May 2022

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 Annual Report on Form 10-K for the year ended December 31, 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 of Key Emerging Targets** including clinical stage IDE397 (MAT2A) and darovasertib (PKC), and maturing preclinical candidates for PARG, Pol Theta and Werner
- **Pharma Collaborations** with GSK (over ~$3 billion in potential milestones) and Pfizer
- **Strong Balance Sheet** with ~$346M in cash anticipated to fund operations into 2025 [1, 2]
- **NASDAQ**: IDYA

- **2022 Target Catalysts**
  - IDE397 (MAT2A) – Phase 1 (Mid-Year)
    - Monotherapy Expansion Cohorts
    - Combination Cohorts Initiation
    - GSK Option Data Package; $50M Option Exercise Fee
  - IDE161 (PARG) – IND (Q4)
  - Pol Theta – Development Candidate (Q2)
  - Darovasertib (PKC) – Phase 1/2 (Mid-Year)
    - Clinical Data Update for Daro + Crizotinib in MUM
    - Regulatory Guidance for Daro + Crizotinib in MUM

(1) IDEAYA Form 10-Q filed with the U.S. Securities and Exchange Commission on May 10, 2022
(2) Includes cash, cash equivalents and marketable securities as of March 31, 2022

Synthetic Lethality

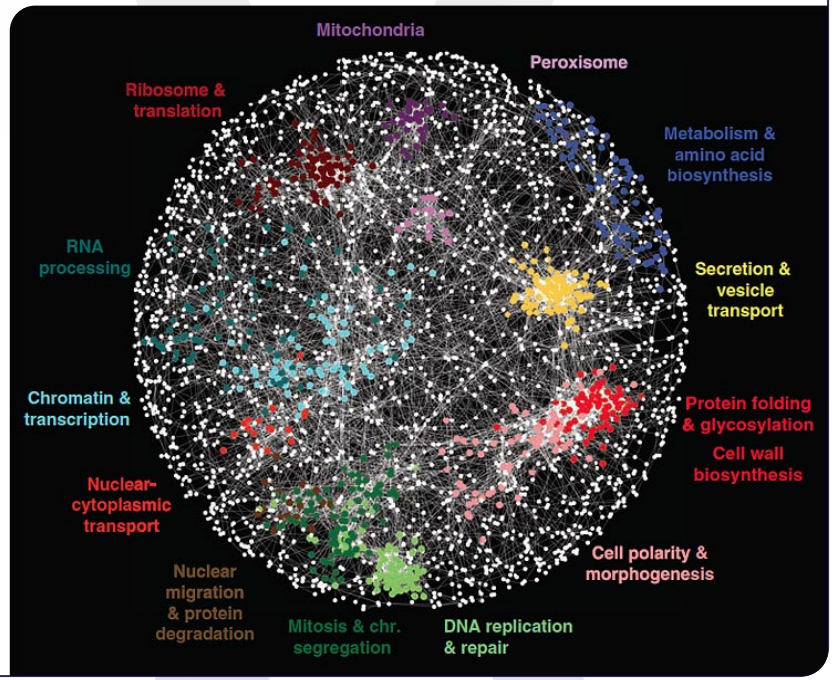
The Next Frontier in Precision Medicine Oncology

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 Mid-2022 GSK Option Data Package Mid-2022	gsk (1)	US 50/50 Profit Share Ex-US Royalties
	Combinations Solid Tumors	MTAP					Ph 1 Initiation Mid-2022		
PARG	Ovarian, Gastric, Breast Cancers	HRD					IND Q4 2022	CANCER RESEARCH UK (2)	WW Commercial Rights
Pol Theta	Small Molecule Protein Degraders	HRD					Development Candidate Q2 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 Combination MUM, Basket	GNAQ/11					Daro + Crizo Clincal Update in MUM Mid-2022 Regulatory Guidance in MUM Mid-2022	Pfizer (3)	WW Commercial Rights
	Monotherapy UM Adjuvant	GNAQ/11					UM Adjuvant – Phase 1 IST H1 2022		
	+cMET[3],+KRAS Combo NSCLC, HCC	MET KRAS					cMET[3] - Preclinical Validation / IND Q4 2022 KRAS – Preclinical Evaluation H2 2022	Pfizer (3)	

(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; IDEAYA controls all Commercial Rights
(3) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreements, including for Darovasertib/Crizotinib Combination in MUM and in cMET-driven Tumors; IDEAYA retains all Darovasertib 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 = tyrosine kinase protein MET , Crizo = crizotinib, NSCLC = non-small cell lung cancer, HCC= hepatocellular carcinoma WW = worldwide

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, including $465M Dev/Reg
- Evaluating multiple clinical combination opportunities

Werner Helicase (MSI High)

- 50/50% US Profit Share and ex-US Royalties
- Milestones: ~$1B, incl up to $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
- Milestones: ~$1B, incl up to $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 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
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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

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UCSF, Professor and former Director, Helen Diller Cancer Center
Former President AACR; Founder and CSO, Onyx

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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

IDEAYA BIOSCIENCES

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

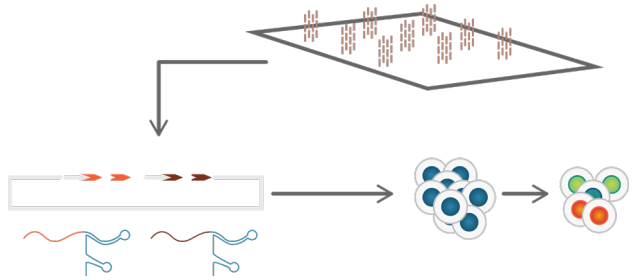
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

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™

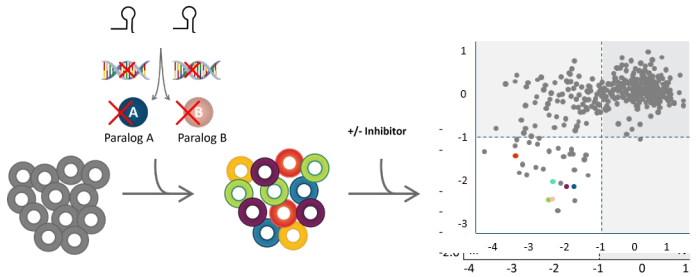
Dual CRISPR SL Library in DNA Damage Repair [2]



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]

IDEAYA BIOSCIENCES

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

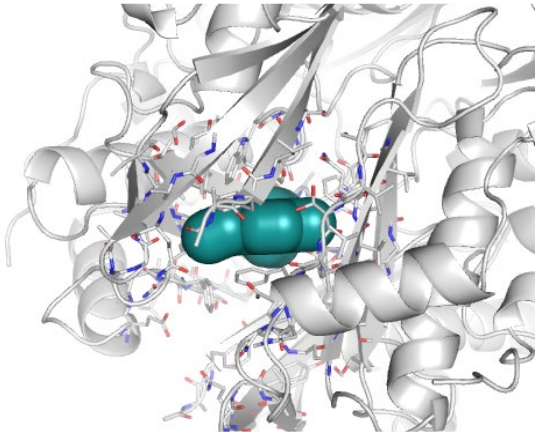
Multiple potential "first-in-world" co-crystal structures resolved, including for PARG, Pol Theta Helicase and Werner Helicase

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

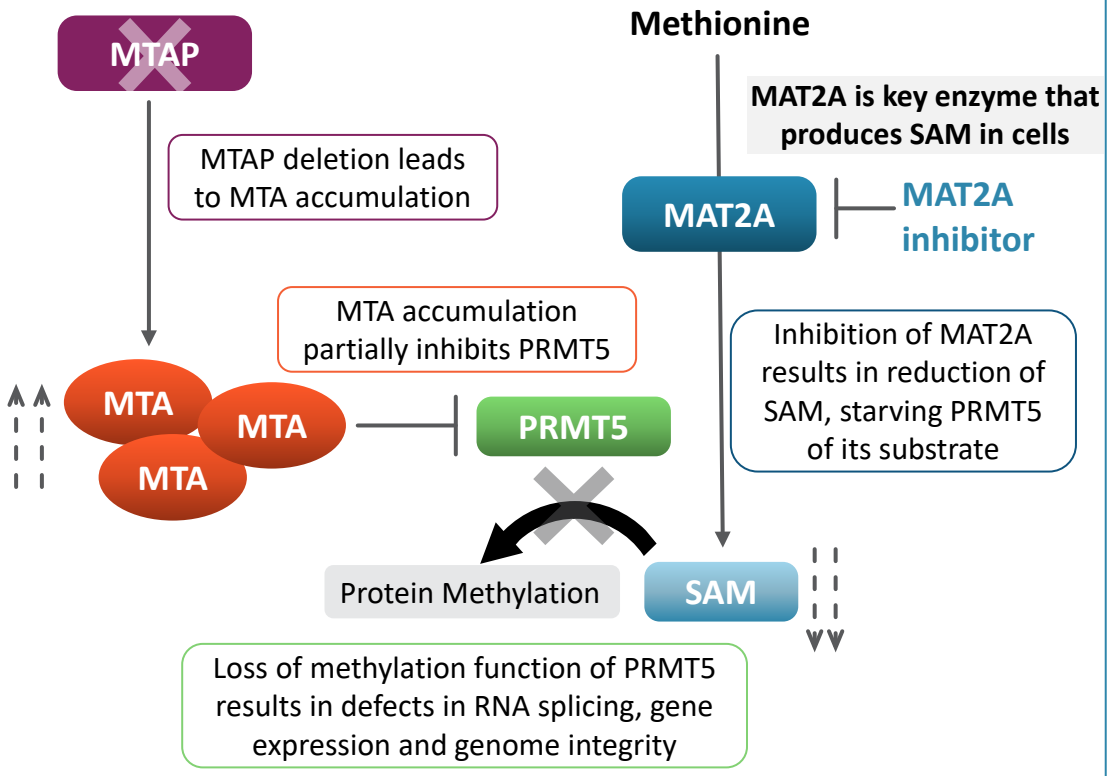
MTAP Deletion	HRD / BRCA	MSI-High	GNAQ/11 MET Driven Tumors	SL Platform
IDE397 (Ph1) MTAP-SL (PC)	IDE161 (DC) Pol Theta Inhibitor (Late PC) Pol Theta Degrader (PC)	Werner (PC)	Daro + cMET in MUM (Ph2) and in HCC / NSCLC (PC) Daro + KRAS G12C (PC)	First-in-Class-SL (Hit ID) DDR (PC) Novel Targets

PC = Preclinical Stage, DC = Development Candidate Stage, Ph 1 = Phase 1, 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

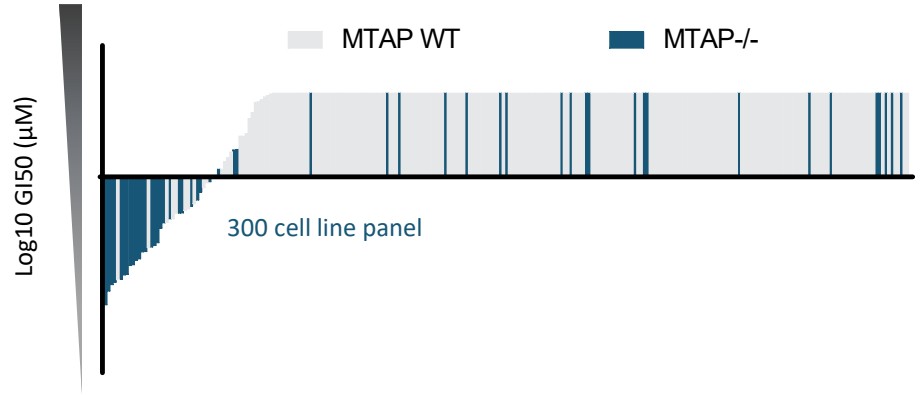
IDE397: MAT2A Inhibitor

Differentiated Profile: Potent and Selective with Sensitivity in MTAP-/- Cell Lines

IDE397 Target Product Profile

- Superior cellular potency and selectivity vs AG-270
- No observed preclinical liver injury or increased bilirubin and does not inhibit UGT1A1 or BSEP transporters
- Favorable physical properties (e.g., solubility)
- *In vivo* efficacy and PD modulation at 5 to 30mg/kg

IDE397 is Selective for MTAP-/- Cell Lines



Biochemical and *in vitro* Potency		
	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		
BSEP inhibition @10µM (%)	1	**25.2**
UGT1A1 inhibition (%)	34	83
PXR Emax @30 µM (%)	9	**35**
Solubility @pH 7.4 (µM)	>100µM	**BLOQ***

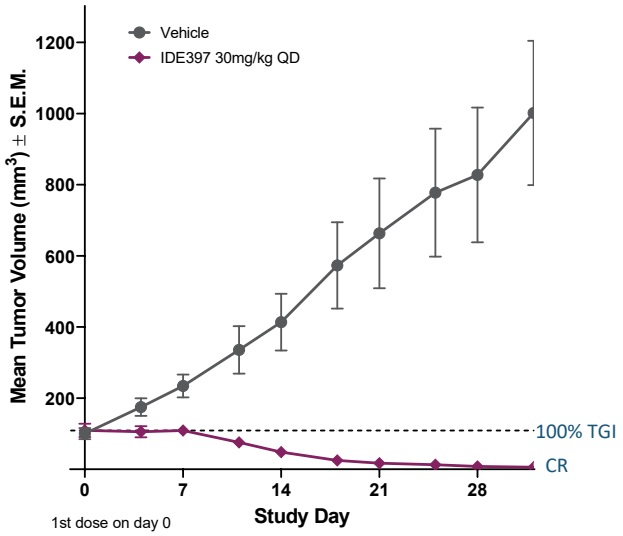
*BLOQ = below limit of quantitation

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

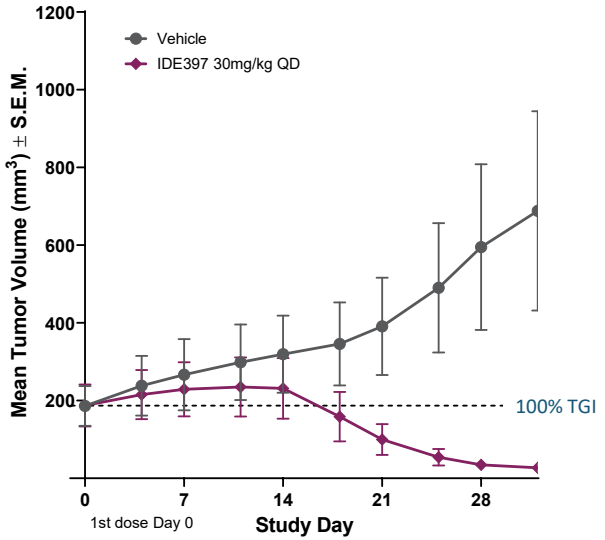
Monotherapy Tumor Regressions & Significant TGI Across Multiple Solid Tumor Types

NSCLC and Bladder Cancer MTAP-/- PDX Models

NSCLC PDX Model

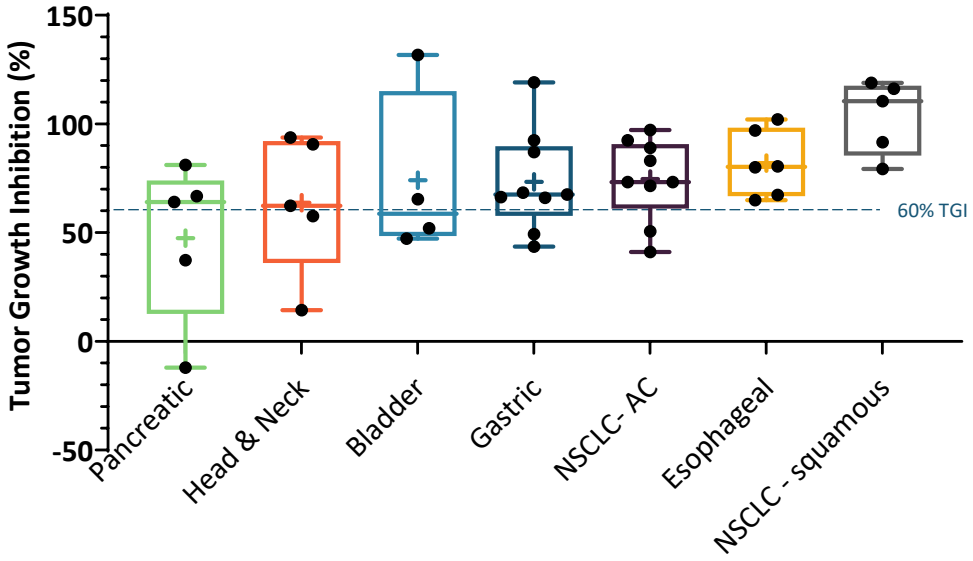


Bladder PDX Model



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

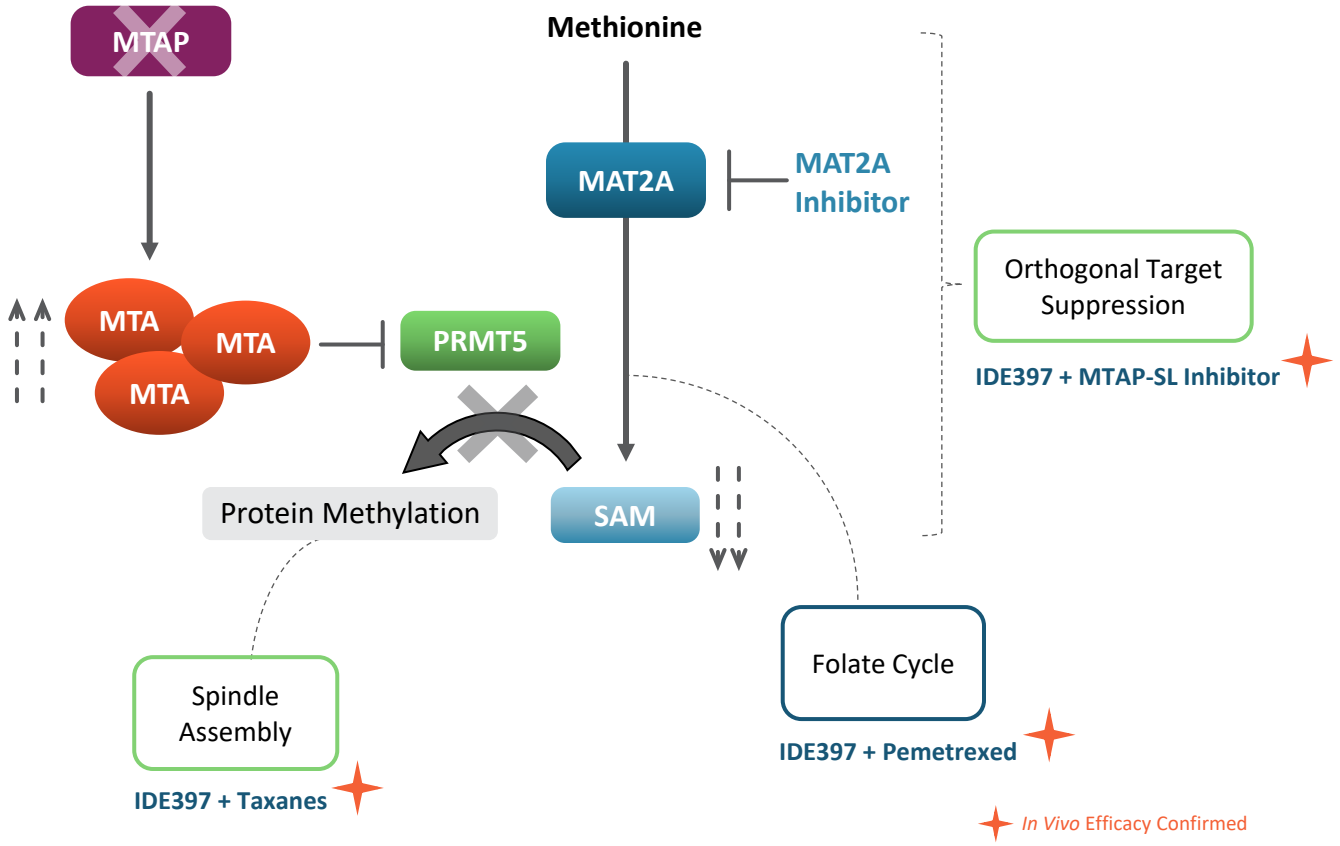
- Tumor Regressions (≥ 100% TGI) observed in multiple PDX models / indications, including in 3 of 5 NSCLC squamous models, with 1 CR
- Observed > 60% TGI in 12 of 14 NSCLC PDX models, including in 7 of 9 adenocarcinoma and in 5 of 5 squamous carcinoma PDX models
- Observed 95%-100% tumor SDMA reduction in multiple MTAP-/- PDX models, with 9 of 12 models showing 80-100% reduction in SDMA

TGI = Tumor Growth Inhibition, CR = Complete Response

IDE397 Combinations Demonstrate Enhanced Anti-Tumor Response

Evaluating Multiple MAT2Ai Rational Combination Strategies

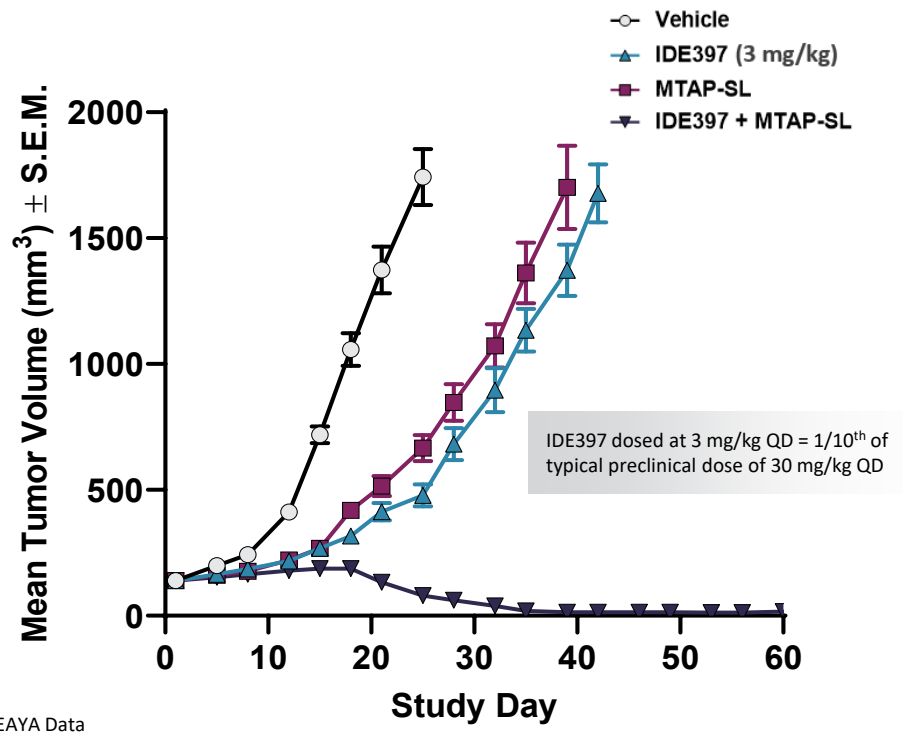
Combination Strategies Based on Mechanistic Hypotheses



MAT2A + MTAP-SL Combination

IDE397 + MTAP-SL Inhibitor *

Complete Response (CR) in NSCLC MTAP-/- CDX Model



IDEAYA Data

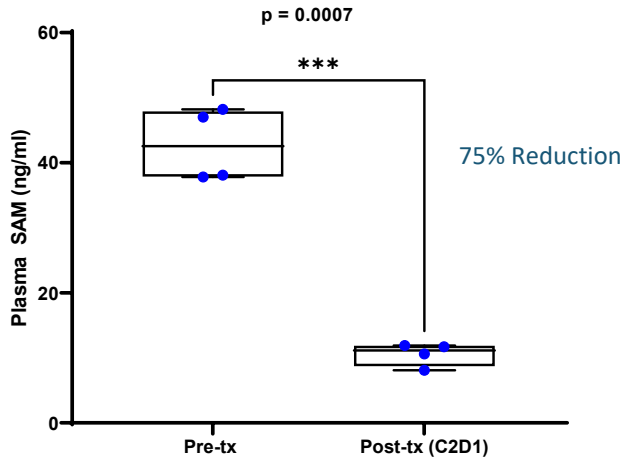
* MTAP-SL Inhibitor = representative tool compound inhibitor of MTAP-SL target

IDE397 Clinical Data Summary

Robust SAM Reduction, Exposure-Dependent SDMA Modulation, Observed Tumor Shrinkage

Maximal Plasma SAM Reduction

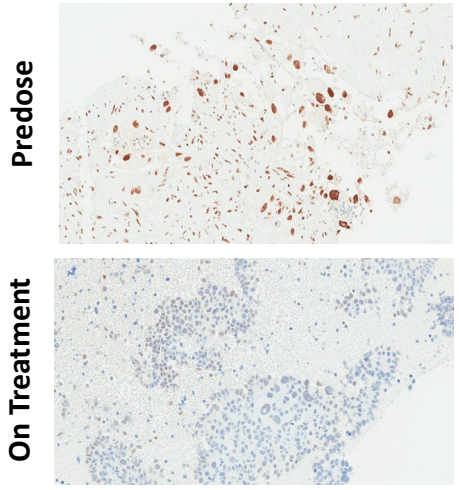
Observed 75% Reduction in mean Plasma SAM Reduction for Cohort 5



Tumor PD – Cohort 5 NSCLC

95% Reduction of Tumor SDMA

Tumor SDMA IHC, 20X

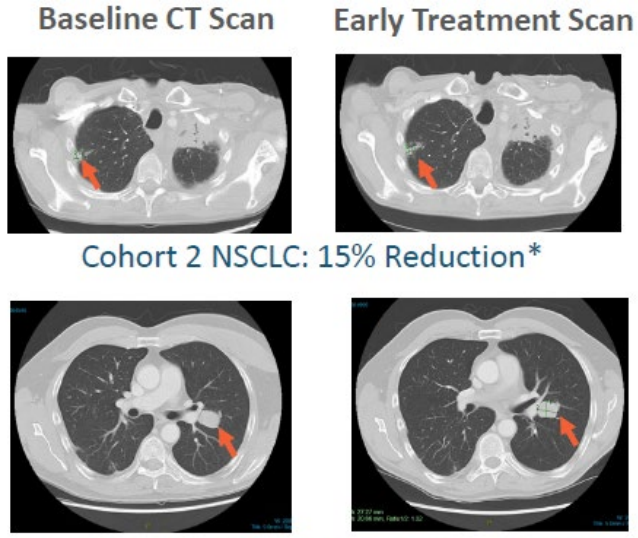


AUC_{ss} [2] = 5.9 x

[2] AUC_{SS} values normalized to Cohort 3 value

Observed Tumor Shrinkage

Preliminary Signal of Clinical Activity



Favorable Preliminary Risk / Benefit Profile

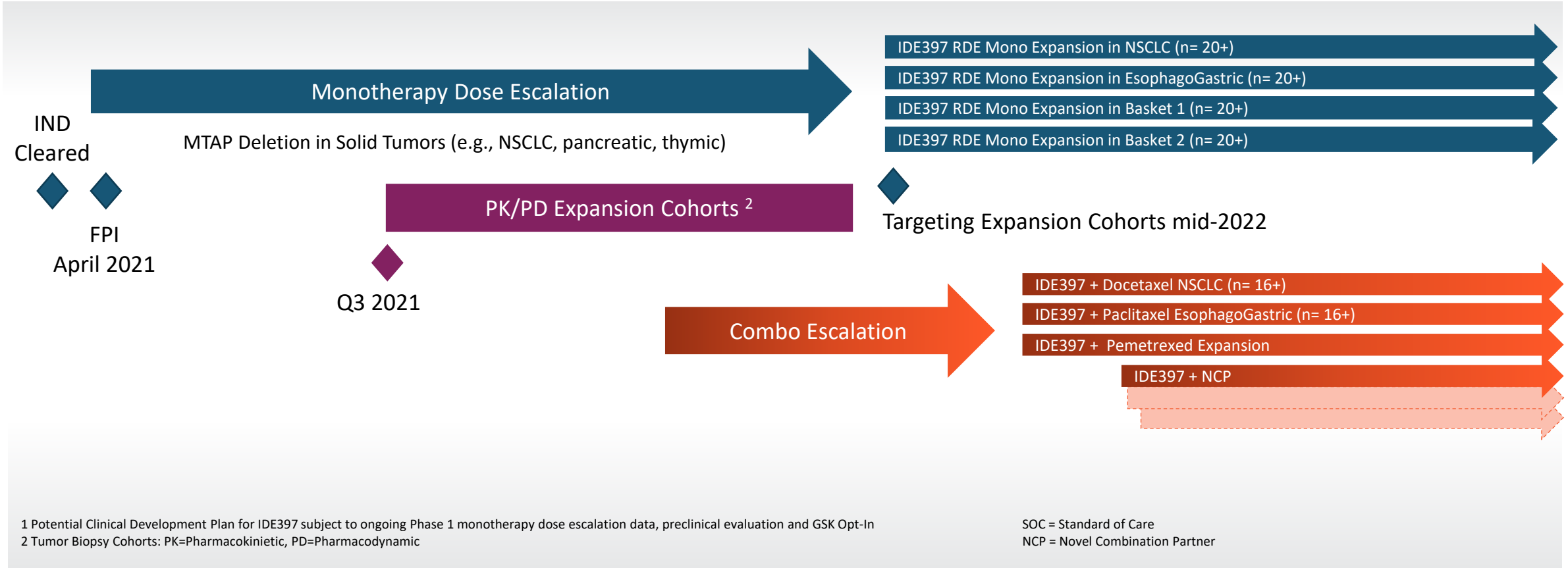
- Observed preliminary signals of clinical activity, including exposure-dependent tumor pharmacodynamic modulation and tumor shrinkage
- Dose-proportional exposures (AUC and C_{max}) Cohort 1 to 5, with low C_{max}/C_{min} ratio, in target efficacious exposure range based on *in vivo* preclinical models
- No Drug-Related Serious Adverse Events (SAEs) and MTD Not Yet Observed through Cohort 5

IDEAYA Data: % Reduction of Tumor SDMA measured by IHC H-Score

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

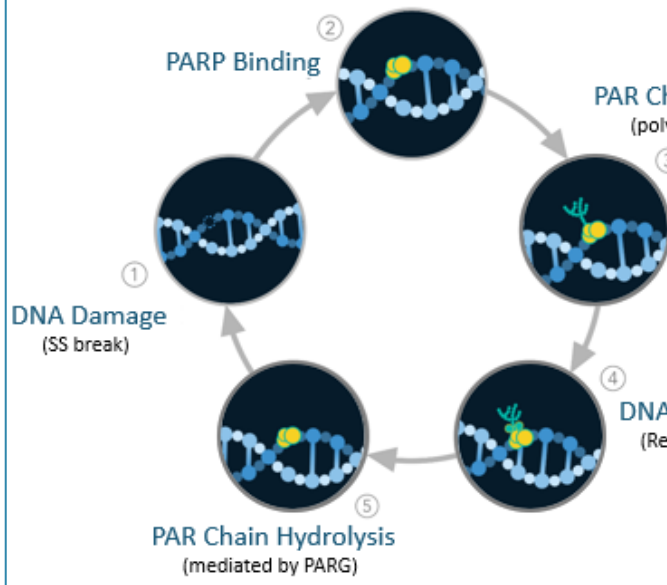
PARG Synthetic Lethality Program

Targeting IND Q4 2021 for Development Candidate IDE161

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

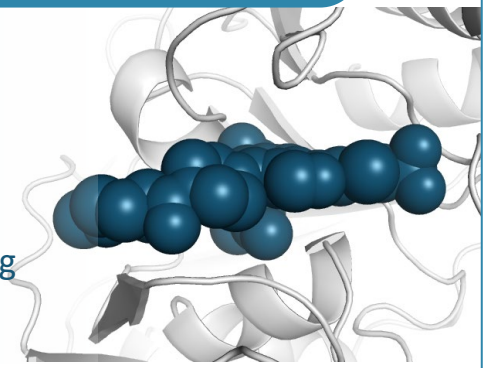


- PARP and PARG inhibitors have distinct efficacy profiles in HRD models
- Potential opportunities for PARG inhibitors beyond BRCA

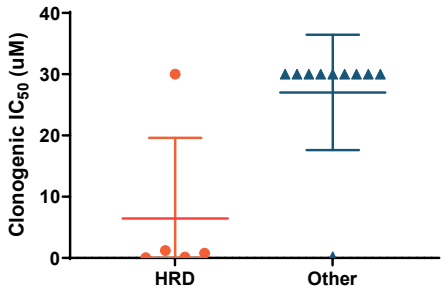
Cancer Research (Aug 2019), Cancer Research (Jul 2019), Cancer Cell (Mar 2019)

PARG Drug Discovery Program

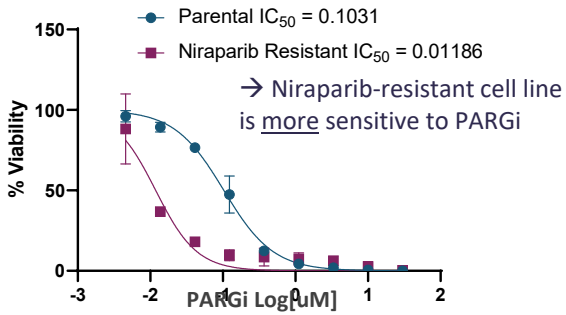
- Project structurally enabled
- Multiple potent cellularly active compounds demonstrate efficacy in defined biomarker setting
- IDE-161 delivers properties supporting development candidate selection



PARGi Sensitivity Enriched in HRD Models



Acquired PARPi Resistance Can Sensitize Tumor Cell to PARGi

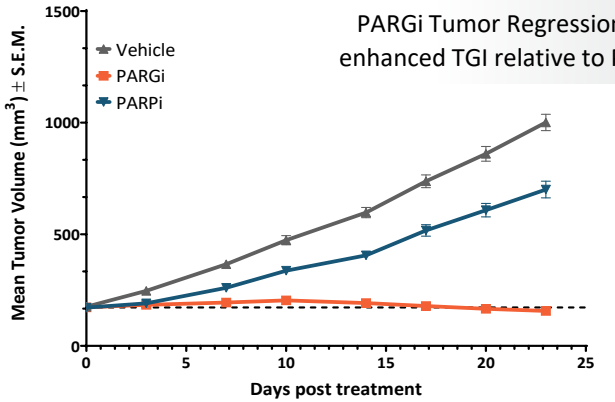


IDEAYA Data

Biomarker Selected CDX and PDX Models are Sensitive to PARGi

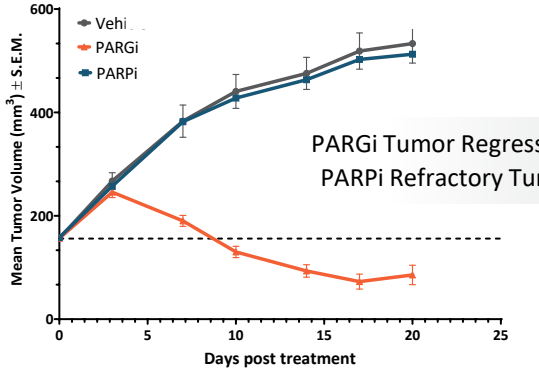
Differentiated Activity to PARP inhibition in Ovarian, Gastric and Breast Cancer Models

Ovarian Cancer HRD CDX Model



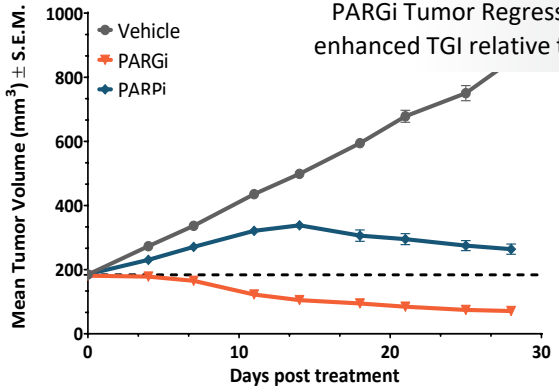
PARGi Tumor Regression and enhanced TGI relative to PARPi [1]

Gastric Cancer HRD CDX Model



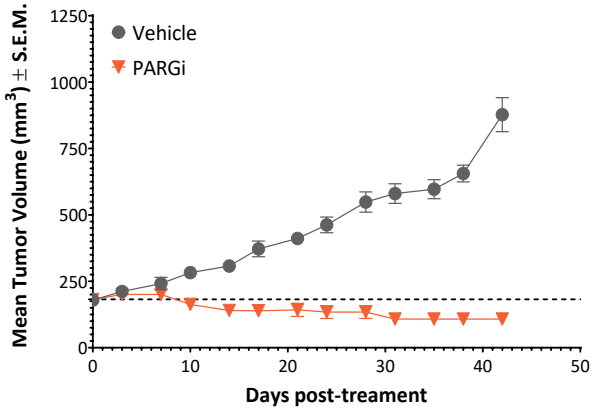
PARGi Tumor Regression in PARPi Refractory Tumor [1]

Breast Cancer HRD CDX Model

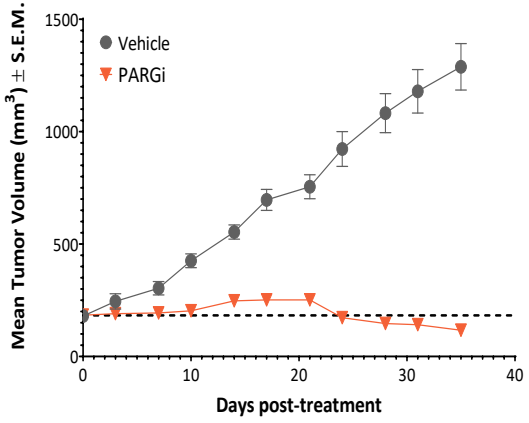


PARGi Tumor Regression and enhanced TGI relative to PARPi [1]

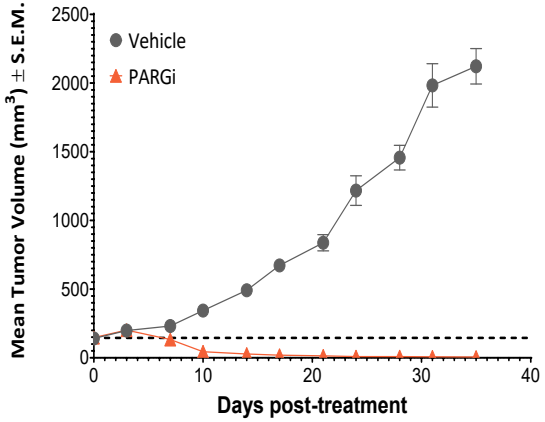
Breast Cancer PDX Model 1



Breast Cancer PDX Model 2



Breast Cancer PDX Model 3



IDEAYA Data; [1] PARPi (Niraparib) dosed at MTD ; IDB-156 dosed at <MTD (100mg/kg)

IDE161 Efficacy Profile Differentiates from PARPi

Multiple Endogenous HRD Cell Lines are Selectively Sensitive to IDE161 vs PARPi

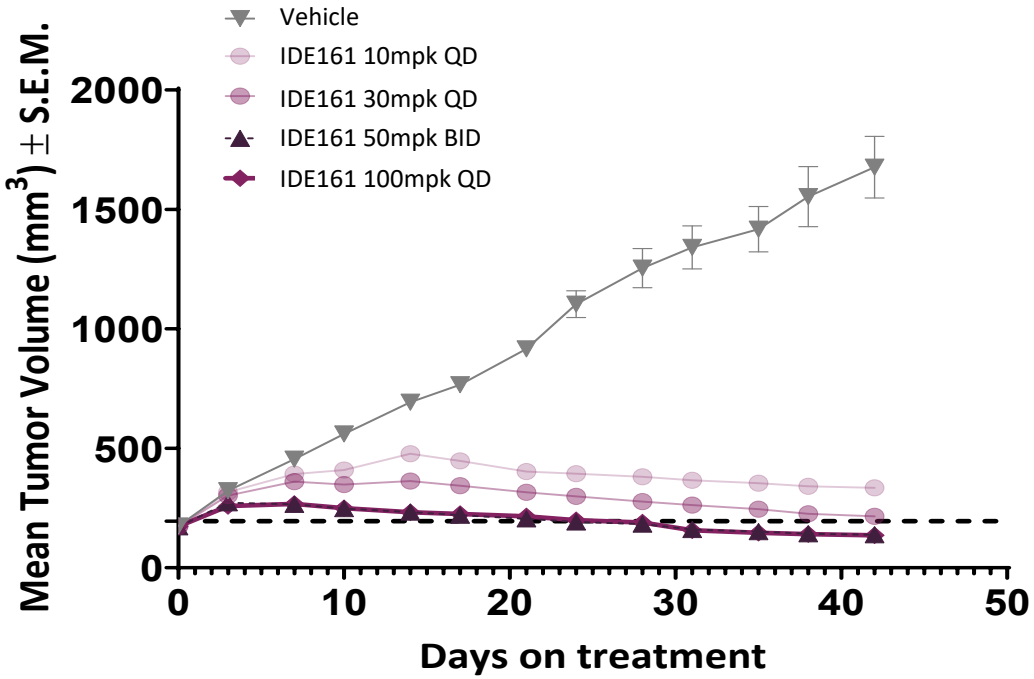
Ovarian HRD

Cell Line	IDE161 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

Breast HRD

Cell Line	IDE161 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	sensitive
Line H	0.64	0.72	insensitive

PARP-resistant HRD Model is Sensitive to PARG inhibition



PARGi Tumor Regression and enhanced TGI relative to PARP inhibitor (Niraparib) which observed ~35% TGI in this model

Pol Theta Synthetic Lethality Program

Targeting Development Candidate Q2 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

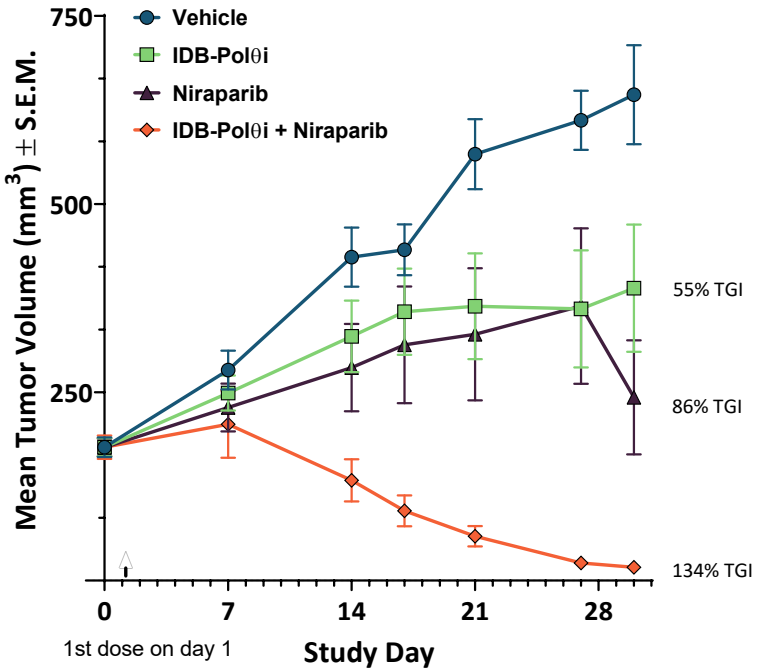
IDEAYA Data

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 in multiple *in vivo* xenograft models in combination study

Durable response, e.g., out to 80 days, in multiple models



IDEAYA Data

Werner Helicase Synthetic Lethality Program

Targeting Development Candidate in 2023

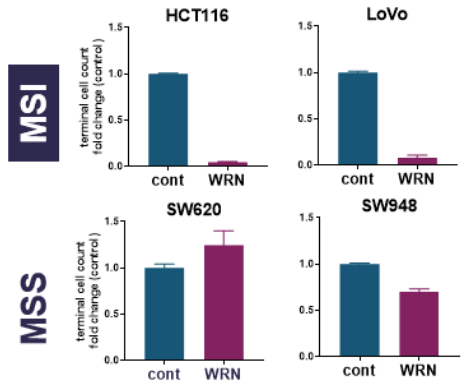
Werner Helicase Synthetic Lethal with High-MSI

CellPress

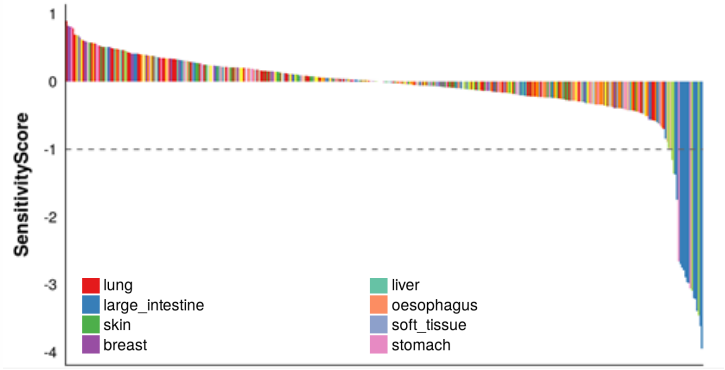
Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al



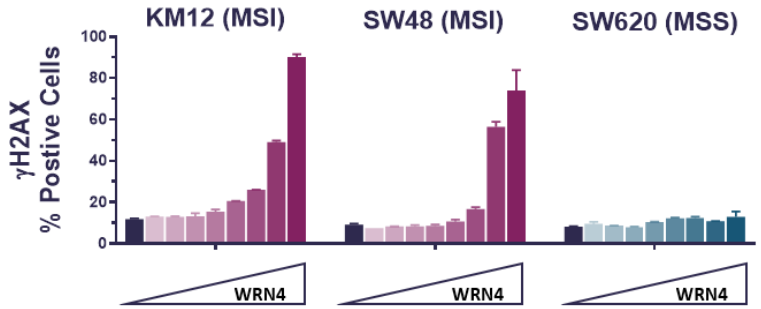
Project Drive: WRN is essential in High MSI cancer cell lines



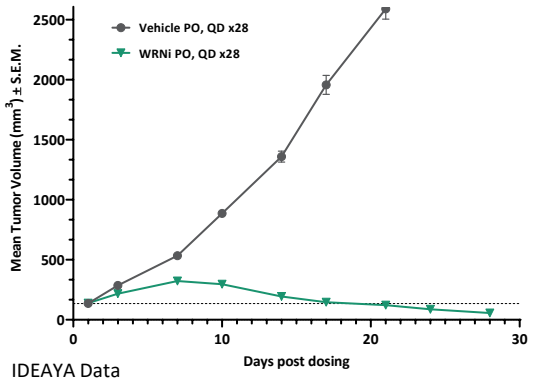
Project Drive

Werner Inhibitor Cellular PD and *In Vivo* Efficacy

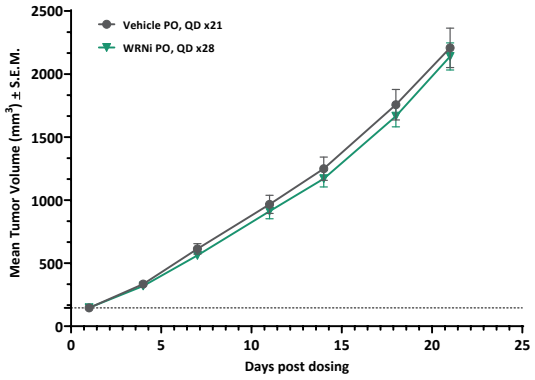
WRN inhibitor PD and *in vivo* efficacy with ~100% TGI and tumor regression



High MSI Xenograft Model



MSS Xenograft Model



IDEAYA Data

[1] Cancer Res., November 1998

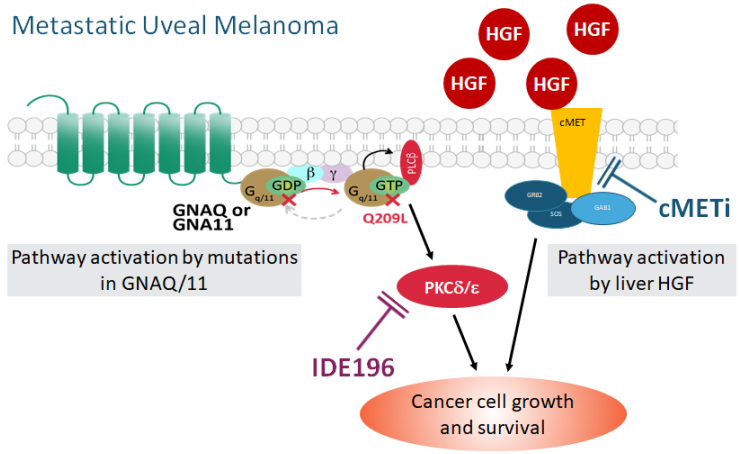
High-MSI (15% GI Cancers and 16% CRC) [1]

Darovasertib: Phase 2 PKC Inhibitor

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

PKC + cMET Synthetic Lethal Discovery

High cMET expression Associated with Metastatic Progression

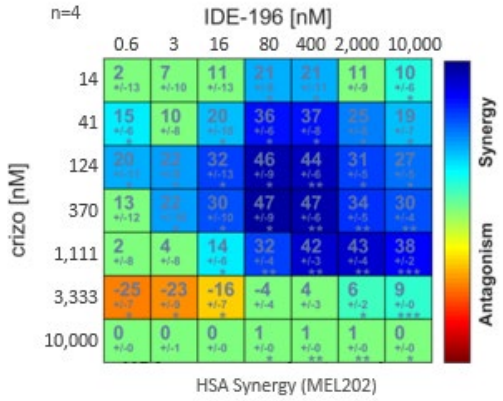


- HGF promotes cancer cell growth and survival
- Translational Research hypothesis: HGF-induced cMET signaling in the liver microenvironment activates an alternative pathway for MUM tumor progression

IDEAYA Darovasertib Investor Day, 2021

Preclinical Synergy

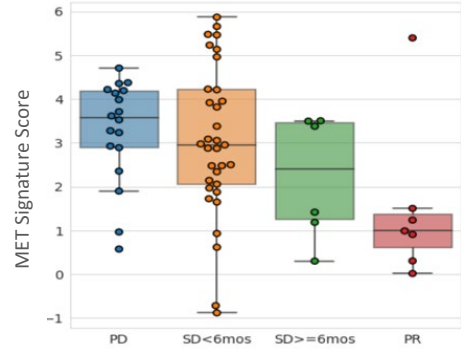
Darovasertib + Crizotinib Synergy in MUM Cells



IDEAYA Data AACR 2021

Clinical Phase 1 Data Association

Darovasertib Ph 1 Association with cMET Activity



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

IDEAYA Data

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 targeting PKC

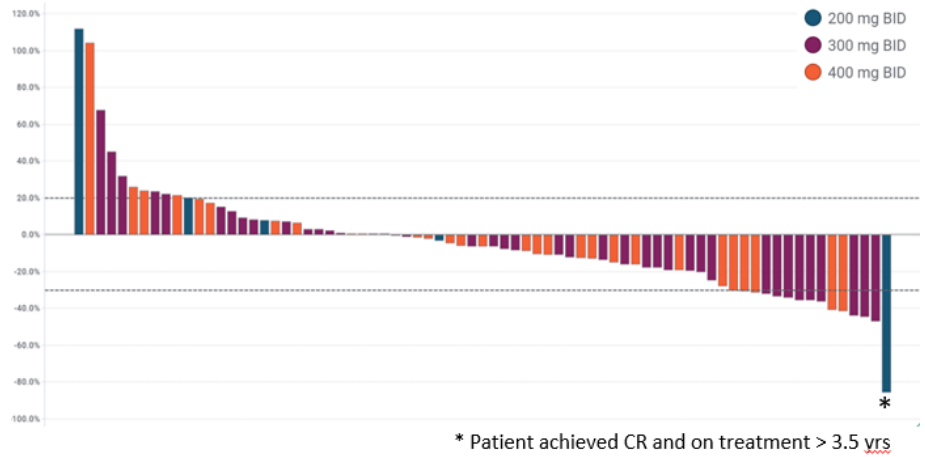
Darovaserib advantages vs current MUM therapy: no patient selection, oral, ↑ response rate

Darovasertib Clinical Experience in Heavily Pre-Treated MUM

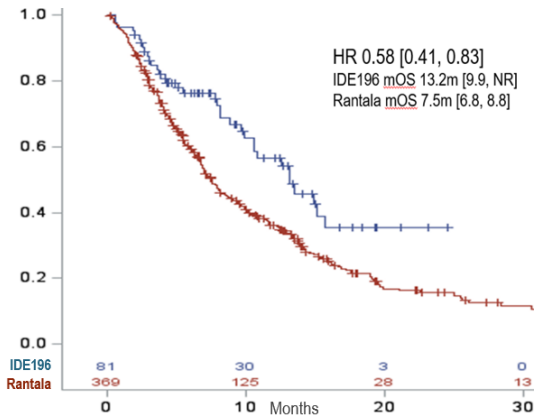
Darovasertib + Crizotinib Combination – Preliminary Efficacy Data for Phase 2 Expansion

Darovasertib Monotherapy in MUM [1]

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



* Patient achieved CR and on treatment > 3.5 yrs

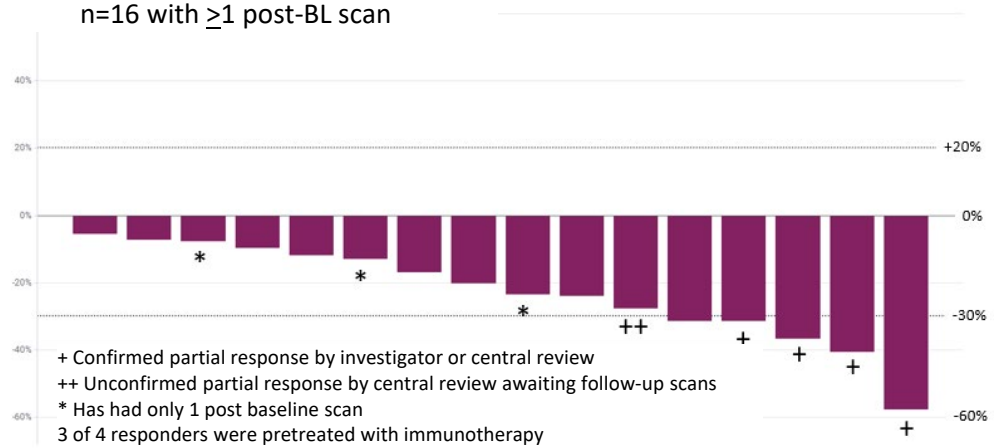


n = 81 with 75 evaluable patients
Observed monotherapy mDOR ~10 mo
Observed monotherapy mOS 13.2 mo

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

Darovasertib + Crizotinib Combination in MUM [3]

n=16 with ≥1 post-BL scan



+ 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)
- Encouraging ORR% in heavily pre-treated MUM patients with ≥2 post-baseline scans (n=13)
- 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%

[1] IDEAYA Data – Monotharpy data is based on preliminary analysis of unlocked database of 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)
[3] IDEAYA Data – Combination data is based on 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

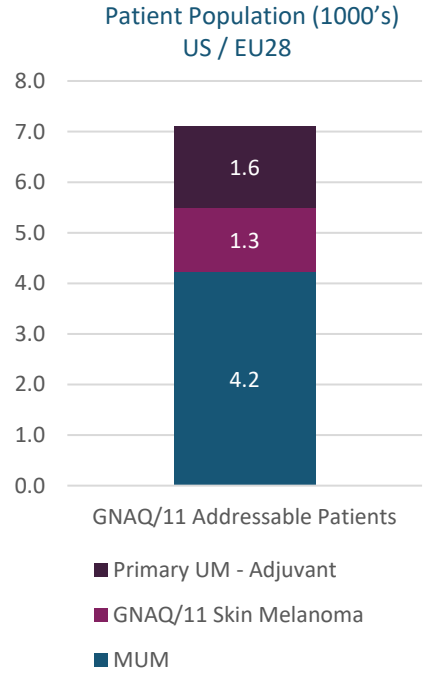
^^^ Journal of Clinical Oncology, Carjaval, et. al, 2018; 1232-1239

IDEAYA BIOSCIENCES

Darovasertib Patient Population Analysis

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

Addressable GNAQ/11 Patients



IDEAYA Analysis

Orphan Drug Designation (ODD) received from U.S. FDA for Darovasertib in Uveal Melanoma, including MUM

MUM, Adjuvant UM and GNAQ/11 Skin Melanoma

- No FDA Approved Precision Medicine 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
- Planning to clinically evaluate Darovasertib + Crizotinib combination in HCC and NSCLC pursuant to Pfizer clinical collaboration and drug supply agreement

	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

* not reported
δ = delta ε = epsilon

Synthetic Lethality Focused Precision Medicine Oncology Biotech

First-in-Class Synthetic Lethality Pipeline and Leading SL Platform

Broad Pipeline of Potential First-in-Class Synthetic Lethality Programs with large addressable patient populations in major solid tumor types, including Phase 2 (Darovasertib) and Phase 1 (IDE397) clinical-stage programs, and late preclinical (PARG, Pol Theta) programs

Validating and Value-Accretive Pharma Partnerships and Collaborations with Pfizer on Darovasertib (Clinical Collaboration and Drug Supply) and with GSK on MAT2A (Opt-In, 80% GSK Cost Share, Milestones, 50/50 US Profits), Pol Theta (100% GSK Cost Share, Milestones, WW Royalties) and Werner Helicase (80% GSK Cost Share, Milestones, 50/50 US Profits)

Strong Balance Sheet with ~$346 M in cash anticipated to fund operations into 2025 [1, 2] and experienced leadership team

Multiple 2022 Target Catalysts for Clinical and Late Preclinical Programs

MTAP-Deletion

IDE397 (MAT2A)
Mono Expansions – Mid-Year
Combo Initiations – Mid-Year
GSK Option Package – Mid-Year

MTAP-SL
Lead Series ID

HRD/BRCA

PARG
IDE161 IND Filing – Q4

Pol Theta
Dev Candidate – Q2

MSI-High

Werner Helicase
Lead Optimization
Dev Candidate 2023

GNAQ/11 and/or **MET-Driven Tumors**

SL Combo: PKC + cMET
Clinical Update – Mid-Year
FDA Guidance – Mid-Year

Expansion Opportunities
cMET (HCC, NSCLC) Ph1 – Q4
KRAS Preclinical – Q4

SL Platform

First-in-Class – Lead Series ID
DDR – Lead Optimization
Novel SL Targets

(1) IDEAYA Form 10-Q filed with the U.S. Securities and Exchange Commission on May 10, 2022
(2) Includes cash, cash equivalents and marketable securities as of March 31, 2022