November 2022

NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicines

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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 darovasertib (PKC) and IDE397 (MAT2A), development candidates IDE161 (PARG) and Pol Theta Helicase Development Candidate, and Werner Helicase preclinical lead optimization
- **Pharma Collaborations** with GSK (over ~$2 billion in potential milestones), Amgen and Pfizer
- **Balance Sheet** of ~$394M anticipated to fund operations into 2026 [1, 2]
- **NASDAQ**: IDYA

- **2022 / 2023 Catalysts**
  - Darovasertib (PKC) – Phase 1/2
    - – Daro Neoadjuvant UM – IDEAYA Phase 1 Q4 2022
    - – Daro/Crizo MUM Registrational Trial Initiation Q1 2023
  - IDE397 (MAT2A) – Phase 1/2
    - √ Monotherapy Expansion Phase 2 Initiation
    - √ Combination Cohorts Phase 1 Initiation
  - IDE161 (PARG) – Targeting IND (Q4 2022)
  - Pol Theta Helicase
    - √ Development Candidate for IND-Enabling Studies
    - – Targeting First-in-Human Studies H1 2023
  - Werner Helicase
    - – Targeting Development Candidate (2023)

(1) Includes aggregate of ~$393.9M cash, cash equivalents and marketable securities as of September 30, 2022
(2) IDEAYA Form 10-Q dated November 8, 2022, as filed with the U.S. Securities and Exchange Commission

Synthetic Lethality

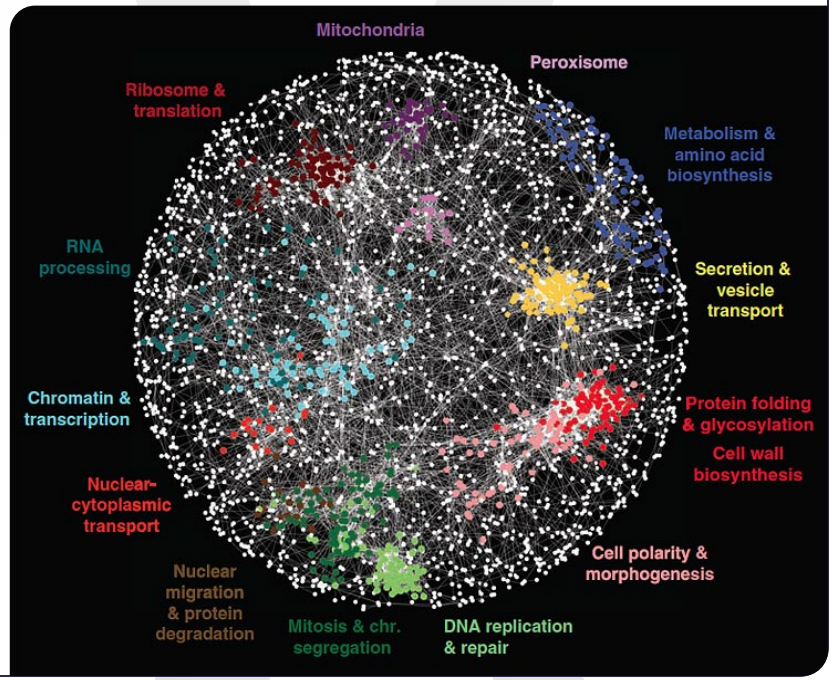
The Next Frontier in Precision Medicine Oncology

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)
Darovasertib *PKC*	+cMET[1] Combination MUM, Basket	GNAQ/11					Daro + Crizo Clincal Update in MUM √ Daro + Crizo Reg Trial in MUM Q1 2023	Pfizer (1)	WW Commercial Rights
	Adjuvant UM	GNAQ/11					(Neo)Adjuvant UM – Phase 1 IST √ Neoadjuvant UM – IDEAYA Phase 1 Q4 2022		
	+cMET[1],+KRAS Combo NSCLC, HCC	MET KRAS					+cMET[3] – Preclinical Evaluation +KRAS – Preclinical Evaluation	Pfizer (1)	
IDE397 *MAT2A*	Monotherapy NSCLC, Esophagogastric	MTAP					Mono Expansion Phase 2 Initiation √		WW Commercial Rights
	Combinations Solid Tumors	MTAP					Combination Cohorts Ph1 Initiation +Pemetrexed √ +Taxanes √ +AMG 193	AMGEN (2)	
IDE161 *PARG*	Ovarian, Gastric, Breast Cancers	HRD					IND Q4 2022	CANCER RESEARCH UK (3)	WW Commercial Rights
Pol Theta	Small Molecule Helicase Inhibitor	HRD					Development Candidate Q2 2022 √ First-in-Human Studies H1 2023	GSK (4)	Global Royalties
WRN	GI Cancers	High-MSI					Development Candidate 2023	GSK (4)	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

(1) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreements for Darovasertib/Crizotinib Combination in MUM and in cMET-driven Tumors; IDEAYA retains all Darovasertib Commercial Rights
(2) Pursuant to Amgen Clinical Trial Collaboration and Supply Agreement for IDE397 + AMG 193, an investigational MTA-cooperative PRMT5 inhibitor; Amgen will sponsor the study and the parties will jointly share external costs of the study
(3) Pursuant to CRUK Evaluation, Option and License Agreement; IDEAYA controls all PARG Commercial Rights
(4) Pursuant to GSK Collaboration, Option and License Agreement: Polθ: Global Royalties; WRN: 50/50 US Profits + ex-US Royalties

= Target Program Milestones

MAT2A=methionine adenosyltransferase 2a, MTAP=methylthioadenosine phosphorylase, MTA=methylthioadenosine, PRMT5=protein arginine methyltransferase 5 (PRMT5), 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 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 Medical Officer
Pfizer · pharmacyclics · AMGEN

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

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

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

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

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SVP, Head of Drug Discovery
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SVP, General Counsel
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IDEAYA Scientific Advisory Board

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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

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
- Differentiated clinical / candidate compounds discovered, including IDE397, IDE161 and Pol Theta Helicase Development Candidate
- Protein degrader capabilities for select targets

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

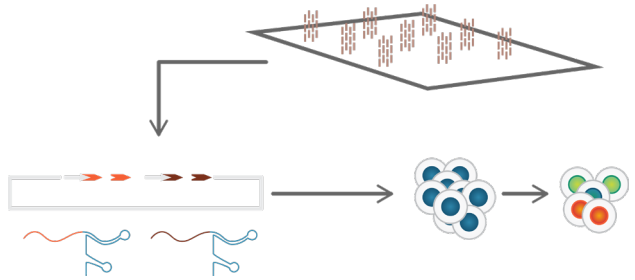
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

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 and *in vivo*

DECIPHER™

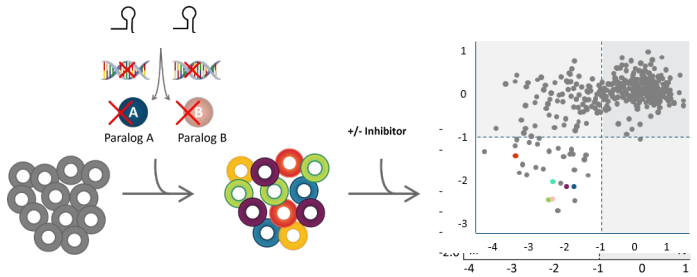
Dual CRISPR SL Library in DNA Damage Repair [2]



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 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

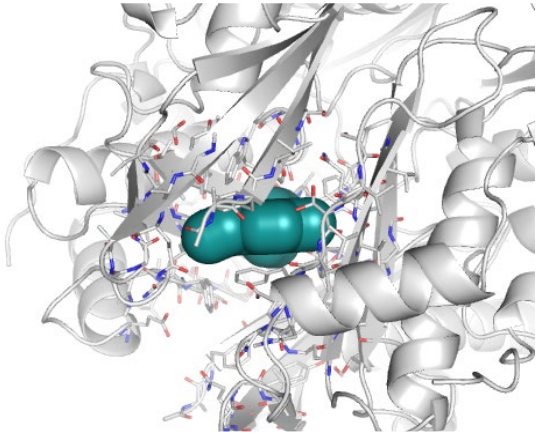
- MAT2A
- PARG
- Pol Theta (polymerase & helicase)
- Werner Helicase
- 2 Undisclosed SL Targets

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

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 Enable Breakthrough Therapies

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

GNAQ/11 MET Driven Tumors	MTAP Deletion	HRD / BRCA	MSI-High	SL Platform
Daro + cMET in MUM (Ph2) (Neo)Adjuvant UM (Ph1) Daro + cMET in HCC, NSCLC (PC) Daro + KRAS G12C (PC)	IDE397 (Ph2) Monotherapy IDE397 (Ph1) Combinations MTAP-SL (PC)	IDE161 (DC) Pol Theta Helicase Inhibitor (DC)	Werner (PC)	First-in-Class SL Targets (PC) Target Identification / Validation

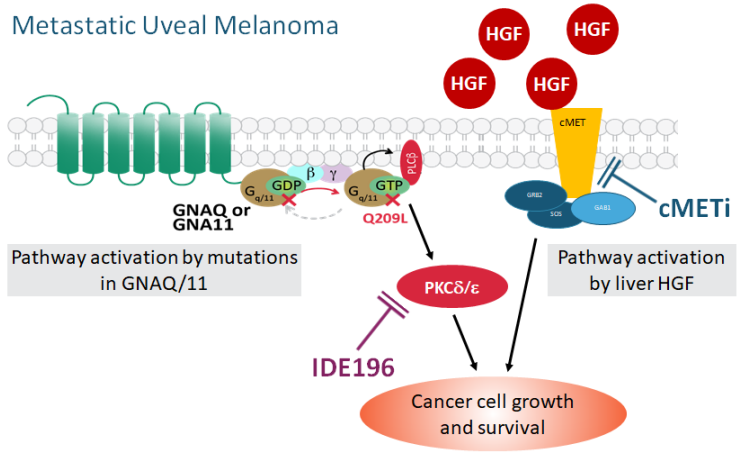
PC = Preclinical Stage, DC = Development Candidate Stage, Ph 1 = Phase 1, Ph2 = Phase 2

Darovasertib + Crizotinib – Phase 2 Synthetic Lethal Combination

Potential First-in-Class and Best-in-Class in MUM, Adjuvant UM and Other GNAQ/11 Tumors

PKC + cMET Synthetic Lethal Discovery

High cMET expression Associated with Metastatic Progression

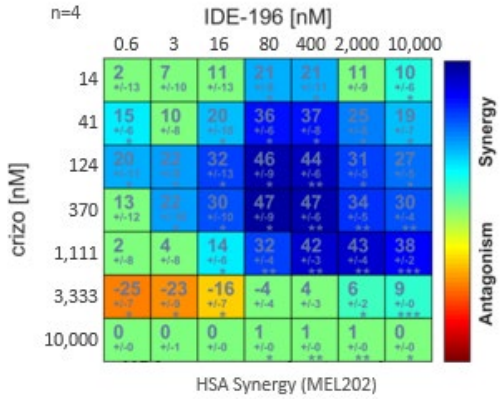


- HGF promotes cancer cell growth and survival
- Translational Research hypothesis: HGF-induced cMET signaling in the liver microenvironment activates an alternative pathway for MUM tumor progression

IDEAYA Darovasertib Investor Day, 2021

Preclinical Synergy

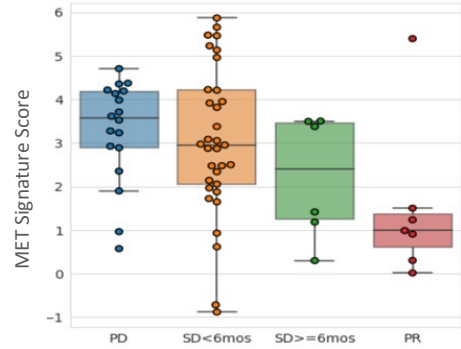
Darovasertib + Crizotinib Synergy in MUM Cells



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

Daro + Crizo Combo in Comparatively High-Risk, Poor Prognosis Population

Disease Burden Significantly Higher in Both Any-Line and First-Line MUM Population+

Baseline Characteristics		IDE196-001 Study* Darovasertib + Crizotinib		Tebentasfusp Phase 3#
		Any-Line n=37 (%)	First-Line n=8 (%)	n=252 (%)
Age	< 65	20 (54)	3 (38)	64 Median
	≥65	17 (46)	5 (62)	
Sex	F	20 (54)	4 (50)	124 (49)
	M	17 (46)	4 (50)	128 (51)
ECOG PS	0	25 (68)	3 (38)	192 (76)
	1	12 (32)	5 (63)	49 (19)
Baseline LDH	Normal	11 (30)	2 (25)	
	>ULN	**25 (68)**	**6 (75)**	**90 (36)**
	Missing	1 (3)	0	
Largest metastatic lesion	≤3.0 cm	10 (27)	2 (25)	139 (55)
	3.1 to 8.0	**22 (60)**	**4 (50)**	**92 (37)**
	≥ 8.1	**5 (14)**	**2 (25)**	**21 (8)**
Location of metastases	Hepatic only	7 (19)	2 (25)	131 (52)
	Extrahepatic only	1 (3)	0	9 (4)
	Hepatic and Extrahepatic	**29 (78)**	**6 (75)**	**111 (44)**

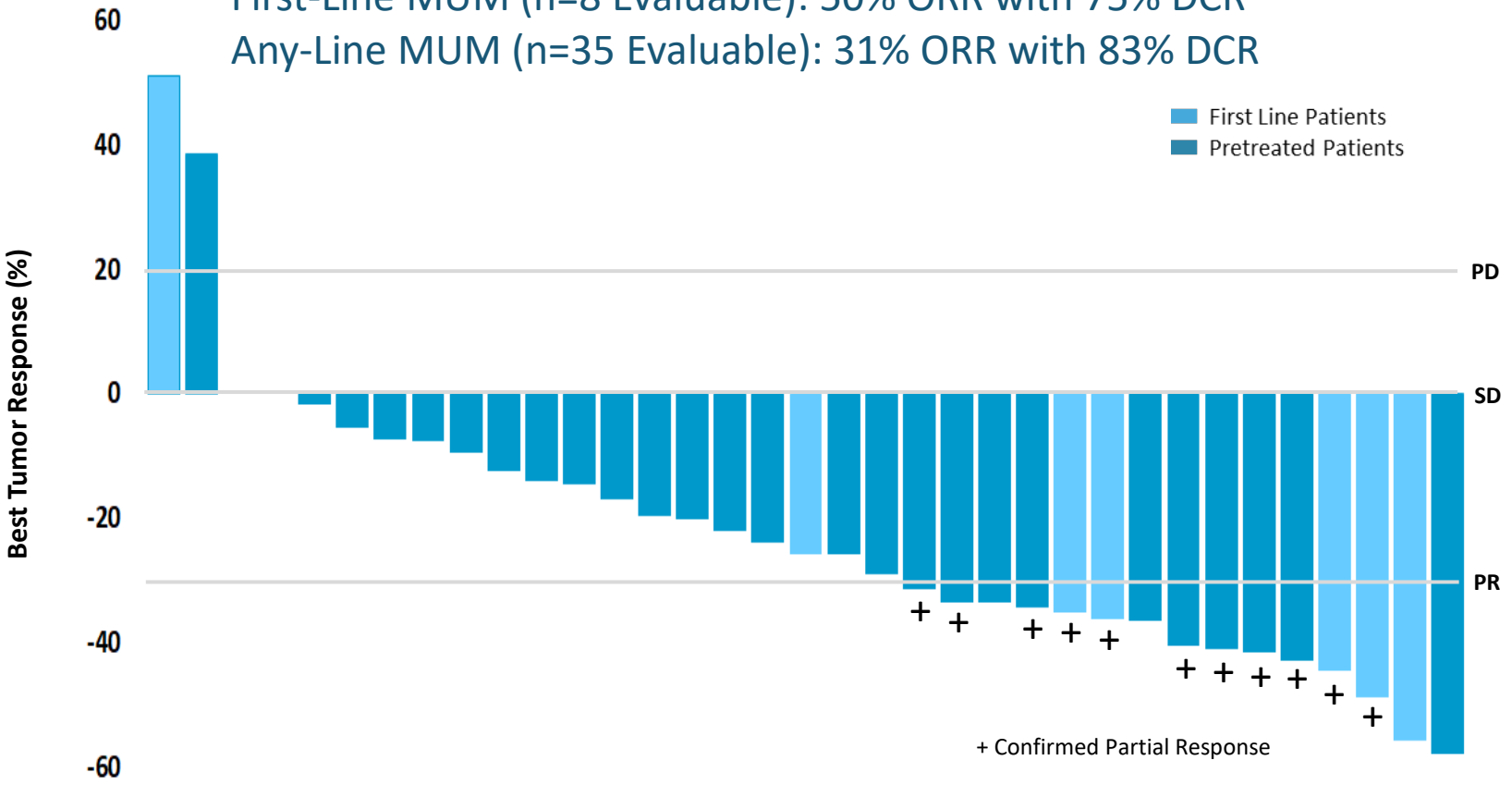
+ Cross-trial comparisons are not based on head-to-head studies and are presented for informational purposes; no direct comparisons are being made
*IDEAYA Data as of June 26, 2022 (based on preliminary analysis of unlocked database); # N Engl J Med 2021; 385:1196-1206

Darovasertib + Crizotinib – Clinical Experience in Heavily Pretreated MUM

Observed Unprecedented ORR% and DCR% with Potential First-Line Differentiation

First-Line MUM (n=8 Evaluable): 50% ORR with 75% DCR

Any-Line MUM (n=35 Evaluable): 31% ORR with 83% DCR



First-Line MUM *	Evaluable (n=8)
ORR (4/8)	50%
Tumor Shrinkage (6/8)	75%
>30% Tumor Shrinkage (5/8)	63%
cPR (4/8)	50%
DCR (6/8)	75%

Any-Line MUM *	Evaluable (n=35)
ORR(11/35)	31%
Tumor Shrinkage (31/35)	89%
>30% Tumor Shrinkage (15/35)	43%
cPR (11/35)	31%
DCR (29/35)	83%

* Response by RECIST 1.1

Manageable Side Effect Profile with No Drug Related Grade 4/5 AEs

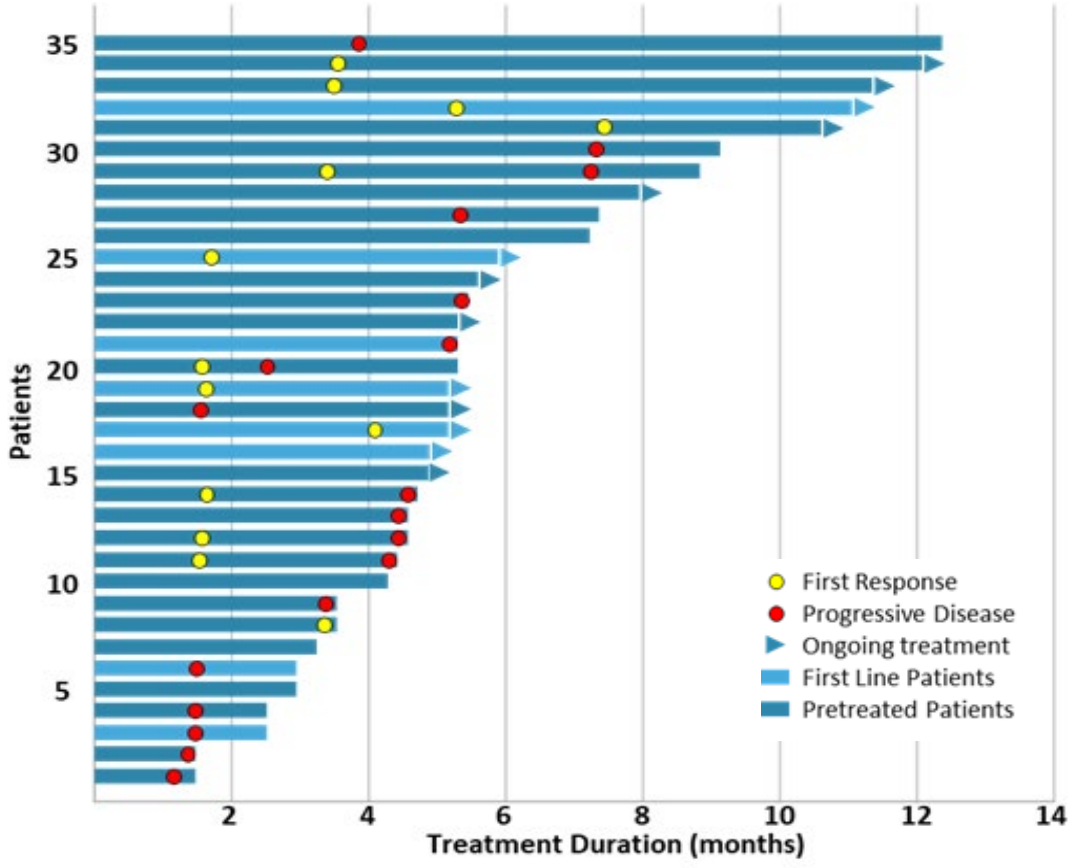
IDEAYA Data: preliminary analysis of unlocked database as of 06/26/2022 by investigator review (n=37); efficacy based on evaluable patients (n=35 for all lines; n=8 for first line), including one PR confirmed after cutoff date; two non-evaluable patients, both pretreated, did not progress due to disease: one (1) patient withdrew consent and one (1) patient discontinued early due to fatigue

ORR = Overall Response Rate by RECIST 1.1; DCR = Disease Control Rate, including cPR, uPR or SD as best overall response; cPR = Confirmed Partial Response; uPR = Unconfirmed Partial Response; SD = Stable Disease

Darovasertib + Crizotinib Combo Phase 2 Clinical Efficacy

Encouraging mPFS and mDOR in 1L and Any-Line MUM versus historical data in MUM

Darovasertib + Crizozotinib Any-Line MUM (n=35)



Clinical Efficacy Summary in Any-Line and First-Line MUM

Median Study Follow-Up *

- Any-Line: 7.8 months
- First-Line: 6.5 months

Median Duration-of-Response

- not reached in Any-Line or in First-Line
- 7 of 11 cPRs in Any-Line MUM remain in response
- 4 of 4 cPRs in First-Line MUM remain in response

Median Progression Free Survival ^

- Any-Line: ~5 months
- First-Line: Not yet reached and >5 months

IDEAYA Data: preliminary analysis of unlocked database as of 06/26/2022 by investigator review
* Median Study Follow-up: Cycle 1 Day 1 to data cut-off date (n=37)
^ mPFS Analysis: median assessment estimated, based on efficacy-evaluable patients (n=35)

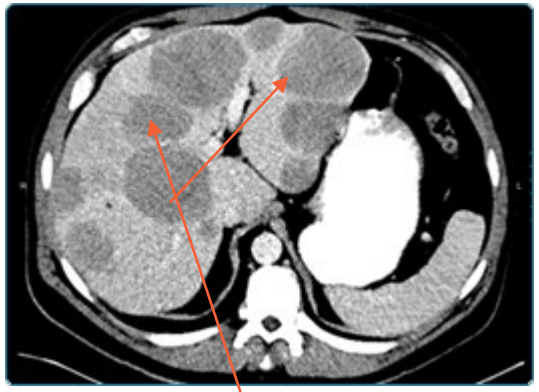
Darovasertib + Crizotinib First-Line MUM Combo Efficacy

Examples of Confirmed PRs with Significant Tumor Shrinkage in First-Line MUM Patients

First-Line MUM Patient

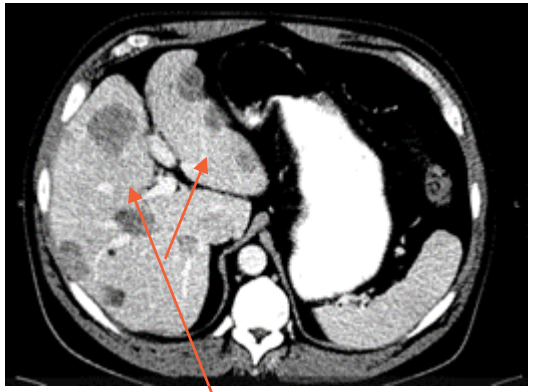
- 40+ year old patient with ongoing response at 12 months
- Diffuse disease in liver and pelvis with elevated LDH of 800 that normalized within one month
- Large tumors (SLD = 210 mm) reduced by 49%

Baseline



Many lesions distorting and replacing the liver

12 months

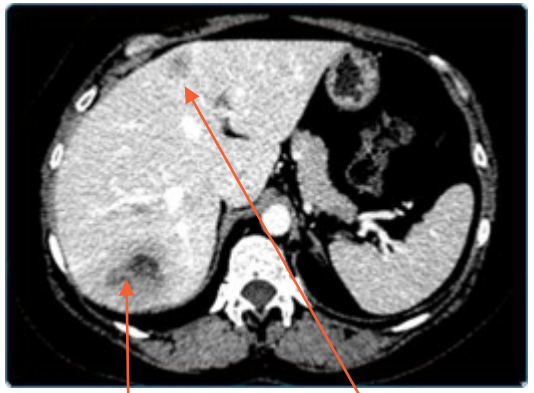


Marked improvement across all lesions

First-Line MUM Patient

- 50+ year old patient with ongoing response at 5 months
- Diffuse disease in liver & lymph nodes with elevated LDH
- Many liver lesions with target lesions reduced by 53%
- Intact orbital lesion reduced by 67%

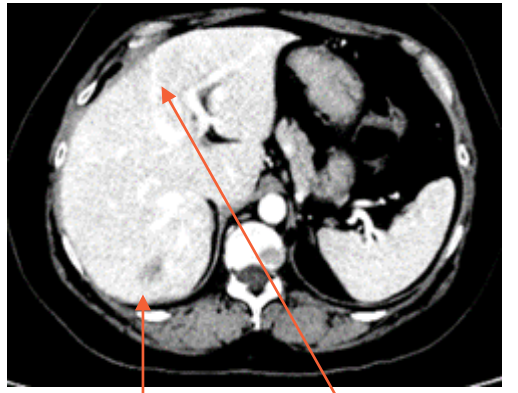
Baseline



Large necrotic lesion

Lesion

5 months



Markedly improved

Lesion Not Visible

IDEAYA Data as of 06/26/2022 (based on preliminary analysis of unlocked database); tumor lesion reductions by investigator review

Darovasertib + Crizotinib Synthetic Lethality Combination Therapy

Differentiated Clinical Efficacy in MUM+

ESMO 2022: IPI + Nivo Combo in HLA-A2-0201 MUM reports ~6% ORR (2 PRs out of 33 patients)++

	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	1L/2L/3L+ MUM (n=35 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 (~40-45% of MUM)
Drug Form	Oral Tablets (BID)	Oral Capsules (QD)	Oral Capsules (BID) plus chemo	IV Infusion (Weekly)
Tolerability (Grade ≥3 Drug-Related AE)	**24%**	**51.6%**	**63% ^^^ (All Cause)**	**46.5%**
% of Pts with Tumor Shrinkage	**89%***	**23% ^^**	**35%^^**	**44%#**
Overall Response Rate (ORR%, by RECIST 1.1)	**All-Line = 31% / First-Line = 50%* (confirmed PRs only)**	**0%**	**3% ^^^**	**4.7%#**
Progression Free Survival (mPFS)	**All-Line: ~5 months / First-Line: >5 months**	**2 months**	**2.8 months ^^^**	**2.8 months#**

+ Cross-trial comparisons are not based on head-to-head studies and are presented for informational purposes; no direct comparisons are being made

++ ESMO 2022: F. Dimitriou, et.al

* IDEAYA Data: preliminary analysis of unlocked database as of 06/26/2022 by investigator 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 + Crizotinib Clinical Development Plan in First-Line MUM

Targeting Potential Registration Enabling Trial Initiation in Q1 2023[1]

Key Considerations

- Strategic Implications
  - Technical / Regulatory POS
  - Time / Cost to Approval
  - Commercial Opportunity
- 1st Line vs All-Line
  - Unmet Need
  - Better Assessment
  - FDA Project Frontrunner
- HLA-A*02:01 Serotype (+/-)
  - All Comers or HLA-Negative Focus
  - Negative is 55-60% of Patients with No FDA Approved Therapies
  - NCCN Guidelines as potential approach for HLA-Positive
- Single-Arm vs Randomized
- Surrogate Endpoint for AA
  - Single Arm – ORR with DOR
  - Randomized – ORR or PFS

Single-Arm Phase 2

Single-Arm Phase 2 Trial (Expand Ongoing) in 1L Patients

Darovasertib + Crizotinib

Phase 2 Endpoint – ORR, Target ≥ 20%
Phase 2 Data → Accelerated Approval

Randomized Phase 3 Confirmatory Study in 1L Patients

Phase 3 Endpoints – PFS or OS
PFS Target ≥ 5-6 months

Randomized Integrated Phase 2/3

Randomized Integrated Phase 2/3 Trial in 1L Patients

Phase 2 Endpoints – ORR or PFS
ORR Target ≥20%, PFS Target ≥ 5-6 months
Phase 2 Data → Accelerated Approval

Expand within same Study Protocol → Phase 3 Confirmation

Phase 3 Endpoints – PFS or OS
PFS Target ≥ 5-6 months

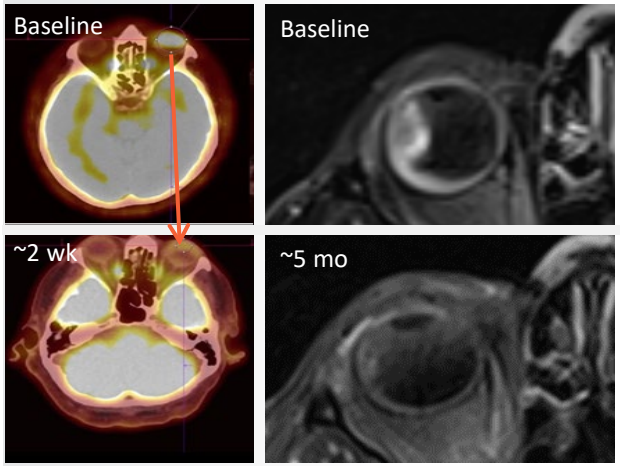
[1] Potential scenarios for accelerated approval (AA), including Single Arm Phase 2, Randomized Phase 2 (with Randomized Ph 3 Confirmatory Study, not shown), and Integrated Ph 2/3, subject to clinical investigator and regulatory guidance

Darovasertib Monotherapy in (Neo)Adjuvant Uveal Melanoma

Preliminary Clinical Proof-of-Concept Supports Evaluation of UM Expansion Opportunity

MUM Patients with Intact Primary

Daro Monotherapy | Daro + Crizo Combination

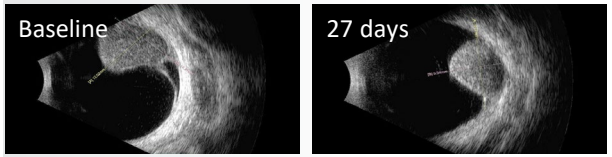


~74% Tumor Reduction at 2-weeks [+]

~67% Tumor Reduction at 5-months [#]

Neoadjuvant UM Patient

Daro Monotherapy

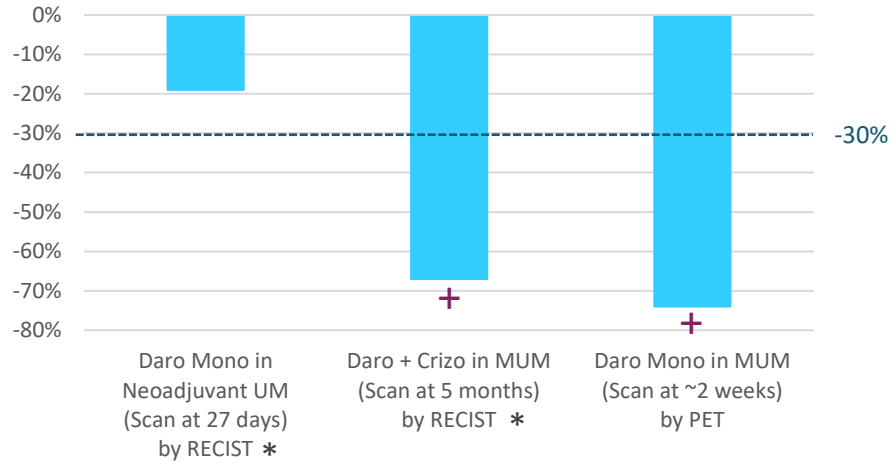


~20% Tumor Reduction [~]

Patient on Treatment 27 Days Prior to Enucleation

Preliminary (Neo)Adjuvant UM Clinical PoC

Reduction in Uveal Melanoma Lesions in UM or MUM



+ Patient observed improvement in visual symptoms

- Preliminary clinical POC for potential use in (neo)adjuvant UM with **observed responses in primary orbital lesions**
- **Tumor shrinkage observed in 5 of 5 (100%) primary UM lesions^**
- Evaluating **novel near-term clinical endpoints** such as vision preservation and organ preservation (avoid enucleation)

Phase 2 Study for (Neo)Adujvant UM [1]

Primary Uveal Melanoma Patients without Metastases and Ineligible for Radiation

↓

Darovasertib Monotherapy Until Maximum Benefit

↓

Radiation

Potential Clinical Endpoints:
Vision / Organ Preservation

↓

Follow-up

Targeting Phase 2 Clinical Trial to Evaluate Darovasertib in (Neo)Adjuvant UM in Q4 2022

[1] Preliminary Phase 2 study plan, pending investigator and regulatory guidance

[+] Images (PET) courtesy of Matthew Carlino, MBBS, FRACP, PhD
[#] Images (MRI) courtesy of Marcus Butler, MD
[~] Images (Ultrasound) courtesy of Ocular Oncology Unit Royal Victorian Eye and Ear Hospital

* Patient remains on treatment as of August 19, 2022 data cutoff; based on preliminary analysis of unlocked database
^ Including two additional patients (not shown) after data cut-off date based on preliminary observation of tumor reductions in uvea lesion of (i) a Daro + Crizo MUM patient with an intact primary lesion, and (ii) a Darovasertib monotherapy UM patient enrolled in the (neo)adjuvant IST (NADOM) study

IDEAYA BIOSCIENCES

Uveal Melanoma and MUM Treatment Paradigm

US/EU Annual Incidence and Prevalence

Darovasertib Monotherapy – Neoadjuvant UM

Clinical Approach: administer darovasertib as a neoadjuvant therapy to reduce ocular tumor size

- → Enable primary interventional procedures which preserve the eye and/or eye function
- → Estimates of ~8,500-11,000 addressable patients for Choroidal Melanoma subset of UM^
- → Targeting IDEAYA-Sponsored Trial Q4 2022

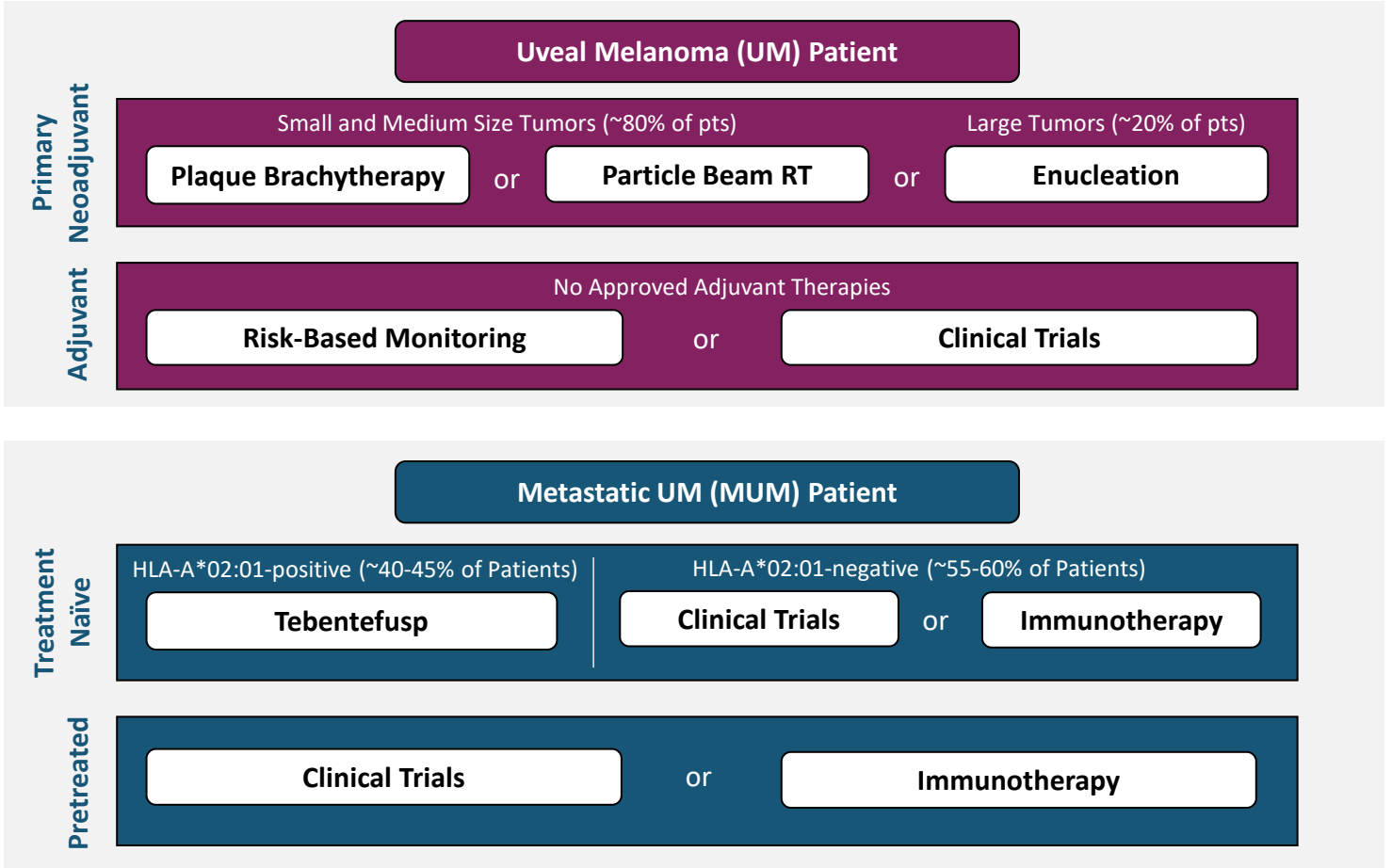
US/EU28 UM Annual Incidence	US/EU28 UM Total Prevalence
~8.7 K	~99.7 K

Darovasertib + Crizotinib – MUM

Clinical Approach: Daro+Crizo as synthetic lethality combination with enhanced clinical efficacy

- → Targeting Potential Registrational Trial Q1 2023

US/EU28 MUM Annual Incidence	US/EU28 MUM Total Prevalence
~4.5 K	~14.4 K



Total Annual Incidence of over 13,000 Patients

Orphan Drug Designation (ODD) for Darovasertib in UM and MUM

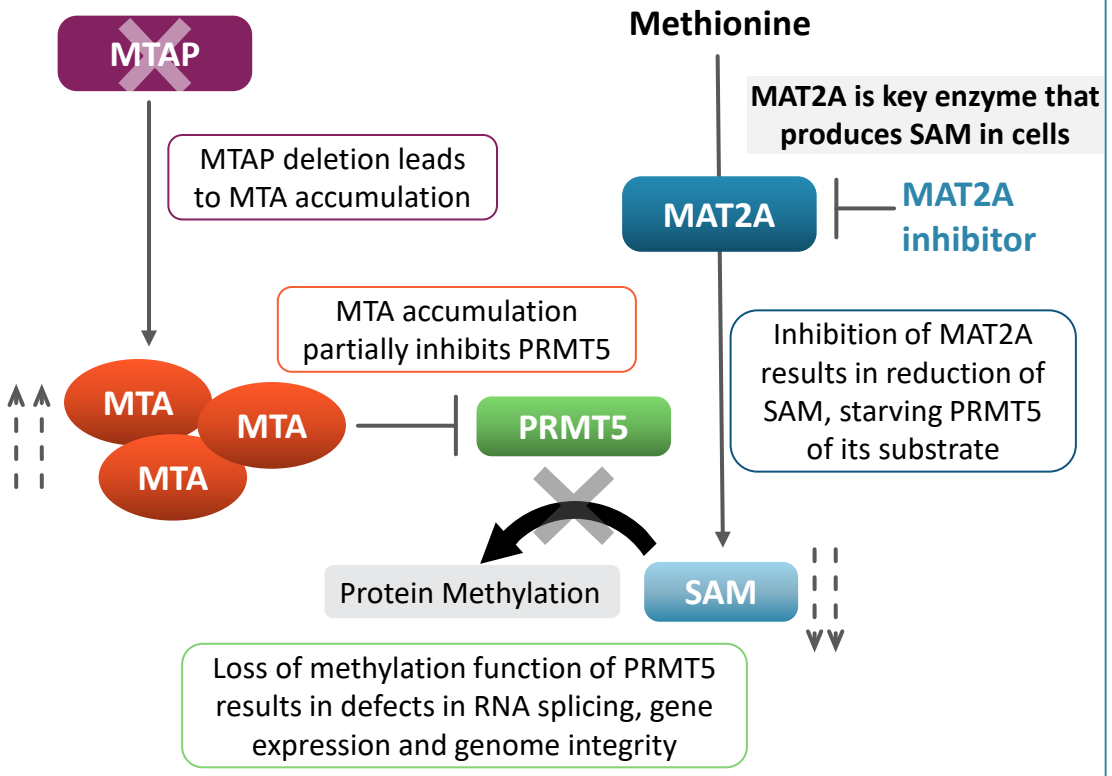
IDEAYA / ClearView Analysis; RT: Radiation Therapy; UM: Uveal Melanoma

^ Estimated addressable patient population for US / EU (Sources: Evercore, Cowen), with projected peak revenues for Aura Biosciences AU-011 in Choroidal Melanoma ranging from $600M to ~$1B (Sources: Evercore, Cowen, SVB Leerink)

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

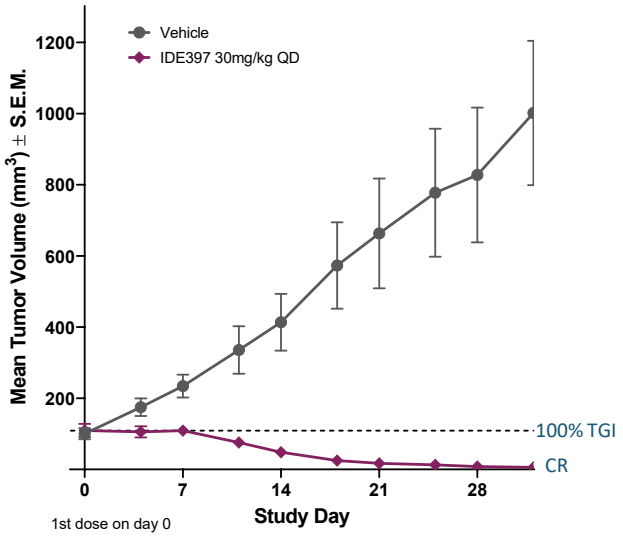
Data from The Cancer Genome Atlas in cBioPortal

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

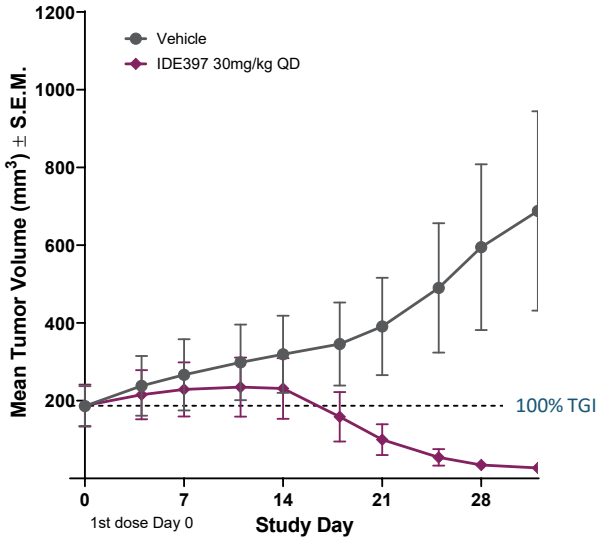
Monotherapy Tumor Regressions & Significant TGI Across Multiple Solid Tumor Types

NSCLC and Bladder Cancer MTAP-/- PDX Models

NSCLC PDX Model

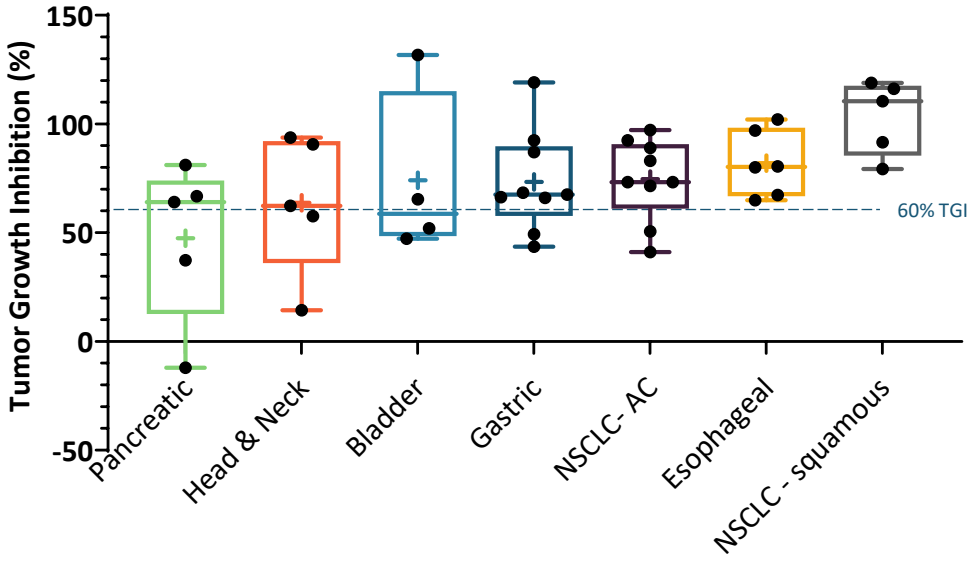


Bladder PDX Model



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 Clinical Data Summary – Monotherapy Dose Escalation Cohorts

ctDNA Molecular Response demonstrates Tumor Pharmacodynamic Modulation

GUARDANT OMNI™

- Comprehensive genomic profiling platform for clinical development programs in targeted therapies
- 500-gene panel incorporating vast majority of genes being evaluated in cancer drug development pipelines and biomarkers, including tumor mutational burden

GUARDANT 360 CDx
Lead with Liquid

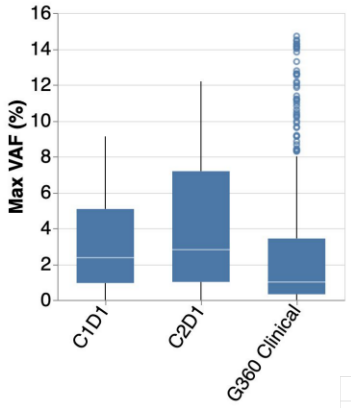
- FDA-approved CDx for patient genomic profiling
- MTAP anticipated to be included in next generation of GUARDENT 360® CDx

Molecular Response

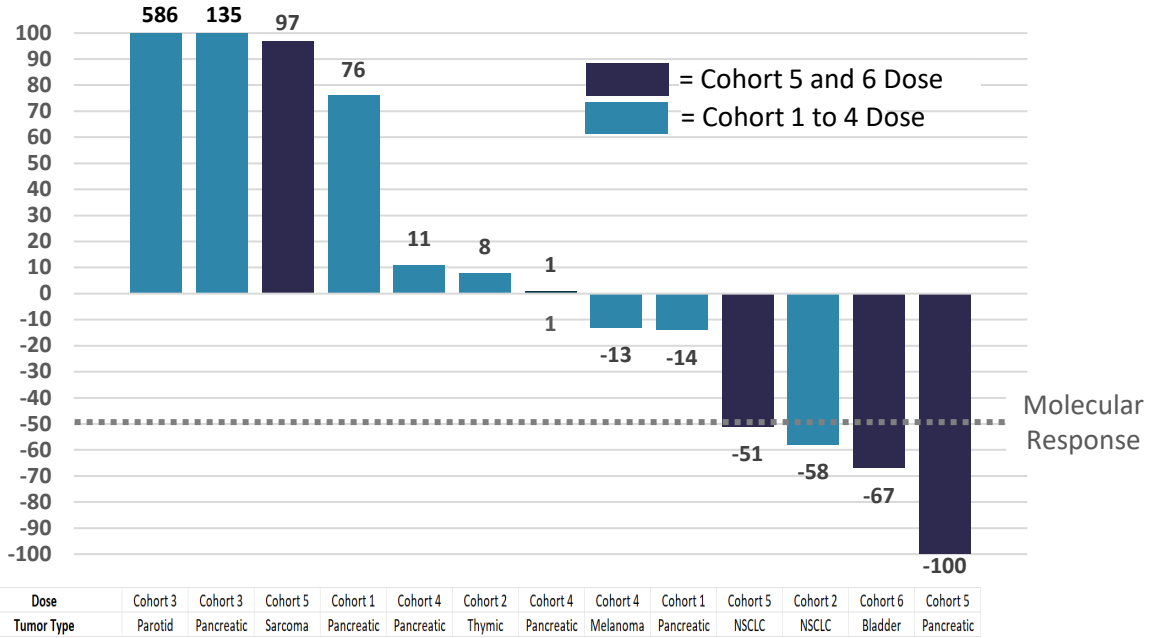
Assess changes in ctDNA during treatment 4-10 weeks vs. baseline

20+ Publications

IDE397 Ph 1 Samples have Higher Tumor Shedding relative to broad-based Guardant360® Clinical Cohort



Molecular Response Waterfall (Baseline to C2D1)



Dose	Cohort 3	Cohort 3	Cohort 5	Cohort 1	Cohort 4	Cohort 2	Cohort 4	Cohort 4	Cohort 1	Cohort 5	Cohort 2	Cohort 6	Cohort 5
Tumor Type	Parotid	Pancreatic	Sarcoma	Pancreatic	Pancreatic	Thymic	Pancreatic	Melanoma	Pancreatic	NSCLC	NSCLC	Bladder	Pancreatic

Molecular response is calculated as the ratio of mean VAF on-treatment to baseline, as in Zhang et al using a cutoff of 50% to define molecular responders (< 50%) or molecular nonresponders (≥ 50%)*

* Zhang Q et al. Cancer Discovery (Aug, 2020)

ctDNA Molecular Response: IDE397 Dose-Dependent Tumor Pharmacodynamic Modulation

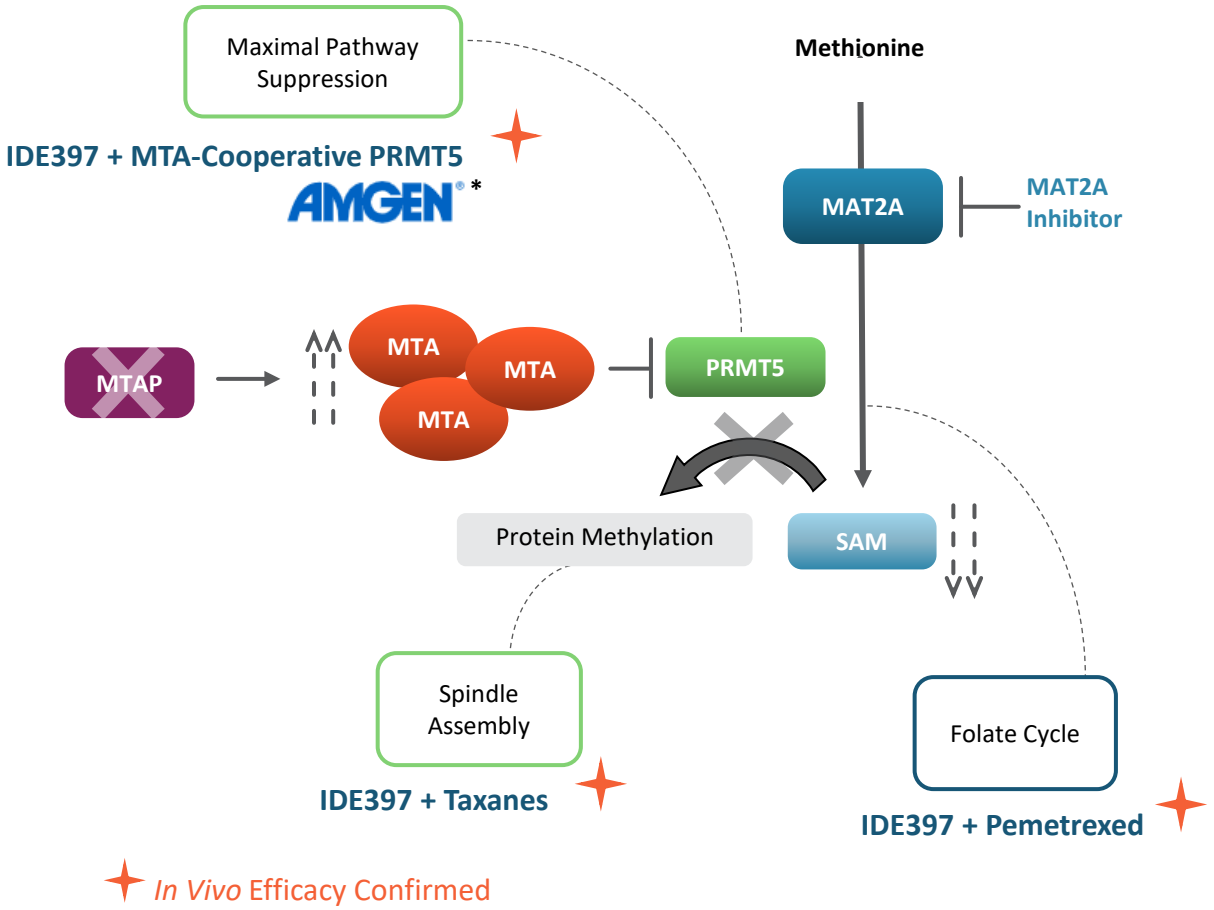
- 100% (2 of 2) Molecular Responders in NSCLC
- 75% (3 of 4) Molecular Responders in Cohort 5 and Cohort 6 Patients
- 31% (4 of 13) Molecular Responders across all Cohorts 1 to 6

IDEAYA Data: Guardant OMNI™ ctDNA Molecular Response (n=13 evaluable IDE397 Phase 1 dose escalation samples)

IDEAYA BIOSCIENCES

Clinically Evaluating Multiple MAT2Ai Rational Combination Strategies

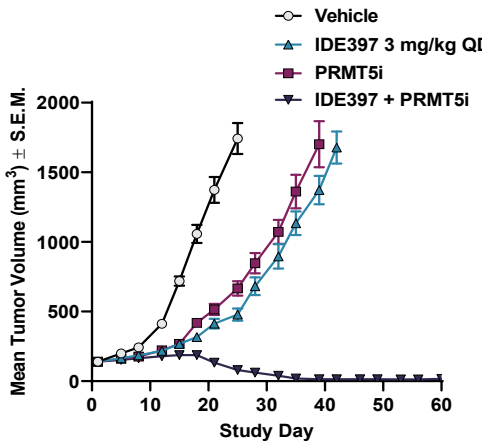
Combination Strategies based on Mechanistic Hypothesis and Preclinical Efficacy



IDE397 Novel Combinations

IDE397 + MTA-Cooperative PRMT5i

(NSCLC MTAP-/- CDX Model)



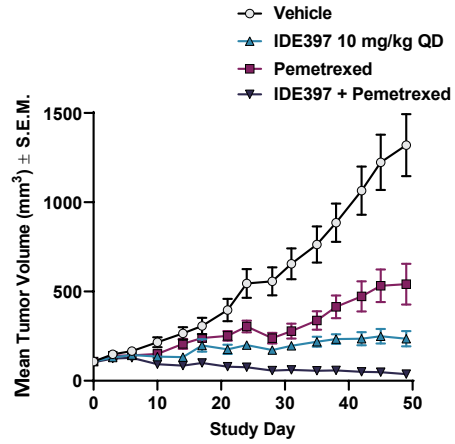
Observed Complete Response (CR) @ Study Day ~40+ durable to Study Day ~60+

IDE397 dosed at 3 mg/kg QD = 1/10th of typical preclinical dose of 30 mg/kg QD

Observed selective sensitivity in MTAP-null tumors (no observed TGI in MTAP-wt tumors)+

IDE397 + Pemetrexed

(NSCLC MTAP-/- PDX Model)



Observed Tumor Regressions (>100% TGI) by Study Day ~30+ durable to Study Day ~50+

IDE397 dosed at 10 mg/kg QD = 1/3 of typical preclinical dose of 30 mg/kg QD

IDEAYA Data; + HCT-116 engineered +/- MTAP CDX models
PRMT5 Inhibitor = representative tool compound PRMT5i

IDEAYA / GSK Data

* Pursuant to Amgen Clinical Trial Collaboration and Supply Agreement for clinical evaluation of IDE397 and Amgen's AMG 193, an investigational MTA-cooperative PRMT5 inhibitor; Amgen will sponsor the study; IDEAYA and Amgen will jointly share external costs of the study

IDE397 Phase 1/2 Clinical Development Plan

Evaluation of Monotherapy Expansion and Combinations

IDE397 Development Candidate – Clinical Profile

- Exposure-Dependent Pharmacokinetic (PK) Profile with low C_{max}:C_{min}
- Robust, Exposure-Dependent Pharmacodynamic (PD) Response
- Monotherapy Expansion at Projected Clinically Active Dose *
- Maximum Tolerated Dose Not Yet Observed ^

IDE397 is uniquely positioned to evaluate efficacy in MTAP pathway, with a favorable PK/PD profile and observed therapeutic window

Mono Expansion Cohorts – Select MTAP-null Tumor Histologies

- IDE397 RDE Mono Expansion in NSCLC (n= 10+)
- IDE397 RDE Mono Expansion in EsophagoGastric (n=10+)

Combination Cohorts – Clinical Proof of Concept in MTAP-null Tumors

Combo Escalation

- IDE397 + Docetaxel NSCLC (n= 10+)
- IDE397 + Paclitaxel EsophagoGastric (n= 10+)
- IDE397 + Pemetrexed (10+)
- AMGEN IDE397 + AMG 193 MTA-Cooperative PRMT5i#

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

* Monotherapy Expansion at Cohort 5 dose, projected to be a potentially efficacious dose based on clinical PK/PD and preclinical data and models
^ Continuing with concurrent dose escalation cohorts (e.g., Cohort 6)
# AMG193 = Amgen's investigational MTA-cooperative PRMT5 inhibitor

IDEAYA BIOSCIENCES

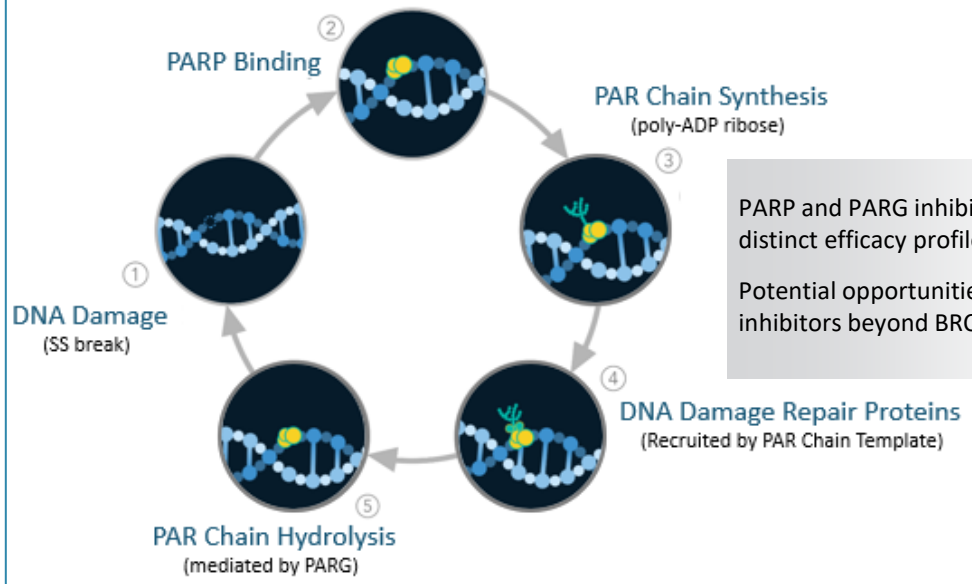
PARG Synthetic Lethality Program

Targeting IND Q4 2022 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



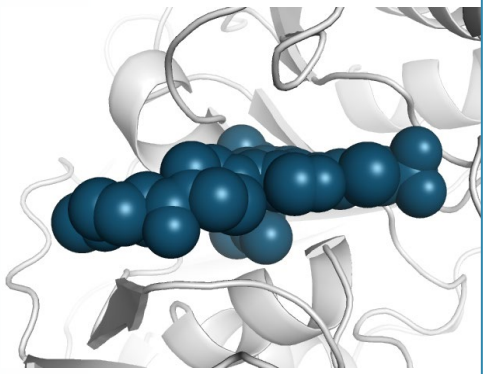
PARP and PARG inhibitors have distinct efficacy profiles in HRD

Potential opportunities for PARG inhibitors beyond BRCA

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

IDE161 Drug Discovery and Profile

- Structurally-Based Drug Design
- IDE161 is a potent, selective small molecule compound; demonstrated cellular activity and efficacy in biomarker defined settings
- IDE161 development candidate in IND-enabling studies
- Targeting IND Q4 2022



Clinical Development Thesis

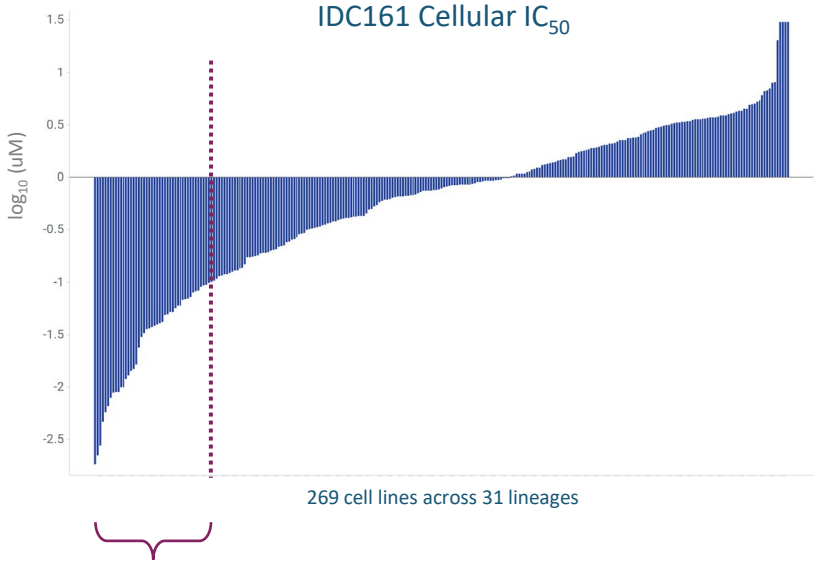
- Activity in setting of PARPi intrinsic and acquired resistance
- Differentiation from PARPi activity across HRD and beyond HRD
- Improved safety profile relative to 1st generation PARPi → potentially enables durable combination regimens

IDEAYA Data

IDE161 Cell Panel Activity Informs Selection of Predictive Biomarkers

HRD Cell Lines are Selective Sensitivity to IDE161

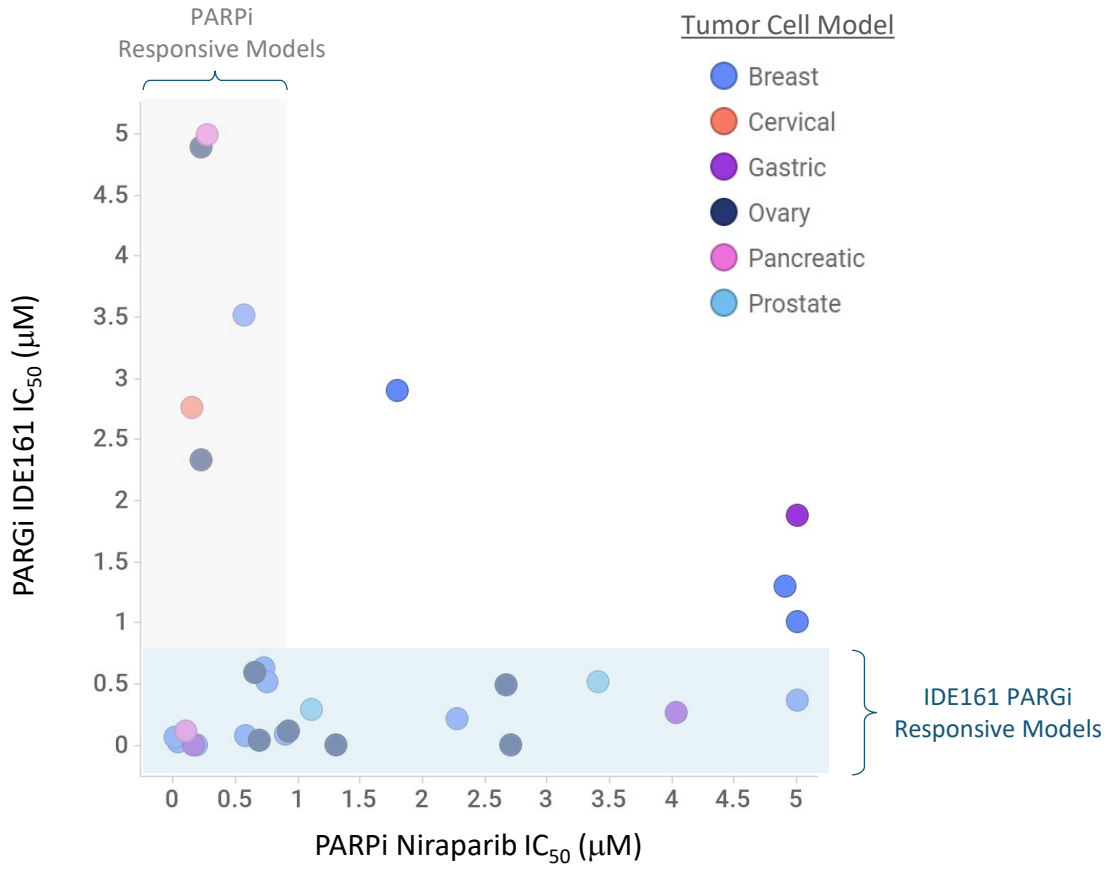
Cellular Response Profiles inform Mechanistic Basis - PARGi Sensitivity within and Beyond HRD



Top predictive response biomarkers* include HRD, replication stress, nucleotide excision repair and parylation cycle

* Based on univariate and multivariate pan-cancer and lineage-specific molecular feature analysis

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

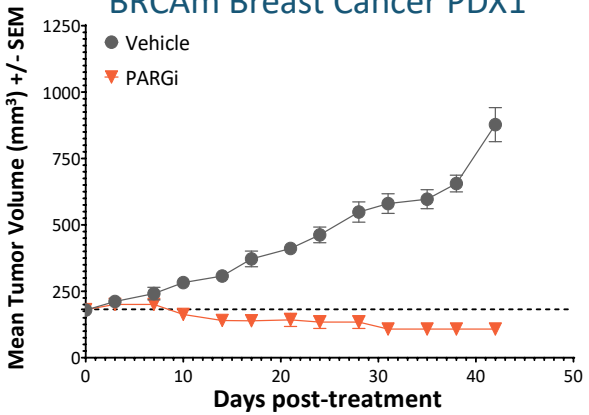


Homologous Recombination Deficient (HRD) Models are Sensitive to PARGi

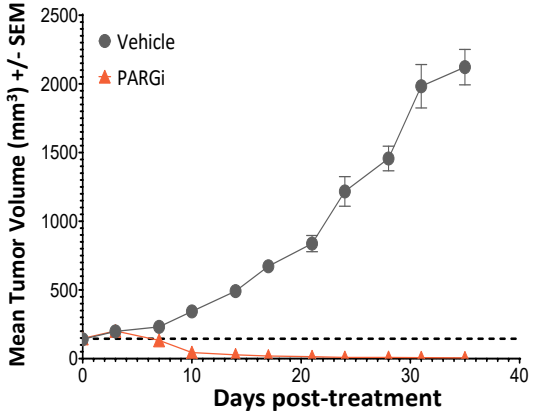
Observed PARGi Activity Distinct to PARP Inhibition in Breast, Gastric and Ovarian Models

Robust activity in HRD PDX setting

BRCAm Breast Cancer PDX1

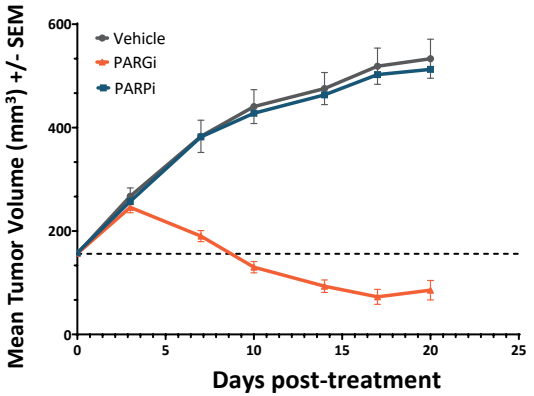


BRCAm Breast Cancer PDX2

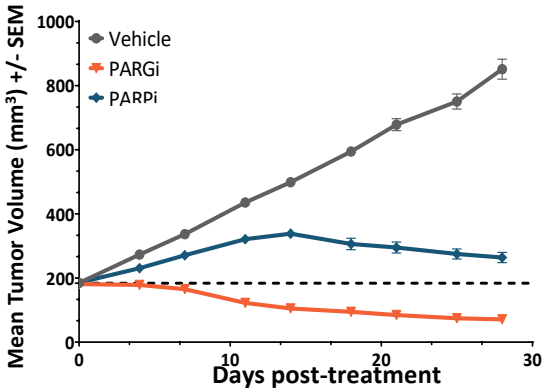


Regression in PARPi refractory models

HRD Gastric Cancer CDX

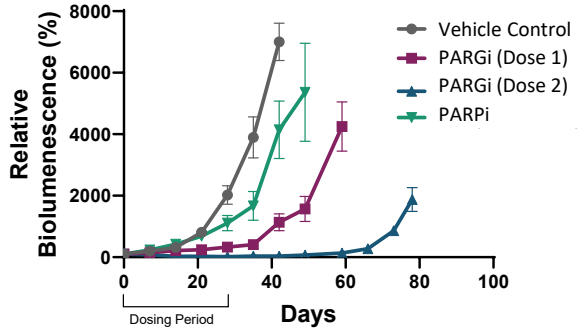


BRCAm Breast Cancer CDX

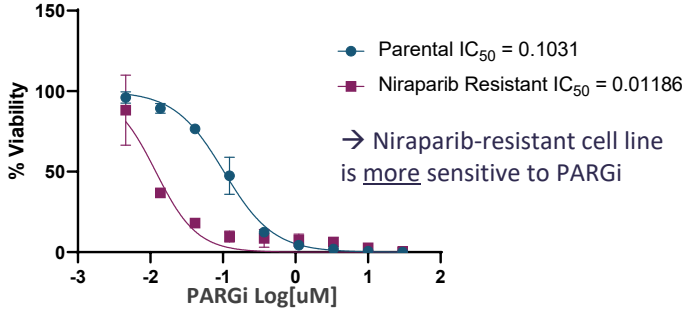


Defense against acquired resistance

Clinically derived PARPi Resistant Orthotopic Ovarian Cancer PDX is Responsive to PARGi



Laboratory derived PARPi Resistance Can Sensitize Tumor Cells to PARGi

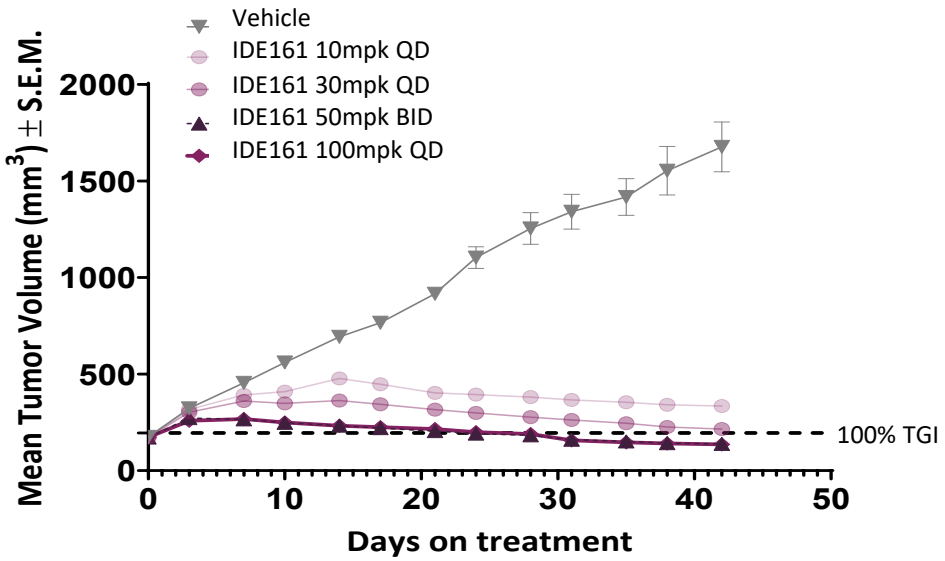


IDEAYA Data; PARPi (Niraparib) dosed at MTD ; PARGi dosed at <MTD

IDE161 Demonstrates Favorable Efficacy and ADME/PK Profile

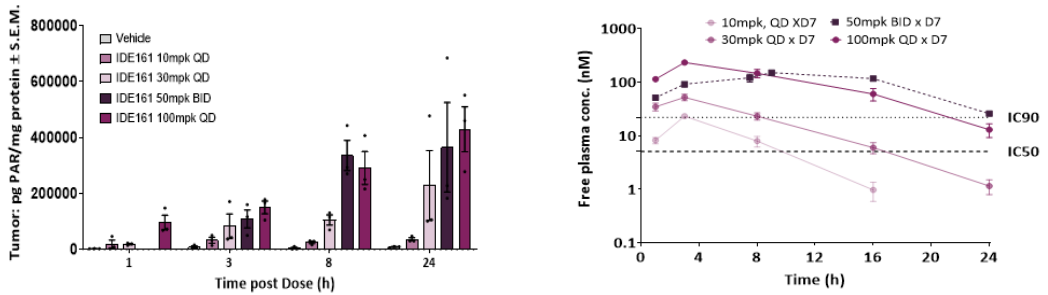
Preliminary Safety Data Suggests Differentiated Target Product Profile vs PARP Inhibitors

Observed Tumor Regressions in PARP-Resistant HRD Model



Observed Exposure-Dependent Responses with Tumor Regressions

Robust PD Modulation and Sustained PK



Observed PK/PD/Efficacy Relationship supports Favorable Dosing Regime

IDE161 Preliminary Safety Data shows Acceptable Safety Profile in Toxicology Studies with Differentiation vs PARP Inhibitors

- Target Product Profile (TPP) supports potential for enhanced therapeutic window vs PARPi, with lower risk for myelosuppression at projected clinically relevant exposures
- TPP supports potential combination opportunities with Chemo or Immuno Oncology agents
- GLP Tox studies ongoing; completed “in-life” phase in two species

Potential First-in-Class Opportunity to Broadly Impact Patients with Breast, Ovarian & Other Tumors

Pol Theta Helicase Synthetic Lethality Program

Targeting First-in-Human Phase 1 Clinical Trial Initiation in H1 2023

Clinical Development Strategy

Pol Theta Helicase Inhibitor + PARP Inhibitor

Pol Theta Helicase Inhibitors Disrupt MMEJ Alternative DNA Damage Repair:

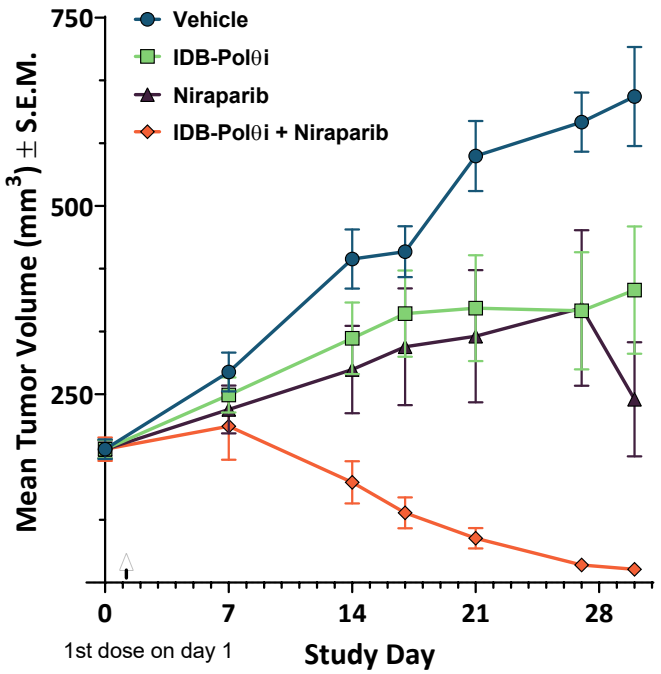
- Inhibit DSB Repair by MMEJ
- Dysregulate Replication Fork Stabilization

- Potentiate PARPi Efficacy
- Overcome PARPi Resistance
- Prevent PARPi Resistance

Potential Clinical Opportunities

Pol Theta Helicase *In Vivo* Activity

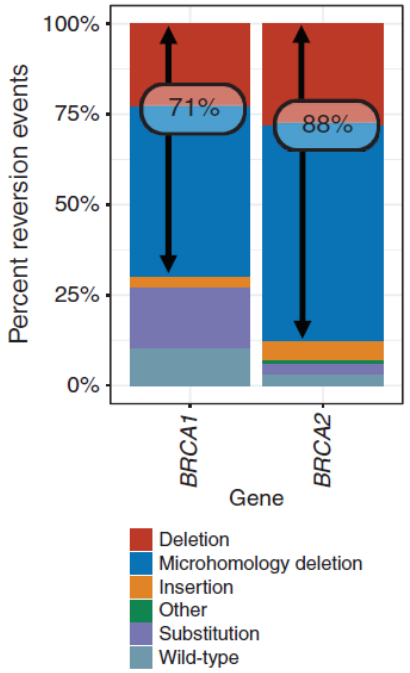
Pol Theta Helicase Inhibitor + PARPi



IDEAYA Data

BRCA 1/2 Clinical Reversions

BRCA Reversions Mediated by MMEJ



Cancer Res. 2020, DOI: 10.1158/2159-8290

GSK Strategic Partnership: Global Royalties with GSK covering all Costs; ~$1B Milestones, incl up to $20M Preclinical / Ph1 Clinical; Potential Combination with GSK's Zejula™, a PARP Inhibitor

Werner Helicase Synthetic Lethality Program

Targeting Development Candidate in 2023

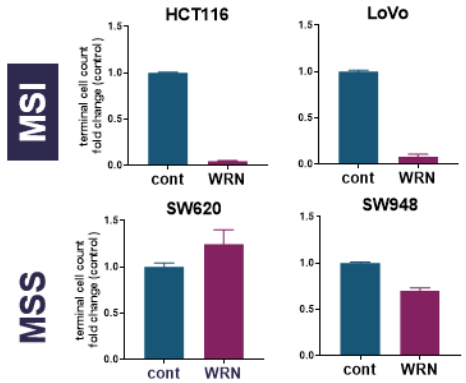
Werner Helicase Synthetic Lethal with High-MSI

CellPress

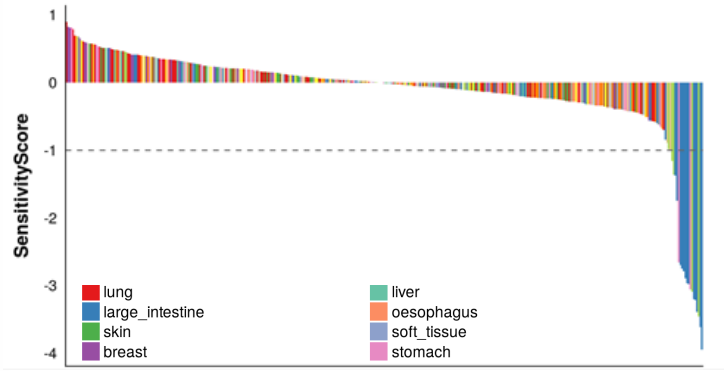
Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al



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



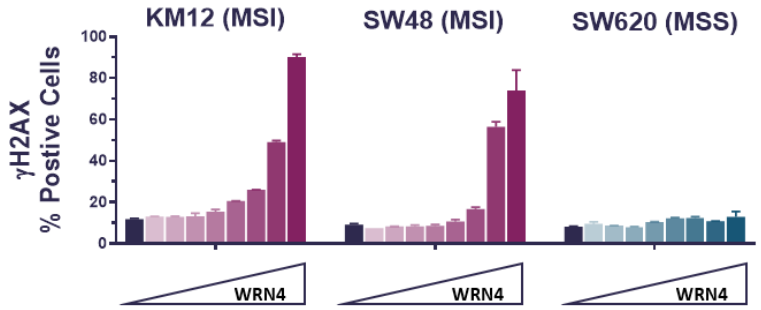
Project Drive

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

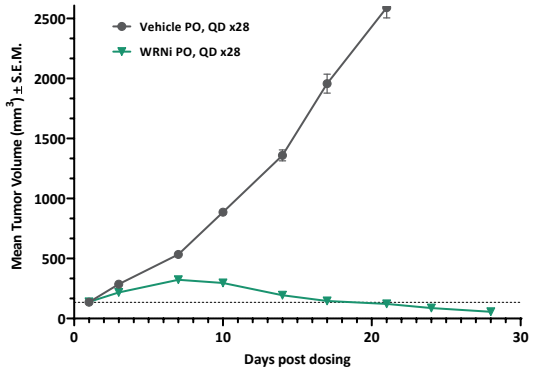
[1] Cancer Res., November 1998

Werner Inhibitor Cellular PD and *In Vivo* Efficacy

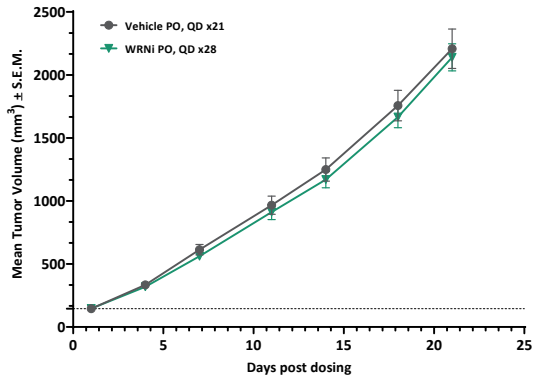
WRN inhibitor PD and *in vivo* efficacy with ~100% TGI and tumor regression



High MSI Xenograft Model



MSS Xenograft Model



IDEAYA Data

GSK Strategic Partnership: 50/50% US Profit Share and ex-US Royalties, ~$1B Milestones, incl up to $20M Preclinical / Ph1 Clinical; Cost Share 80% (GSK) / 20% (IDEAYA); Potential Combination with GSK's Jemperli™, a PD-1 IO Agent

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 clinical-stage (IDE397, Darovasertib) and late preclinical (PARG, Pol Theta) programs

Validating and Value-Accretive Pharma Partnerships and Collaborations with Amgen on MAT2A-PRMT5 Combination,[3] Pfizer on Darovasertib-Crizotinib Combination,[3] GSK on Pol Theta (100% GSK Cost Share, Milestones, WW Royalties) and GSK on Werner Helicase (80% GSK Cost Share, Milestones, 50/50 US Profits)

Strong Balance Sheet with ~$394 M in cash anticipated to fund operations into 2026 [1, 2]

Multiple 2022 / 2023 Target Catalysts for Clinical and Late Preclinical Programs

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

PKC + cMET in MUM
Clinical Data Update √
Reg Trial Initiation – Q1 2023

Expansion Opportunities
Neoadjuvant UM – Q4 2022
cMET (HCC) – Preclinical
KRAS – Preclinical

MTAP-Deletion

IDE397 (MAT2A)
Mono Expansions – Ph 2 √
Combo Initiations – Ph 1 √

MTAP-SL
Lead Series ID

HRD/BRCA

PARG
IDE161 IND Filing – Q4

Pol Theta
Dev Candidate – Q2 √
First-in-Human – H1 2023

MSI-High

Werner Helicase
Lead Optimization
Dev Candidate 2023

SL Platform

First-in-Class – SL Targets
Target ID and Validation

(1) Includes aggregate of ~$393.9M cash, cash equivalents and marketable securities as of September 30, 2022
(2) IDEAYA Form 10-Q dated November 8, 2022, as filed with the U.S. Securities and Exchange Commission
(3) Clinical Trial Collaboration and Supply Agreements, independently with Pfizer (Darovasertib + Crizotinib) and Amgen (IDE397 + AMG193); IDEAYA retains all commercial rights