J.P. Morgan 40th Annual Healthcare Conference
January 2022
NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicines

IDEAYA BIOSCIENCES

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 (H1 2022)
    - Cohort Expansions
    - GSK Option Package & Clinical Data Update
  - PARG IND-Filing (Q4 2022)
  - Pol Theta Initiate IND-enabling Studies (H1 2022)
  - Darovasertib (IDE196) Phase 1/2 (H1 2022)
    - Clinical Update on mPFS for Daro + Crizotinib
    - Regulatory Guidance for Daro + Crizotinib

(1) IDEAYA Form 10Q and Q3 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

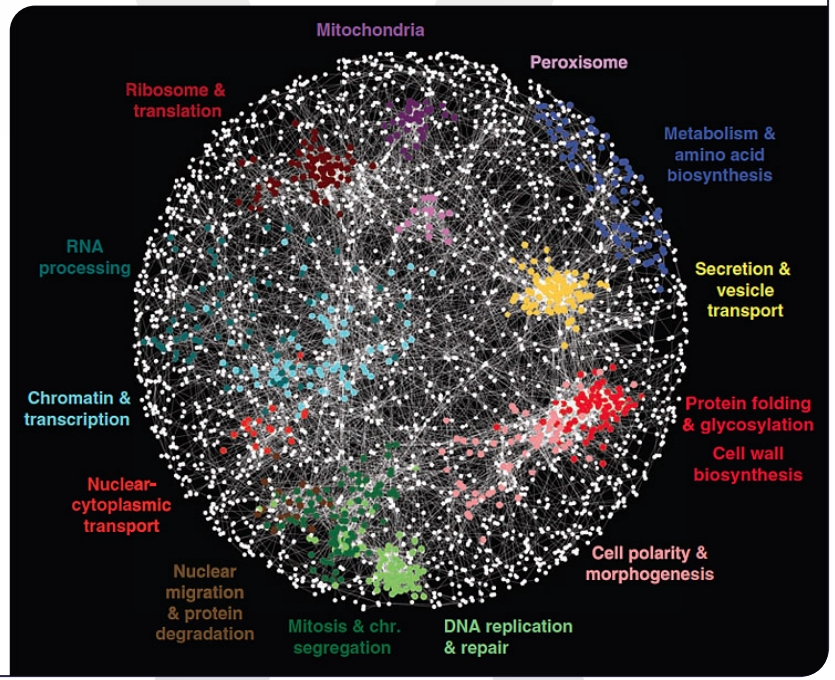
The Next Frontier in Precision Medicine Oncology

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

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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					Ph 1 Initiation H1 2022		
PARG	Ovarian, Gastric, Breast Cancers	HRD					IND-filing by Q4 2022	CANCER RESEARCH UK (2)	WW Commercial Rights
Pol Theta	Small Molecule Protein Degraders	HRD					Initiate IND Enabling Studies H1 2022	gsk (1)	Global Royalties
WRN	GI Cancers	High-MSI					Development Candidate 2023	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*	+cMET Combo MUM, Basket	GNAQ/11					Daro + Crizo mPFS Update in MUM H1 2022 Regulatory Guidance in MUM H1 2022	Pfizer (3)	WW Commercial Rights
	Monotherapy MUM, UM Adjuvant	GNAQ/11					Expand to UM Adjuvant - IST H1 2022		
	MET-Amplified / High-Expression Tumors	MET					Evaluate Potential Indication Expansion into additional MET-driven Tumors		

(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 cMET Combinations; IDEAYA retains all IDE196 Commercial Rights

= 2022 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, cMET = crizotinib, 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

Michael White, Ph.D.
SVP, Chief Scientific Officer, Head of Research
Pfizer · UT Southwestern Medical Center

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

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

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

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

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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
- 20/80% IDEAYA/GSK cost share for MAT2A and 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 Milestones, incl $20M Preclinical / Ph1 Clinical
- Potential Combination with GSK's Dostarlimab, a PD-1 IO Agent

Pol Theta (BRCA/HRD)

- Global Royalties with GSK covering all Costs
- ~$1B potential Milestones, incl $20M Preclinical / Ph1 Clinical
- 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
- INQUIRE™ Chemical Library - proprietary, expert-curated small-molecule library of over 200,000 compounds
- 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

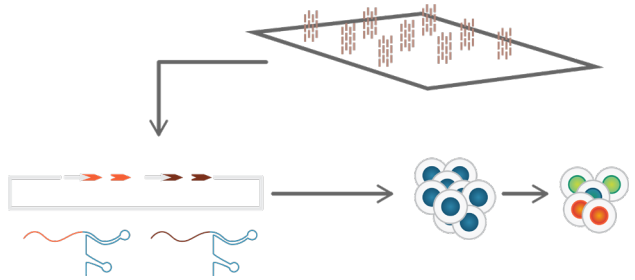
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

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™

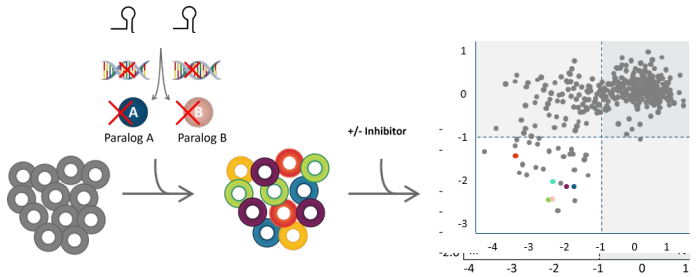
Dual CRISPR SL Library in DNA Damage Repair [2]



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]

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IDEAYA Synthetic Lethality Bioinformatics Platform

Vast Data Sets Being Analyzed to Prioritize Novel Synthetic Lethality Targets

Synthetic Lethality Target Identification

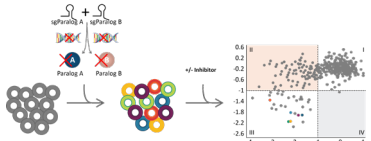
- Computational effort to mine data sets for SL pairs
- IDEAYA algorithms developed for SL target and biomarker discovery and patient stratification

DepMap Consortium

- DepMap consortium membership deepens access to genome-wide CRISPR SL screen data to inform IDEAYA programs

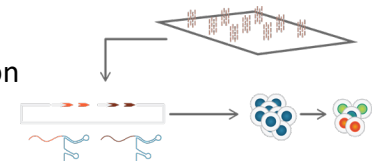
PAGEO™ Paralog Screens

- Ovarian Dual gRNA CRISPR paralog screens with functional redundancy that are hidden in single gRNA CRISPR screens
- Comprehensive set of paralog gene pairs involved in DDR



DECIPHER™ Dual CRISPR Screens

- Dual CRISPR DDR Library data analysis and hit prioritization
- Results demonstrate encouraging pairwise interaction effects and target validation ongoing



Big Data

IDEAYA Integrates Proprietary, Partner and Public Synthetic Lethality Data Sets

Hundred of Millions of Synthetic Lethality Data Points being analyzed

Data sets are growing rapidly with SL data points anticipated to reach billions

IDEAYA Bioinformatics

Machine Learning / AI

Data integration and unsupervised machine learning

Iterative process with SL Biologists to develop most powerful algorithms for SL target & biomarker discovery

Determine SL pairs with the strongest signal to noise ratio

Enables SL Target and Biomarker Discovery and Prioritization

IDEAYA Synthetic Lethality Drug Discovery Platform

Structure-Based Drug Design & Proprietary Chemical Library Enable "Hard to Drug" Targets

Structural Biology & Structure Based Drug Design

Full suite of capabilities in structural biology, biophysics, & computational chemistry

Ligand bound co-crystal structures resolved to enable Structure Based Drug Design for each of 6 Synthetic Lethality Programs

- MAT2A
- PARG
- Pol Theta (polymerase & helicase)
- Werner Helicase
- 2 undisclosed targets

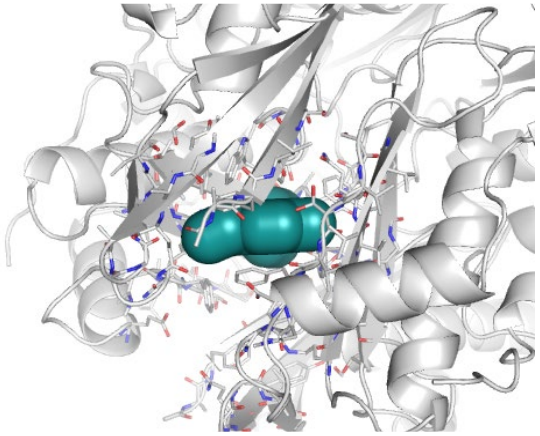
Multiple potential "first-in-world" co-crystal structures resolved, including for PARG, Pol Theta Helicase and Werner Helicase

INQUIRE™ Proprietary Chemical Library

Expert-curated HTS library to enhance hit discovery capabilities against novel SL targets classes, such as helicases and endonucleases

Over 200,000 compounds in IDEAYA proprietary library

Enhances IDEAYA's SL Drug Discovery Platform and competitive differentiation



IDEAYA 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

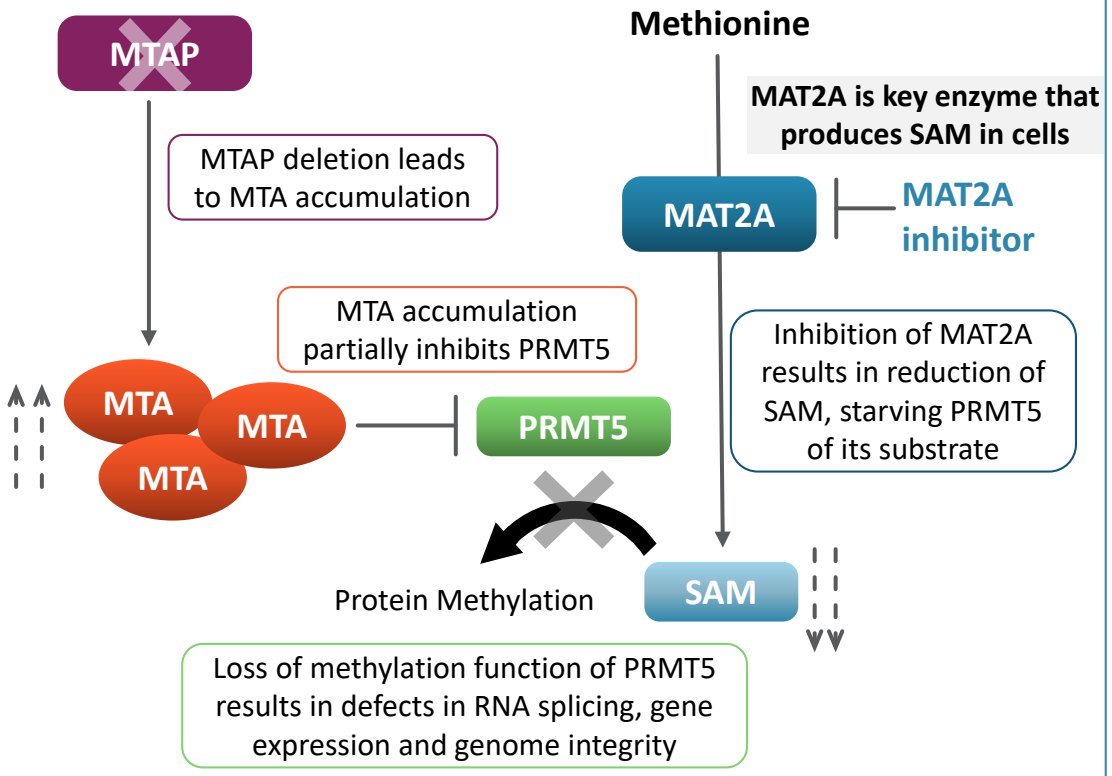
MTAP Deletion	HRD / BRCA	MSI-High	GNAQ/11 MET Driven Tumors	SL Platform
IDE397 (Ph1) MTAP-SL (PC)	PARG (DC) Pol Theta (Late PC) Pol Theta Degrader (PC)	Werner (PC)	Daro + cMET (Ph2) (SL Combination)	First-in-Class-SL (Hit ID) DDR (PC) Novel Targets

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

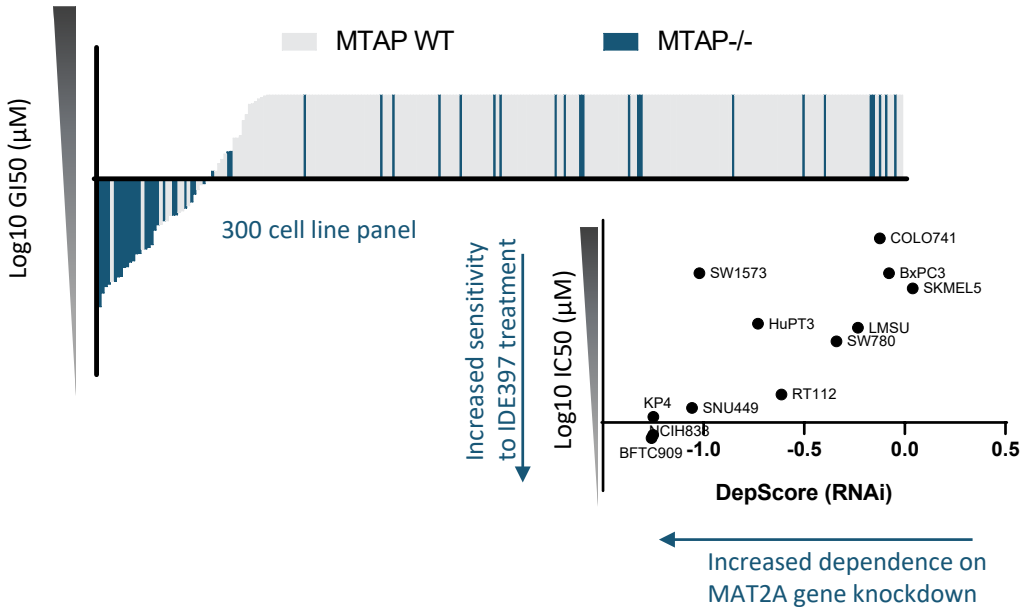
Cancer Type	N	MTAP Deletions (%)
Glioblastoma	592	41
Mesothelioma	87	32
Esophageal	95	28
Bladder	411	26
Pancreatic	184	22
Melanoma	448	16
Lung Cancer (NSCLC)	1053	15
Head and Neck	523	14
Sarcoma	255	10
Esophagogastric	514	10
Diffuse Glioma	513	9
Breast	1084	3
Ovarian	585	3
Adrenocortical	92	3
Thymic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

Data from The Cancer Genome Atlas in cBioPortal

IDE397: MAT2A Development Candidate *in vitro* Profile

IDE397 is selective for MTAP-/- Cell Lines

IDE397 is Selective for MTAP-/- Cell Lines

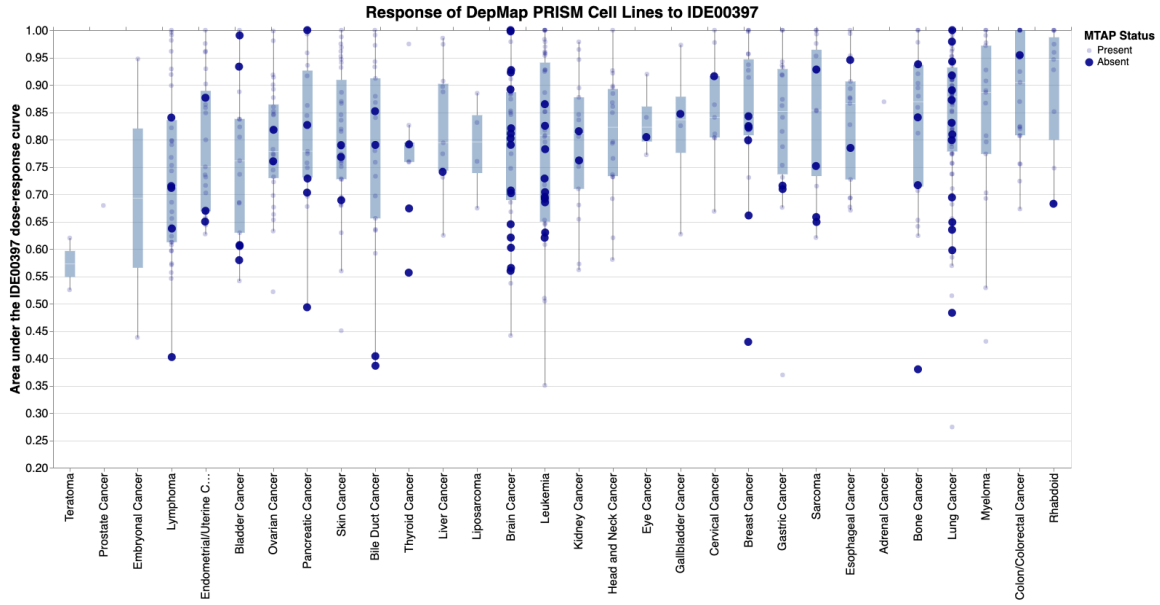


MTAP-/- cell lines are sensitive to IDE397

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

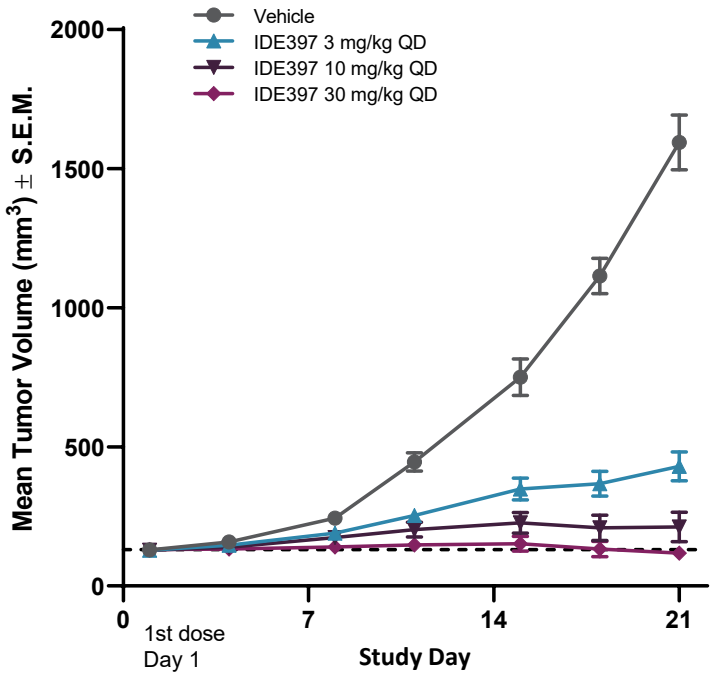
*BLOQ = below limit of quantitation

(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 SAM and SDMA Tumor PD Modulation in CDX Xenograft models

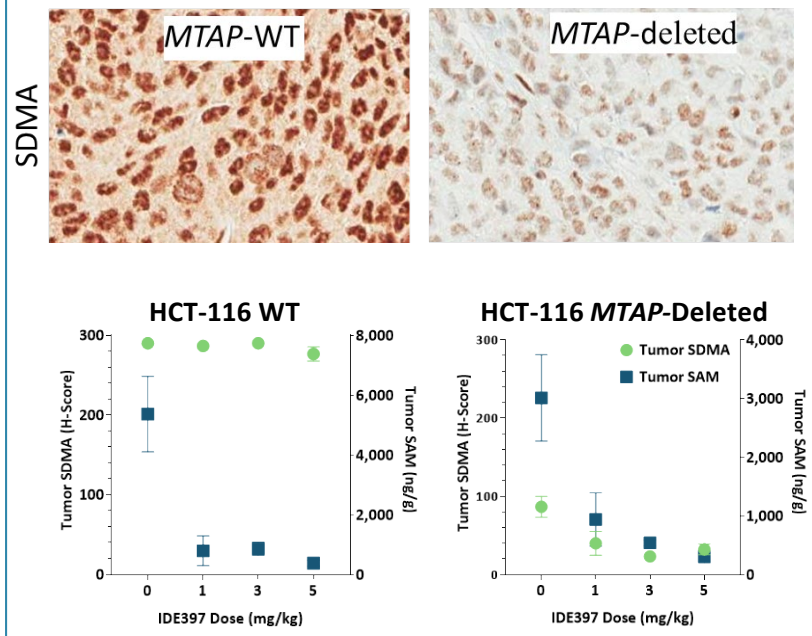
NSCLC Endogenous MTAP-/- CDX Model



IDEAYA Data

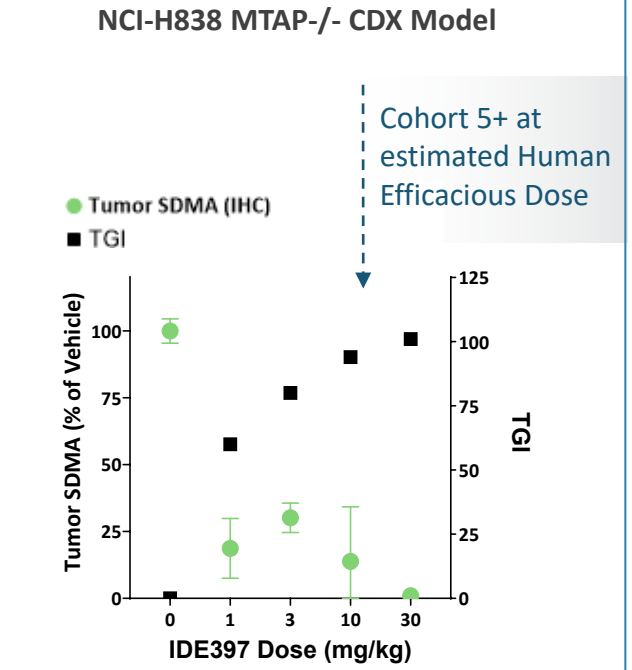
SDMA and SAM are Proximal PD Biomarkers of MAT2A inhibition

IDE397 modulates SDMA and SAM



IDEAYA Data: Fischer et. al., AACR 2021

SDMA modulation correlates to TGI



IDEAYA Data

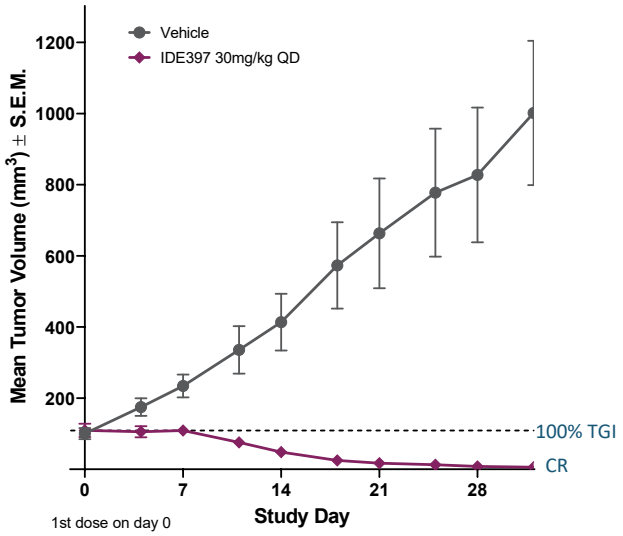
Robust dose-dependent efficacy and PD modulation observed in NSCLC CDX Model

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

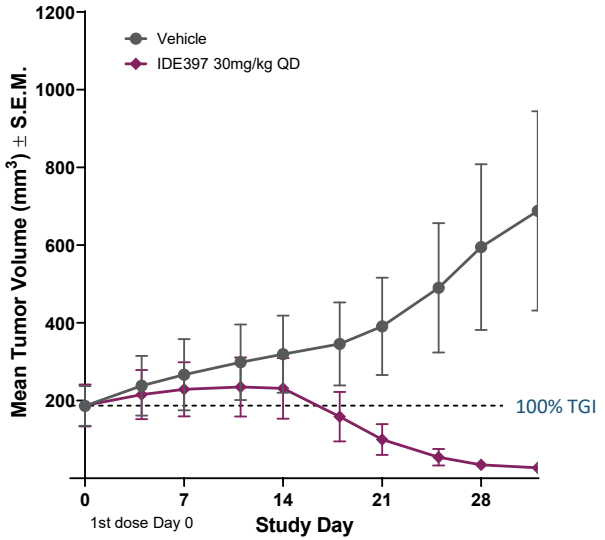
Monotherapy Tumor Regressions & Significant TGI Across Multiple Solid Tumor Types

NSCLC and Bladder Cancer MTAP-/- PDX Models

NSCLC PDX Model

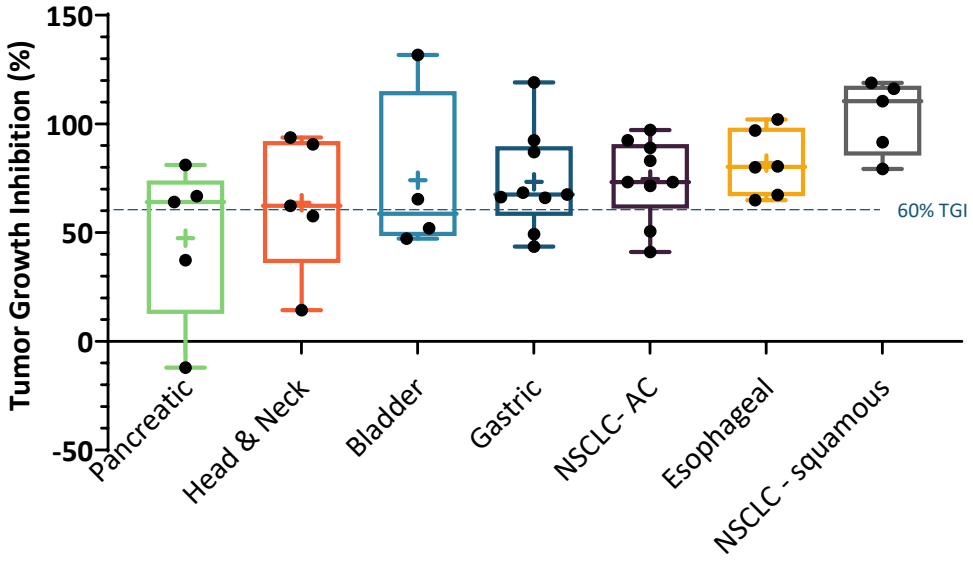


Bladder PDX Model



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

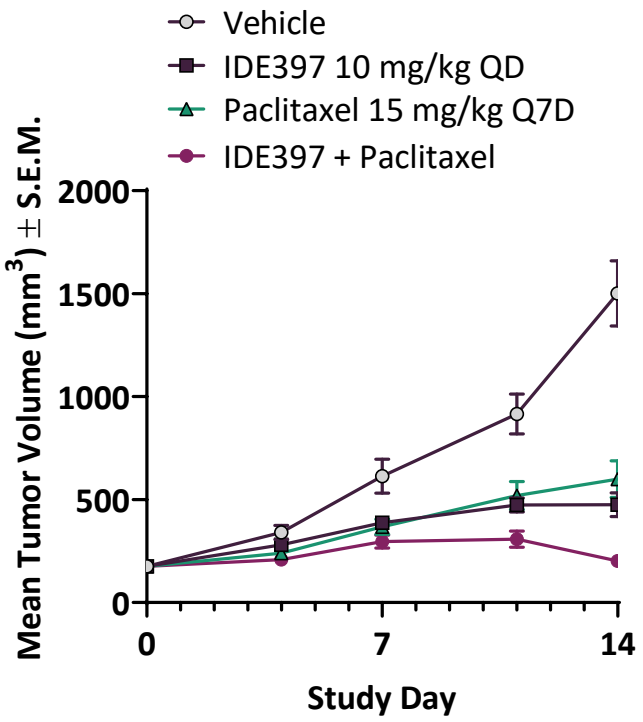
TGI = Tumor Growth Inhibition, CR = Complete Response

IDE397 Combination Partners Enhance Anti-Tumor Response

Evaluating Standard of Care (SOC) Combinations and Novel Combination Partners

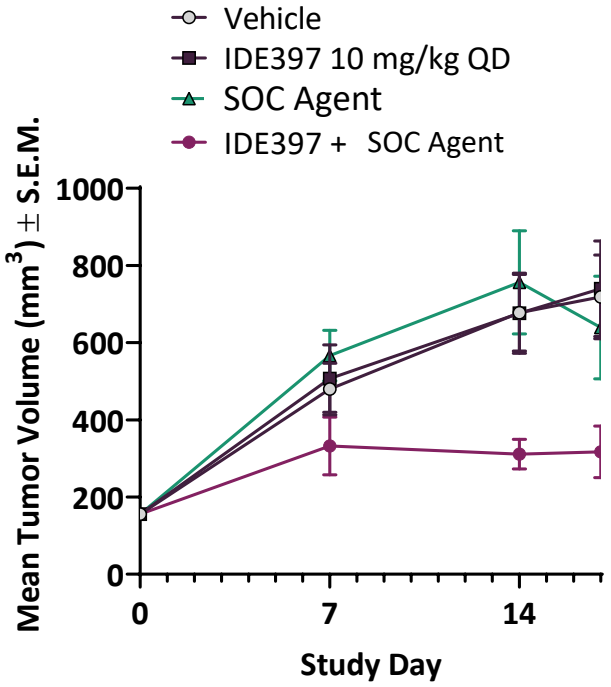
IDE397 + Paclitaxel – Head / Neck PDX

Combination Enables Tumor Regressions



IDE397 + SOC Agent – Solid Tumor CDX

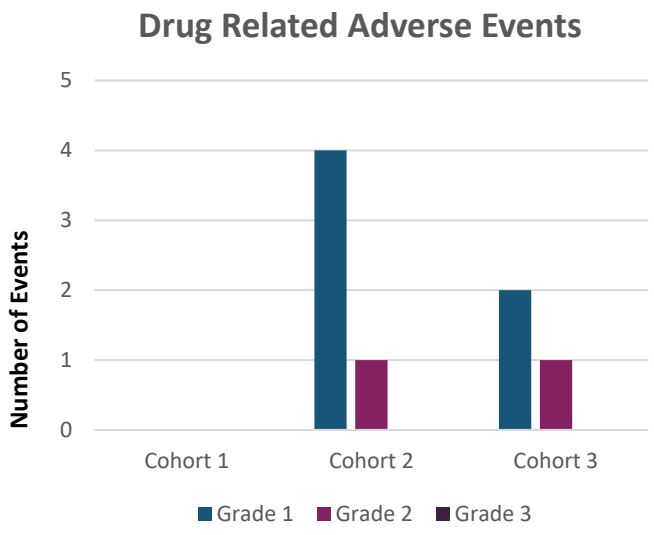
Combination Significantly Enhances Efficacy over Standard of Care (SOC)



Observed Preliminary IDE397 Clinical Activity and Tolerability

Plasma PD Reduction and Tumor Shrinkage in MTAP Deletion Patients

IDE397 Safety / Tolerability

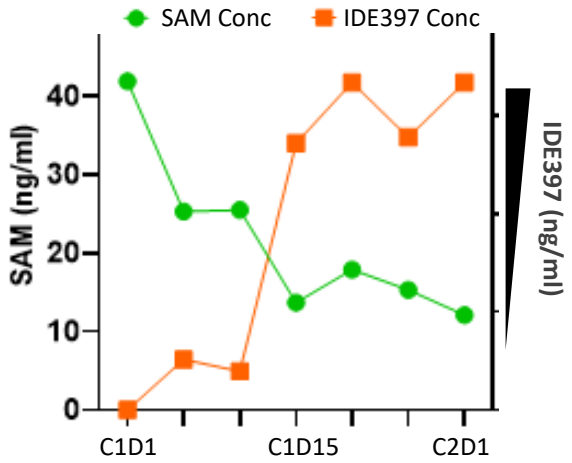


Cohorts 1 thru 3

IDE397 Plasma SAM PD

PK / PD Analysis

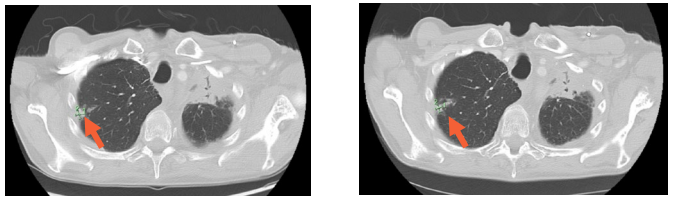
Plasma SAM vs IDE397 Concentration



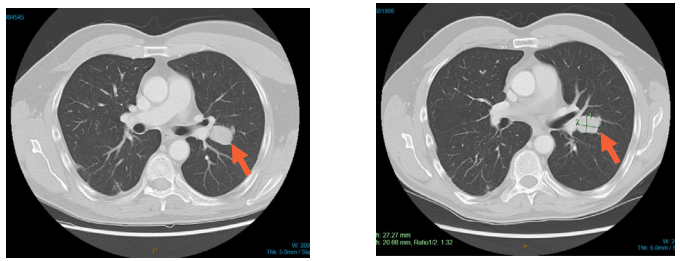
Cohort 3 Patient

Observed Tumor Shrinkage

Baseline CT Scan | Early Treatment Scan



Cohort 2 NSCLC: 15% Reduction*



Cohort 3 ACC with Lung Mets: 11% Reduction*

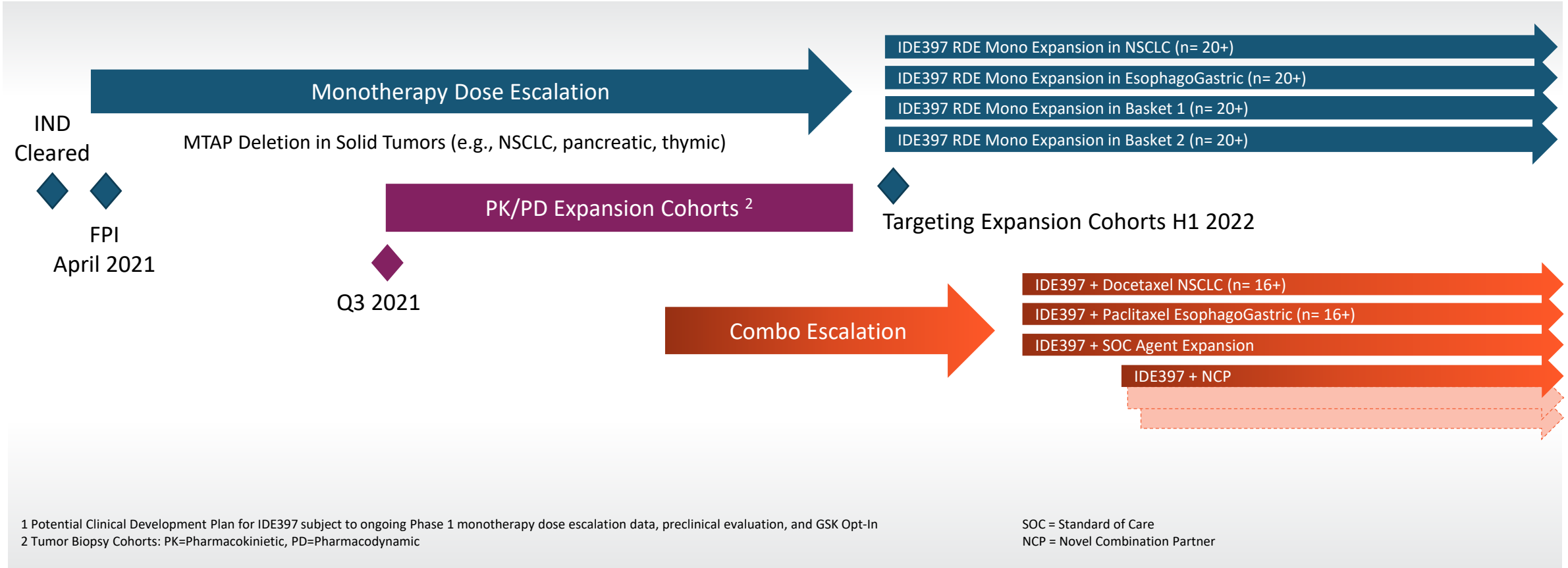
- No drug-related Serious Adverse Events: drug-related adverse events have been Grade 1/2, with no reported myelosuppression or liver toxicity
- Observed plasma SAM PD reduction in early dose escalation Cohorts 1 thru 3, achieving predefined target ≥ 60% plasma SAM suppression
- Observed tumor shrinkage 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
- Completed Enrollment into 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

SOC = Standard of Care
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

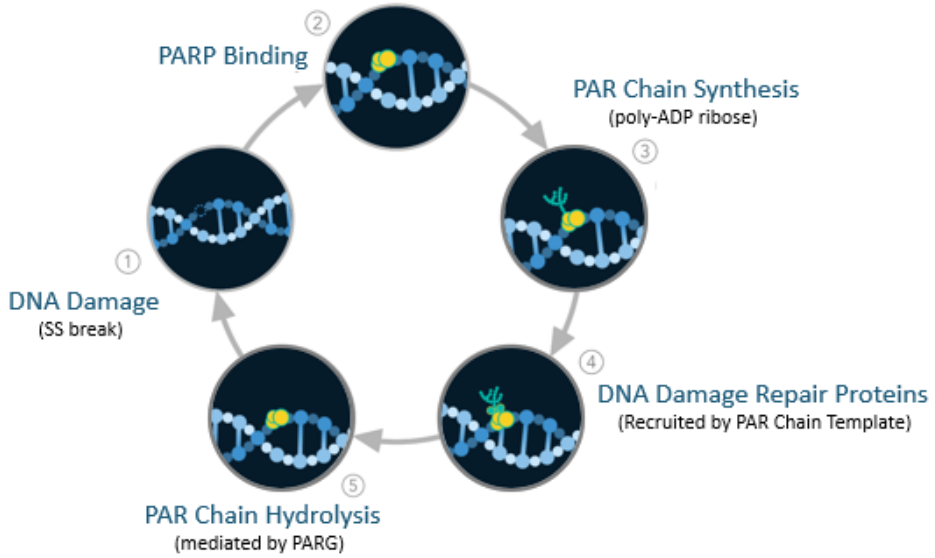
PARG Synthetic Lethality Program

Development Candidate Lead Selected

PARG Biology

Novel target in Clinically Validated Pathway

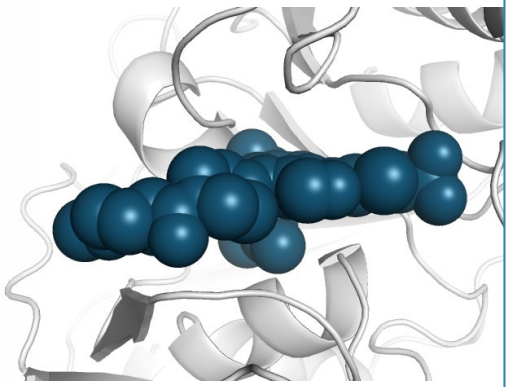
Poly(ADP-ribose) glycohydrolase (PARG) regulates DNA repair by hydrolyzing PAR chains in final step of DDR cycle



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

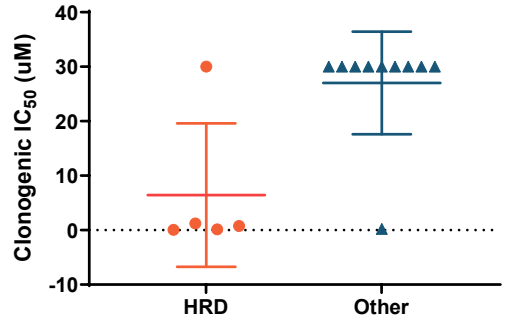


- Multiple potent cellularly active compounds demonstrate *in vitro* and *in vivo* PAR accumulation (PD) and *in vivo* efficacy in defined biomarker setting
- Collaboration with Bill Sellers lab (Broad) established to identify additional genetic sensitizers to PARGi

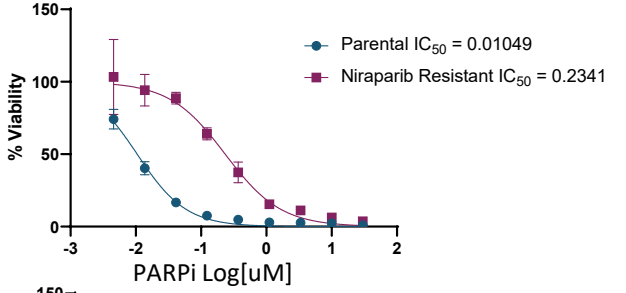
IDEAYA Data

PARG Inhibitors are Synthetic Lethal to HRD and Differentiate from PARPi

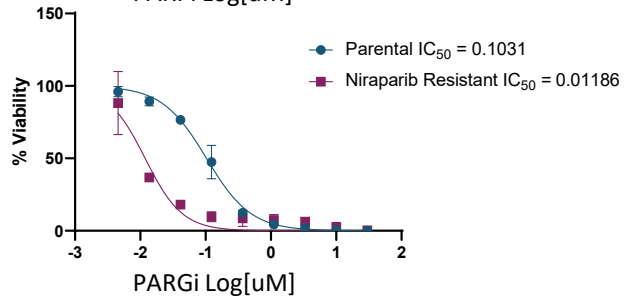
Cellular PARGi Sensitivity enriched in HRD Models



Acquired PARPi Resistance Can Sensitize Cells to PARGi



22-fold ***right*** shift in IC_{50}
→ Niraparib-resistant cell lines are less sensitive to PARPi



11-fold ***left*** shift in IC_{50}
→ Niraparib-resistant cell lines are more sensitive to PARGi

Multiple Endogenous HRD Cell Lines are Selectively Sensitive to PARGi (vs PARPi)

Ovarian HRD

Cell Line	PARG2 IC_{50} (μM)	Niraparib IC_{50} (μM)
Line A	0.009	1.3
Line B	0.008	2.7
Line C	0.05	0.68
Line E	4.9	0.22
Line F	2.34	0.22
Line G	0.6	0.65

sensitive
insensitive

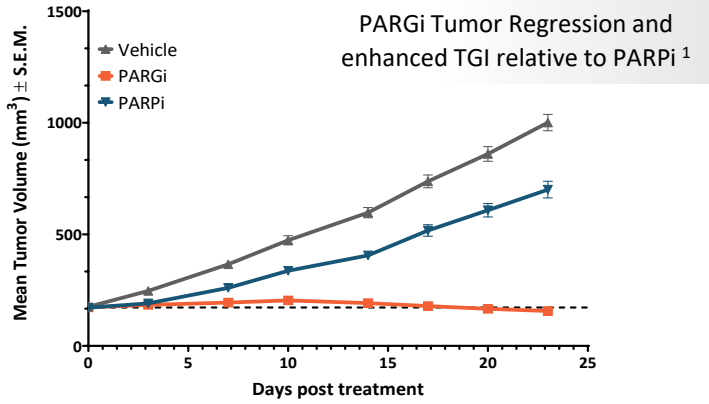
Breast HRD

Cell Line	PARG2 IC_{50} (μM)	Niraparib IC_{50} (μM)
Line A	0.01	0.18
Line B	0.03	0.03
Line C	0.07	0.007
Line D	0.08	0.57
Line E	0.37	17.6
Line F	0.1	0.89
Line G	0.22	2.27
Line H	3.5	0.56
Line I	1.02	5
Line J	1.31	4.9
Line H	0.64	0.72

Biomarker Selected CDX and PDX Models are Sensitive to PARGi

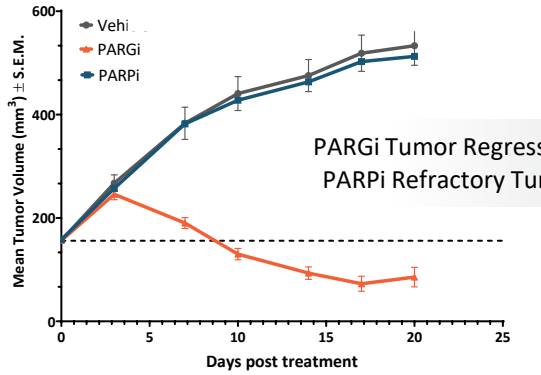
Differentiated Activity to PARP inhibition in Ovarian, Gastric and Breast Cancer Models

Ovarian Cancer HRD CDX Model



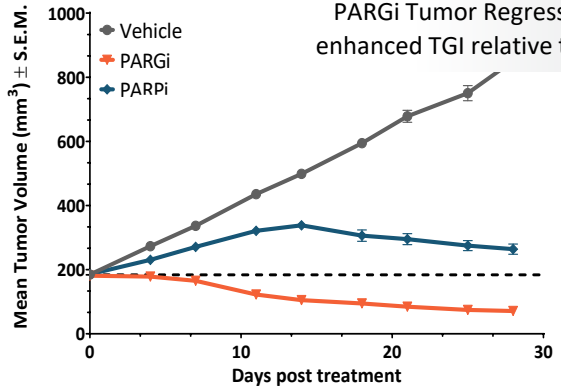
PARGi Tumor Regression and enhanced TGI relative to PARPi [1]

Gastric Cancer HRD CDX Model



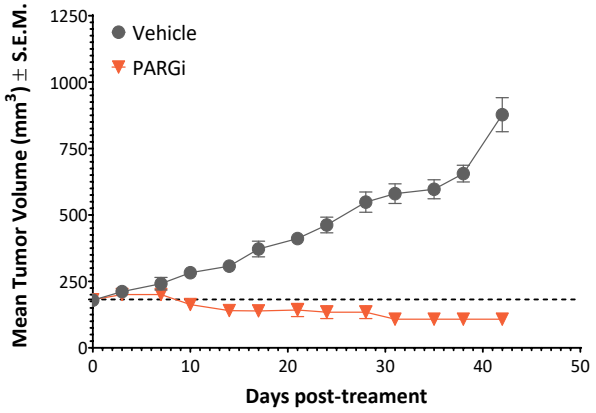
PARGi Tumor Regression in PARPi Refractory Tumor [1]

Breast Cancer HRD CDX Model

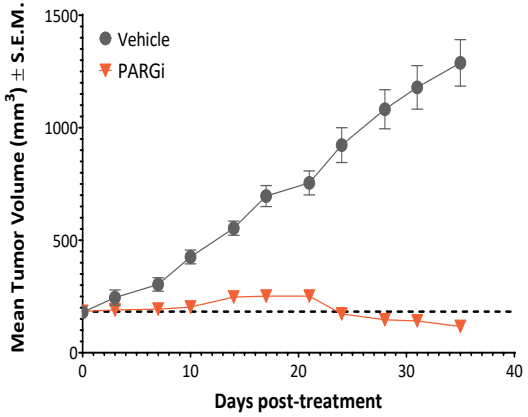


PARGi Tumor Regression and enhanced TGI relative to PARPi [1]

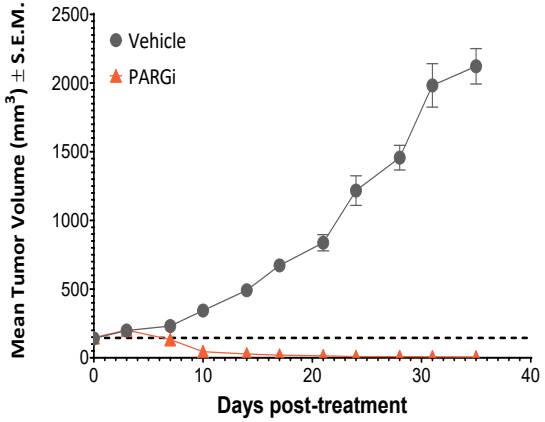
Breast Cancer PDX Model 1



Breast Cancer PDX Model 2



Breast Cancer PDX Model 3



IDEAYA Data; [1] PARPi dosed at MTD ; PARGi dosed at <MTD

Pol Theta Synthetic Lethality Program

Initiate IND-Enabling Studies in H1 2022

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

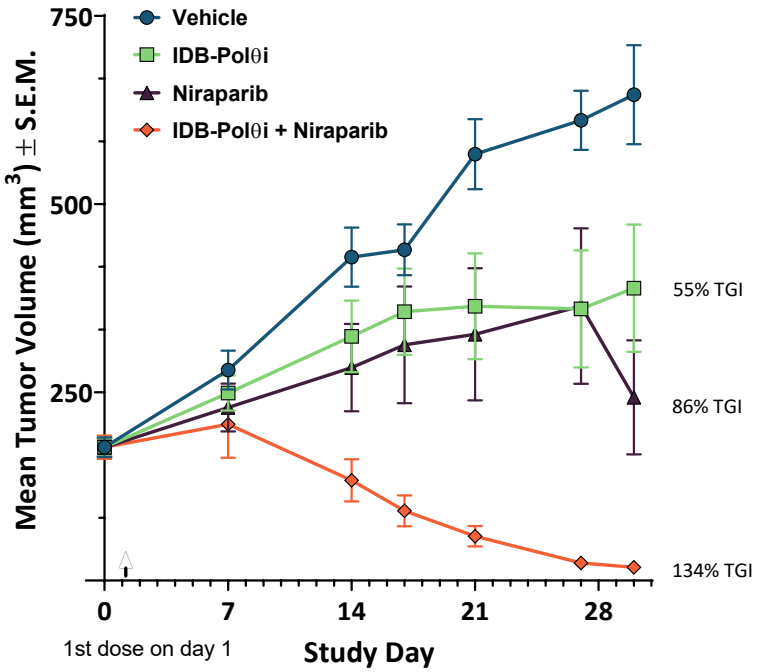
Advancing both small molecule inhibitors and protein degraders

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]

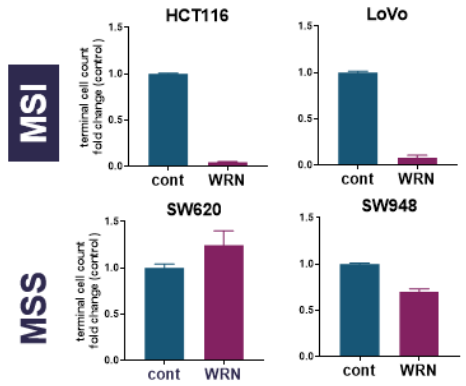
Werner Helicase Synthetic Lethal with High-MSI

CellPress

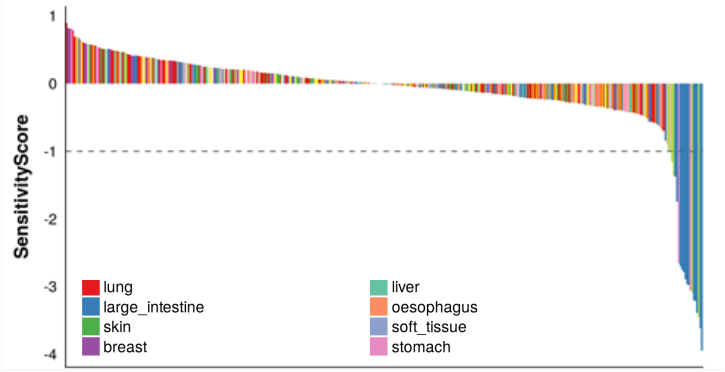
Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al



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



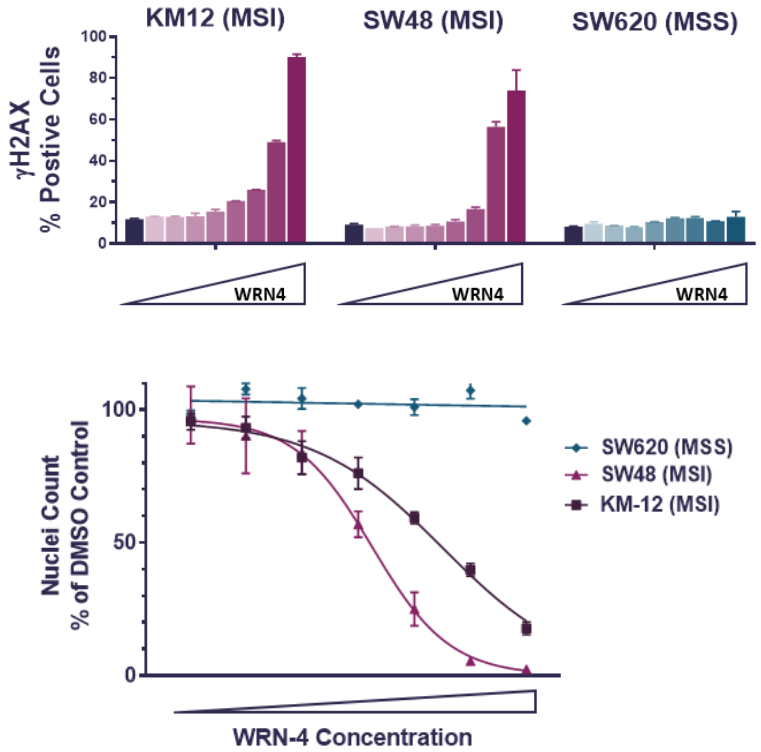
Project Drive

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**: WRN inhibitor *in vivo* PD and efficacy, with ~100% TGI



IDEAYA Data

[1] Cancer Res., November 1998

Darovasertib, a Phase 2 PKC Inhibitor

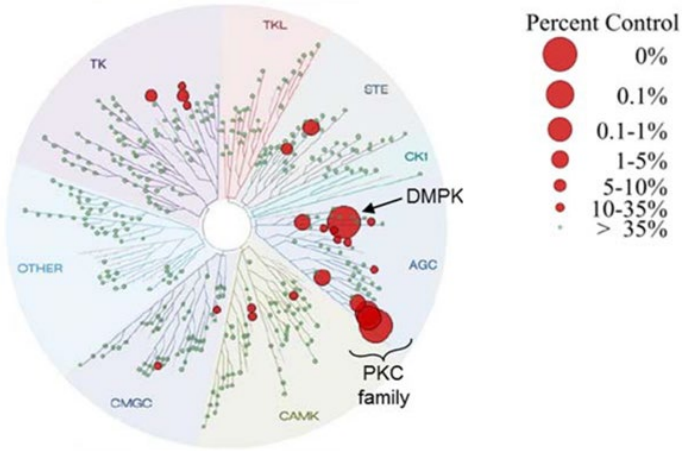
Potential First-in-Class and Best-in-Class Precision Medicine Oncology Program

Darovasertib Compound Profile

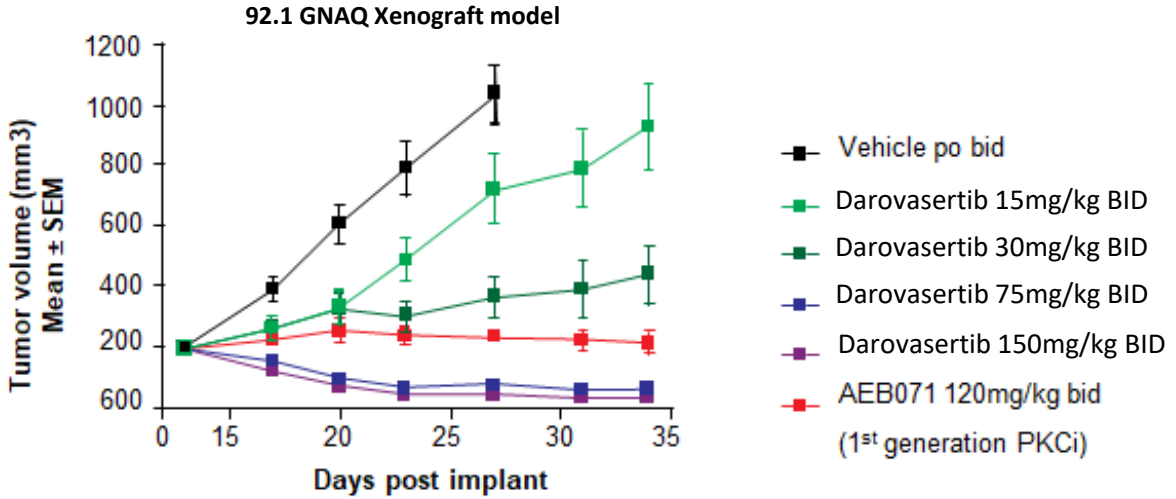
- Enhanced potency across novel PKC isoforms
- Single agent tumor regressions in *GNAQ/GNA11* xenografts
- Long-term 13-week toxicology studies in two species completed to enable potential registration (oncology)

Darovasertib IC_{50} (nM) PKC Activity								
Classical				Novel				Atyp.
alpha	beta 1	beta 2	gamma	delta	epsilon	eta	theta	zeta
25	66	58	11	4	3	1	3	>2000

High Kinome Selectivity



Single Agent Darovasertib Induces Tumor Regressions



- 1st Generation PKCi, AEB071, only demonstrated stasis *in vivo*
- Darovasertib led to tumor regressions *in vivo*, with enhanced cell potency vs. novel PKC isoforms (delta, epsilon, eta and theta)
- Enhanced selectivity vs. AEB071 to improve overall tolerability, including GI-related

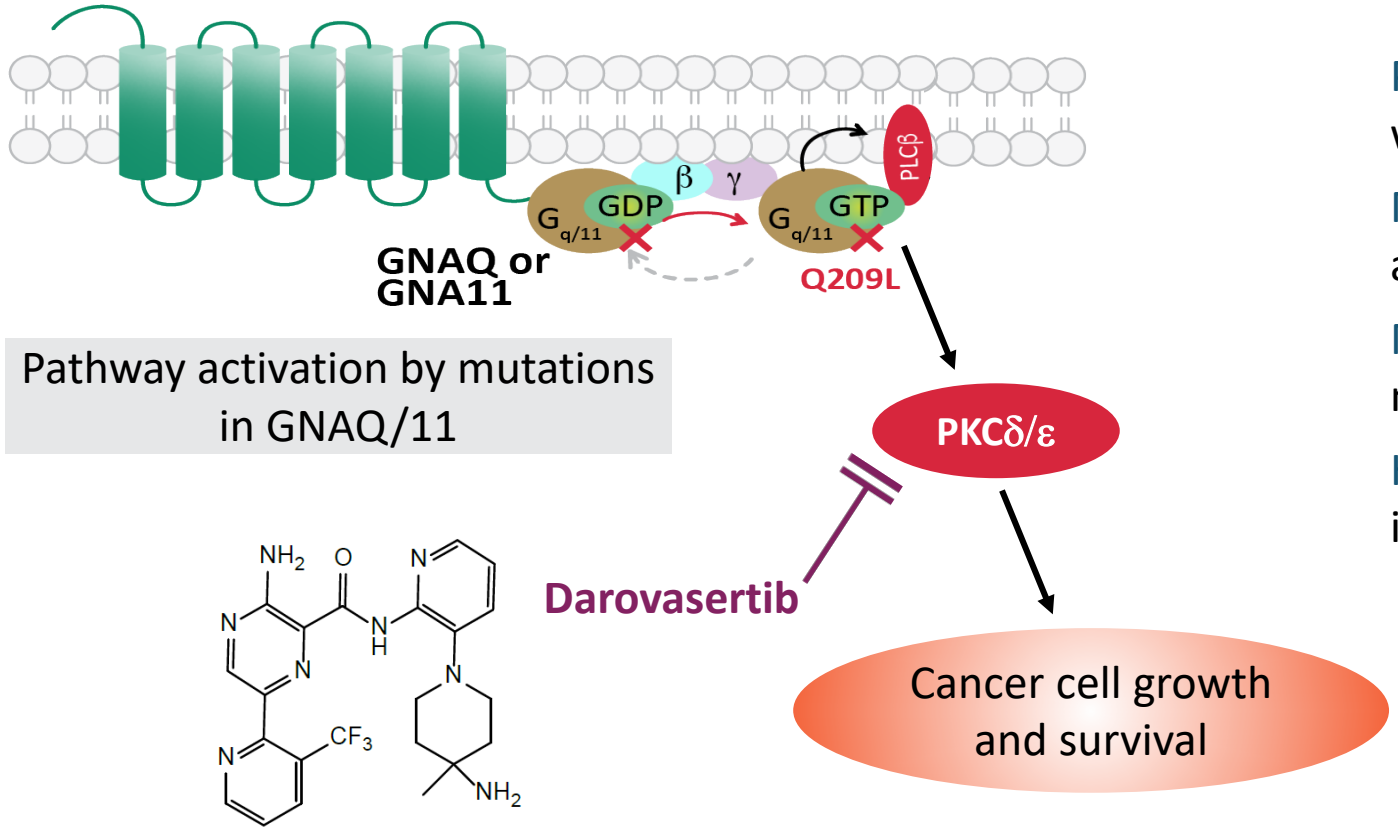
AEB071 = Novartis 1st generation PKC inhibitor
Darovasertib (LXS196 / IDE196) = 2nd generation PKC inhibitor

Reference: ACS National Meeting, 2017, Visser, et. al

Darovasertib, a PKCδ/ε Inhibitor Targeting GNAQ/11 Mutation Tumors

GNAQ/11 mutations (>90% UM) highjack PKC signaling for tumorigenic transformation

GNAQ/11 Mutation



Pathway activation by mutations in GNAQ/11

Primary Uveal Melanoma is typically treated with radiation and/or enucleation

Metastatic Uveal Melanoma (MUM) occurs in approximately 50% of patients

MUM presents predominantly as liver metastasis in ~90% of patients

Historical treatment approaches have been ineffective with no approved therapies

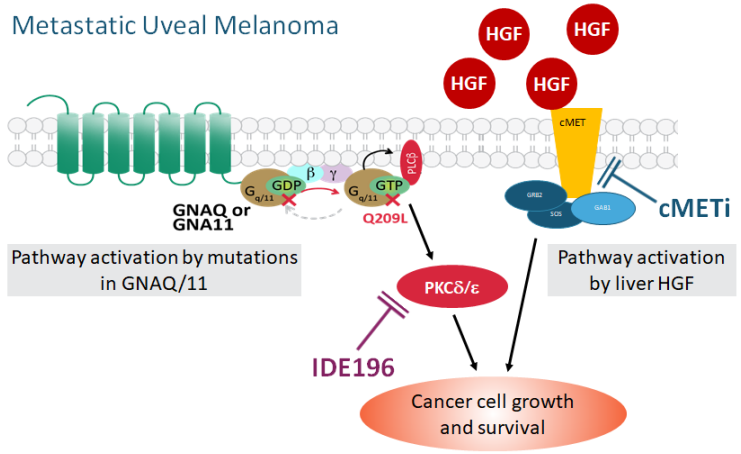
δ = delta ε = epsilon

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

cMET inhibitor reduces HGF activation of cMET signaling to Synergize with Darovasertib

PKC + cMET Synthetic Lethal Discovery

High cMET expression is associated with metastatic progression

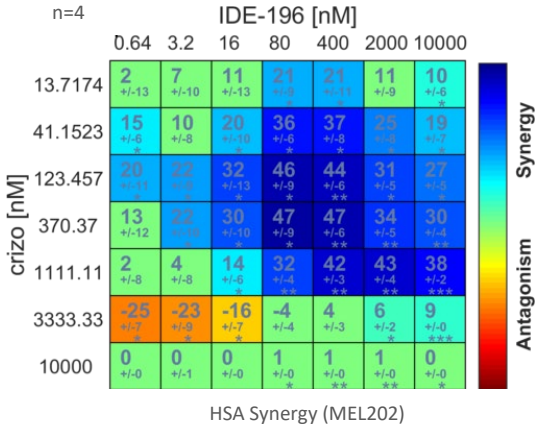


- HGF promotes cancer cell growth and survival
- Translational Research hypothesis: HGF-induced cMET signaling in the liver microenvironment activates an alternative pathway for MUM tumor progression

IDEAYA Darovasertib Investor Day, 2021

Preclinical Synergy

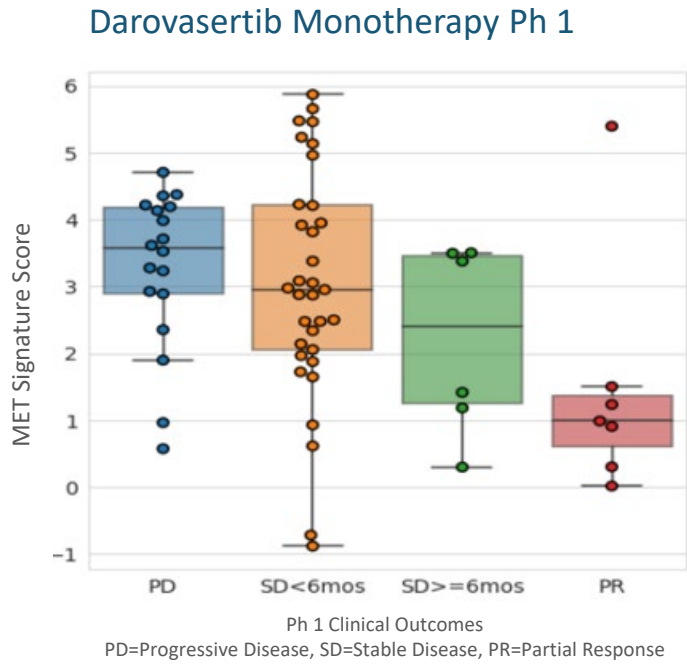
Darovasertib + Crizotinib synergy exhibited in Mel202 (MUM) cell line



IDEAYA Data AACR 2021

Clinical Phase 1 Data Association

Clinical response to Darovasertib monotherapy associates with low cMET activity

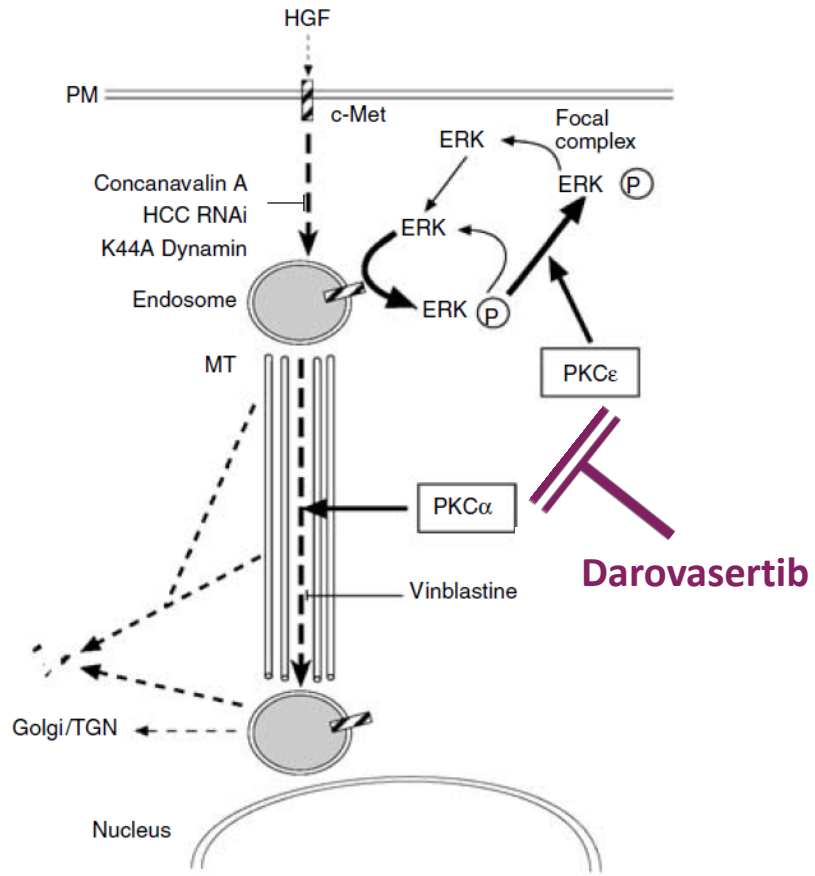


IDEAYA Data

PKC-cMET SL: Evaluation of Potential Indication Expansion Ongoing

Additional MET-Amplified / MET High Expression Tumors

PKC-epsilon and MET Amplified Tumors



EMBO 2004, Parker et al, modified by IDEAYA

PKC-epsilon has been reported in literature to control HGF-dependent cMET traffic, signaling and cell migration

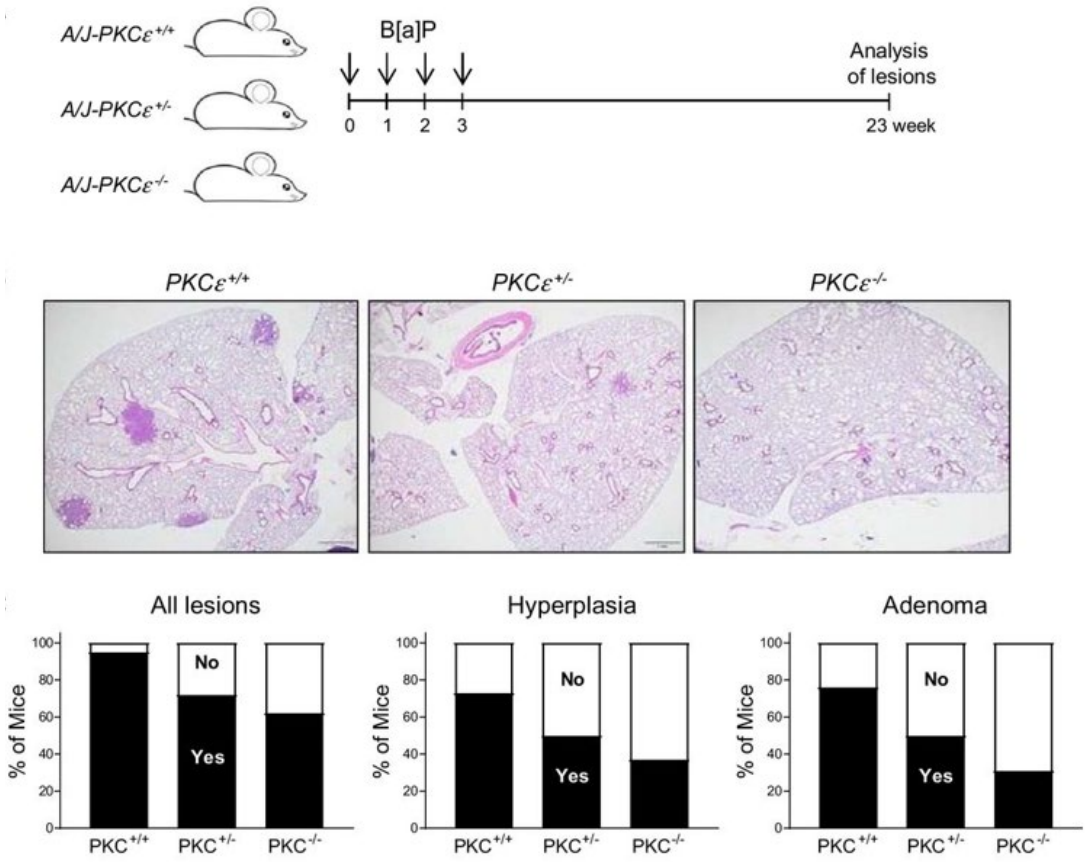
Evaluating potential opportunities to expand clinical PoC of Darovasertib (PKC) + cMET combo to additional MET-amplified / high expression tumors, such as Hepatocellular Carcinoma

Darovasertib demonstrates activity vs PKC-epsilon isoform with strong cell potency (<100nM EC50)

PKC δ/ε are Required for KRAS-Driven Lung Tumorigenesis

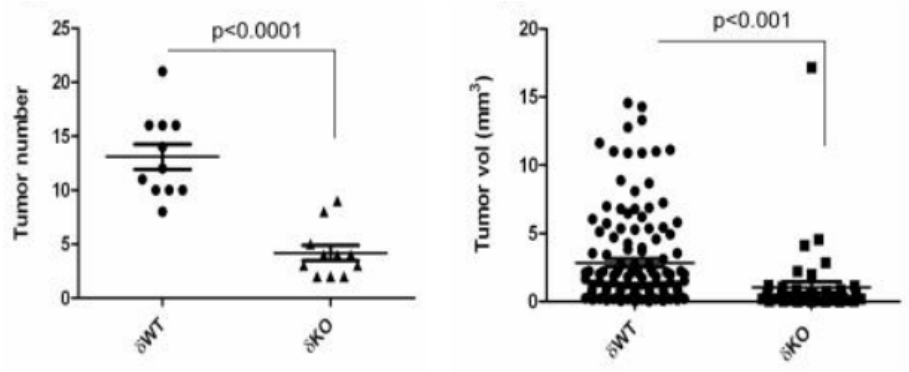
Evaluation of Potential Darovasetib plus KRAS Combinations

Germline knockout of PKCε reduced number and size of carcinogen-induced KRAS mutant lung tumors

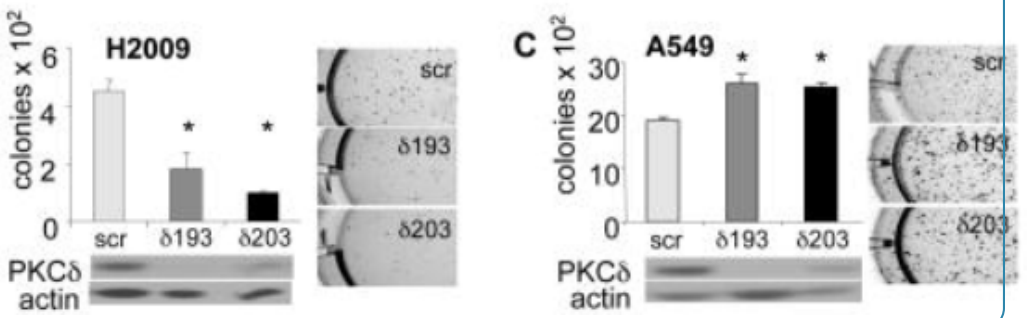


Reference: Kazanietz lab, U Penn (Garg et al., 2020, Cancer Research)

Germline knockout of PKCδ reduced number and size of carcinogen-induced KRAS mutant lung tumors



PKCδ is required for anchorage-independent growth of KRAS mutant/KRAS addicted lung cancer cells



Reference: Reyland lab, U Col (Symonds et al., 2011, Cancer Research)

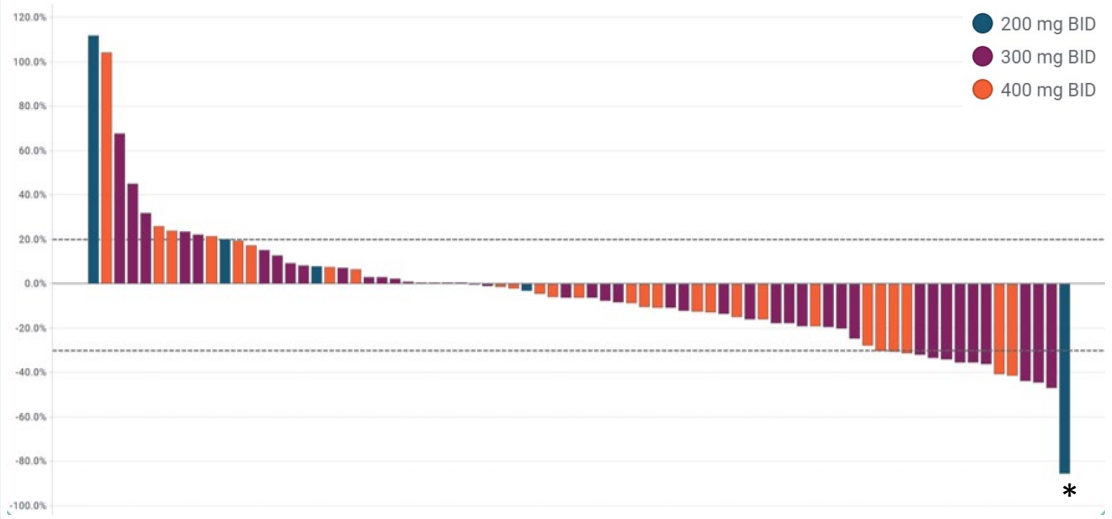
δ = delta ε = epsilon

Darovasertib Monotherapy BID Experience in Heavily Pre-Treated MUM

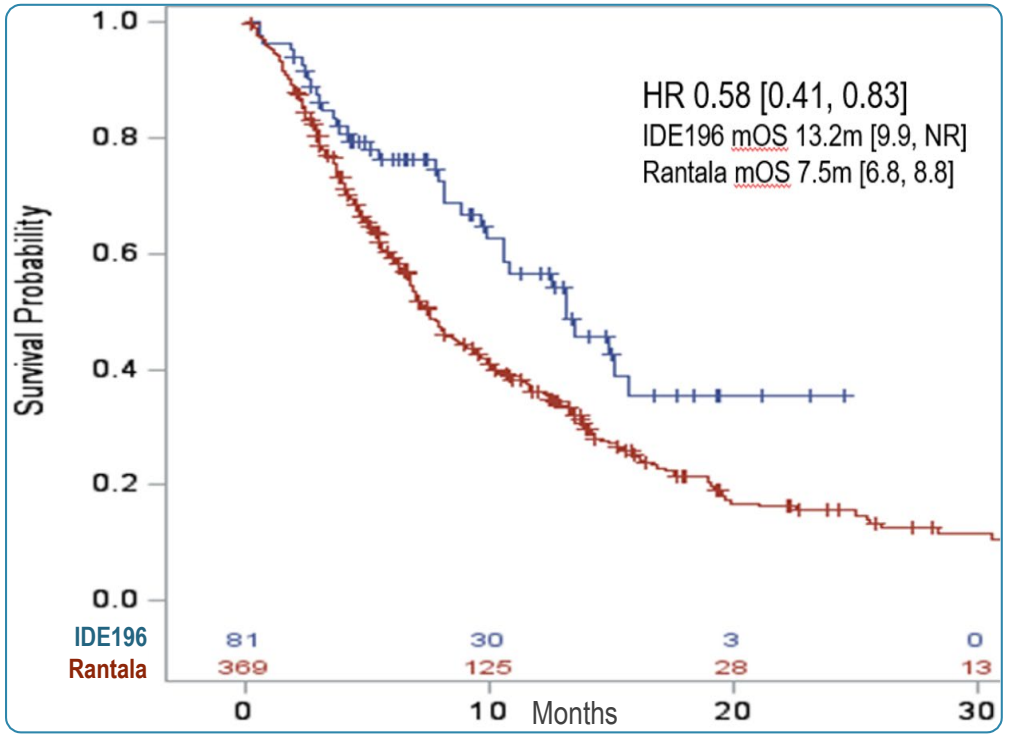
Overall Survival favorable compared to Historical Pretreated Synthetic Control Arm [1,2]

Darovasertib (IDE196) BID in MUM

n=81 (75 patients with ≥ 1 post-baseline scan)



* Patient achieved CR and on treatment > 3.5 yrs



Pooled Analysis IDEAYA + Novartis Clinical Data BID Monotherapy
n = 81 with 75 evaluable patients
46 patients (61%) with target lesion reduction
15 patients (20%) with ≥30% target lesion reduction
Observed monotherapy mOS 13.2

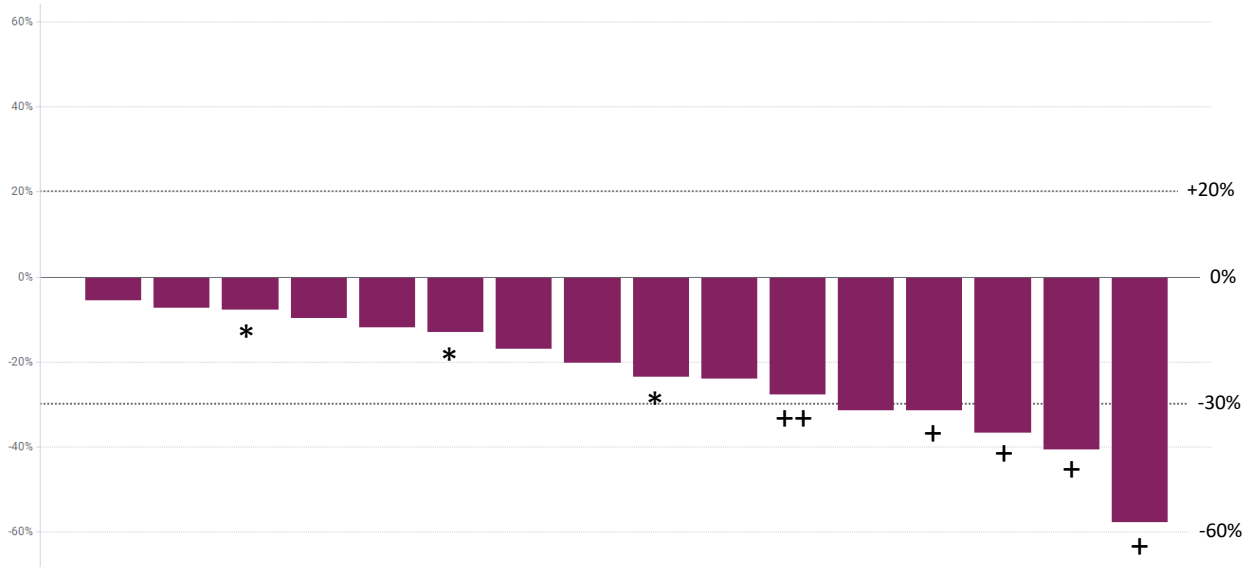
[1] IDEAYA Data (based on preliminary analysis of unlocked database, including: pooled IDEAYA and Novartis BID monotherapy clinical data as of Apr 13, 2021)
[2] Synthetic Control Arm based on Rantala 2019 (meta-analysis of overall survival of patients with metastatic uveal melanoma over 1980 to 2017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

Preliminary Darovasertib + Crizotinib Phase 2 Expansion Dose Efficacy

Encouraging Clinical Activity in heavily pretreated Metastatic Uveal Melanoma

Daro + Crizo Expansion Dose Cohort, n=16 with ≥1 post-BL scan

100% of patients observed tumor shrinkage (100% DCR)
31% ORR in patients with ≥2 post baseline scans



+ Confirmed partial response by investigator or central review
++ Unconfirmed partial response by central review awaiting follow-up scans
* Has had only 1 post baseline scan
3 of 4 responders were pretreated with immunotherapy

Early Clinical PoC of PKC + cMET Synthetic Lethal

- 100% of patients show tumor reduction in target lesions (n=16 evaluable patients with ≥ 1 scan)
  - 100% Disease Control Rate
- Encouraging ORR% in heavily pre-treated MUM patients with ≥2 post-baseline scans (n=13)*
  - 4 patients with confirmed PRs (31% ORR)
  - 6 patients (46%) demonstrate >30% tumor reduction, including 1 uPR awaiting follow-up scan(s)
  - IMC-GP100/IMCR: 4.7% ORR; Pembro: 5% ORR**
- Baseline Characteristics of n=22 total patients, including 6 patients awaiting 1st scan
  - LDH > ULN in 65% of patients
  - 91% with prior therapies
  - 59% with 2 or more prior therapies
- Program Goal: ORR >20%

* No patients off-treatment prior to 2nd scan

IDEAYA Data: preliminary analysis of unlocked database as of 11/25/2021

* CT scan read by investigator or central review
** Immunocore Corporate Presentation, November 2021

Darovasertib + Crizotinib Combination Preliminary Efficacy

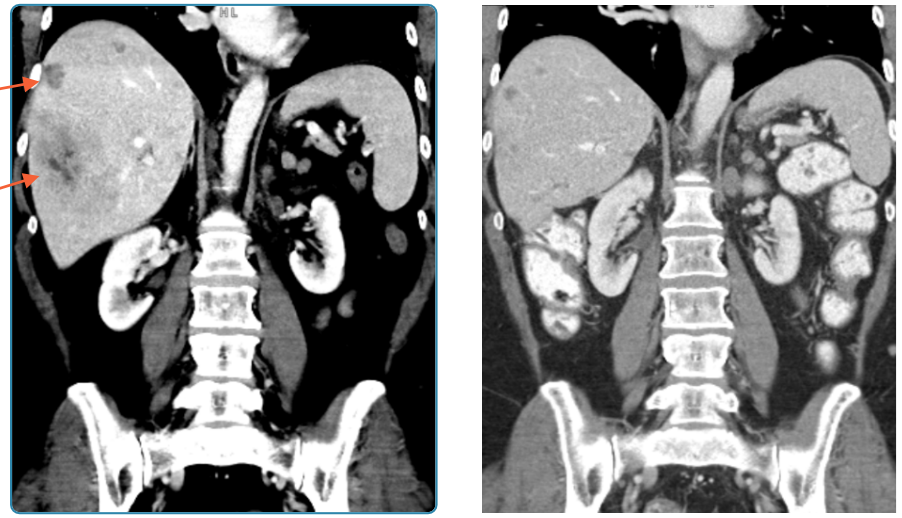
Examples of Responses with significant Anti-Tumor Activity

Patient Example 1

- 70+ year old patient with ongoing response at 6 months
- Priors: Ipi+Nivo, Chemoembolization, Radioembolization
- Diffuse disease in liver, lung, LN, subcut and elevated LDH

Baseline

5 months

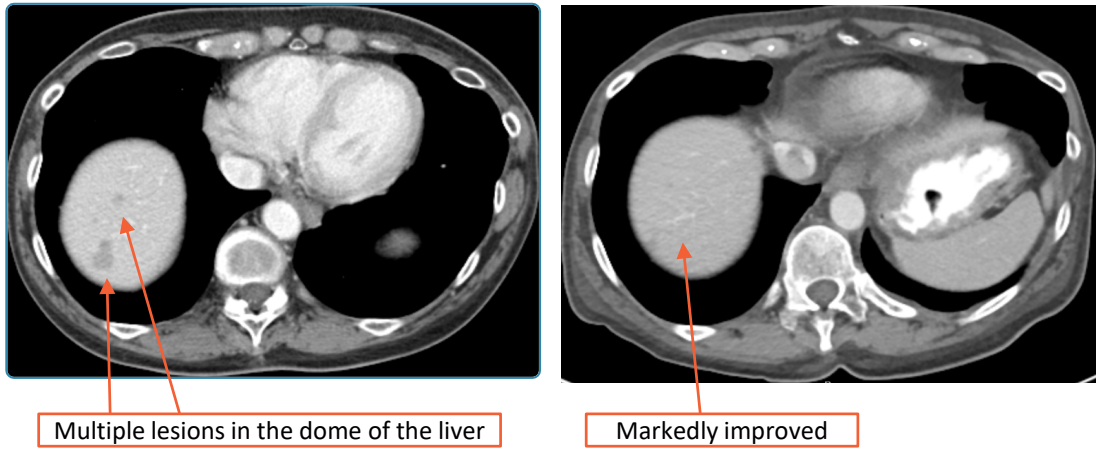


Patient Example 2

- 60+ year old patient with ongoing response at 4 months
- Priors: Ipi+Nivo
- Numerous liver lesions, normal LDH

Baseline

4 months



IDEAYA Data: preliminary analysis of unlocked database as of 11/25/2021

Darovasertib + Crizotinib SL Combination Therapy

Differentiated Novel Treatment Mechanism in MUM

	Darovasertib + Crizotinib	Cabozantinib	Selumetinib + Dacarbazine	Tebentafusp
Target / Mechanism	PKC + cMET	cMET	MEK + Chemotherapy	HLA-A2-0201 Bi-Specific Ab
Study Name	NCT03947385	Alliance A091201^	SUMIT (NCT01974752)	IMCgp100-102
Population	2L/3L+ MUM (n=16 eval)	1L+ MUM (n=31 eval)	1L+ MUM (n=97)	2L+ MUM (n=127)
Patient Selection	N/A (100% of MUM)	N/A (100% of MUM)	N/A (100% of MUM)	HLA-A2-0201 (~40-50% of MUM)
Drug Form	Oral Tablets (BID)	Oral Capsules (QD)	Oral Capsules (BID) plus chemo	IV Infusion (Weekly)
Tolerability (Grade ≥3 Drug-Related AE)	27%	51.6%	63% ^^^ (All Cause)	46.5%
% of Pts with Tumor Shrinkage	100%*	23% ^^	35%^^	44%#
Overall Response Rate (ORR)	31%*	0%	3% ^^^	4.7%#
Progression Free Survival (PFS)	Targeting mPFS update in H1 2022	2 m	2.8 m ^^^	2.8 m#
Overall Survival (OS)	[TBD]	6.4 m	Not reported	16.8 m#

* IDEAYA Ph 1/2 (ongoing): based on preliminary analysis of unlocked database as of 11/25/2021 by investigator or central review

Based on Immunocore reported 2L+ study data (to reflect comparative patient population) and by independent review

^ Randomized Phase II Trial and Tumor Mutational Spectrum Analysis from Cabozantinib versus Chemotherapy in Metastatic Uveal Melanoma (Alliance A091201); Clin Cancer Res 2020;26:804–11

^^ Estimated from Waterfall plot

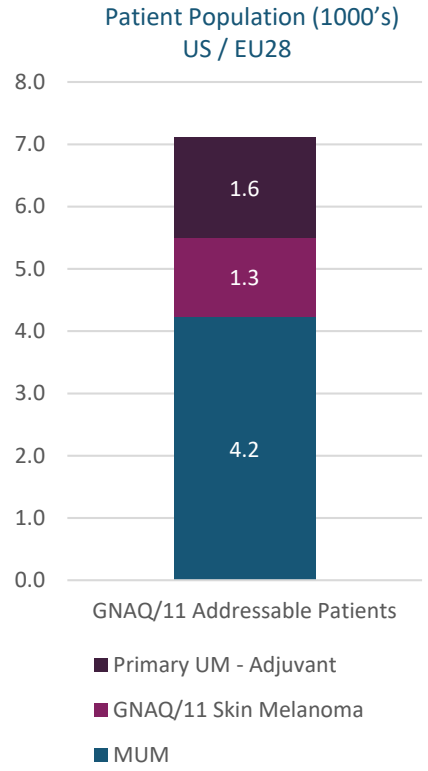
^^^ Journal of Clinical Oncology, Carjaval, et. al, 2018; 1232-1239

IDEAYA BIOSCIENCES

Darovasertib Patient Population Analysis

GNAQ/GNA11 Melanoma & Additional MET-Amplified / High Expression Tumors

Addressable GNAQ/11 Patients



IDEAYA Analysis

MUM, Adjuvant UM and GNAQ/11 Skin Melanoma

- No FDA Approved Therapies for MUM or GNAQ/11-Tumors
- Clinical evaluation of opportunities in MUM (Ph2), Adjuvant Uveal Melanoma (Ph 1 IST) and GNAQ/11 Skin Melanoma (Ph1)
- Total Addressable Patient Population (US, EU28) ~7.1K pts/year

Evaluating Additional MET-Amplified / High Expression Tumors

- Patient selection based on CLIA-validated assays for MET-amplification (e.g., NGS, FISH) or high MET expression (e.g., IHC)
- HCC focus on refractory / resistant patients based on hypothesis of constitutively active cMET/HGF axis

Validating Additional Mechanistic Relationships

- nPKC (δ or ε) knockout mice protected from KRAS induced lung adenocarcinoma[4,5]
- PKC epsilon supports aneuploid cancer cell mitosis[6]

	MET-amplification	High MET Expression
NSCLC	~1-5% [1,2]	~3-4% [2]
CRC	*	~3-9% [2]
Gastric Cancer	*	~9-20% [2]
HCC	~9% [3]	~27% [3]

1 Drilon et al., Journal of Thoracic Oncology, 2017, 12: 15-26
2 Sierra et al., Therapeutic Advancers in Medical Oncology, 2011, 3: S21-S35
3 Lee et al., Anticancer Research, 2013, 33: 5179-5186
4 Symonds et al., Cancer Research, 2011, 71: 2087-2097
5 Garg et al., Cancer Research, 2020, 80: 5166-5173
6 Parker et al., Advances in Biolgical Regulation, 2020, 78: 100759

* not reported
δ = delta ε = epsilon

Building a Premier Synthetic Lethality Precision Medicine Oncology Biotech

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
Lead Series ID

HRD/BRCA

PARG
IND Filing – Q4 2022

Pol Theta
Initiate IND Enabling – H1 2022
Advance Protein Degraders

MSI-High

Werner Helicase
Lead Optimization
Dev Candidate 2023

GNAQ/11 MET-Driven Tumors

SL Combo: PKC + cMET
mPFS Update – H1'22
FDA Guidance on Registration Trial - H1'22
Evaluate Expansion Opportunities in MET

SL Platform

First-in-Class – Lead Series ID

DDR – Lead Optimization

Novel SL Targets

Target Milestones to Advance Industry Leading Synthetic Lethality Pipeline