



March 2024

NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives
Through Transformative
Precision Medicines

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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 and the IDEAYA logo are trademarks of IDEAYA Biosciences, Inc. All other trademarks used herein are the property of their respective owners.

IDEAYA Biosciences Highlights

Leading Precision Medicine Oncology Biotechnology Company Advancing Potential First-in-Class Therapies

Broad Pipeline of 4 Clinical Programs with Multiple 2024 Target Milestones and Catalysts

PHASE 2/3	PHASE 1/2	PHASE 1	IND-ENABLING	PRECLINICAL
<p>DAROVASERTIB (PKC)</p> <ul style="list-style-type: none"> Daro + Crizo (cMET) 1L MUM Registrational Ph2/3 Program Update(s) – 2024 Daro + Crizo Phase 2 expansion in GNAQ/11 Cutaneous Melanoma Neoadjuvant UM Phase 2 Clinical Efficacy Updates – Mid 2024 Regulatory guidance update in Neoadjuvant UM – 2024 	<p>IDE397 (MAT2A)</p> <ul style="list-style-type: none"> Phase 1/2 expansion in MTAP NSCLC and Bladder <p>IDE397 + AMG 193 (PRMT5)</p> <ul style="list-style-type: none"> Ongoing Phase 1 enrollment and development of joint publication strategy – 2024 <p>IDE397 + Trodelvy® (Trop2-ADC)</p> <ul style="list-style-type: none"> Phase 1 FPI in MTAP Bladder – Mid 2024 	<p>IDE161 (PARG)</p> <ul style="list-style-type: none"> Phase 1/2 Expansion in HRD Program Update(s) - 2024 Enable Combination(s) - 2024 <p>IDE161 + KEYTRUDA® (pembrolizumab)</p> <ul style="list-style-type: none"> Phase 1 in Endometrial Cancer <p>GSK101 (POL THETA)</p> <ul style="list-style-type: none"> Ongoing Phase 1 dose escalation 	<p>WERNER HELICASE</p> <ul style="list-style-type: none"> IND Submission (\$7M Milestone upon successful IND clearance) – 2024 	<p>NEXT GEN PROGRAMS</p> <ul style="list-style-type: none"> Development Candidate Nominations, including in MTAP-deletion – 2024

Pharma Collaborations



~\$2B in potential milestones

Financials and Investor Relations

~\$975M to fund operations into 2028^{1, 2}

NASDAQ: IDYA

IND = Investigational New Drug, UM = Uveal Melanoma, MUM = Metastatic Uveal Melanoma, NSCLC = Non Small Cell Lung Cancer, HRD = Homologous Recombination Deficiency, MTAP = methylthioadenosine phosphorylase

(1) Includes aggregate of \$632.6M cash, cash equivalents and marketable securities as of December 31, 2023, plus pro forma \$342.3M estimated net proceeds from sales of common stock through at-the-market offerings in January 2024

(2) IDEAYA Form 10-K dated February 20, 2024 as filed with the U.S. Securities and Exchange Commission



Leading Functional Genomics and Synthetic Lethality Platform

The Next Frontier in Precision Medicine Oncology

Functional Genomics and 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, Others), and high-MSI (15% GI Cancers)



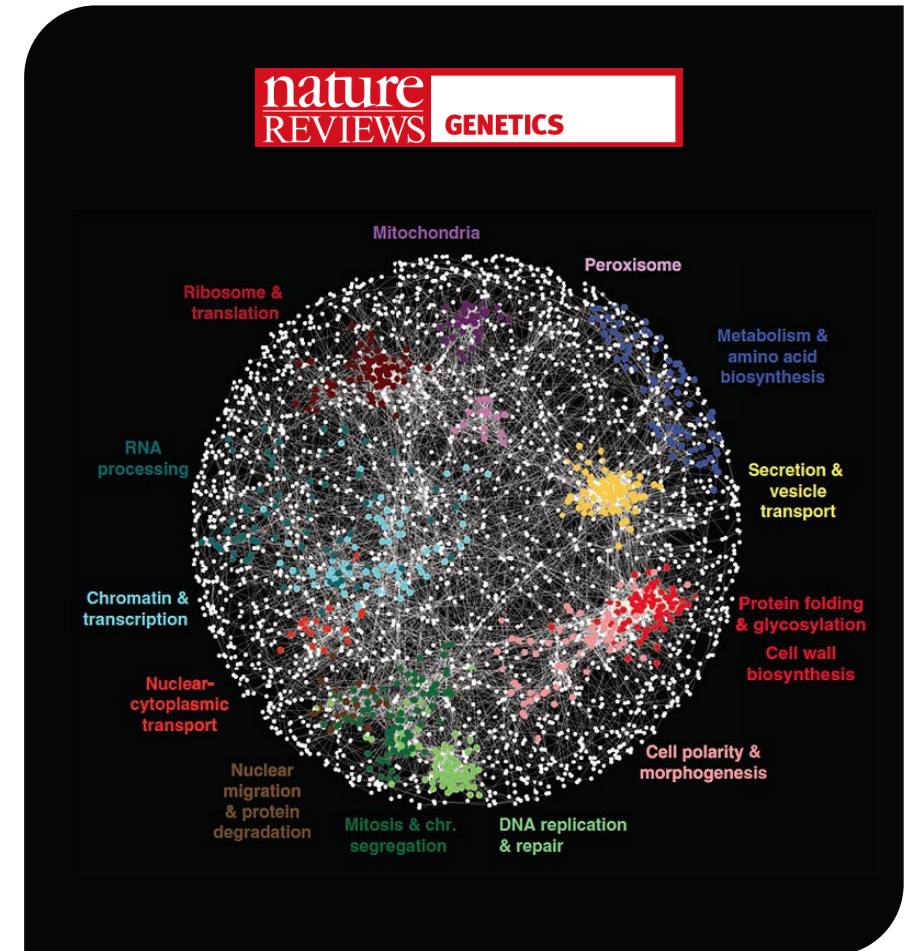
Functional genomics combines human genetics with advances in AI and machine learning to develop effective precision medicines



Synthetic lethality occurs when the simultaneous perturbation of two genes results in cell death



Large-scale screening for novel synthetic lethal targets has progressed through advances in molecular biology (e.g., RNA interference, CRISPR-Cas9 editing) and bioinformatics



IDEAYA Precision Medicine Oncology Platform

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

Target & Biomarker Discovery and Validation



Bioinformatics, including AI Algorithms
Dual CRISPR, CRISPR, Chemogenomics
Genetically Engineered Models

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

Drug Discovery and Pharmacological Validation



Structure Based Drug Design
Small Molecule Chemistry
Protein Degradation Capabilities

- Crystal structures for SL discovery programs obtained to enable structure-based design
- INQUIRE™ Chemical Library - proprietary, expert-curated small-molecule library
- HARMONY™ Machine-Learning engine empowers drug discovery platform
- Differentiated clinical / candidate compounds discovered, including IDE397, IDE161 and GSK101 / IDE705 (Pol Theta Helicase)

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 and transformative combinations
- Opportunity expansion through broad cell panel screening
- Pharmacodynamic biomarker analysis to confirm target modulation and correlation with clinical activity

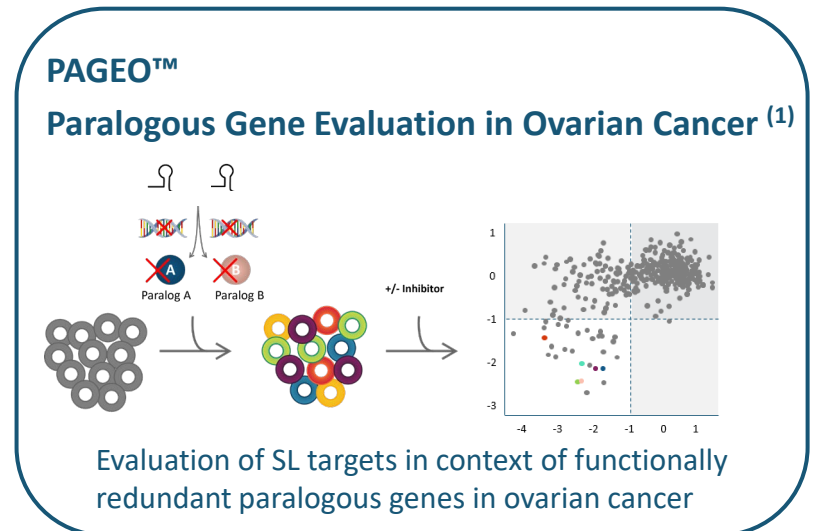
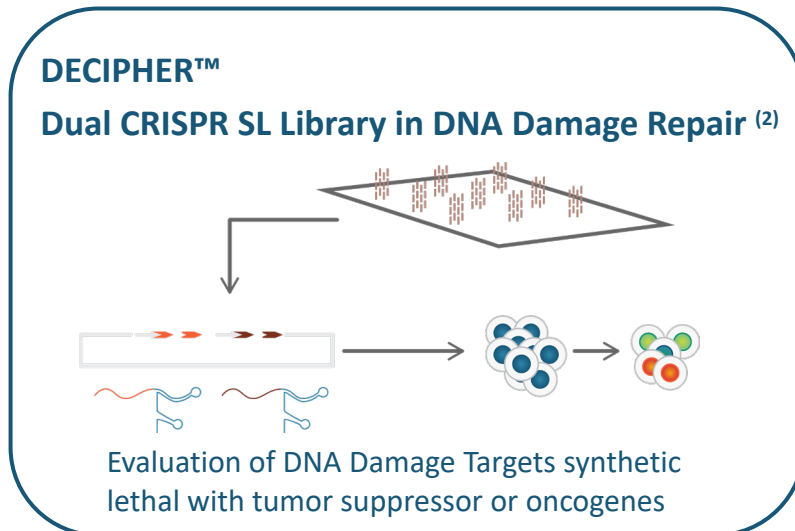
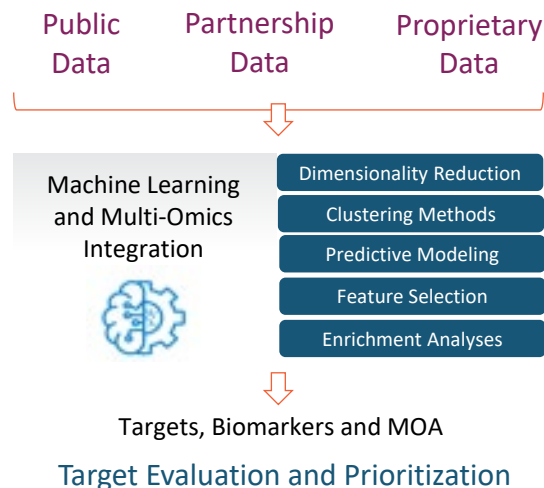
IDEAYA Functional Genomics and Synthetic Lethality Platform

Novel Target and Biomarker Discovery and Validation

Target and Biomarker Discovery & Validation Platform

IDEAYA Functional Genomics Platform integrates 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*

Data-to-Knowledge Enterprise fueled by multi-omic patient and molecular data across public, partnership and proprietary data sets via IDEAYA Bioinformatics Platform



IDEAYA Precision Oncology Drug Discovery Platform & IND Engine

AI/ML & Structure Based Drug Design to Deliver First-in-Class Development Candidates

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 the Synthetic Lethality drug-discovery programs

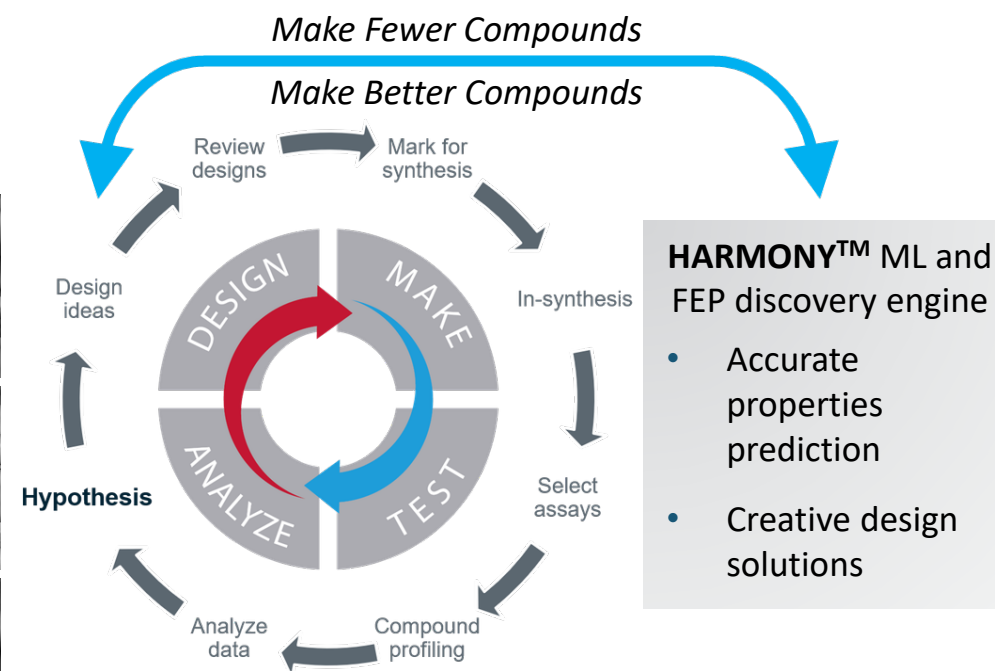
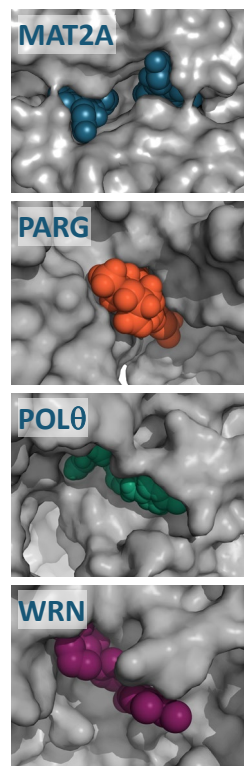
Multiple potential “first-in-world” co-crystal structures resolved, including for PARG, Pol Theta Helicase and Werner Helicase

INQUIRE™ Proprietary Chemical Library

Expert-curated HTS library to enhance hit discovery capabilities against novel SL targets classes

Enhances IDEAYA's SL Drug Discovery Platform and competitive differentiation

AI/ML Enabled Computational Drug Discovery*



AI/ML to Accelerate Time to IND for First-in-Class Targets

IDEAYA's Potential First-in-Class Precision Medicine Oncology Pipeline

	Modality/Indication	Biomarker	Pre-clinical	IND Enabling	Phase 1	Phase 2	Potential Registrational	Program Goals / Achievements	Collaborations	Commercial (IDEAYA)	
Darovasertib <i>PKC</i>	+cMET ¹ Combination 1L HLA-A2(-) MUM	GNAQ/11	[Progress bar]					Phase 2 (AA) / Phase 3 Registrational Trial ^ Program Update(s) - '24		Pfizer (1)	WW Commercial Rights
	cMET ¹ Combination HLA-A2(+) MUM ^	GNAQ/11	[Progress bar]					HLA-A2(+) Clinical Trial ^^			
	cMET ¹ Combination Cutaneous Melanoma	GNAQ/11	[Progress bar]					Phase 2 Expansion in Metastatic Cutaneous Melanoma			
	(Neo)Adjuvant UM	GNAQ/11	[Progress bar]					Phase 2 Clinical Efficacy – Mid '24 Regulatory Guidance – '24			
IDE397 <i>MAT2A</i>	Monotherapy Solid Tumors	MTAP	[Progress bar]					Phase 2 Monotherapy Expansion in NSCLC, Bladder		AMGEN (2)	WW Commercial Rights
	Combination Solid Tumors	MTAP	[Progress bar]					Phase 1 IDE397 + AMG 193 (PRMT5 ^{iMTA}) ongoing enrollment and joint publication strategy – '24			
	Combination Bladder Cancer	MTAP	[Progress bar]					Phase 1 IDE397 + Trodelvy® FPI – Mid '24	GILEAD (3)		
IDE161 <i>PARG</i>	Monotherapy Solid Tumors	HRD	[Progress bar]					Phase 2 expansion in priority tumor types (Breast, CRC, Endometrial, Prostate) – '24		MERCK (4)	WW Commercial Rights
	Combination Endometrial Cancer	High-MSI, MSS	[Progress bar]					Phase 1 IDE161 + KEYTRUDA® in endometrial cancer			
	Combinations Solid Tumors	HRD, Others	[Progress bar]					Enable IDE161 combination(s) – '24			
GSK101 <i>Pol Theta Helicase</i>	+Niraparib Combo ⁴ Solid Tumors	HR Mutations	[Progress bar]					Ongoing Phase 1 dose escalation	GSK (5)	Global Royalties	
WRN <i>Werner Helicase</i>	GI Cancers	High-MSI	[Progress bar]					Targeting IND submission in 2024 (\$7M Milestone upon successful IND clearance)	GSK (5)	50% US Profits and 20% costs	
Platform	Solid Tumors	Defined Biomarkers	[Progress bar]					Targeting Multiple DC Nominations, including in MTAP-deletion – '24		WW Commercial Rights	

^ Integrated Phase 2/3 enables potential Accelerated Approval (AA, Phase 2) and potential Full Approval (Phase 3) based on FDA Type C Meeting Q1 2023, ^^ Targeting enrollment of additional HLA-A2(+) patients in a separate clinical trial (e.g., ongoing IDE196-001 Phase 2 clinical trial)

(1) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreements for Darovasertib/Crizotinib Combination; 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 is the sponsor the study and the parties jointly share external costs of the study

(3) Pursuant to Gilead Clinical Study Collaboration and Supply Agreement for IDE397 + Trodelvy®, a Trop-2 directed antibody-drug conjugate (ADC); the Company will sponsor the study and Gilead will provide Trodelvy at no cost

(4) Pursuant to Merck Clinical Trial Collaboration and Supply Agreement for IDE161 + Keytruda®, an anti-PD-1 therapy; the Company will sponsor the study and Merck will provide Keytruda at no cost

(5) Pursuant to GSK Collaboration, Option and License Agreement: Polθ: Global Royalties; WRN: 50/50 US Profits + ex-US Royalties

MAT2A=methionine adenosyltransferase 2a, MTAP=methylthioadenosine phosphorylase, MTA=methylthioadenosine, PRMT5=protein arginine methyltransferase 5 (PRMT5), PARG= poly (ADP-ribose) glycohydrolase, WRN = Werner Helicase, Polθ = DNA Polymerase Theta, HRD = homologous recombination deficiency,

MSI = microsatellite instability, PKC = protein kinase C, MUM = metastatic uveal melanoma, UM = uveal melanoma, Crizo = crizotinib, NSCLC = non-small cell lung cancer, WW = worldwide, HLA-A2(-) = HLA-A2*02:01 Negative; HLA-A2(+) = HLA-A2*02:01 Positive, DC = development candidate

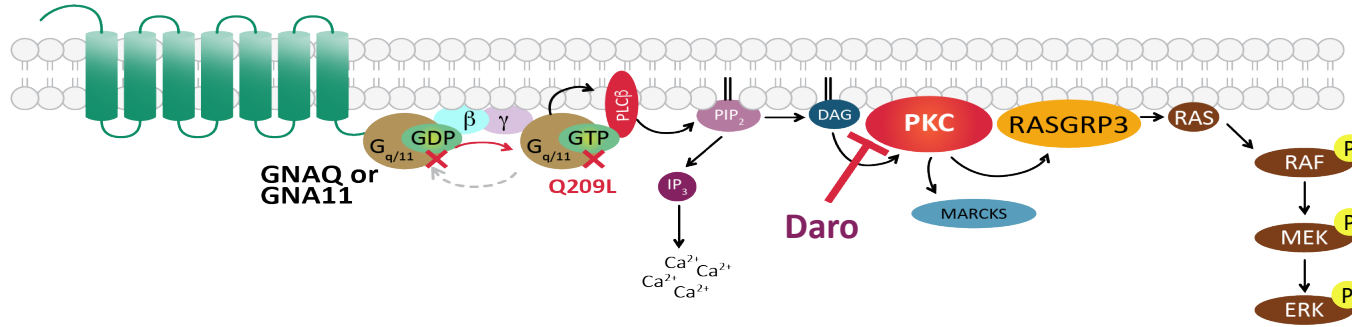
[Hatched pattern] = Target 2024 Program Milestones



Darovasertib – Potential to Broadly Impact Uveal Melanoma

Potential First-in-Class and Best-in-Class in (Neo)adjuvant UM and Metastatic UM

Mutations in GNAQ / GNA11 activate PKC Signaling, a genetic driver of Uveal Melanoma

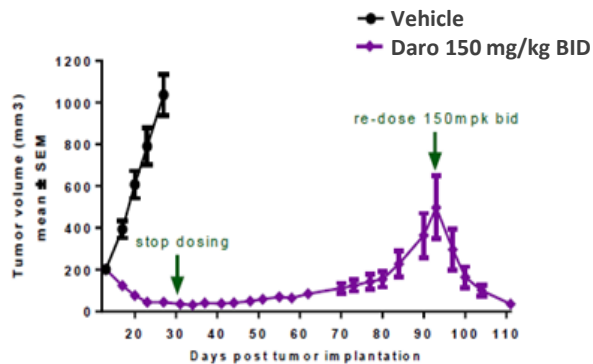


Darovasertib is an oral, potent and selective PKC inhibitor. GNAQ or GNA11 (~95%) and other upstream mutations activate PKC signaling in UM and MUM patients.

UM is typically treated with radiation and/or enucleation, with no approved systemic therapies for Neoadjuvant UM. MUM occurs in approximately 50% of UM patients and predominantly as liver metastasis in ~90% of MUM patients, with no approved therapies for HLA-A*02:01 negative MUM.

Daro Mono Rationale in Primary UM

Single Agent Daro Induces Tumor Regression
Uveal Melanoma Xenograft (92.1 mutant GNAQ)

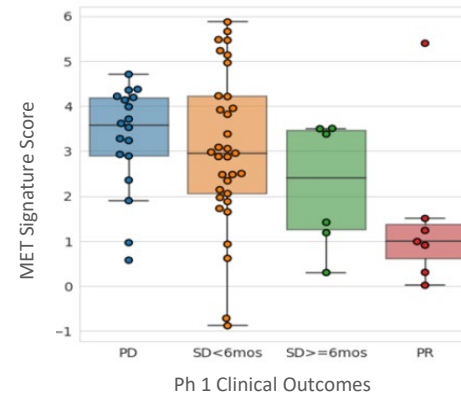


Van Raamsdonk, CD, et. al, Nature 2009; Van Raamsdonk CD, et. al, NEJM 2010; Piperno-Neumann S, et. al, J Clin Oncol 2014

Daro + Crizo Combo Rationale for Use in Metastatic Uveal Melanoma (MUM)



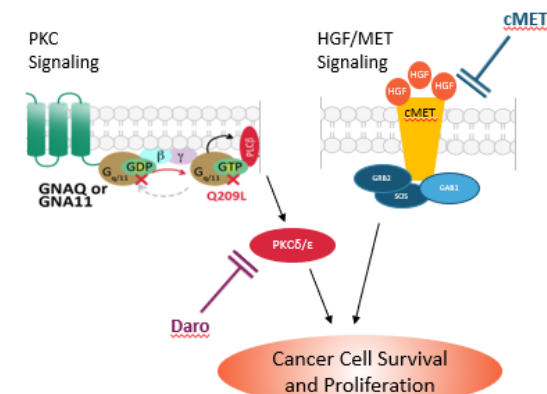
Daro Phase 1 Monotherapy Efficacy Association with cMET Expression



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

IDEAYA Data, AACR 2021

Activation of PKC and cMET Pathways with Observed cMET Overexpression in MUM Liver Metastases



Phase 2 Clinical Trial - Comparatively High-Risk, Poor Prognosis Population

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

Baseline Characteristics		IDE196-001 Phase 2* Darovasertib + Crizotinib		Tebentafusp First-Line Phase 3 [#]	
		Any-Line n=63 (%)	First-Line n=20 (%)	Tebe Arm n=252 (%)	Control Arm [^] n=126
Age (Years)	< 65	35 (56)	10 (50)	64 Median	66 Median
	≥65	28 (44)	10 (50)		
Sex	F	32 (51)	9 (45)	124 (49)	64 (51)
	M	31 (49)	11 (55)	128 (51)	62 (49)
ECOG PS	0	43 (68)	14 (70)	192 (76)	85 (67)
	1	20 (32)	6 (30)	49 (19)	31 (25)
Baseline LDH	Normal	25 (40)	10 (50)	90 (36)	46 (37)
	>ULN	38 (60)	10 (50)		
Largest metastatic lesion	≤3.0 cm	22 (35)	8 (40)	139 (55)	70 (56)
	3.1 to 8.0 cm	35 (56)	9 (45)	92 (37)	46 (37)
	≥ 8.1 cm	6 (10)	3 (15)	21 (8)	10 (8)
Location of metastases	Hepatic Only	19 (30)	10 (50)	131 (52)	59 (47)
	Extrahepatic Only	3 (5)	0	9 (4)	10 (8)
	Hepatic and Extrahepatic	41 (65)	10 (50)	111 (44)	55 (44)

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

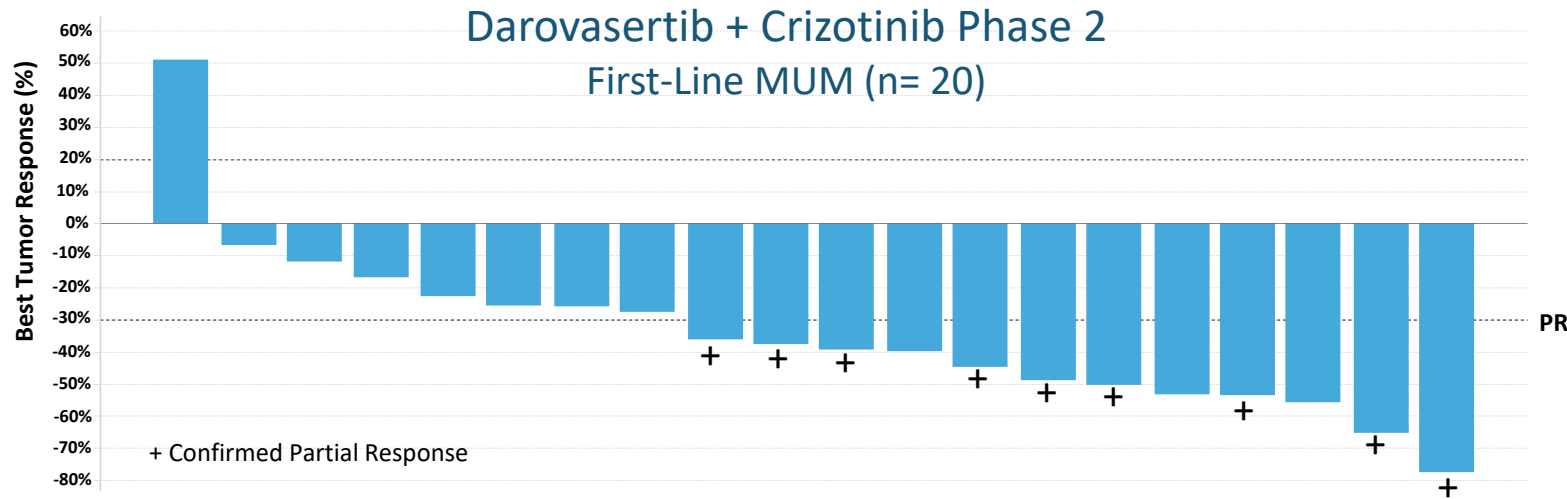
* IDEAYA Data as of August 22, 2023 (based on preliminary analysis of unlocked database by investigator review)

[#] N Engl J Med 2021; 385:1196-1206; ECOG data missing in Tebentafusp and Control arm of 4% and 7% respectively

[^] Investigator Choice distribution in the control group: 103 (82%) received pembrolizumab, 16 (13%) received ipilimumab, and 7 (6%) received dacarbazine

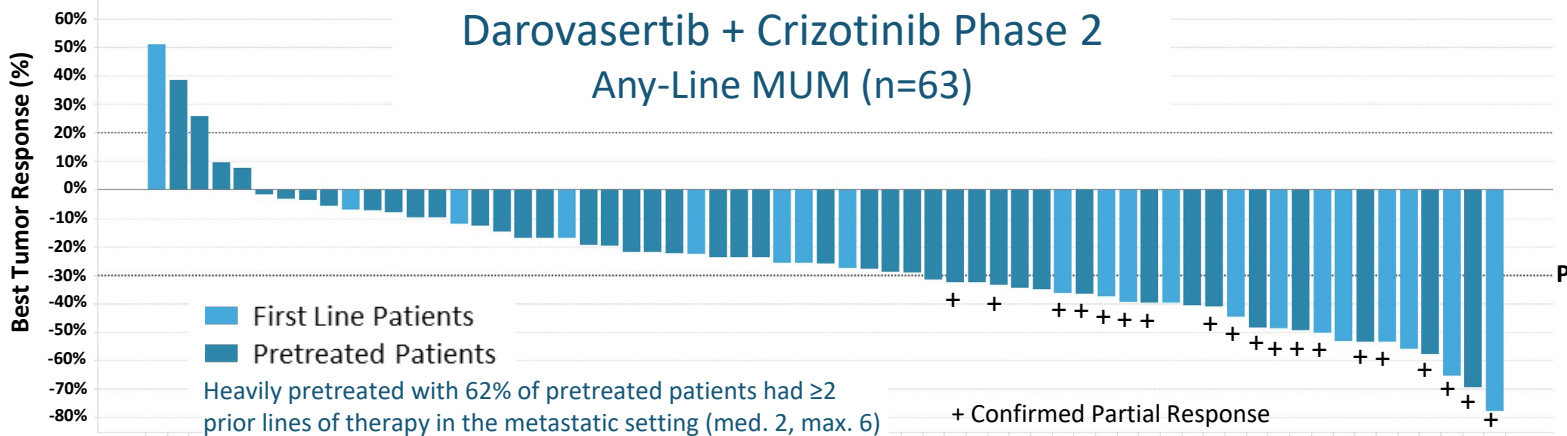
Daro + Crizo Phase 2 Efficacy: First-Line MUM and Any-Line MUM

Compelling Overall Response Rate (ORR) by RECIST 1.1 Observed



Confirmed 45% ORR and 90% DCR

Response by RECIST 1.1 First-Line MUM	Evaluable (N=20)
Confirmed ORR (9/20)	45%
Tumor Shrinkage (19/20)	95%
>30% Tumor Shrinkage (12/20)	60%
Best Overall Response	
cPR (9/20)	45%
SD (9/20)	45%
DCR (18/20)	90%



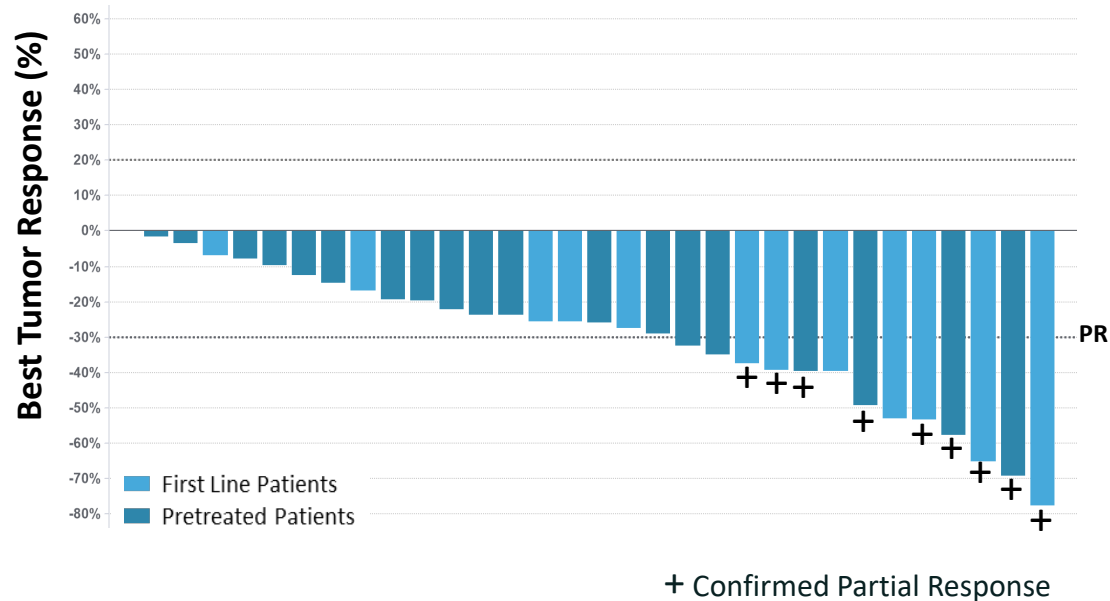
Confirmed 30% ORR and 89% DCR

Response by RECIST 1.1 Any-Line MUM	Evaluable (N=63)
Confirmed ORR (19/63)	30%
Tumor Shrinkage (58/63)	92%
>30% Tumor Shrinkage (27/63)	43%
Best Overall Response	
cPR (19/63)	30%
SD (37/63)	59%
DCR (56/63)	89%

Daro + Crizo Phase 2 Efficacy: HLA-A2-Negative and HLA-A2-Positive MUM Clinical Combination Observes Clinical Efficacy Irrespective of HLA-A2 Status

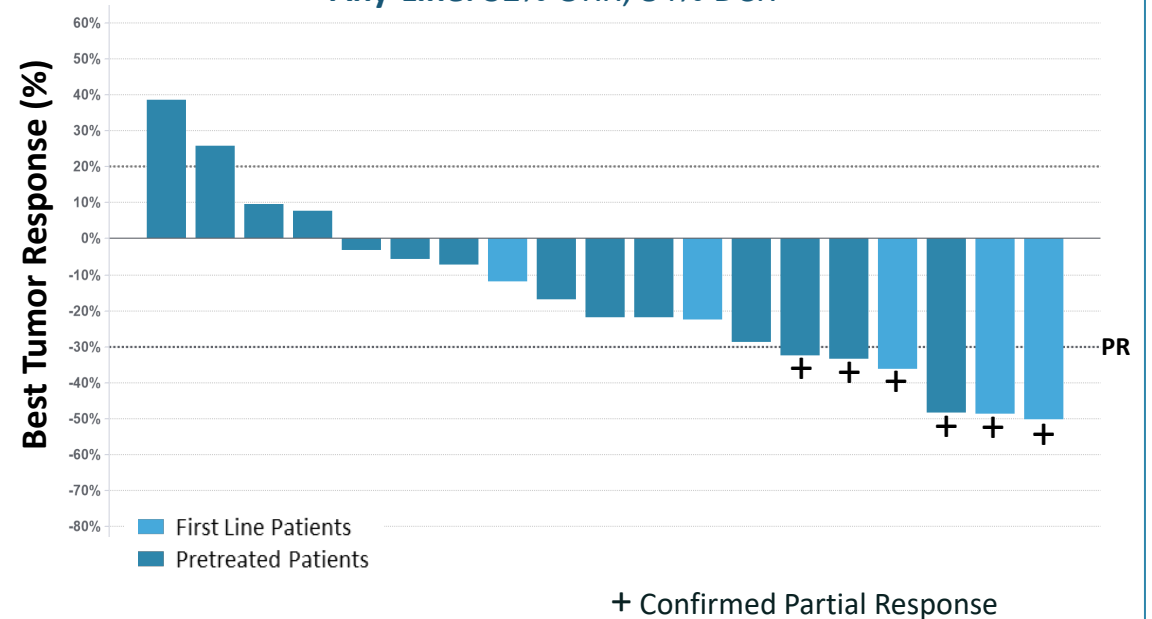
HLA-A2 Negative (n=31)

First-Line: 42% ORR; 100% DCR
Any-Line: 29% ORR; 94% DCR



HLA-A2 Positive (n=19)

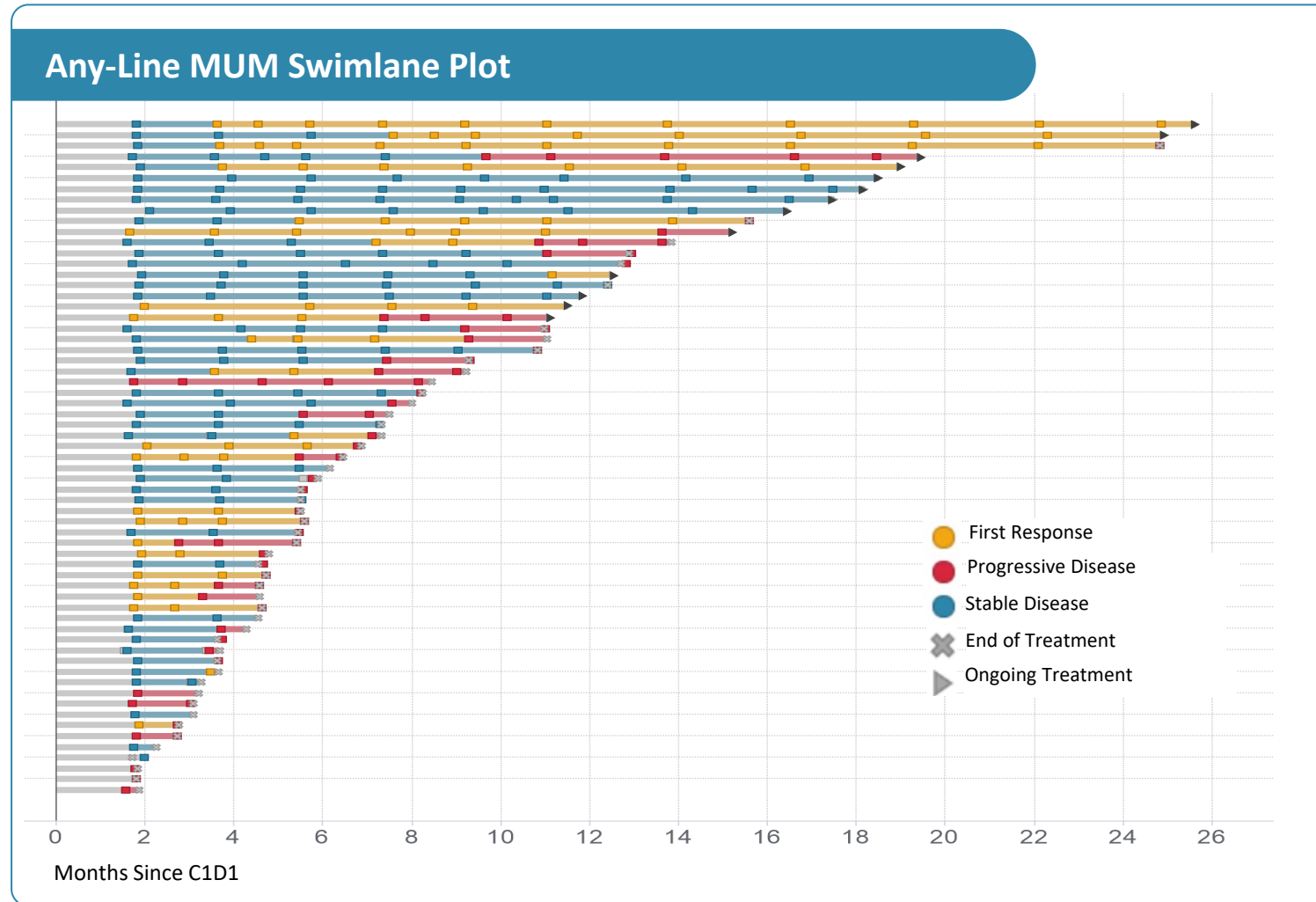
First-Line: 60% ORR; 100% DCR
Any-Line: 32% ORR; 84% DCR



ESMO 2023 Preferred Presentation M McKean et al : preliminary analysis of unlocked database as of 08/22/2023 by investigator review; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) as of 9/22/2022

Median PFS in First-Line, Any-Line and Hepatic-Only MUM

Observed Compelling Median Progression Free Survival with Encouraging Trend



Darovasertib + Crizotinib Phase 2

Median Progression Free Survival

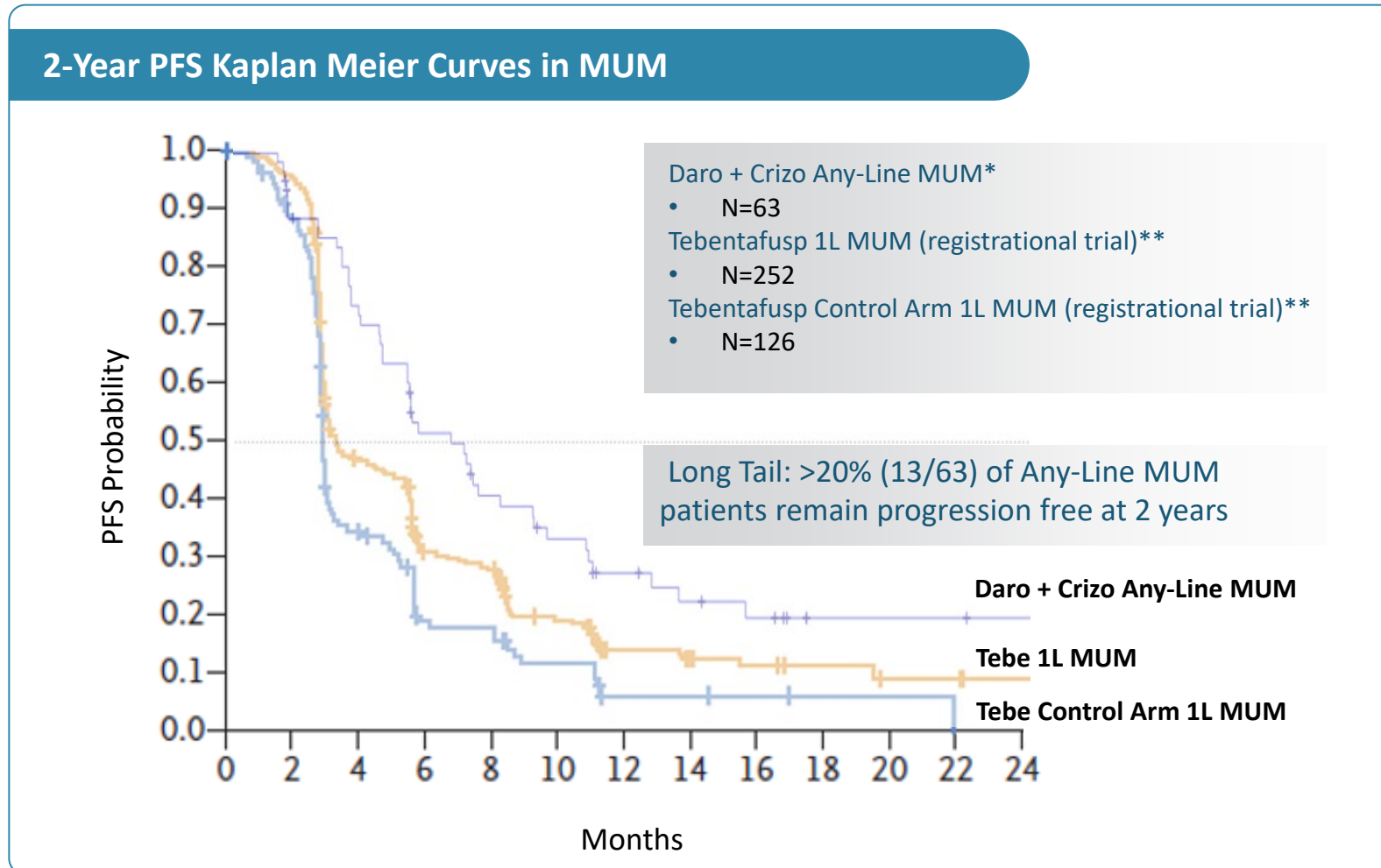
- First-Line (n=20): 7.1 months
- Any-Line (n=63): 6.8 months
- Hepatic-Only (n=19): 11.0 months

Treatment Duration – Observations

- ~50% of patients treated > 6 months
- ~30% of patients treated > 1 year

2-Year PFS Kaplan Meier (KM) Curve: Daro + Crizo in Any-Line MUM*

Daro + Crizo Combo Observes a Promising 2-Year PFS KM Curve and a “Long Tail” Effect



* IDEAYA Data: preliminary analysis of unlocked database as of 08/22/2023 by investigator review, C1D1 cutoff as of 9/22/2022, based on 63 evaluable Any-Line MUM patients. Direct comparisons are not being made and the historical data for tebentafusp is being shared for informational purposes only

** N Engl J Med 2021;385:1196-206; Tebentafusp Phase 3 registrational trial, PFS curves

Darovasertib + Crizotinib Combination Clinical Summary in MUM

Highly Differentiated Clinical Efficacy & AE Profile Observed^{+, ++}

	Darovasertib + Crizotinib	Cabozantinib Mono / Crizotinib Mono	Selumetinib + DTIC	Ipi + Nivo	Tebentafusp
Target / Mechanism	PKC + cMET	cMET	MEK + Chemotherapy	CTLA4 + PD1	HLA-A2-0201 Bi-Specific
Study Name(s)	NCT03947385	A091201 [^] / NCT05063058 ^{^^^^}	NCT01974752 ^{^^^}	NCT02626962 ^{##}	IMCgp100-102 [#]
Population	1L/2L/3L+ MUM (n=63)	1L+ MUM (n=31) / 1L (n=6) 2L (n=1) MUM	1L+ MUM (n=97)	1L MUM (n=52)	2L+ MUM (n=127)
Patient Selection	NA	NA / MET Overexpression	NA	NA	HLA-A2-positive
Drug Form	Oral Tablets	Oral Capsules	Oral Capsules + chemo	IV infusion	IV Infusion (Weekly)
Tolerability (Grade ≥3 Drug-Related AE)	31%	51.6% / NA	63% (All Cause)	58%	46.5%
% of Patients with Tumor Shrinkage	First-Line = 95% / Any-Line = 92% / Hepatic Only = 100%*	23% ^{^^} / NA	35% ^{^^}	27% ^{^^}	44% ^{^^}
Confirmed ORR% (by RECIST 1.1)	First-Line = 45% / Any-Line = 30% / Hepatic Only = 37%*	0% / 0%	3%	11.5% (not confirmed ORR)	4.7%
Median PFS	First-Line: 7.1 months / Any-Line: 6.8 months / Hepatic-Only: 11.0 months*	2 months / NA	2.8 months	3 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: IPI + Nivo Combo in HLA-A2-0201 MUM reports ~6% ORR (2 PRs out of 33 patients)

* ESMO 2023 Preferred Presentation M McKean et al: Preliminary analysis of unlocked database as of 08/22/2023 by investigator review; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) as of 9/22/2022

Based on Immunocore reported 2L+ study data (to reflect comparative patient population) and by independent review and ORR% was with confirmed PRs; ## ASCO 2021, J. Piulats, et. Al, Ipi = ipilimumab, nivo = nivolumab, ORR% did not require PR/CR confirmation

[^] 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; ^{^^^^} European Journal of Cancer, Leyraz, et. al, 2022; 146-155

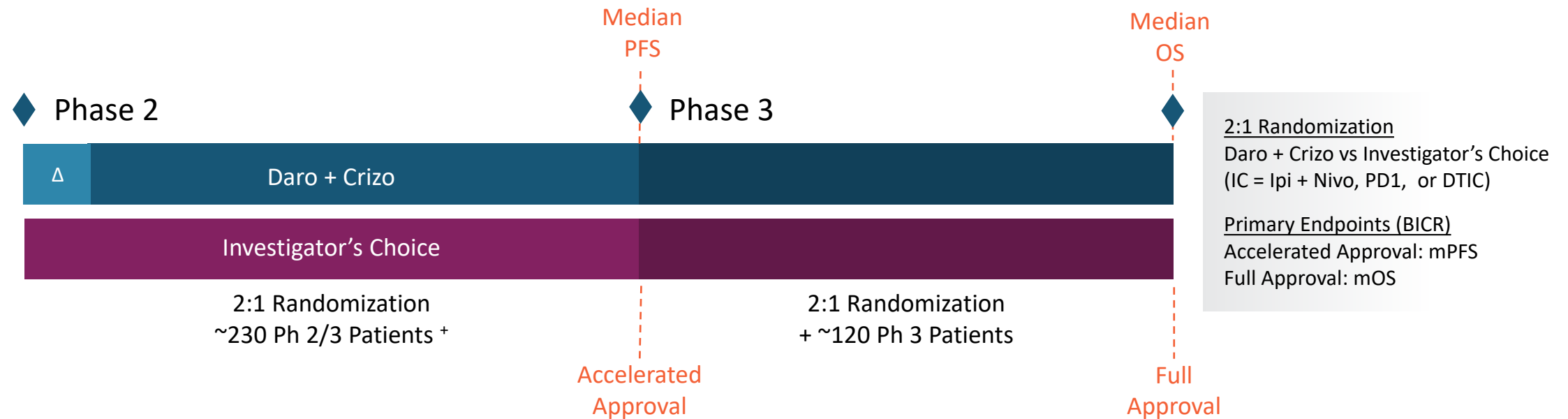
Accelerated Approval Trial Design in First-Line HLA-A2 Negative MUM

FDA Guided Design: Open Label Ph2/3 Evaluation of Daro + Crizo vs. Investigator's Choice [^]

FDA Project FrontRunner: Target First-Line approval strategy to enhance patient benefit in MUM

FDA Accelerated Approval: Address unmet need in MUM, which has limited effective treatment options

Integrated Phase 2/3 Study within Study Enables Potential Accelerated Approval & Full Approval



FDA Fast Track Designation for Daro + Crizo in MUM

[^] Nested study to confirm move forward dose: (i) Daro 300 mg BID + Crizo 200 mg BID or (ii) Daro 200 mg BID + Crizo 200 mg BID

⁺ Phase 2 study contemplates data set of n=200 patients randomized 2:1 with treatment arm at move forward dose in support of potential accelerated approval based on mPFS

Daro = Darovasertib, Crizo = Crizotinib, MUM=Metastatic Uveal Melanoma, HLA-A2 = HLA-A2*02:01 Serotype, IC = Investigator's Choice, Ipi = ipilimumab, nivo = nivolumab; DTIC = dacarbazine

[^] Clinicaltrials.gov: NCT05987332

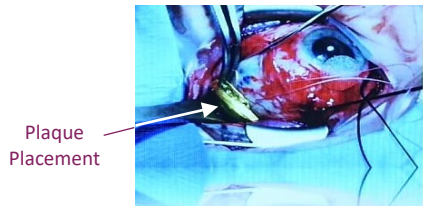
Darovasertib Monotherapy in (Neo)adjuvant Primary Uveal Melanoma

3 of 6 evaluable (50%) UM Patients Observed Eye Preservation in Enucleation Cohort[^]

IDEAYA Phase 2 and IST ongoing to evaluate Darovasertib Current Treatment Approach following diagnosis of UM depends on tumor size and location:

- Enucleation in Large Tumors (~20%)
- Radiation in Small / Medium Tumors (~80%)

Plaque Brachytherapy



Iodine-125 Plaque Surgery, UCLA

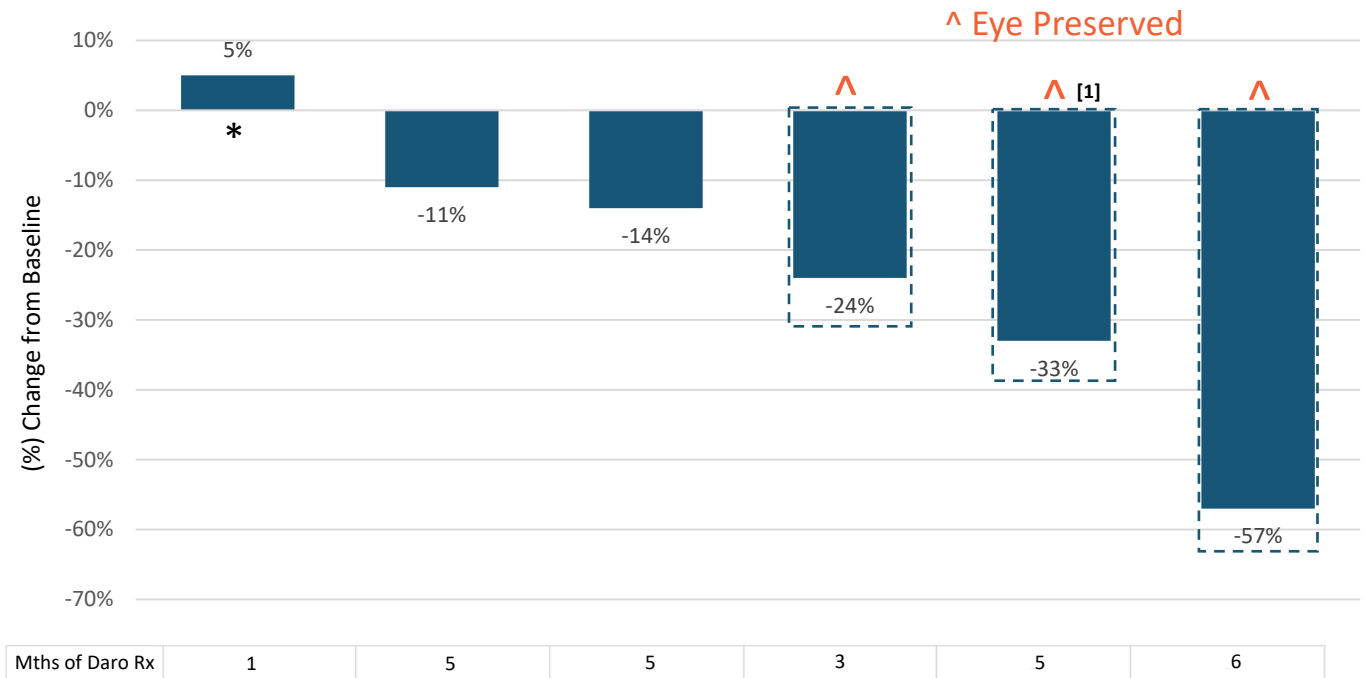
Poor Vision ($\leq 20/200$) occurs in about 70%-80% of patients with UM (including enucleation)

Neoadjuvant / Adjuvant Systemic Therapy goals:

- Avoid Enucleation → Save the Eye
- Reduce Tumors and Radiation Dose → Protect Vision
- Reduce Occurrence of Metastasis → Save Lives

Paradigm Shifting Opportunity to Broadly Impact UM, with annual incidence of ~8,000 – 10,000 patients in US, EU

Evaluable UM Patients Treated to Maximal Benefit Φ^+



2 out of 4 additional patients after the enrollment cutoff date are likely plaque eligible (20% tumor reduction in 2 months, 22% tumor reduction in 1 month) and continuing on darovasertib until maximal benefit

^Φ Data by investigator assessment with enrollment cut-off of July 17, 2023, from NADOM IST courtesy of Professor Anthony Joshua, MBBS, PhD, FRACP, St. Vincent's Hospital

⁺ Maximal % reduction in measured apical height or longest basal diameter

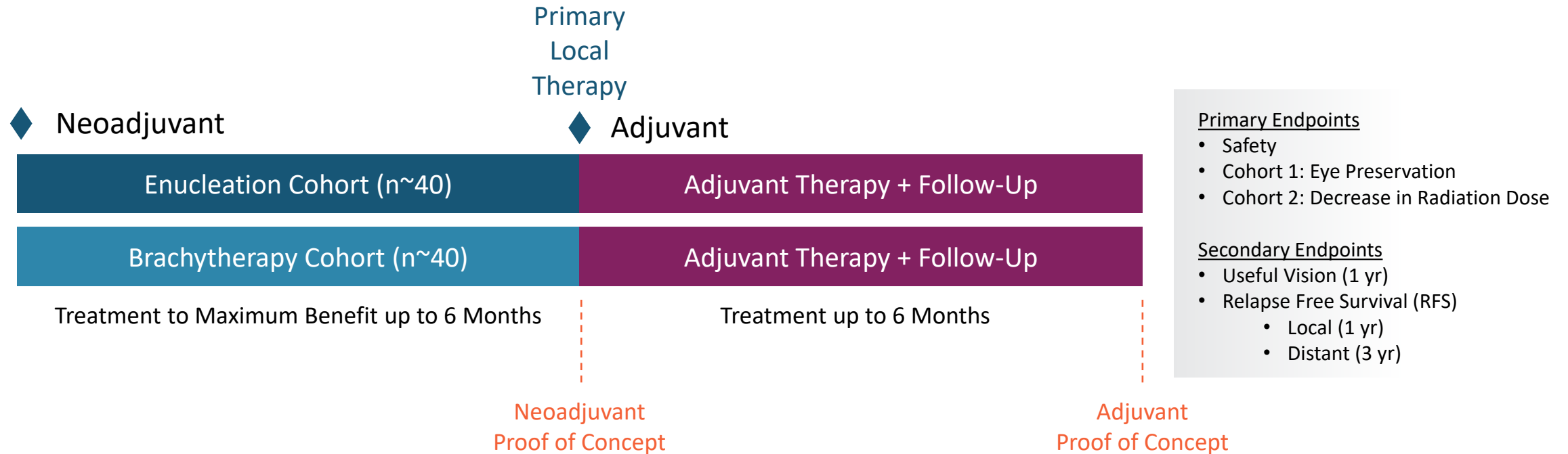
* Patient had sub-retinal blood present at baseline and with lack of shrinkage and visual deterioration discontinued after 6 weeks. One additional patient had Grade 3 drug related dermatitis and discontinued treatment before 1st scan.

[1] Patient was plaque-eligible and ongoing with darovasertib neo-adjuvant treatment to maximal benefit

(Neo)Adjuvant Darovasertib in Primary Uveal Melanoma (UM)

Paradigm Shifting Opportunity to Save the Eye, Protect Vision and Save Lives

Phase 2 Study of Darovasertib Monotherapy as Neoadjuvant Therapy followed by Adjuvant Therapy [^]



Three Independent Approaches for demonstrating Clinical Benefit and defining potential Approval Pathways

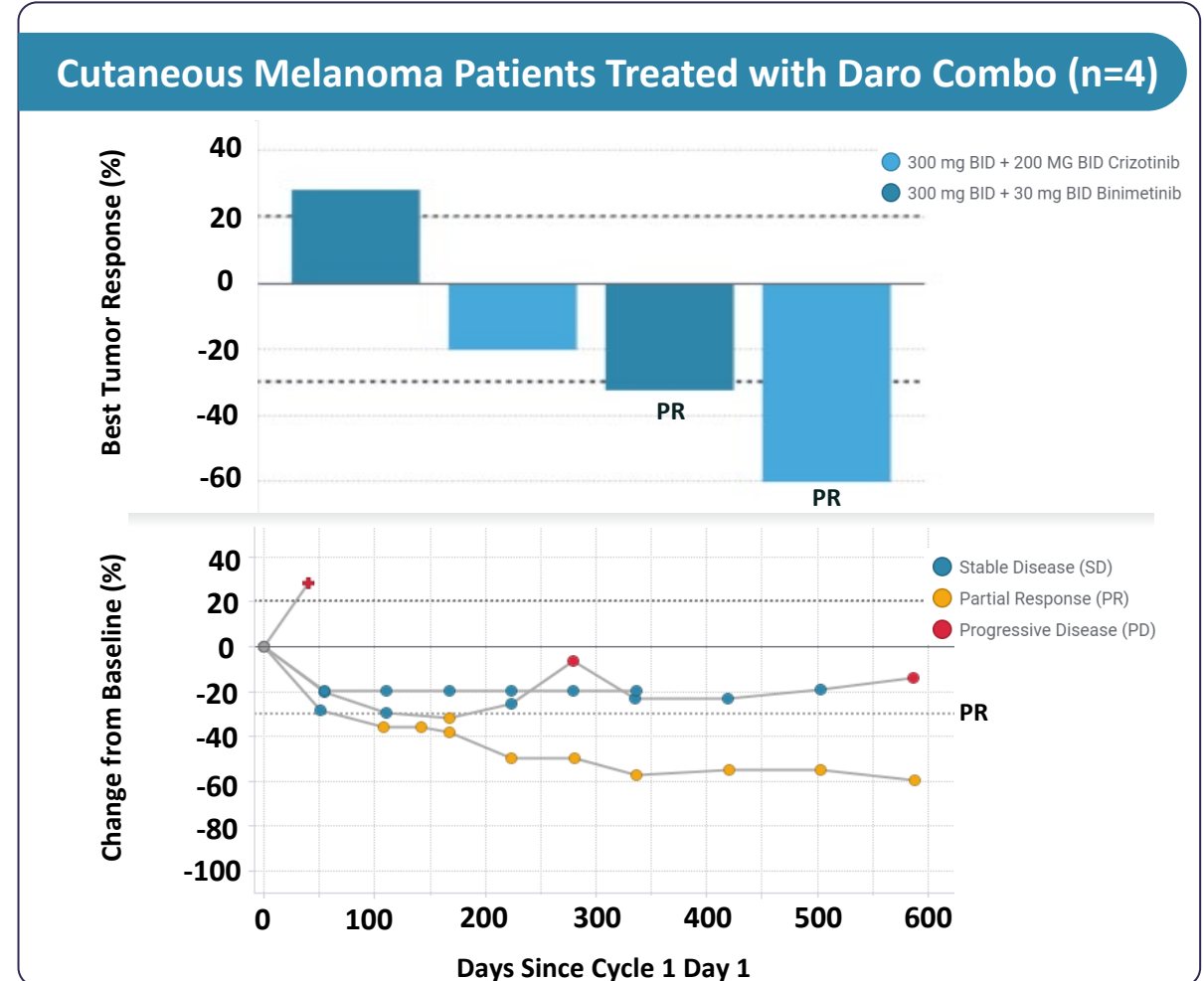
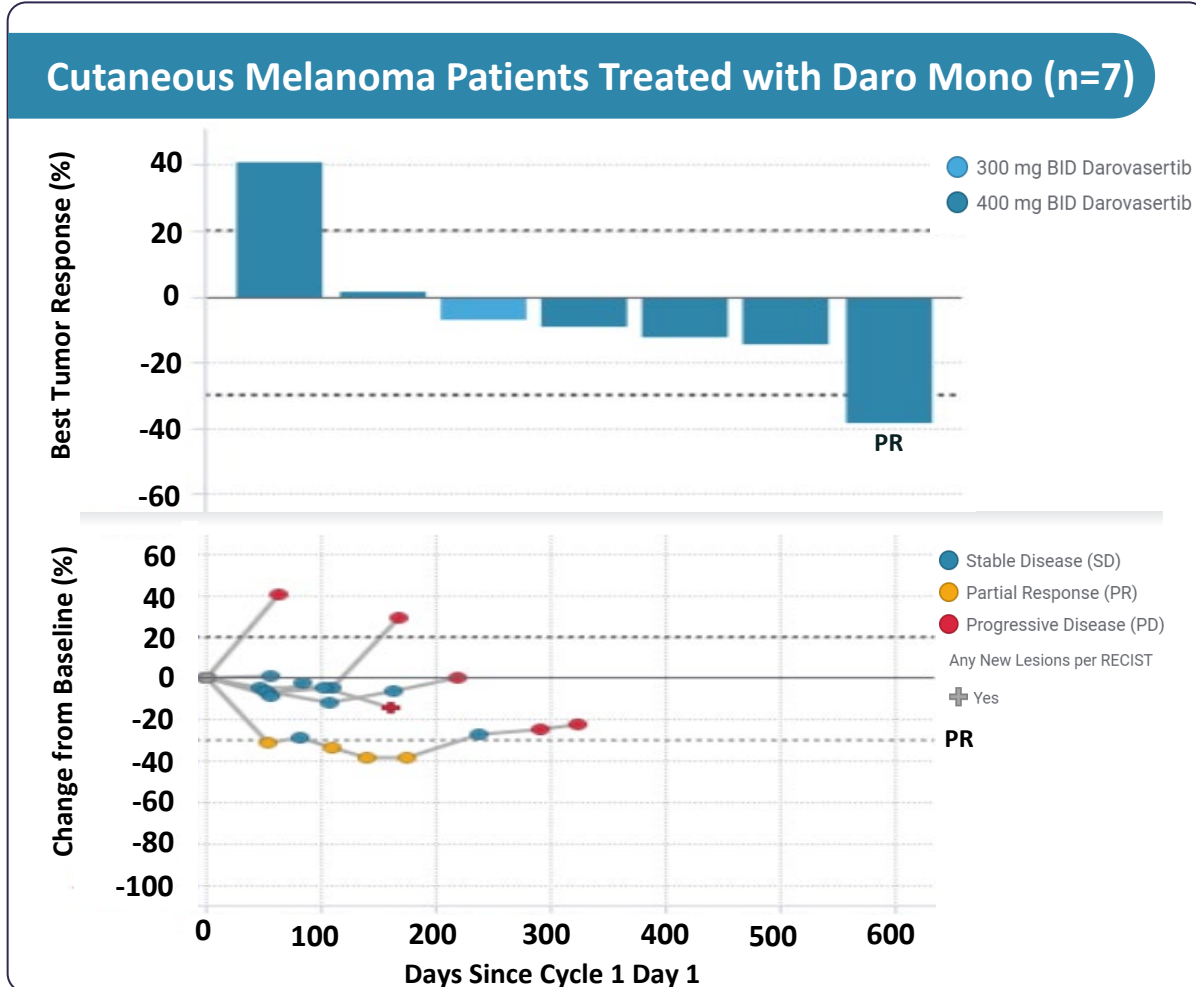
Enucleation Cohort → Save the Eye

Brachytherapy Cohort → Protect Vision

Adjuvant Therapy → Save Lives

GNAQ/11 Cutaneous Melanoma Patients Treated With Darovasertib

2 of 4 (50%) Observed Durable Partial Responses by RECIST 1.1 with Daro Combination



IDEAYA Data: preliminary analysis of unlocked database as of 24Dec2023 by investigator review

Darovasertib Clinical & Commercial Strategy in Uveal Melanoma and CM

High Unmet Need and Multiple First-Line Opportunities

Uveal Melanoma Patient Journey							
	Neoadjuvant UM		Adjuvant UM	MUM	Metastatic CM		
HLA-A2-Negative (~70% of UM / MUM)**	No FDA Approved Therapies*	Daro Phase 2 Enucleation Define Accelerated Approval Path	No FDA Approved Therapies*	Daro Phase 2 Define Accelerated Approval Path	No FDA Approved Therapies*	Daro + Crizo Registrational Trial Accelerated Approval	Daro + Crizo Phase 2 Define Accelerated Approval Path
HLA-A2-Positive (~30% of UM / MUM)**		Daro Phase 2 Radiation Define Accelerated Approval Path				Daro + Crizo Target NCCN / Compendia Listing	
Target Treatment Duration	≥6 months		≥6 months	mPFS + ~3 months	mPFS + ~3 months		
Target Clinical Endpoints	Eye & Vision Preservation		Relapse Free Survival	ORR, mPFS, mOS	ORR, mPFS, mOS		
Annual Incidence US/EU**	~8-10k		~8-10k	~4-5k	>5K [1]		
Total Prevalence US/EU**	~100k		~100k	~14k	~180K[2]		

+95% of UM and ~5% of Cutaneous Melanoma (CM) patients harbor GNAQ/GNA11 mutation

FDA Orphan Drug Designation in Uveal Melanoma⁺

*No FDA approved systemic therapies in multiple UM and MUM indications across the patient journey

**IDEAYA data: ~70% of MUM patients were HLA-A2-negative based on 149 patients tested for HLA-A2 status as presented at ESMO 2023; US/EU MUM annual incidence and total prevalence based on market research analysis

⁺ Orphan Drugs benefit from certain tax credits and may be excluded from certain mandatory price negotiation provisions of the 2022 Inflation Reduction Act

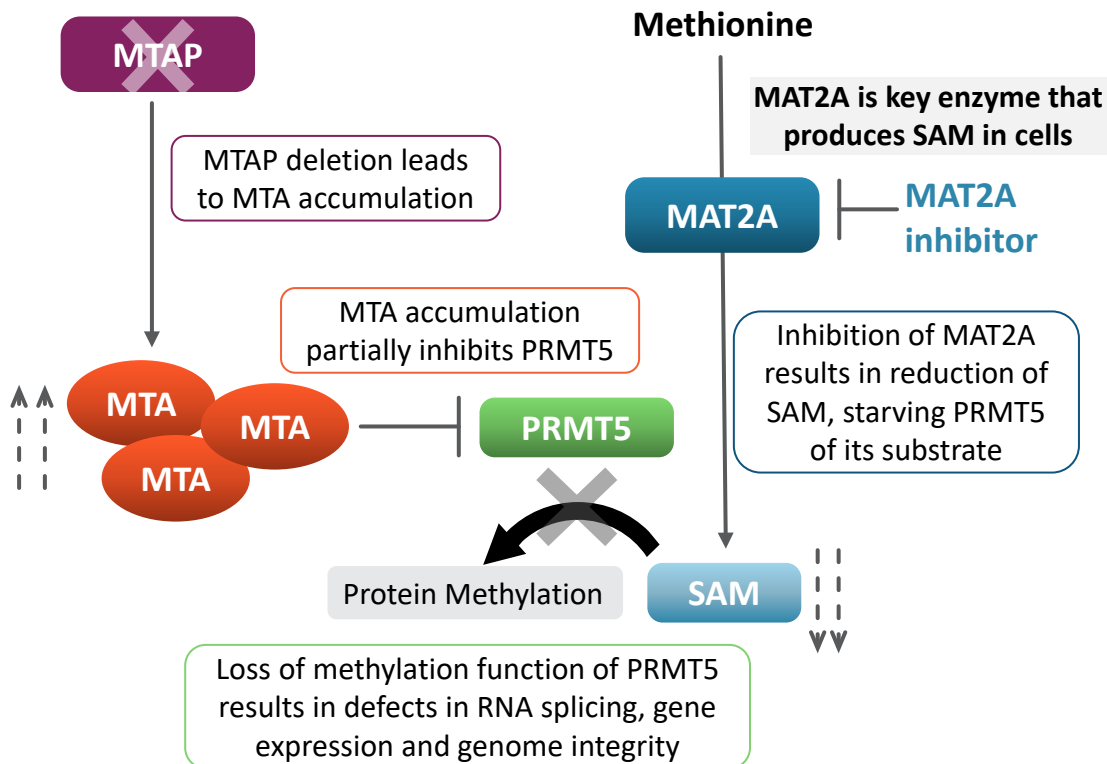
[1] GNAQ/11 cutaneous melanoma estimated annual incidence is approximately 5,000 patients in the US and 8,000 patients in the EU28. Based on several metastatic cancer patient databases, including Memorial Sloan Kettering Cancer Center (MSKCC) Impact, we project GNAQ/11 metastatic cutaneous melanoma has the potential to double or more the annual addressable metastatic patient population of metastatic uveal melanoma alone

[2] The estimated total prevalence of primary GNAQ/11 cutaneous melanoma is approximately 70,000 patients in the US and 110,000 patients in the EU28

MAT2A Inhibition is Synthetic Lethal with MTAP-Deletion

Strategies to address MTAP^{-/-} Prevalence in ~15% of all Solid Tumors

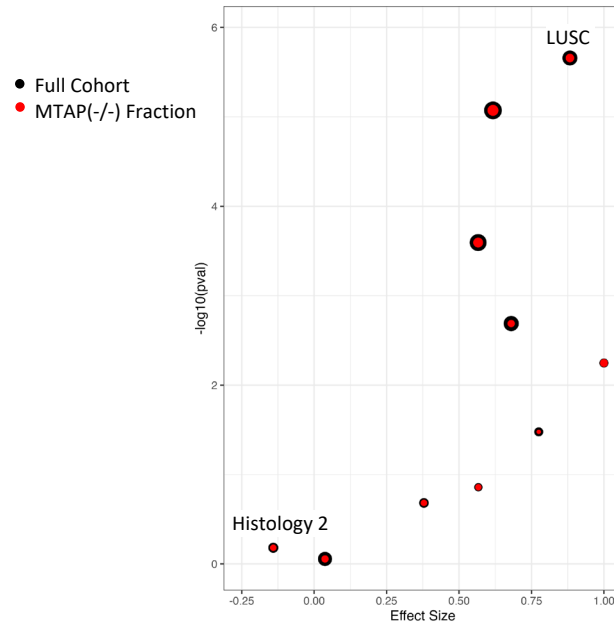
MTAP-MAT2A Synthetic Lethality Biology



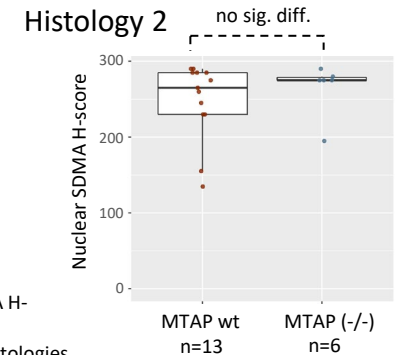
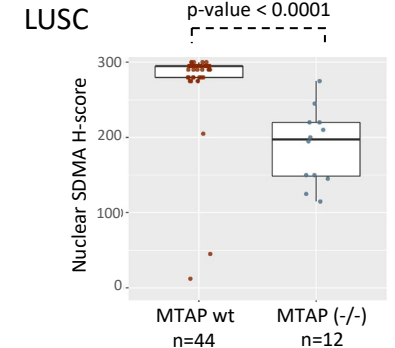
Endogenous Suppression in MTAP^{-/-} PDX Models

Methylation Pathway Suppression in MTAP^{-/-} Squamous Lung (LUSC)

SDMA Effect Size (PDX Tissue Microarray)



IDEAYA Data: AACR 2023 (M. Fischer et al.) – Volcano plot comparing nuclear SDMA H-Score by IHC in MTAP^{-/-} relative to MTAP wt across tissue microarray (TMA) of treatment-naïve PDX models; LUSC shows most significance effect across tumor histologies

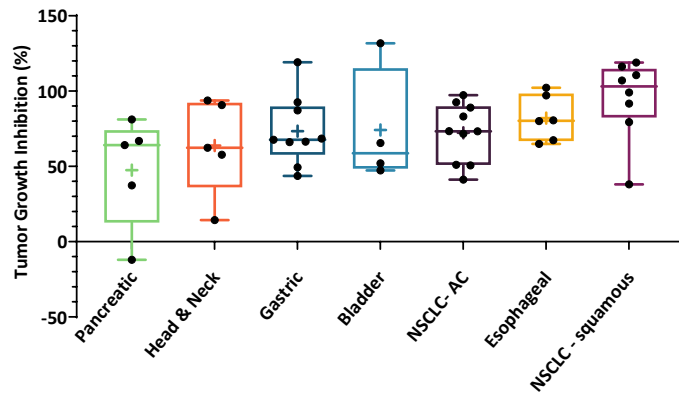


IDE397 Demonstrates Broad Efficacy across MTAP-Deletion PDX Models

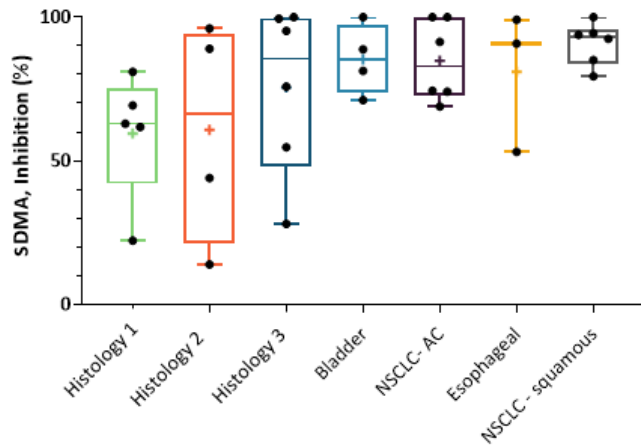
Deep Regressions observed in NSCLC-squamous (LUSC), Esophageal and Bladder Cancers

IDE397 Efficacy: 47 MTAP^{-/-} PDX Models

TGI with IDE397 (30mpk) in MTAP^{-/-} PDX Panel



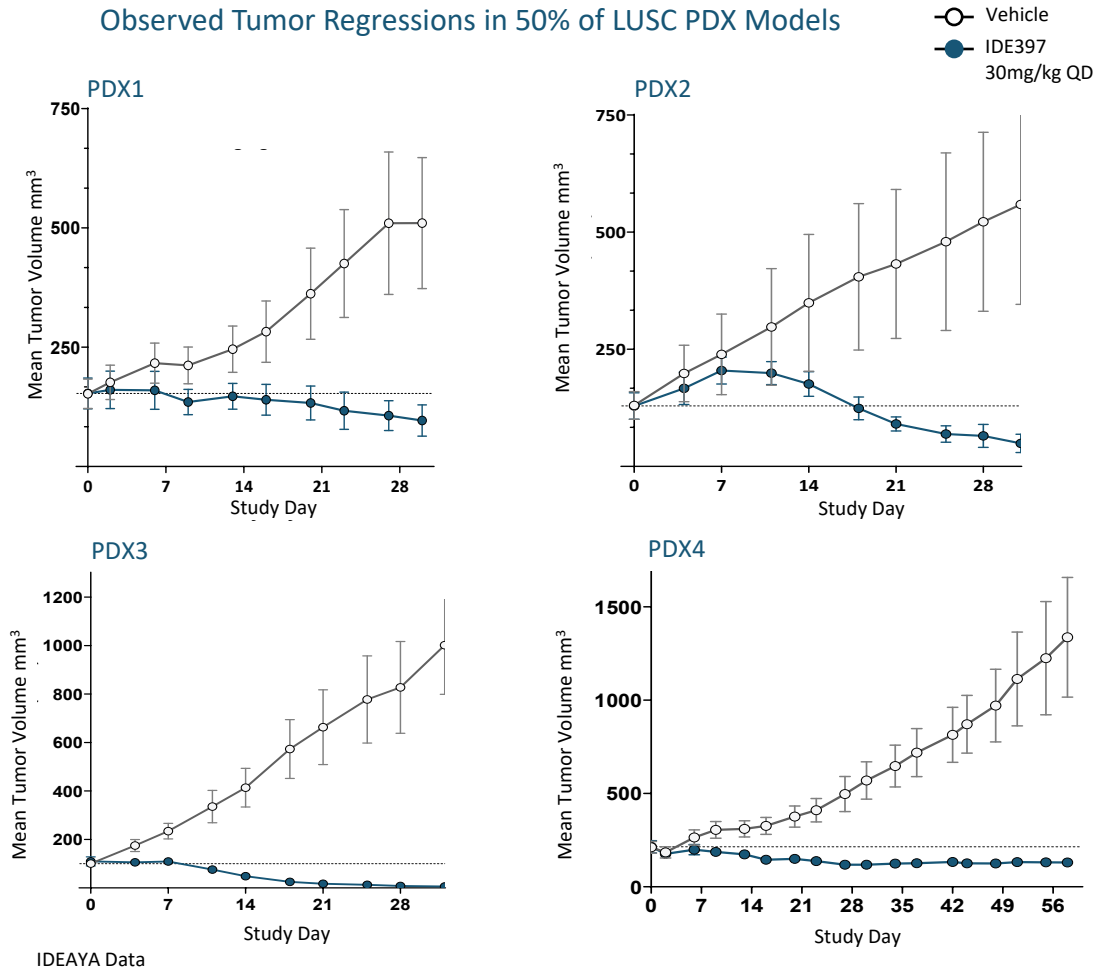
SDMA Suppression in Residual Tumors* at End of Study



IDEAYA Data; *2 of 8 LUSC unevaluable due to insufficient residual tumor burden

IDE397 In Vivo Efficacy in LUSC PDX Models

Observed Tumor Regressions in 50% of LUSC PDX Models



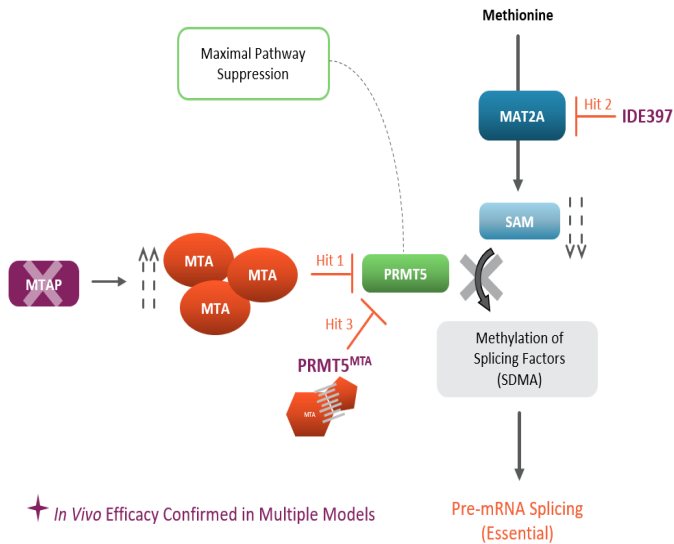
IDE397 Clinical Combination Strategy in MTAP-Deletion NSCLC



Phase 1 Study of IDE397 + AMG 193 (Amgen PRMT5) Clinical Combination Enrolling

IDE397 + MTA-Cooperative PRMT5i

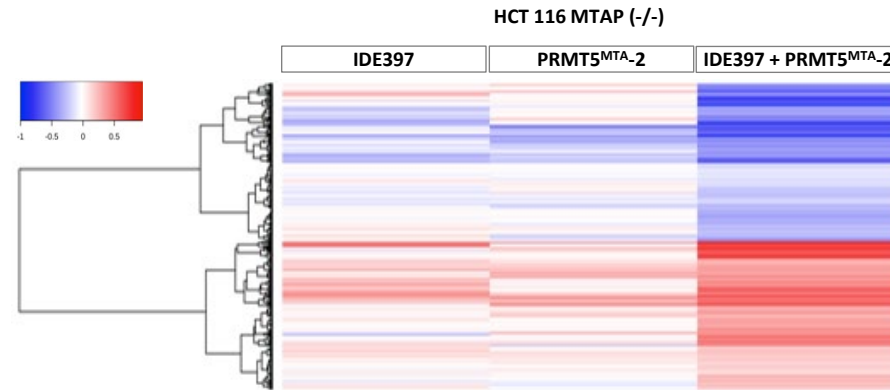
IDE397 + MTA-Cooperative PRMT5 Inhibitor enables Maximal Pathway Suppression



Enhanced Combination Efficacy Observed in multiple Tumor Indications and Across Representative PRMT5^{MTA} Inhibitors

Alternative mRNA Splicing Analysis

Combination Highly Perturbs Splicing Fidelity



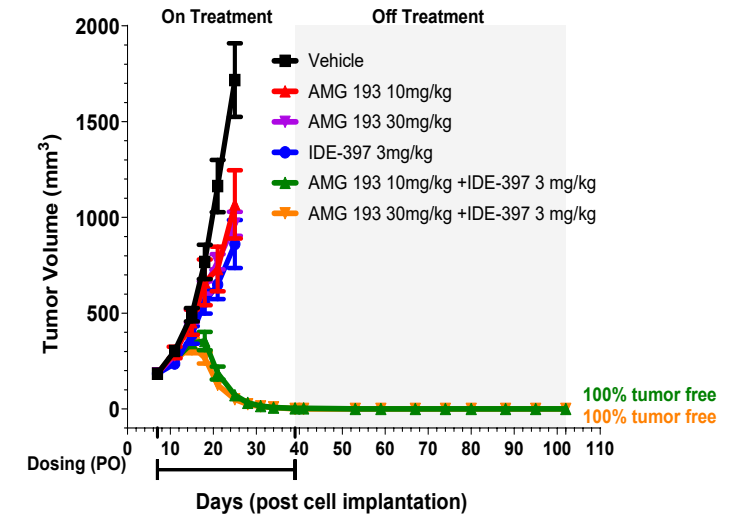
Quantitative Assessment of IDE397 / PMRT5i Effect on pre-mRNA Splicing

>2800 significant Splicing Events only in the Combination Treatment Arm+

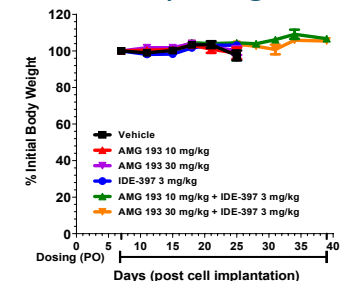
Identified as novel splice junctions or as not meeting significance criteria in monotherapy arms

Preclinical Efficacy

Observed Durable Complete Responses



No Body Weight Loss

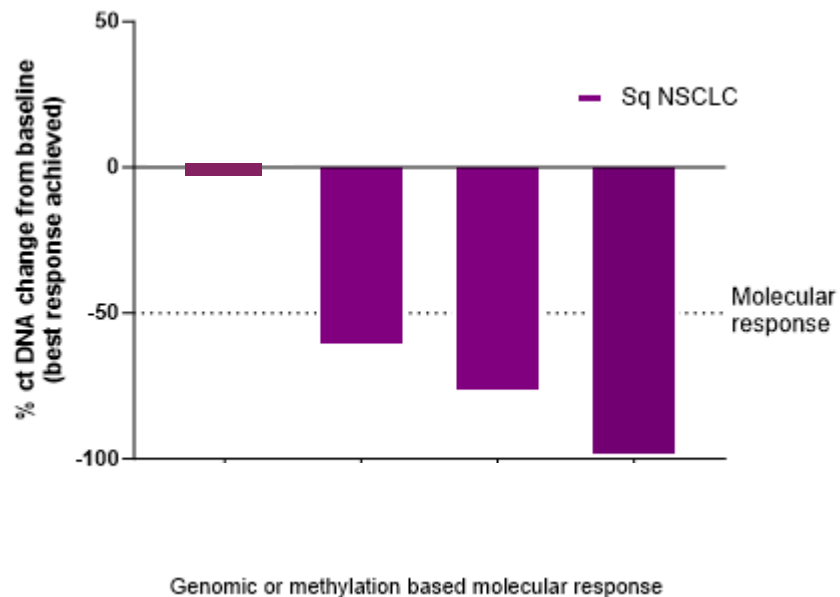


IDE397 Phase 2 Monotherapy Expansion in MTAP-Deletion Squamous NSCLC

Robust Tumor Shrinkage and ctDNA Molecular Responses Observed

Best Response from Baseline among subjects with Squamous NSCLC with evaluable ctDNA samples*

75% Molecular Response Rate

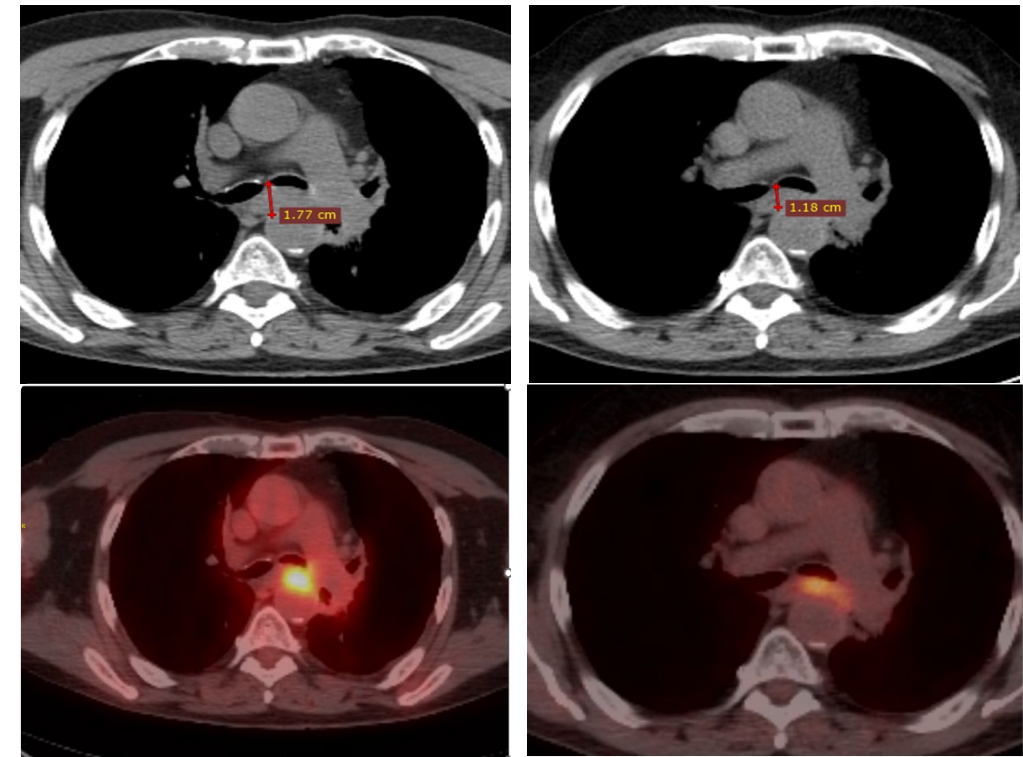


*1 patient sample failed QC for ctDNA analysis

33% shrinkage by PET/CT and decreased hypermetabolism noted in the mediastinal nodal mass in Squamous NSCLC patient**

Baseline PET/CT

12-week on study PET/CT



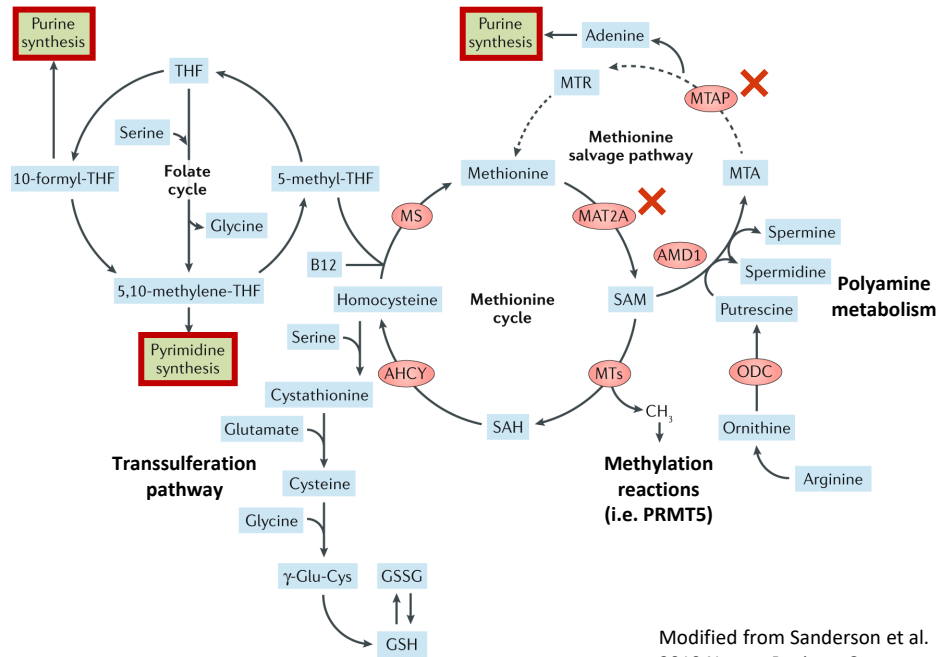
IDEAYA Data: preliminary analysis of unlocked database as of November 21, 2023

** Radiologic and Clinical response noted (decreased dyspnea and hoarseness) in recurrent tumor in the mediastinum after prior platinum chemotherapy and consolidation anti-PD1 antibody treatment

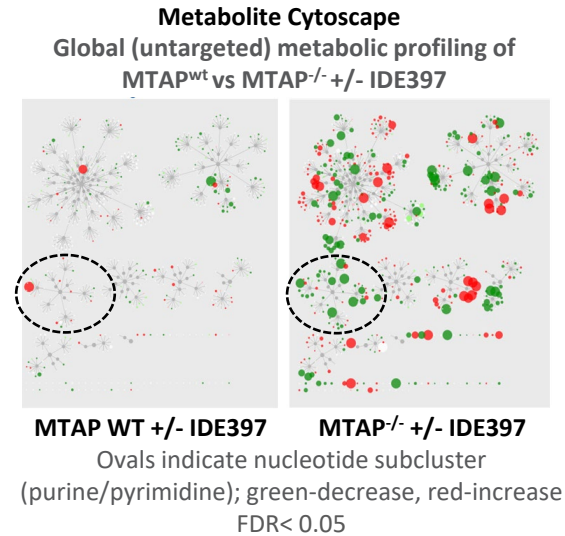
TRODELVY® + IDE397 Combination in MTAP-Deletion Urothelial Cancer

Disordered methionine metabolism underpins IDE397 combination opportunity with TOP1i-based ADC

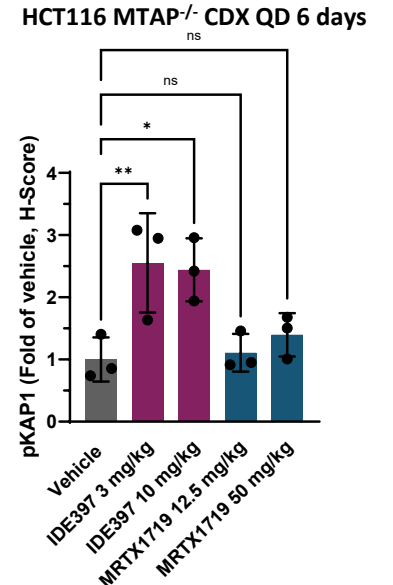
IDE397 perturbs both nucleotide pools and mRNA splicing in MTAP^{-/-} cells



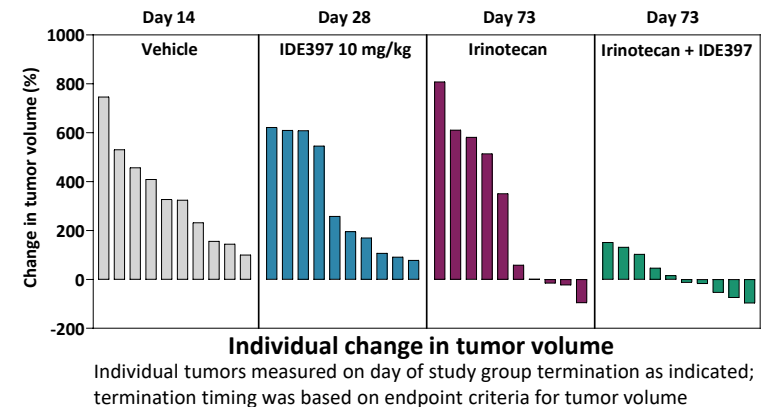
Metabolic perturbation by IDE397 selectively interacts with MTAP



IDE397 provokes DDR response in vivo



TOP1i combination delivers durable benefit in challenging RT112/84 UC CDX model



Key clinical correlates underscore combination opportunity

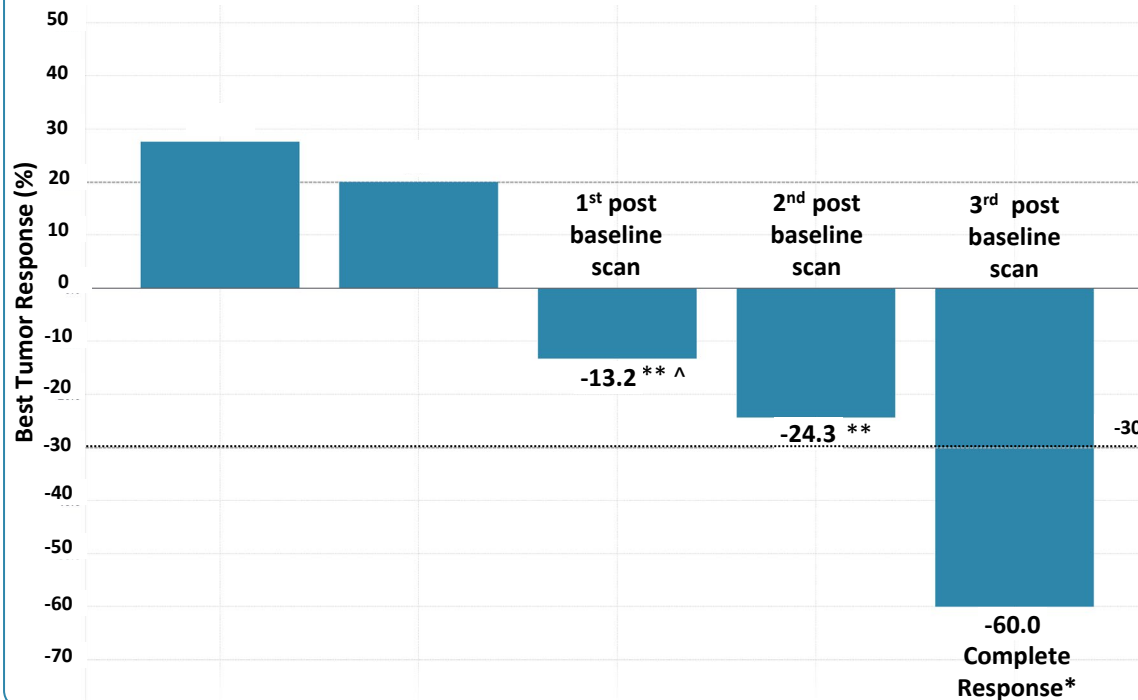
- MTAP^{-/-} UC: shorter survival, lower RR to CPI, shorter PFS and OS with Enfortumab-Vedotin (EV)
- MTAP^{-/-} status is associated with pemetrexed antitumor activity in UC
- A small study evaluating Trodelvy activity in UC post-EV suggested preferential activity in MTAP^{-/-} tumors (RR 50% vs. 19% post EV)
- IDE397 has monotherapy efficacy in MTAP^{-/-} UC (CR observed in a patient with short DFI post platinum and CPI, other tumor reductions and molecular responses seen)

IDE397 Phase 2 Monotherapy Expansion in MTAP-Deletion Urothelial Cancer

Robust Tumor Shrinkage and ctDNA Molecular Responses Observed

Best Overall Response by RECIST 1.1 in Urothelial / Bladder Cancer

Preliminary IDE397 Mono Efficacy Supports Combo Evaluation

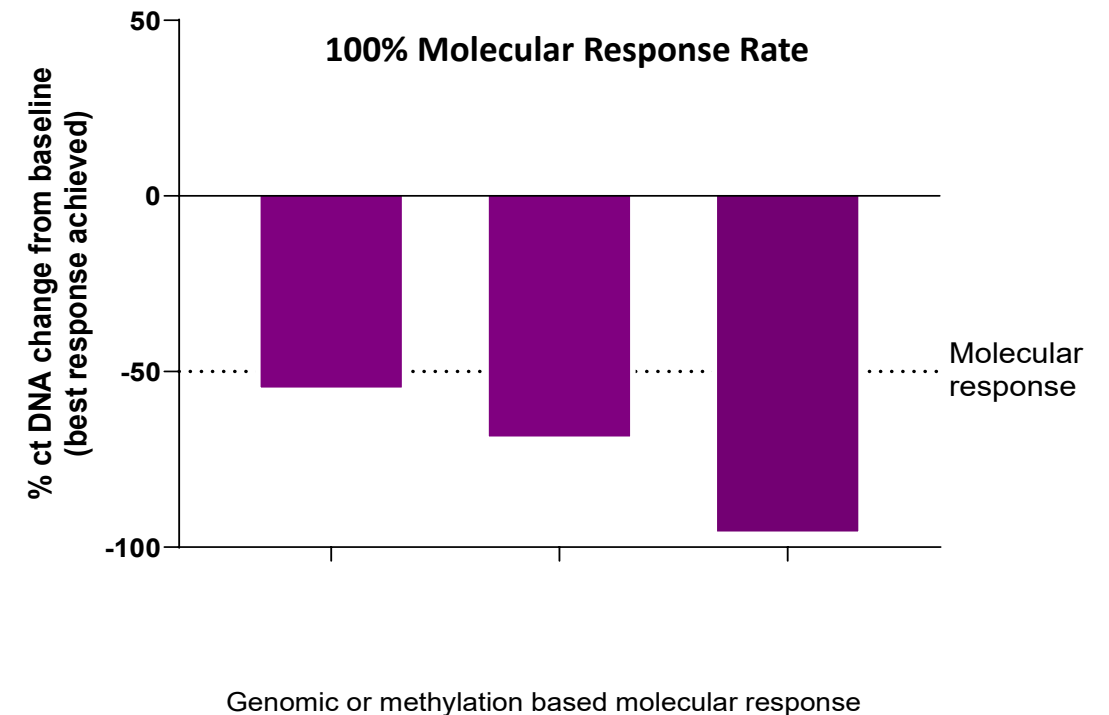


IDEAYA Data: preliminary analysis of unlocked database as of November 21, 2023

* Decrease of all nodes selected as target lesions to < 10mm in short axis is assessed as a complete response per RECIST v1.1 in cases where no other target lesions are present at baseline. Target lesion sum for lymph nodes may not be zero even if CR criteria are met

** Patients had visceral metastases with target lesions in the liver and lung. ^ 6-week on study scan

ctDNA: Best Response From Baseline in Urothelial / Bladder Cancer*



IDEAYA Data: preliminary analysis of unlocked database

*2 of the patient samples failed QC for ctDNA assessment

IDE397 Phase 1/2 Clinical Development Plan in MTAP-Deletion Solid Tumors

Strategic Focus in Select Monotherapy Indications and High Conviction Clinical Combinations

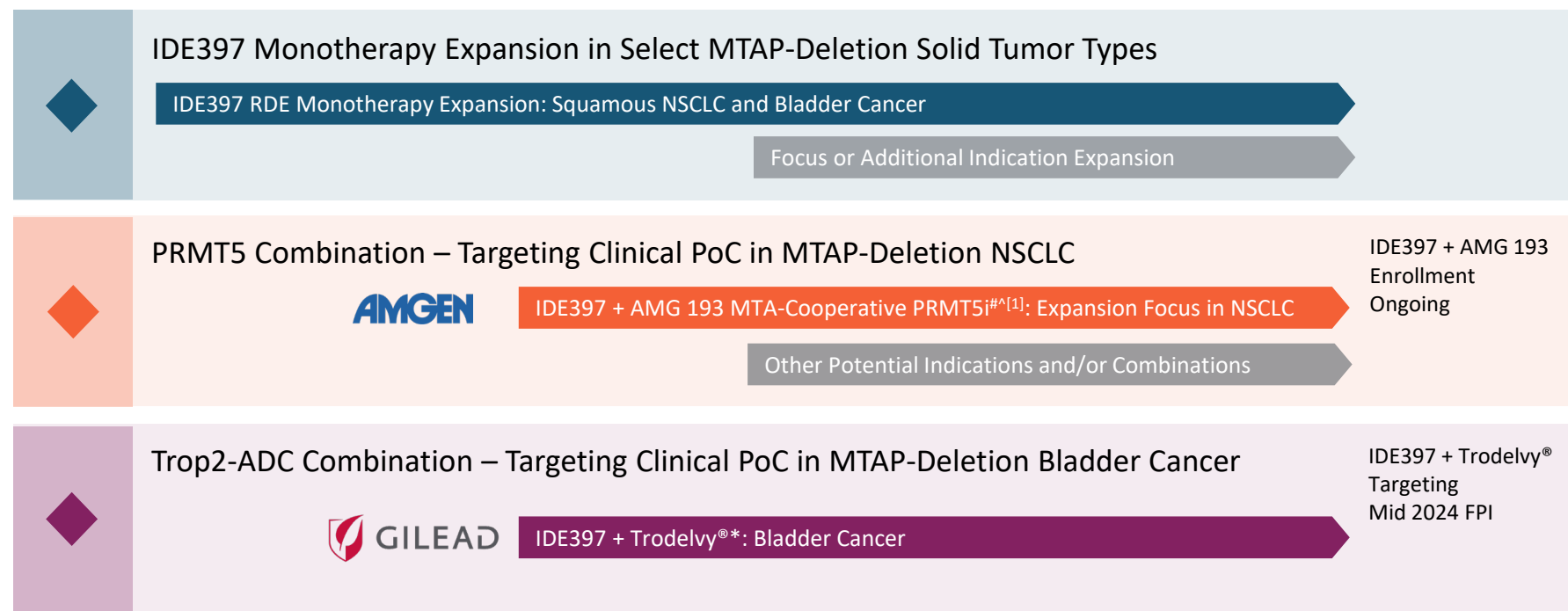
IDE397 – Clinical Profile

Exposure-Dependent
Pharmacokinetic (PK) Profile with
low $C_{max}:C_{min}$

Robust Pharmacodynamic (PD)
Response observed

Monotherapy Expansion
demonstrates clinical efficacy
with Responses in Multiple High-
Priority Tumor Types in Dose
Expansion, including a Complete
Response

IDE397 is strategically well positioned to evaluate both monotherapy and clinical combinations in MTAP-deletion solid tumors



Addressable MTAP-Deletion Annual Incidence of >50,000 patients in the US, EU5 and Japan across priority solid tumor types of NSCLC, bladder, gastric, and esophageal cancers

AMG 193 = Amgen's investigational MTA-cooperative PRMT5 inhibitor; * Trodelvy® = Gilead's Trop-2 directed ADC

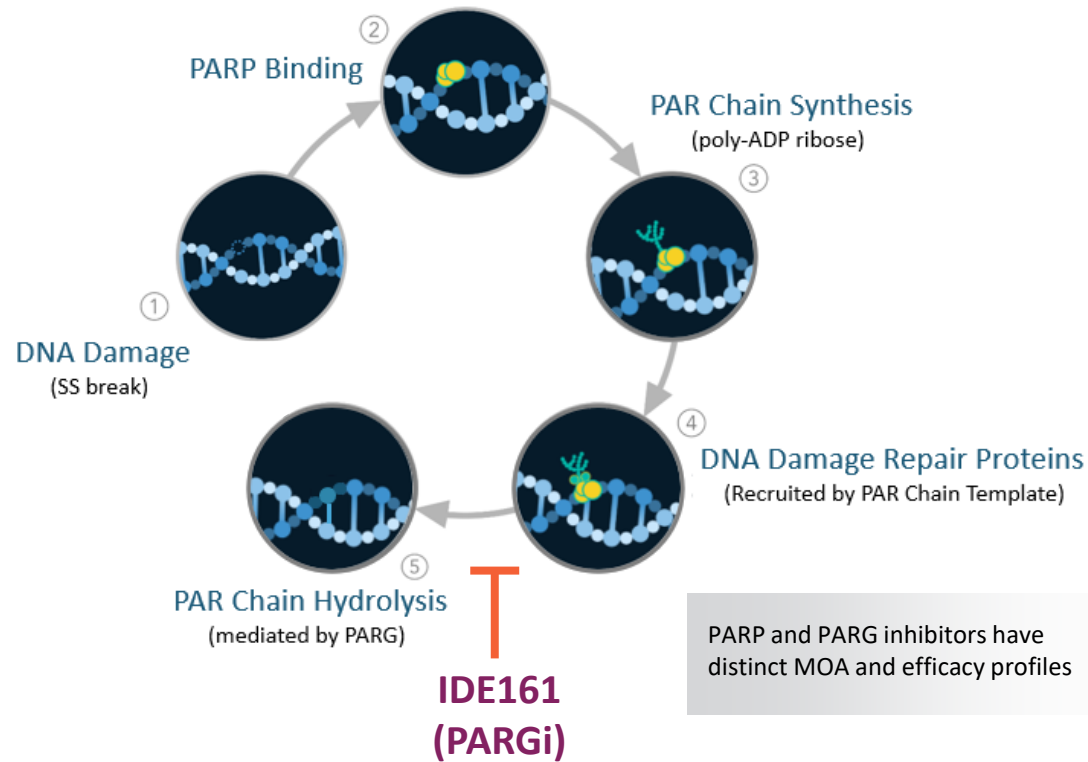
^ Amgen reported initial clinical data at the 2023 AACR-NCI-EORTC that showed 5/18 (ORR=28%) for AMG 193 monotherapy expansion at dose > 800 mg QD in esophageal, pancreatic, renal cell, gallbladder, and Sertoli-Leydig cell cancers

[1] Clinicaltrials.gov: NCT05975073

PARG Inhibition is Synthetic Lethal with HRD

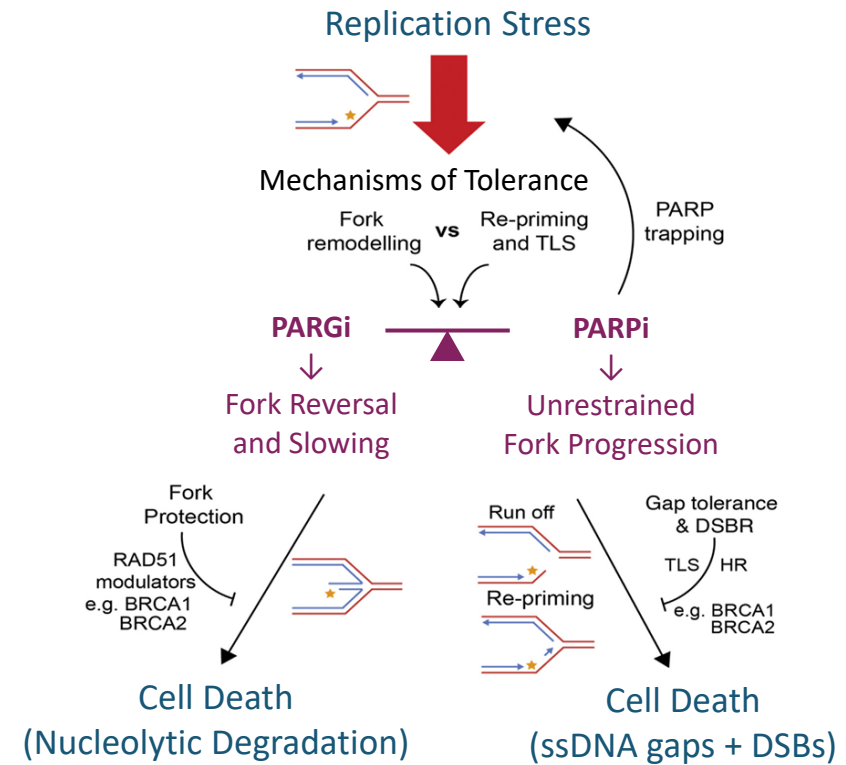
Novel, Mechanistically-Differentiated Target in a Clinically Validated Pathway

PARG Activity is required to resolve DNA Repair



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

PARG Inhibition is Mechanistically Distinct from PARPi

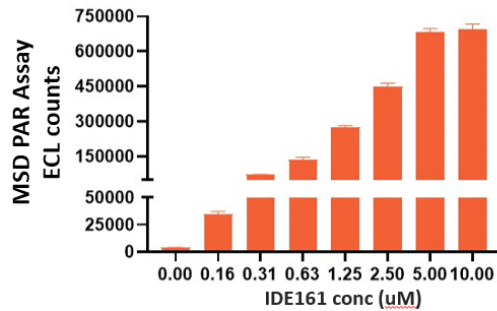


Pillay et al., Progress in Biophysics and Molecular Biology 2021; McDermott et al., Cancer Cell 2019; Zeman and Cimprich, Nature Cell Biology 2014

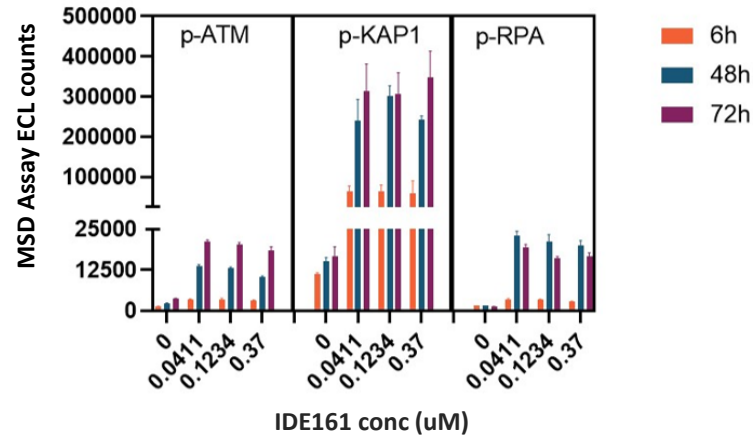
IDE161: Potential First-in-Class Phase 1 PARG Inhibitor

IDE161 Profile: Potent, Selective with Favorable Properties

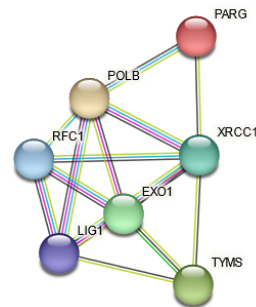
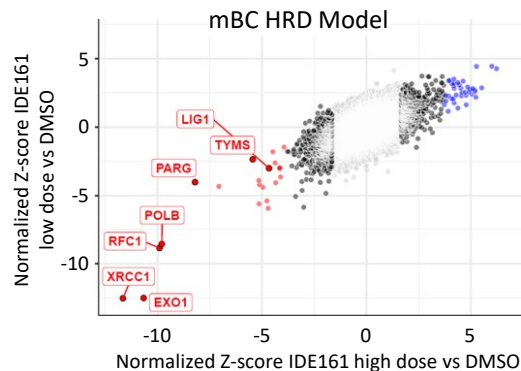
IDE161-induced Cellular PAR Accumulation



IDE161-induced DNA Damage Response



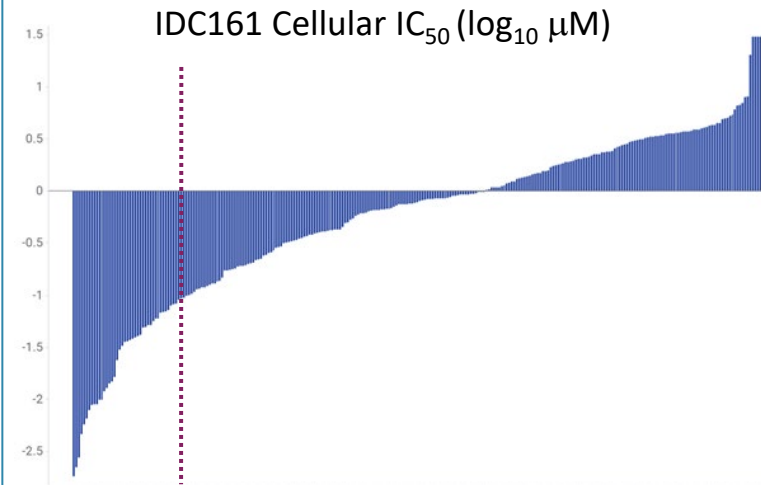
IDE161 is Synthetic Lethal with BER Gene Disruption



Gene Network generated from whole genome CRISPR screens anchored with IDE161 using significant synthetic lethality hits across 4 models

IDE161 Sensitivity Profile in Cell Panel

Cellular response profiles reveal mechanistic associations with PARGi sensitivity



314 cell lines across 31 lineages

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

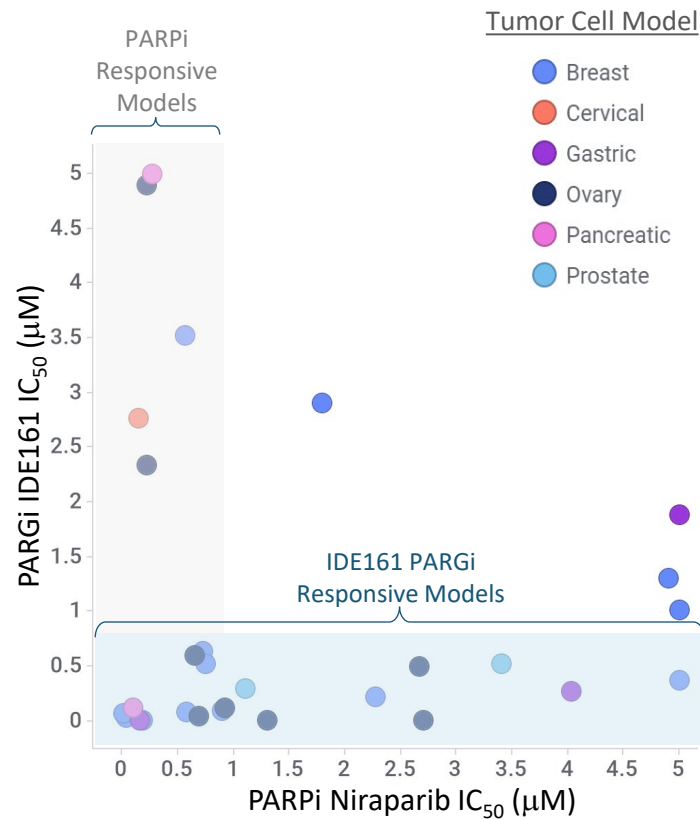
* Based on univariate and multivariate pan-cancer and lineage-specific molecular feature analysis

IDE161 is Active and Well-Tolerated in HRD ER+ Her2- Breast Cancer Models

Observed PARG inhibitor Activity is Distinct from PARP Inhibition

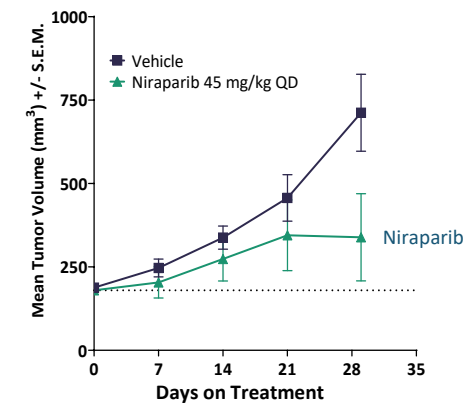
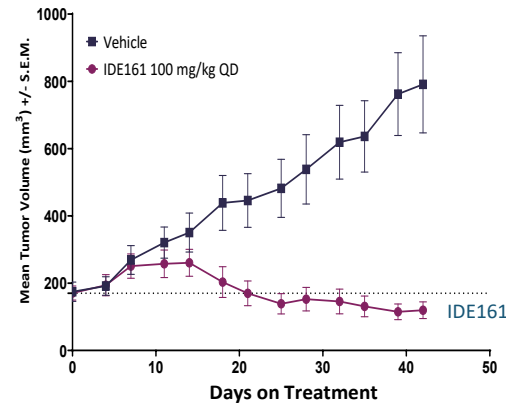
IDE161 Selective Sensitivity vs PARPi

HRD cell lines are selectively sensitive to IDE161 versus PARPi

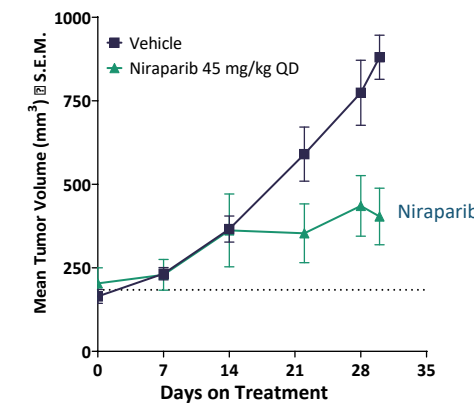
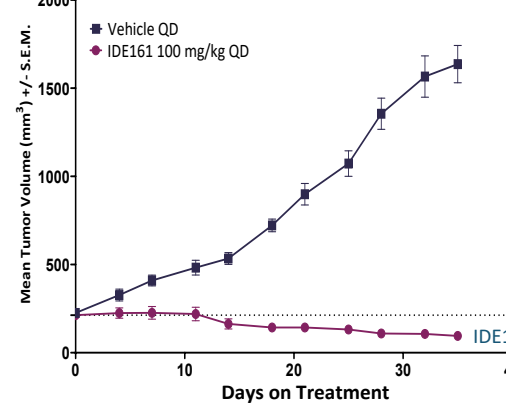


Regression in BRCA-altered Breast Cancer PDX Models

ER+ / Her2- Breast Cancer PDX1



ER+ / Her2- Breast Cancer PDX2



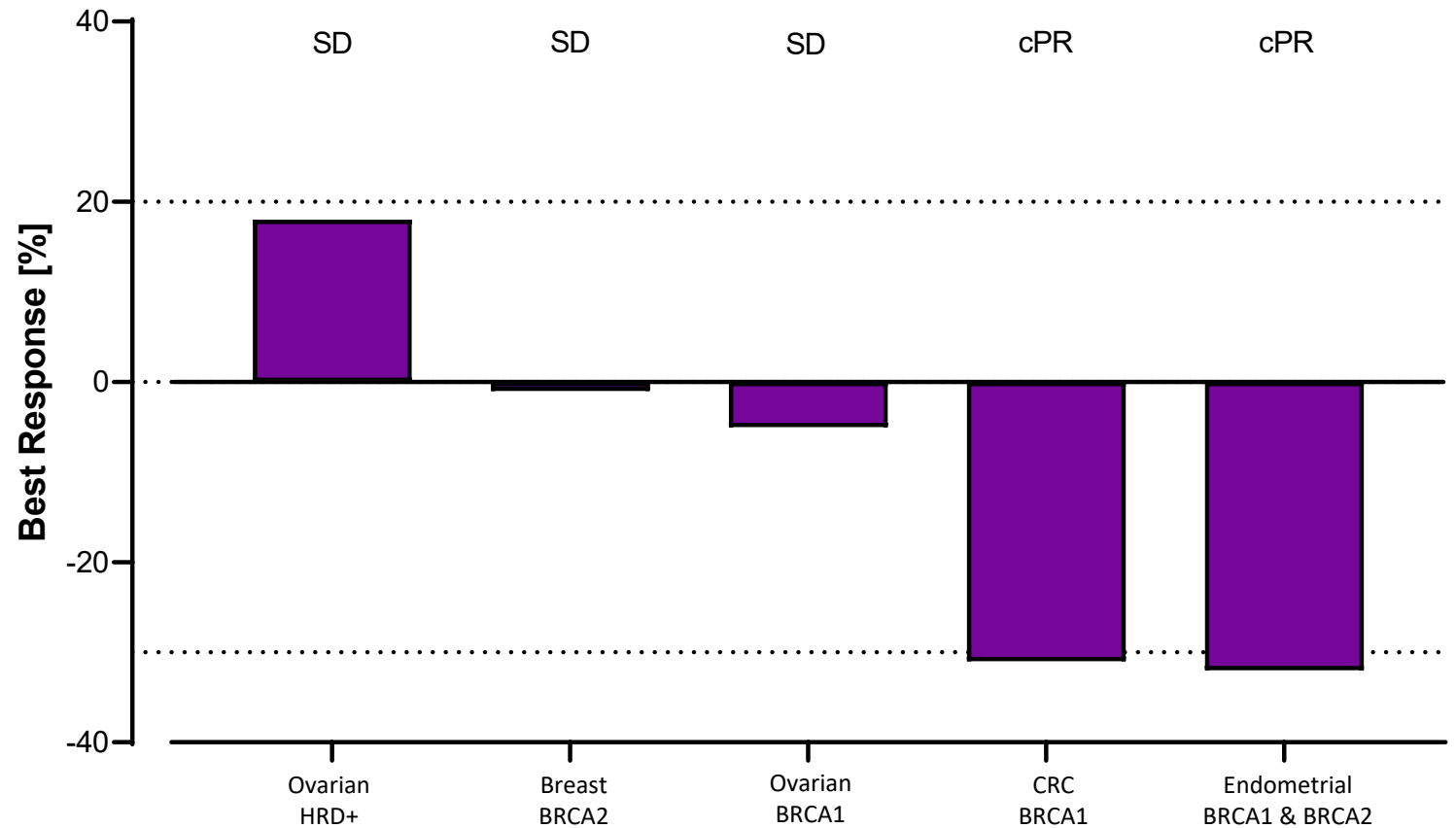
Preliminary IDE161 Clinical Efficacy at Phase 1 Expansion Dose

2 PRs by RECIST 1.1 and 100% DCR in Priority Solid Tumor Types with HRD

Initial tumor scans support favorable efficacy of IDE161 in HRD solid tumors:

- 100% DCR (5 of 5): 4 patients with tumor shrinkage & 3 Stable Disease
- Partial Response in a CRC patient at 2nd scan which was subsequently confirmed.
- Patient with Endometrial Cancer showed 87% reduction in CA125 (2760 U/mL at baseline and 360 U/mL at nadir). First scan showed Partial Response with 31% reduction in tumor size which was confirmed on subsequent scan.
- Fast track designation granted for BRCA1/2 HR+HER2- BC and ovarian cancer post PARPi therapy

Subjects with Priority Tumor Types at Phase 1 Expansion Dose



IDEAYA Data: Preliminary analysis of unlocked database as of 09Nov23; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) of 21Aug23 in patients at clinically relevant doses in priority tumor types; SD = Stable Disease, cPR = confirmed Partial Response

IDE161 Phase 1/2 Clinical Development Plan in HRD Solid Tumors

Strategic Focus in Endometrial, Colorectal, Prostate, Breast & Other Solid Tumor Types

IDE161 Phase 1/2 – Monotherapy and Combination Clinical Development Plan

IDE161 Monotherapy Dose Escalation and Expansion in HRD Solid Tumors^[1]



IDE161 Combination Opportunities Validated Preclinically



Activity in PARPi- and Platinum-Resistant Settings

Differentiated Sensitivity relative to PARPi's

Targeting Improved Safety Profile relative to PARPi's

Preliminary IDE161 monotherapy clinical efficacy observed, including RECIST 1.1 Responses and >50% reduction in PSA

ER+, Her2- Breast Cancer Patients with HRD Tumors → ~10% to ~14% of Breast Cancer

Facile peripheral PD Biomarker for PARGi based on measurement of PAR in blood samples (PBMC's)

FDA Fast Track Designation for IDE161 in BRCA1/2 Ovarian and Breast Cancers*

*Fast Track Designations include (i) Pretreated, Platinum-Resistant Advanced or Metastatic BRCA1/2 mutant Ovarian Cancer, and (ii) Pretreated, Advanced or Metastatic HR+, Her2-, BRCA1/2 mutant Breast Cancer
PARG = poly (ADP-ribose) glycohydrolase; PAR = poly (ADP-ribose); PBMC = peripheral blood mononuclear cells, PSA = prostate specific antigen, EC = endometrial cancer, CRC = colorectal cancer

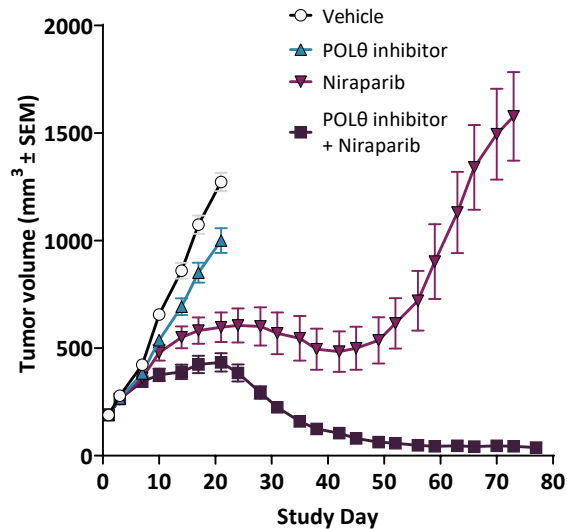
[1] Clinicaltrials.gov: NCT05787587

GSK101 (IDE705): Potential First-in-Class Pol Theta Helicase Inhibitor

Phase 1 in Combination with Niraparib (PARPi)

Pol Theta Helicase *In Vivo* Activity

GSK101 + PARPi

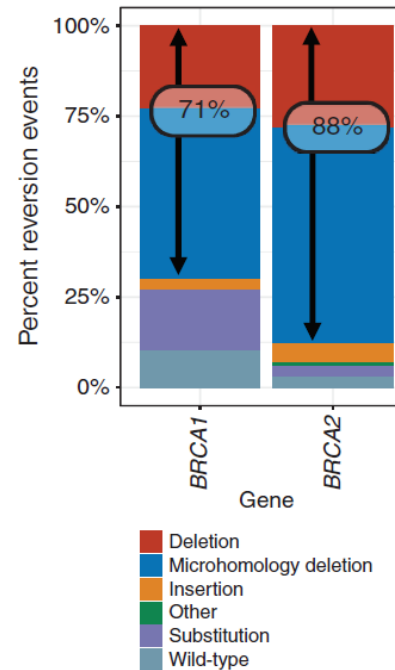


Observed Deep and Durable Responses in Multiple Xenograft Models

IDEAYA / GSK Data

BRCA 1/2 Clinical Reversions

BRCA Reversions Mediated by MMEJ



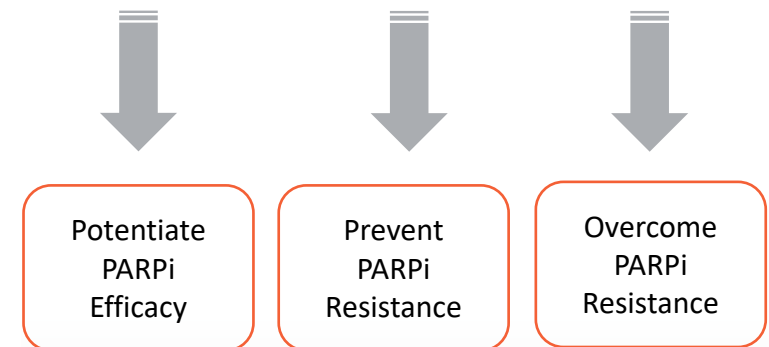
Cancer Res. 2020, DOI: 10.1158/2159-8290

Clinical Development Strategy



Pol Theta Helicase Inhibitors Disrupt MMEJ Alternative DNA Damage Repair:

- Inhibit DSB Repair by MMEJ
- Dysregulate Replication Fork Stabilization



Potential Clinical Opportunities

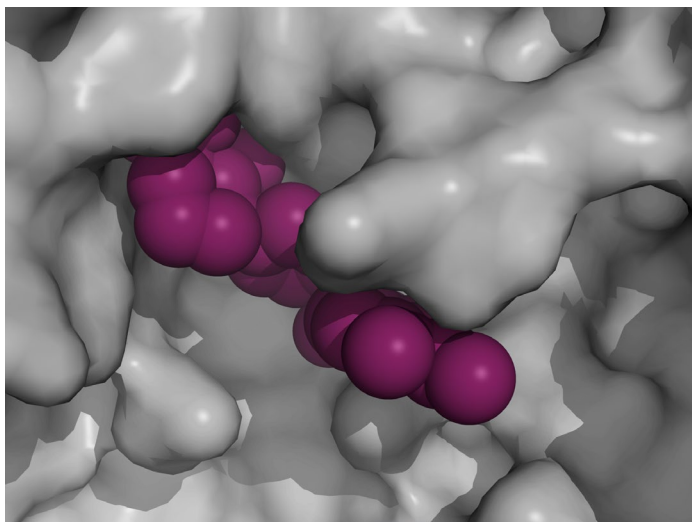
GSK Strategic Partnership: Global Royalties with GSK covering all Costs, ~\$1B Milestones, incl up to \$20M Preclinical / Ph1 Clinical Potential Combination with GSK's Zejula™, a PARP Inhibitor

IDEAYA's AI/ML Enabled Drug Discovery Platform and IND-Engine

IND-Filing and Multiple Potential First-in-Class Development Candidates (DCs) Targeted in 2024

WRN Helicase

Nominated Werner Helicase Development Candidate

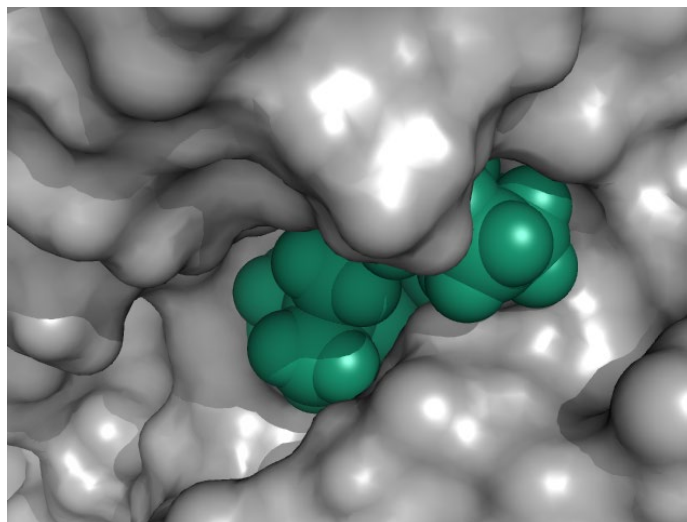


Targeting IND Submission in 2024*
MSI-High Tumor Agnostic

*Pursuant to GSK Collaboration

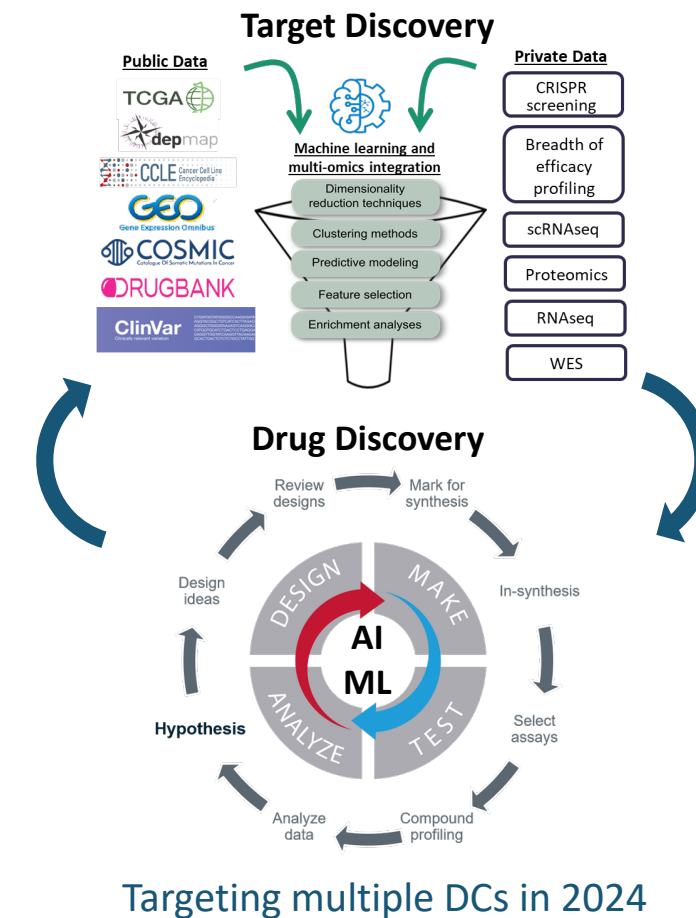
Multi-Pronged Strategy in MTAP^{-/-}

Next Generation Programs



Key mechanistic interaction with MTAP^{-/-} loss, including distinct from PRMT5 pathway

AI/ML-Enabled IND-Engine

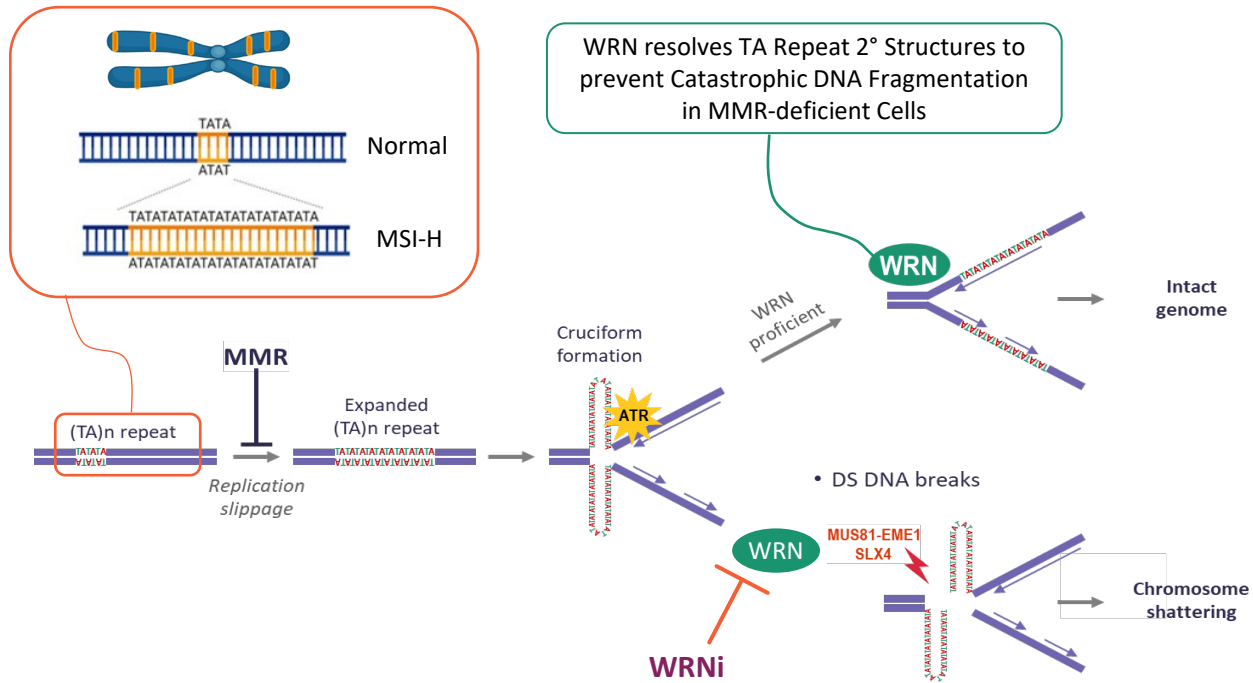


Werner Helicase is Synthetic Lethal with Microsatellite Instability

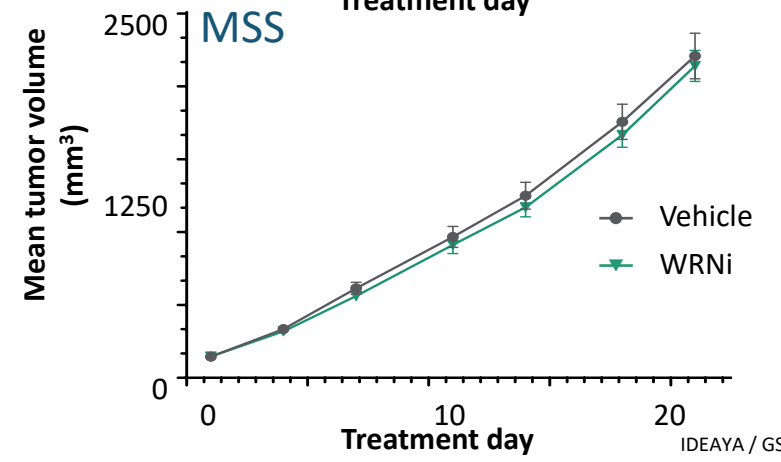
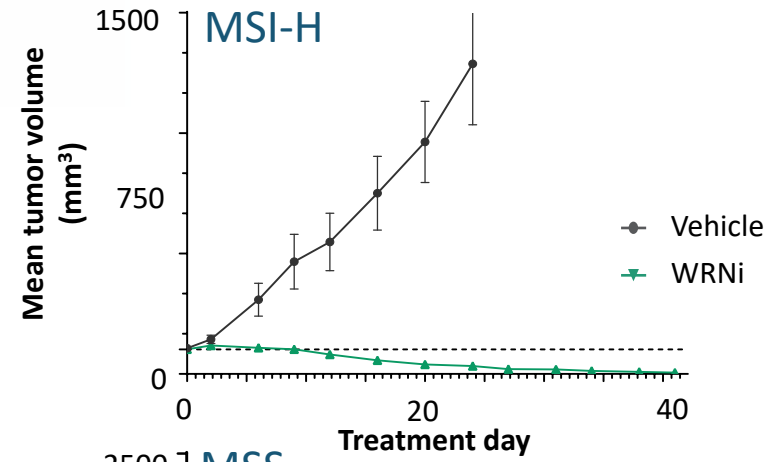
Development Candidate in IND Enabling Studies

Werner Helicase Inhibitors Phenocopy Genetic SL in MSI-High Cancers
 Nanomolar Potency, Biochemical and Cellular Activity, and Selectivity over other RecQ Helicases

Werner Helicase Synthetic Lethality in MSI-High Cancer Cells



Werner Helicase Synthetic Lethal with High-MSI



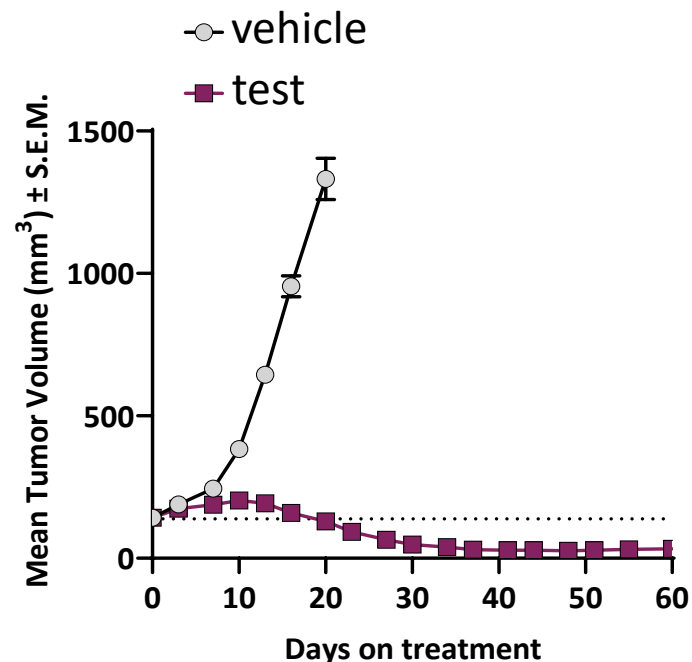
IDEAYA / GSK Data: AACR 2023

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

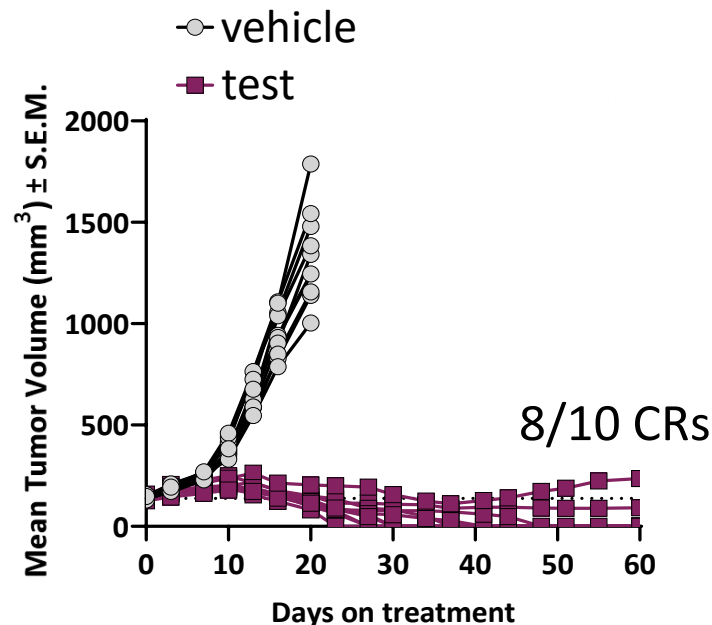
IDEAYA Pipeline: MTAP-Deletion New Target Opportunity

Mechanism-based activity distinct from PRMT5 pathway

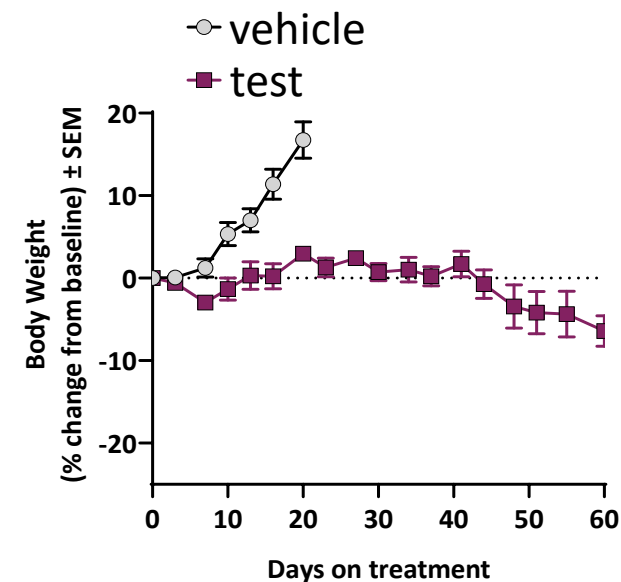
Mean Tumor Volume in NCI-H838



8 of 10 Complete Responses



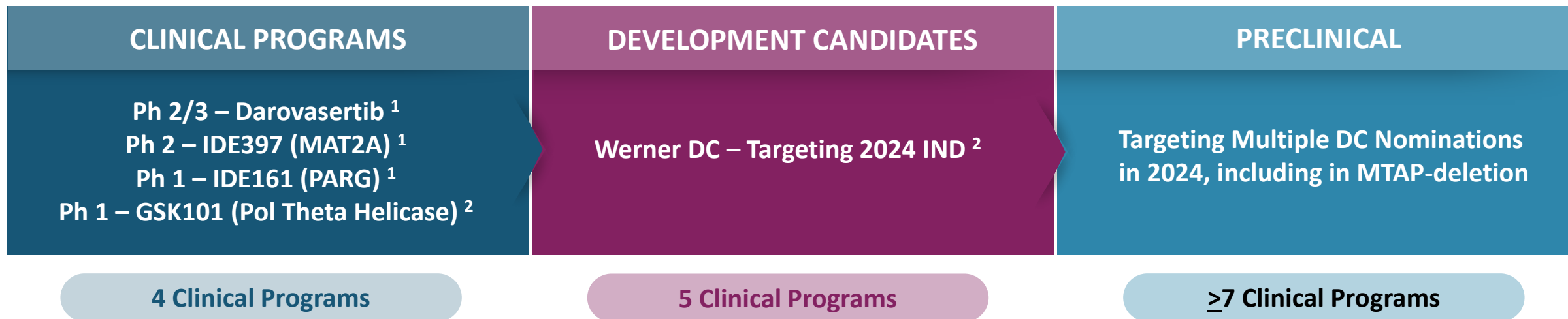
Minimal Body Weight Change



- First-in-class opportunity not yet evaluated in the clinic
- Cellular screens indicate potential for broad therapeutic benefit in MTAP^{-/-} cancers
- Mechanism anticipated to combine well with MAT2A and PRMT5^{MTA} inhibitors

Building a Fully-Integrated Biotech in Precision Medicine Oncology

Foundational Potential First-in-Class Clinical Pipeline and Drug Discovery Platform



Darovasertib Registration-Enabling Trial with Potential Accelerated Approval in HLA-A2(-) MUM is tractable for commercial execution and provides path to potential product revenue to reinvest in broad *first-in-class* pipeline

Potential First-in-Class Precision Medicine Oncology Pipeline, including Darovasertib (Ph2/3), IDE397 (Ph 2), IDE161 (Ph 1), GSK101 (Ph 1), Werner Helicase (IND-enabling), and multiple Development Candidates targeted in 2024, including in MTAP-deletion

Strong Balance Sheet with ~\$975M³ and opportunity for milestones with cash runway to 2028

Pharma Collaborations include combinations with Pfizer, Amgen, Gilead, Merck, and GSK partnership with ~\$2 billion² in potential milestones

(1) Clinical Trial Collaboration and Supply Agreements, independently with Pfizer (Darovasertib + Crizotinib), Amgen (IDE397 + AMG193), Gilead (IDE397 + Trudelvy®), and Merck (IDE161 + KEYTRUDA®); IDEAYA retains all commercial rights to its products

(2) GSK101 Pol Theta Program Cost Share = 100% GSK with ~\$1B Milestones and WW Royalties; Werner Helicase Program Cost Share = 80% GSK / 20% IDEAYA with ~\$1B Milestones, 50/50 US Profit Share and Ex-US Royalties

(3) Includes aggregate of \$632.6M cash, cash equivalents and marketable securities as of December 31, 2023, plus pro forma \$342.3M estimated net proceeds from sales of common stock through at-the-market offerings in January 2024