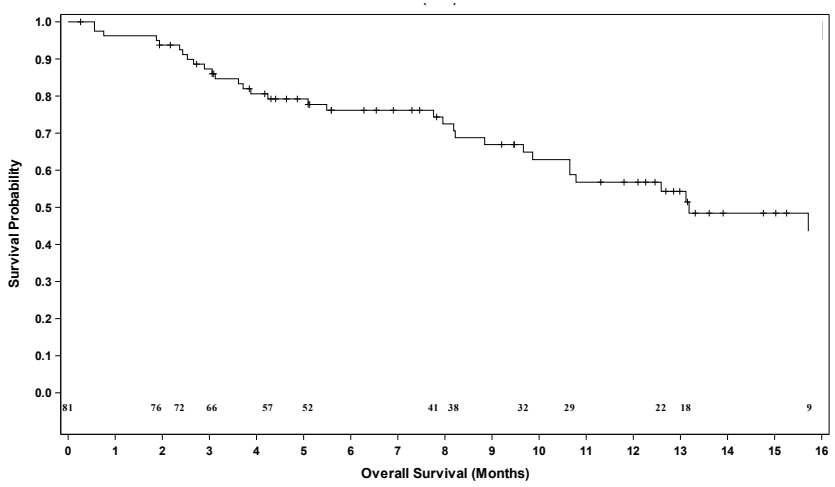
Darovasertib Phase 1/2 Clinical Trial in GNAQ/11 Patients

Robust Mono 1-Year Overall Survival Data and Early Partial Responses in Combinations

Darovasertib Monotherapy Overall Survival in MUM [1]

Monotherapy

n=81 (predominantly 2L/3L and heavily pre-treated to7L/8L)



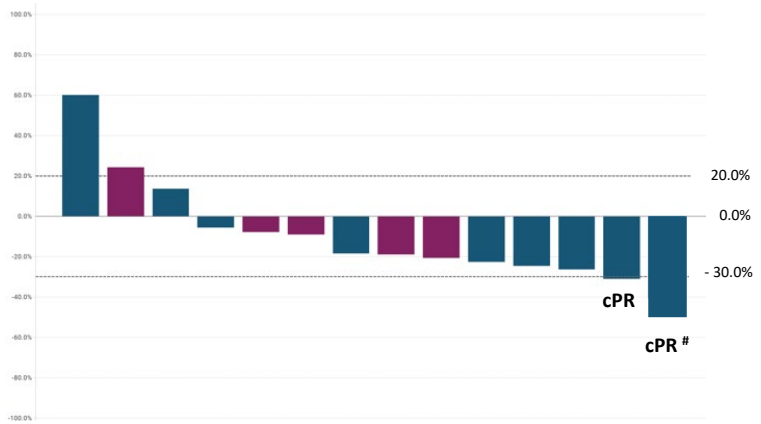
- 57% 1-Year Overall Survival with 95% CI (44%, 69%)
- 13.2 mo Median OS with 95% CI (10.7 mo, Not Reached)
- Historical 1-Year OS = 37% and Median OS = 7mo[2] in similar predominantly 2L/3L+ patient population

Darovasertib Combination Activity in MUM [1]

Darovasertib + Binimetinib

n=24 with 14 evaluable patients

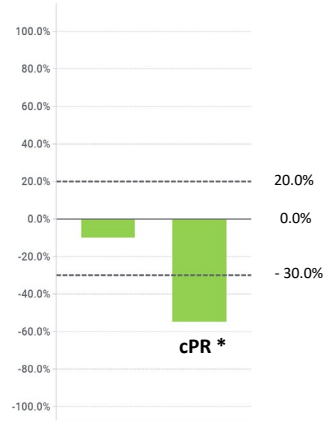
● ≥ 2 post-baseline scans ● 1 post-baseline scan



prior uPR confirmed at subsequent scan (-51.7%)

Darovasertib + Crizotinib

n=4 with 2 evaluable patients



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

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

[1] IDEAYA Data (based on preliminary analysis of unlocked database, including: pooled IDEAYA and Novartis BID monotherapy clinical data as of Apr 13, 2021; and IDEAYA darovasertib + binimetinib as of Apr 13, 2021 and darovasertib + crizotinib as of May 5, 2021)

[2] 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)

Crizotinib Combination – Confirmed Partial Response

Patient shows Deep Response (-56.5%) after 6 Months on Treatment

Patient Profile

56 year old woman

GNAQ mutant MUM

Elevated baseline LDH

2 prior therapies:
– immunoembolization
– chemoembolization

Significant tumor burden
– multiple liver and lung lesions
– axillary adenopathy

Patient Experience

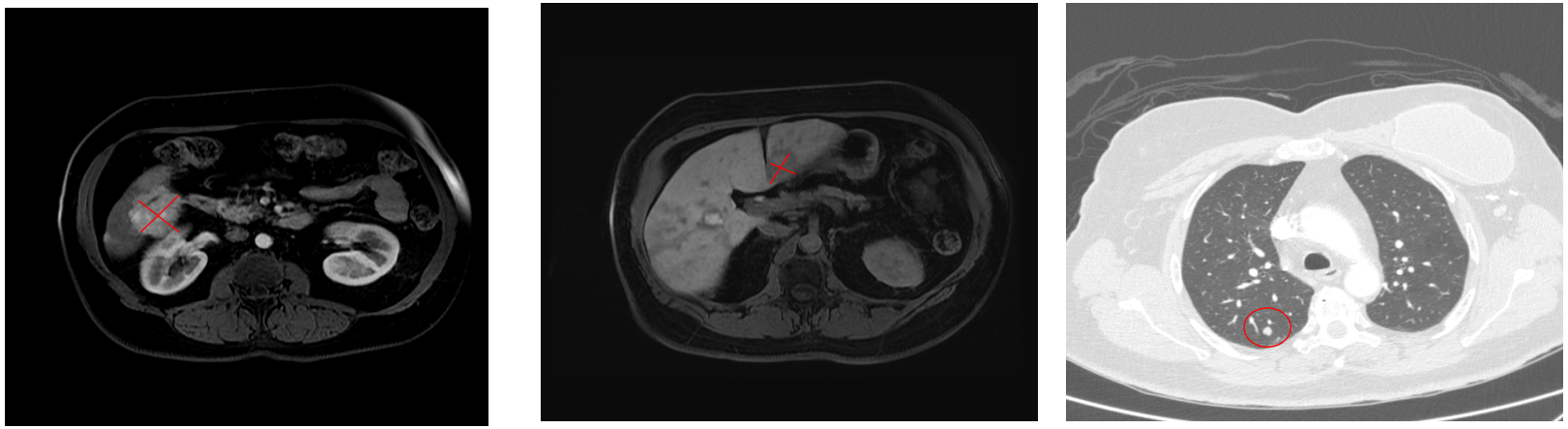
Tolerating treatment well

Initial response at 4 months and confirmed response at 6 months

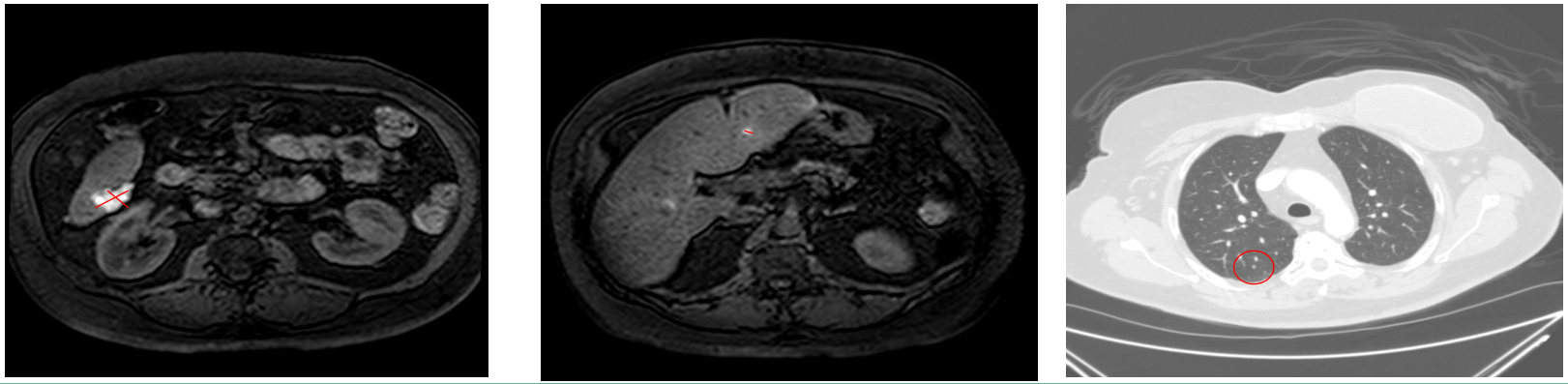
56.5% reduction in target lesions 6 months into therapy

Patient Response

Baseline



4 Months



Darovasertib (IDE196) Phase 1/2 Clinical Program Overview

Clinical Data Supports Potential Registrational Strategies

Metastatic Uveal Melanoma [1, 2]

Darovasertib Monotherapy – Phase 2

- Potential registrational approach: randomized, OS endpoint in 1L or 2L/3L

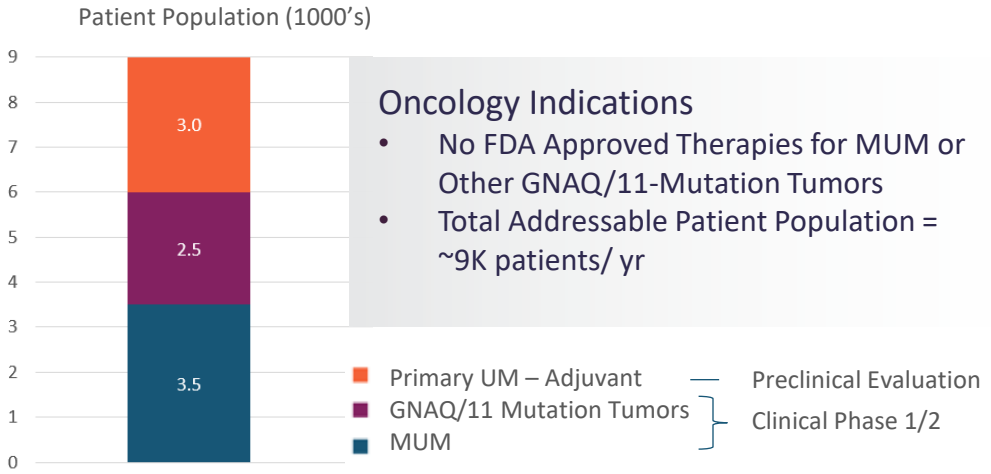
Darovasertib Combination Therapies – Phase 2

- Program goal for darovasertib combination therapies (+ binimetinib, + crizotinib) of >20% ORR and enhance overall survival
- Potential registrational approach: single arm, ORR endpoint with in 1L or 2L/3L with potential Accelerated Approval pathway

Clinical and Regulatory Strategy to Define Registrational Path

- Continue combination studies (+ Bini, +Crizo) with data maturing
- Obtain regulatory guidance in MUM – targeting feedback for monotherapy (H2 2021) and/or on potential registrational path for combination therapy (H1 2022)
- Advance to registrational trial based on monotherapy (current OS data) or combination therapy (maturing ORR data) with potential accelerated pathway
- Evaluate optionality for 1L or 2L/3L+, e.g., considering HLA status and ORR

Addressable GNAQ/11 Patients (US/EU5)



Oncology Indications

- No FDA Approved Therapies for MUM or Other GNAQ/11-Mutation Tumors
- Total Addressable Patient Population = ~9K patients/ yr

GNAQ Mutation-Mediated Rare Disease Indications

- Sturge Weber potential chronic treatment (US/EU5 prevalence ~13-33K)[3]
- Port Wine Stain potential related indication (US/EU5 prevalence ~235K)[4]
- Targeting FDA Clearance in H1 2022 to initiate Phase 1 in SWS / PWS

[1] IDEAYA clinical data based on preliminary analysis of unlocked database, including: pooled IDEAYA and Novartis BID monotherapy clinical data as of Apr 13, 2021; IDEAYA darovasertib + binimetinib data as of Apr 13, 2021; IDEAYA darovasertib + crizotinib data as of May 5, 2021; and IDEAYA GNAQ skin melanoma data as of April 13, 2021

[2] Preclinical rationale and synergy demonstrated for darovasertib combinations IDE196+MEKi Combination Preclinical Data AACR 2020; IDE196+cMET Preclinical Combination Data AACR 2021

3 Singh, et al, Sturge-weber syndrome. 2019; Sturge Weber Foundation

4 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)
Phase 1 Pharmacodynamic Data
Tumor PD Q4 2021

MTAP-SL Target
Lead Series ID

HRD/BRCA

PARG
Development Candidate Nomination
Q4 2021

Pol Theta
Development Candidate Nomination
Q4 2021
Advance Protein Degraders

MSI-High

Werner Helicase
Lead Optimization

2021 Target Catalysts to Build Industry Leading Synthetic Lethality Pipeline