July 2024

NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicines

Safe Harbor Statement

Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future financial performance of IDEAYA Biosciences, Inc. (the “Company”) and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “potential” or other comparable terminology. All statements other than statements of historical fact could be deemed forward-looking, including expectations regarding the clinical activity profile, potential clinical benefit and potential advantages of the Company’s clinical programs; the translation of preliminary clinical trial results into future clinical trial results; the enrollment of clinical trials; whether the Phase 2/3 clinical trial for evaluation of the darovasertib and crizotinib combination in metastatic uveal melanoma will be considered a registrational trial by the U.S. Food and Drug Administration (the “FDA”); the potentially addressable patient population for the Company’s programs; 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, including the estimated funding of operations into 2028; 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. Such risks and uncertainties include, among others, the uncertainties inherent in the drug development process, including IDEAYA’s programs’ early stage of development, the process of designing and conducting preclinical and clinical trials, serious adverse events, undesirable side effects or unexpected characteristics of drug development, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, IDEAYA’s ability to successfully establish, protect and defend its intellectual property, and other matters that could affect the sufficiency of existing cash to fund operations. 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, 2023, its Quarterly Report on Form 10-Q for the quarter ended March 31, 2024, and any current or periodic reports filed with the SEC. 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.

Other

This presentation concerns anticipated products that are under clinical investigation and which have not yet been approved for marketing by the FDA. These anticipated products are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and the Company’s own internal estimates and research. The Company has not independently verified, and makes no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, all of the market data included in this presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions. Finally, the Company's own internal estimates and research have not been verified by any independent source.

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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
DAROVASERTIB (PKC) • Daro + Crizo (cMET) 1L MUM Registrational Ph 2/3 Program Update(s) – 2024 • Daro + Crizo Ph 2 in GNAQ/11 Melanomas • Neoadjuvant UM Ph 2 Company-Sponsored Clinical Data Update and Regulatory Guidance Update – H2 2024	**IDE397 (MAT2A)** • Phase 2 Clinical Data Update at IDE397 expansion dose in MTAP urothelial cancer and NSCLC **IDE397 + AMG 193 (PRMT5)** • Ongoing Phase 1 Enrollment and Development of Joint Publication Strategy – 2024 **IDE397 + Trodelvy® (Trop2-ADC)** • Ongoing Phase 1 Enrollment in MTAP urothelial cancer	**IDE161 (PARG)** • Initial Phase 2 Expansion – H2 2024 • Enable Combination(s) – 2024 **IDE161 + KEYTRUDA® (pembrolizumab)** • Phase 1 FPI in Endometrial Cancer – H2 2024 **GSK101 (POL THETA)** • Ongoing Phase 1 Dose Escalation	**WERNER HELICASE** • IND Submission ($7M Milestone Upon Successful IND Clearance) – H2 2024	**NEXT GEN PROGRAMS** • Development Candidate Nominations, including in MTAP and potential first-in-class in KAT6 pathway – H2 2024

Pharma Collaborations

Pfizer | AMGEN | GILEAD | MERCK | GSK

~$2B in potential milestones

Financials and Investor Relations

~$978M 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 $941.4M cash, cash equivalents and marketable securities as of March 31, 2024, plus pro forma $36.5M estimated net proceeds from sales of common stock through at-the-market offerings in April 2024

(2) $941.4M of cash, cash equivalents and marketable securities as of March 31, 2024, as disclosed in IDEAYA's Form 10-Q dated May 7, 2024 as filed with the U.S. Securities and Exchange Commission

IDEAYA BIOSCIENCES

Leading Functional Genomics and Synthetic Lethality Platform

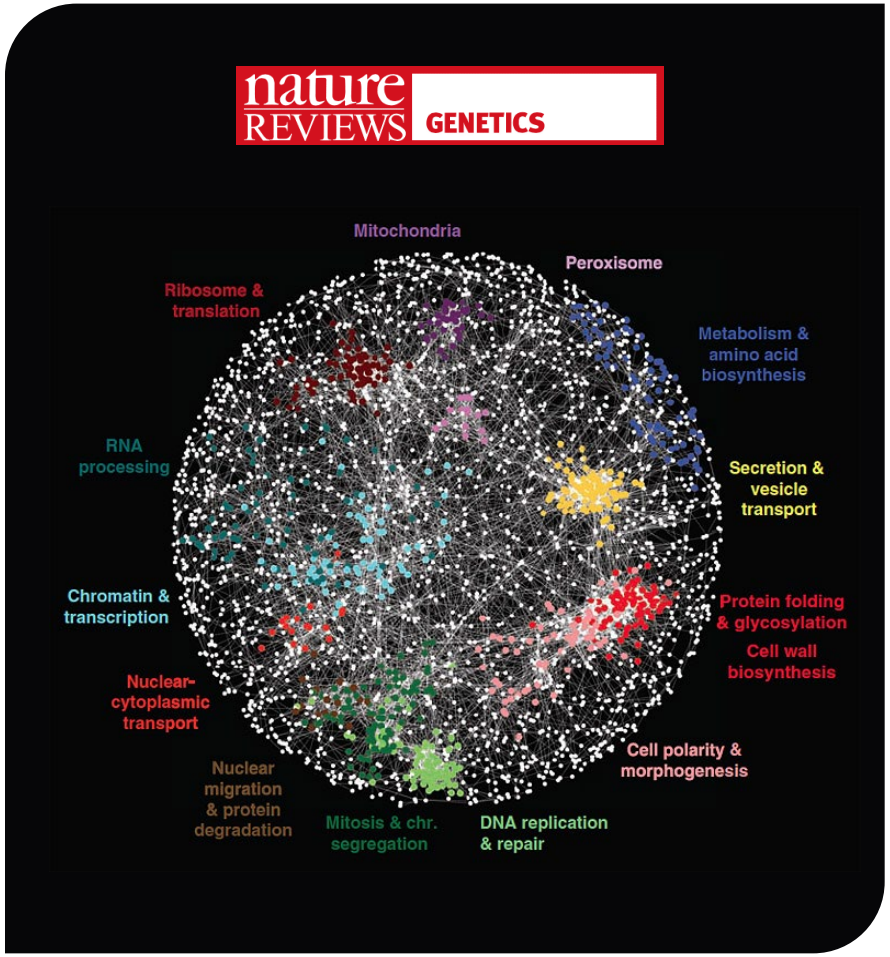
The Next Frontier in Precision Medicine Oncology

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



Nature Reviews Genetics, Vol. 18, 2017, Hieter, et al., as edited by IDEAYA; Image (right) Charles Boone

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 Degrader 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

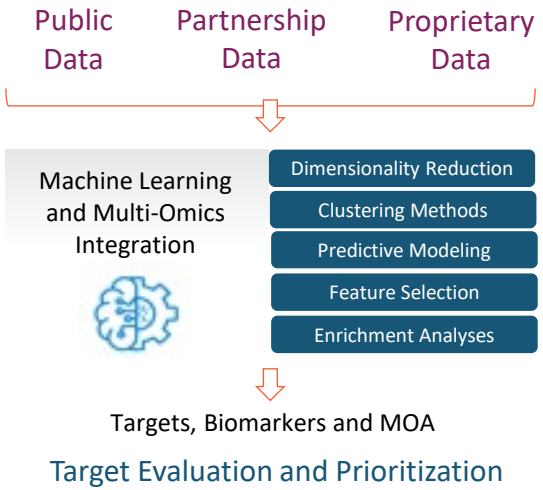
Target and Biomarker Discovery & Validation Platform

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

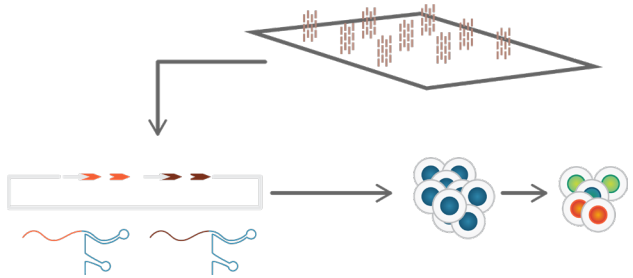
Robust SL interactions validated genetically (Dual CRISPR, paralogues, isogenic pairs, CRISPR/siRNA), pharmacologically and *in vivo*

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



DECIPHER™

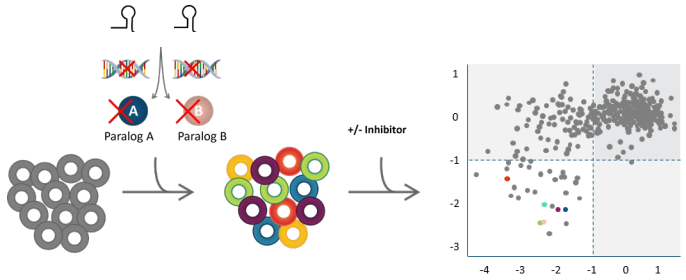
Dual CRISPR SL Library in DNA Damage Repair (2)



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

depmap portal | FOUNDATIONINSIGHTS™

Public Databases

TCGA | BioPortal | CCLE | PROJECTGENIE | Project Achilles | MSK-IMPACT™

(1, 2) IDEAYA Proprietary Libraries and Datasets – Strategic Collaborations with Broad Institute(1) and UC San Diego(2)

IDEAYA Precision Oncology Drug Discovery Platform & IND Engine

AI/ML & Structure Based Drug Design to Deliver Potential 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

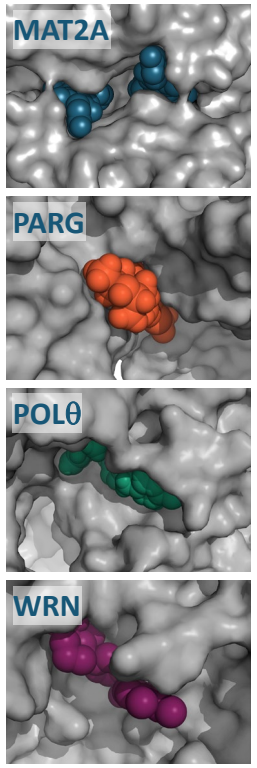
Multiple potential "first-in-world" co-crystal structures resolved, including for PARG, Pol Theta Helicase and Werner Helicase

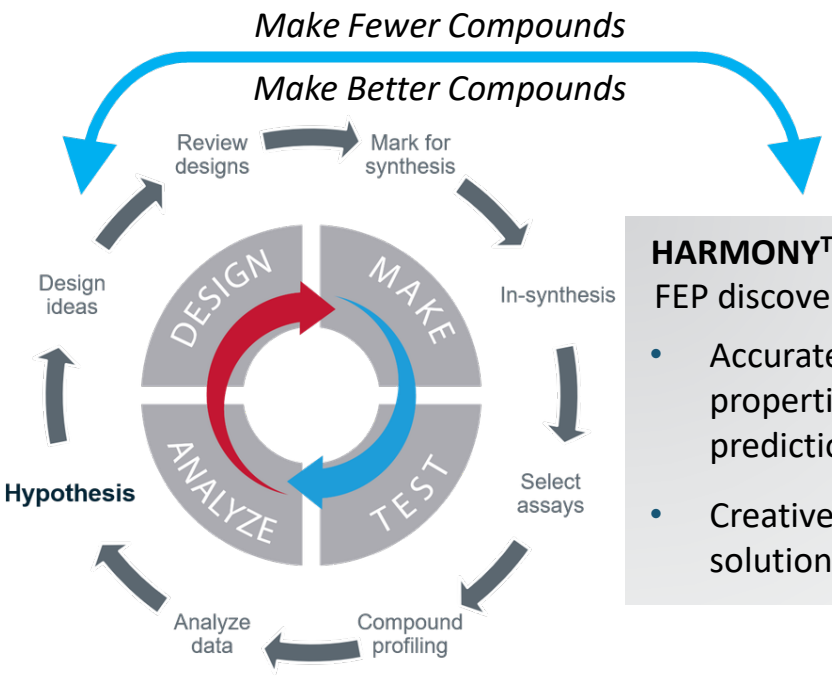
INQUIRE™ Proprietary Chemical Library

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*





HARMONY™ ML and FEP discovery engine

- Accurate properties prediction
- Creative design solutions

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

*HARMONY™ ML: IDEAYA proprietary AI/Machine Learning platform designed to enable computational drug discovery and lead optimization

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 *PKC*	+cMET[1] Combination 1L HLA-A2(-) MUM	GNAQ/11		Phase 2 (AA) / Phase 3 registrational trial ^ program update(s) - '24	Pfizer (1)	WW Commercial Rights
	cMET[1] Combination HLA-A2(+) MUM ^	GNAQ/11		HLA-A2(+) clinical trial ^^		
	cMET[1] Combination Melanomas	GNAQ/11		Phase 2 expansion in GNAQ/11 melanomas, including metastatic cutaneous melanoma		
	(Neo)Adjuvant UM	GNAQ/11		Phase 2 company-sponsored clinical efficacy update and regulatory guidance – H2'24		
IDE397 *MAT2A*	Monotherapy Solid Tumors	MTAP		Phase 2 clinical data update at expansion dose in MTAP urothelial and lung cancer		WW Commercial Rights
	Combination Solid Tumors	MTAP		Phase 1 IDE397 + AMG 193 (PRMT5iMTA) ongoing enrollment and joint publication strategy – '24	AMGEN (2)	
	Combination Urothelial Cancer	MTAP		Ongoing enrollment in Phase 1 IDE397 + Trodelvy®	GILEAD (3)	
IDE161 *PARG*	Monotherapy Solid Tumors	HRD		Phase 2 expansion in priority tumor types (Breast, CRC, Endometrial, Prostate) – H2'24		WW Commercial Rights
	Combination Endometrial Cancer	High-MSI, MSS		Phase 1 IDE161 + KEYTRUDA® FPI – H2 '24	MERCK (4)	
	Combinations Solid Tumors	HRD, Others		Enable IDE161 combination(s) – '24		
GSK101 *Pol Theta Helicase*	+Niraparib Combo[4] Solid Tumors	HR Mutations		Ongoing Phase 1 dose escalation	GSK (5)	Global Royalties
WRN *Werner Helicase*	GI Cancers	High-MSI		Targeting IND submission in H2 2024 ($7M Milestone upon successful IND clearance)	GSK (5)	50% US Profits and 20% costs
Platform	Solid Tumors	Defined Biomarkers		Targeting Multiple DCs, including in MTAP and potential first-in-class in KAT6 pathway – H2'24		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

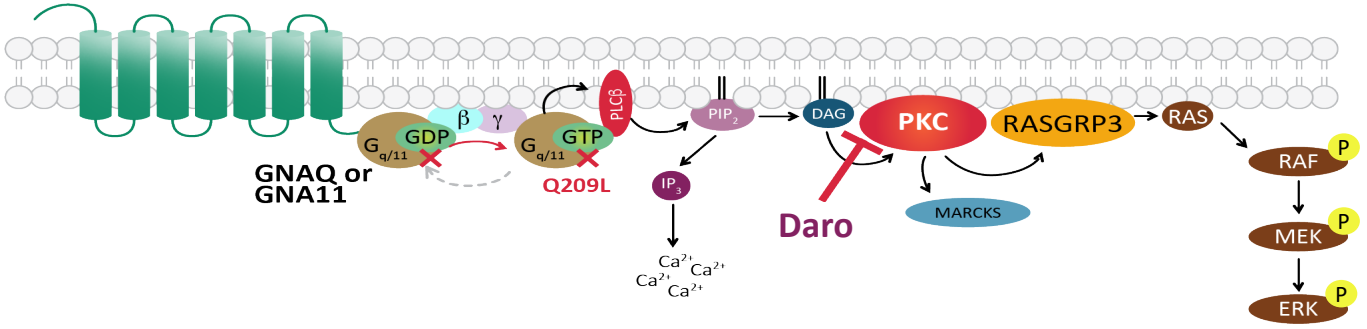
MAT2A=methionine adenosyltransferase 2a, MTAP=methylthioadenosine phosphorylase, MTA=methylthioadenosine, PRMT5=protein arginine methyltransferase 5 (PRMT5), PARG= poly (ADP-ribose) glycohydrolase, WRN = Werner Helicase, Polθ = DNA Polymerase Theta, HRD = homologous recombination deficiency, MSI = microsatellite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

= 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

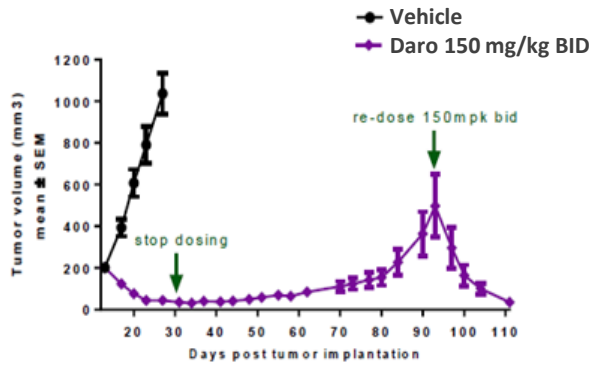
UM is typically treated with radiation and/or enucleation, with no approved systemic therapies for Neoadjuvant UM

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

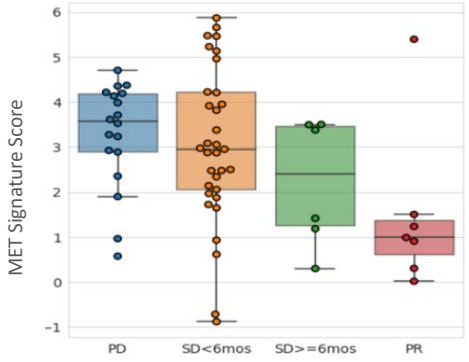
Uveal Melanoma Xenograft (92.1 mutant GNAQ)



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

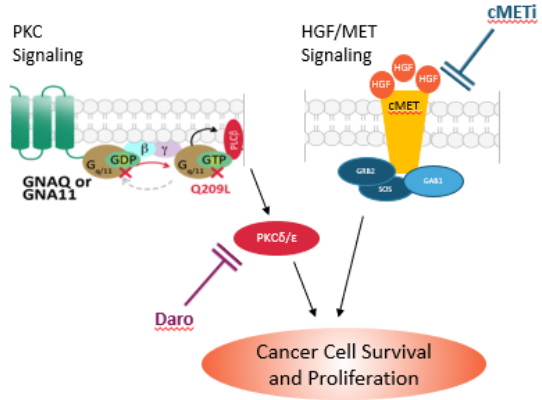


Ph 1 Clinical Outcomes

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



+ Pfizer Clinical Trial Collaboration and Supply Agreements for Darovasertib + Crizotinib Combination in MUM

IDEAYA owns or controls all commercial rights in darovasertib, including in Primary UM and MUM

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

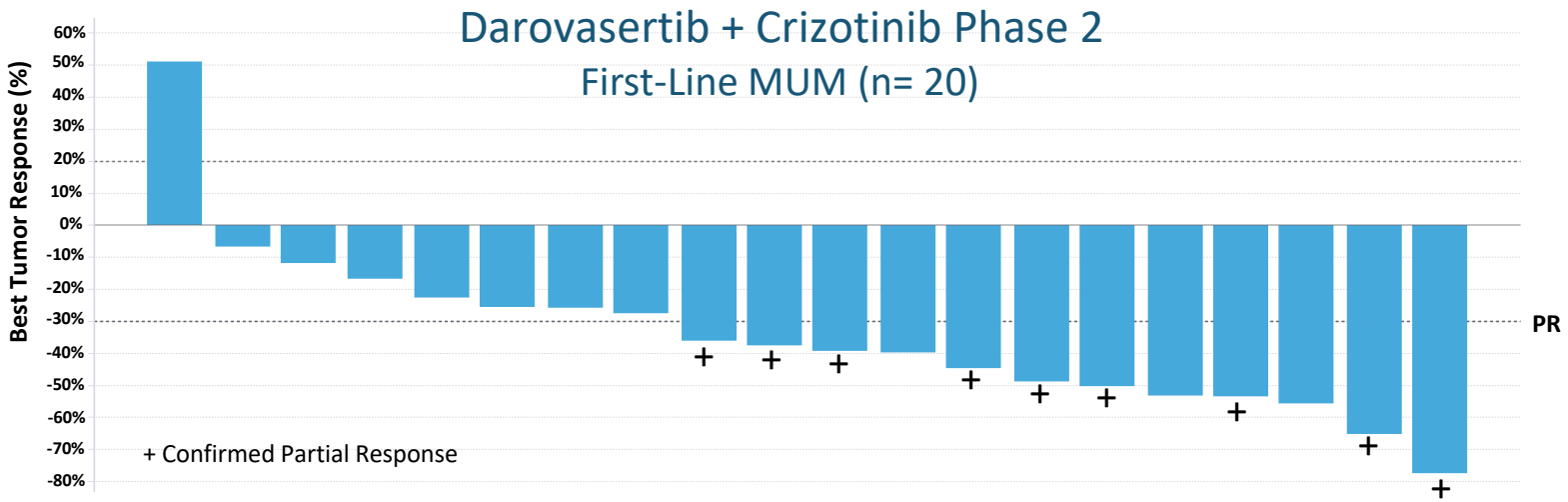
Disease Burden Significantly Higher in Both Any-Line and First-Line MUM Population+

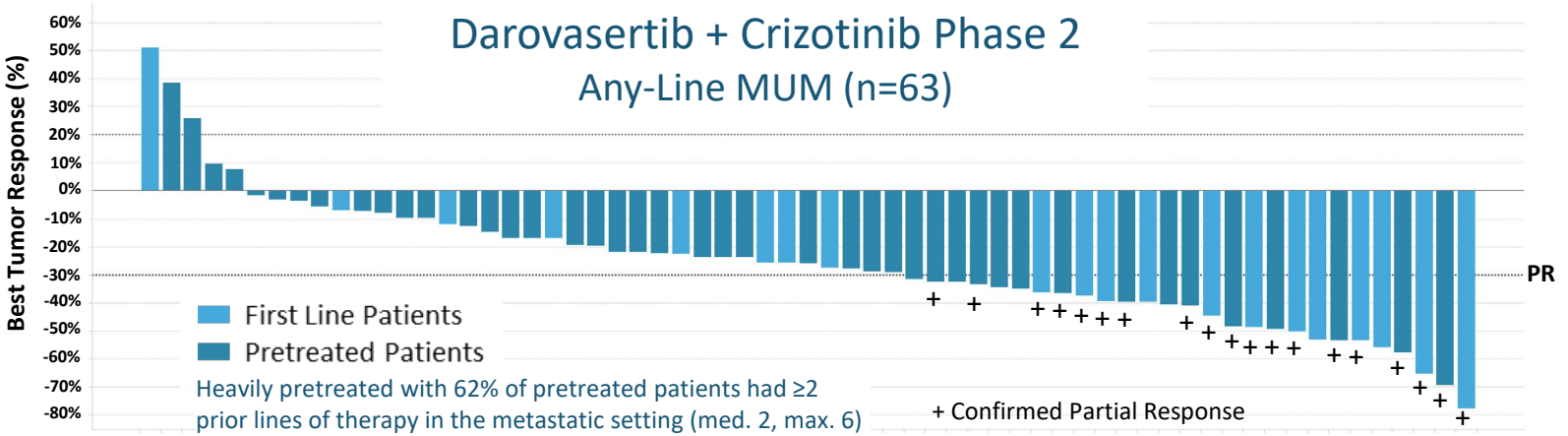
Baseline Characteristics		IDE196-001 Phase 2* Darovasertib + Crizotinib		Tebentasfusp First-Line Phase 3#	
		Any-Line n=63 (%)	First-Line n=20 (%)	Tebe Arm n=252 (%)	Control Arm^ n=126
Age (Years)	< 65	35 (56)	10 (50)	64 Median	66 Median
	≥65	28 (44)	10 (50)		
Sex	F	32 (51)	9 (45)	124 (49)	64 (51)
	M	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)		
	>ULN	**38 (60)**	**10 (50)**	**90 (36)**	**46 (37)**
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%

ESMO 2023 Proferred Presentation M McKean et al: preliminary analysis of unlocked database as of 8/22/2023 by investigator review, C1D1 cutoff as of 9/22/2022, based on 20 evaluable 1L MUM patients and 63 evaluable Any-Line (includes 1L and 2L+/pre-treated) MUM patients

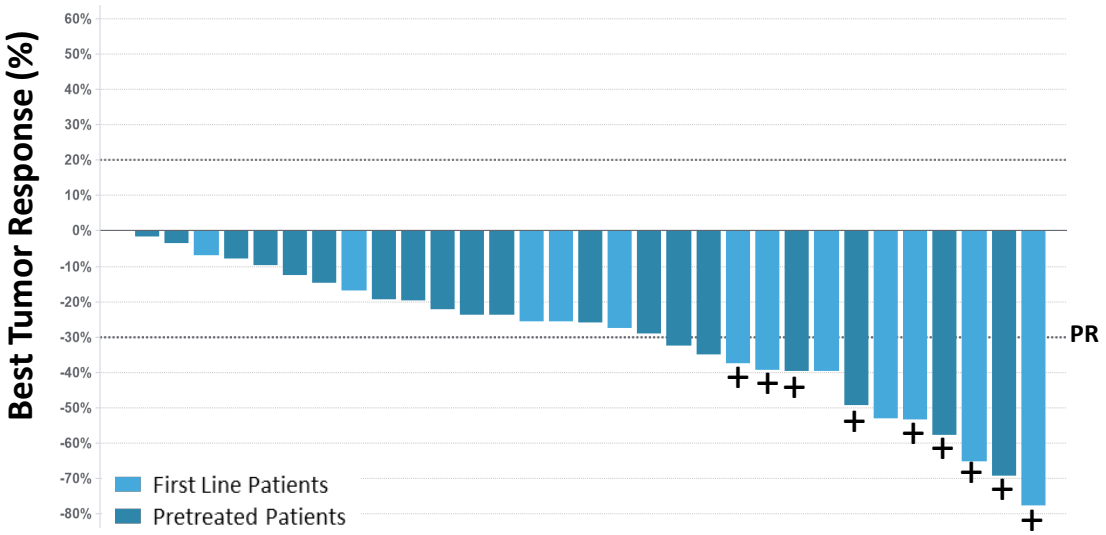
ORR = Overall Response Rate; DCR = Disease Control Rate; cPR = Confirmed Partial Response; uPR = Unconfirmed Partial Response; SD = Stable Disease

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)

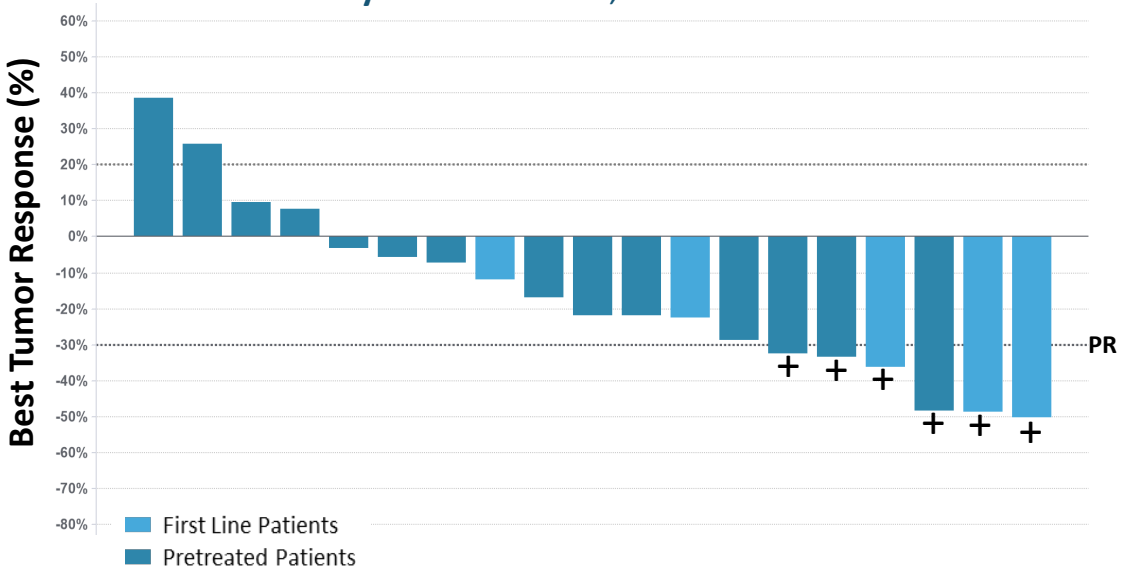
First-Line: 42% ORR; 100% DCR
Any-Line: 29% ORR; 94% DCR



+ Confirmed Partial Response

HLA-A2 Positive (n=19)

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



+ Confirmed Partial Response

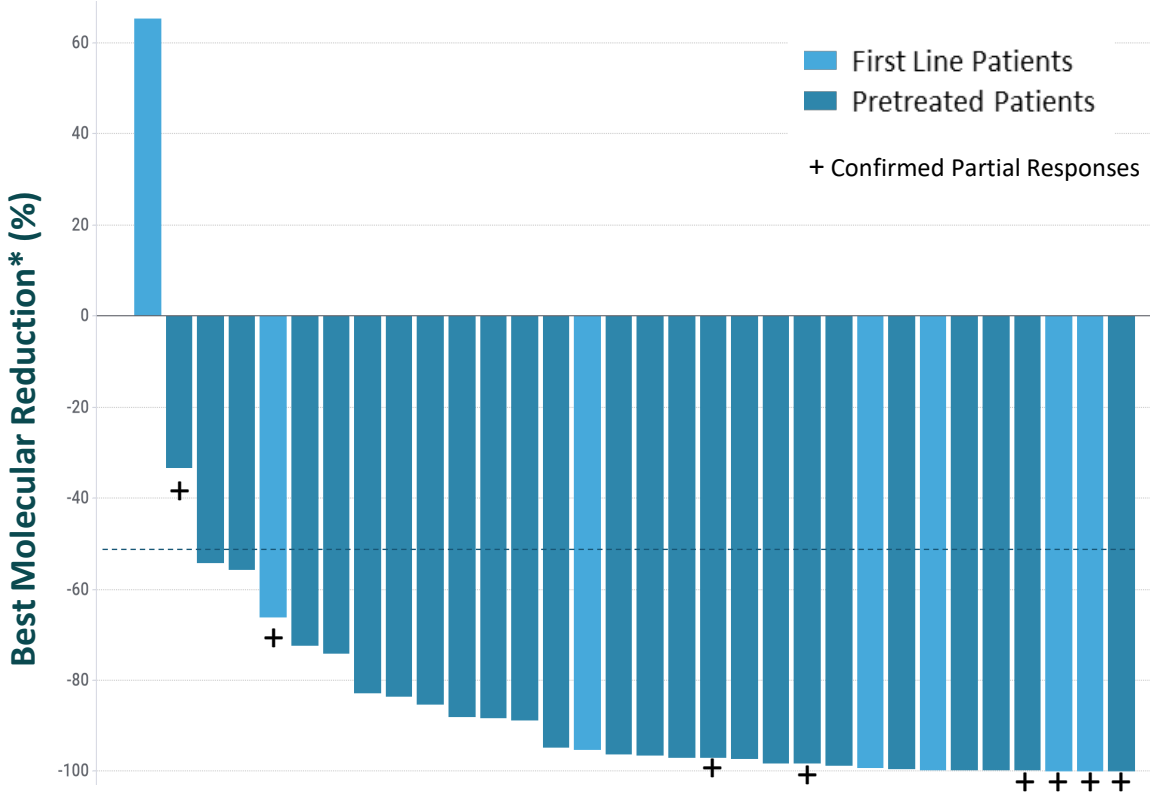
ESMO 2023 Proferred Presentation M McKean et al : preliminary analysis of unlocked database as of 08/22/2023 by investigator review; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) as of 9/22/2022

IDEAYA BIOSCIENCES

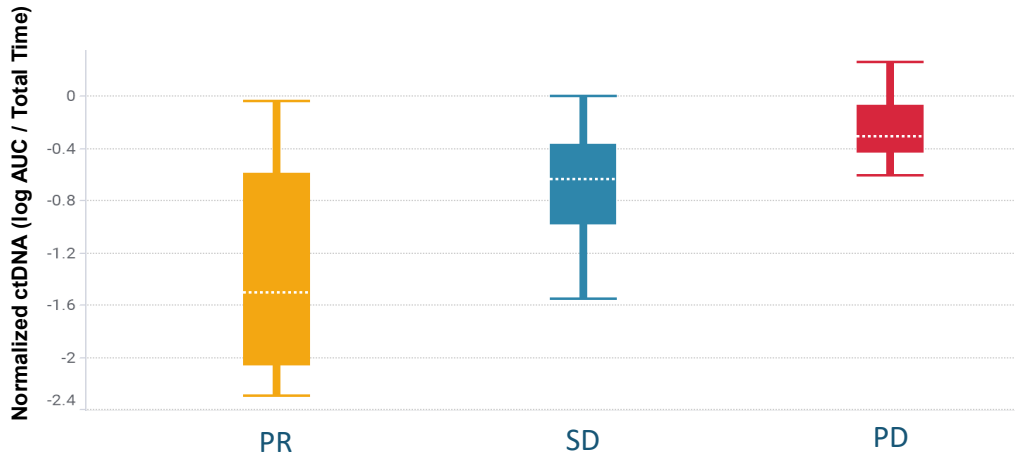
Observed 94% ctDNA Molecular Response Rate with Deep & Sustained MRs*

Any-Line MUM Patients Treated with the Darovasertib + Crizotinib Combination

Molecular Response Regardless of BAP1 Mutation



Molecular Response Correlates with RECIST Response ^



High ctDNA Molecular Response Rate of 94% in Any-Line MUM

Deep and Sustained MRs with approximately 80% of patients showing >80% reduction in MAF

ctDNA MRs correlate with Clinical Efficacy (PR, SD, PD) by RECIST

ESMO 2023 Proferred 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
*Molecular response (MR) defined as at least 50% reduction in percentage of Mean Allele Frequency (MAF) at any timepoint
^ Best Overall Response

IDEAYA BIOSCIENCES

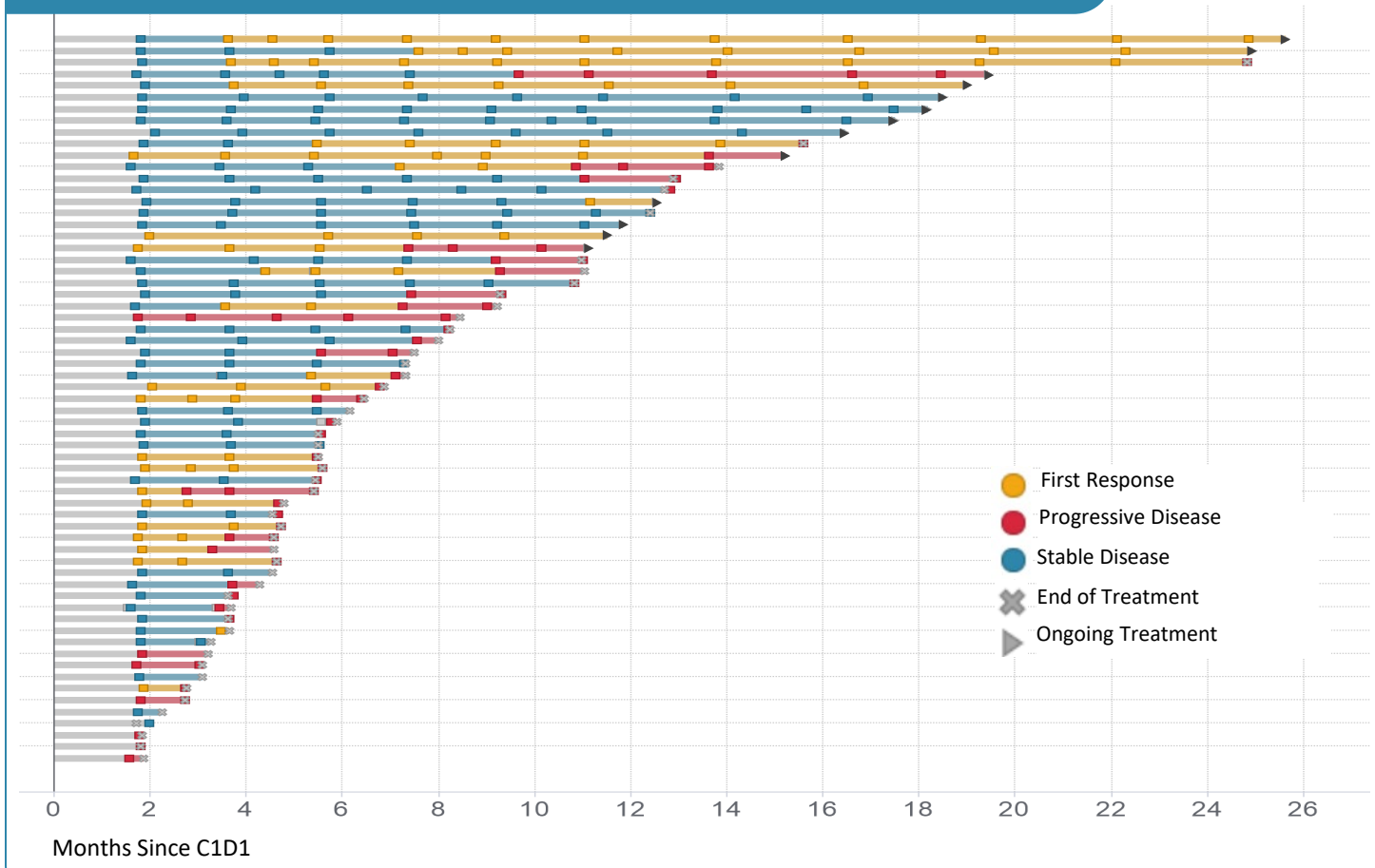
MADRID 2023 ESMO congress

Oral Presentation

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

Observed Compelling Median Progression Free Survival with Encouraging Trend

Any-Line MUM Swimlane Plot



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

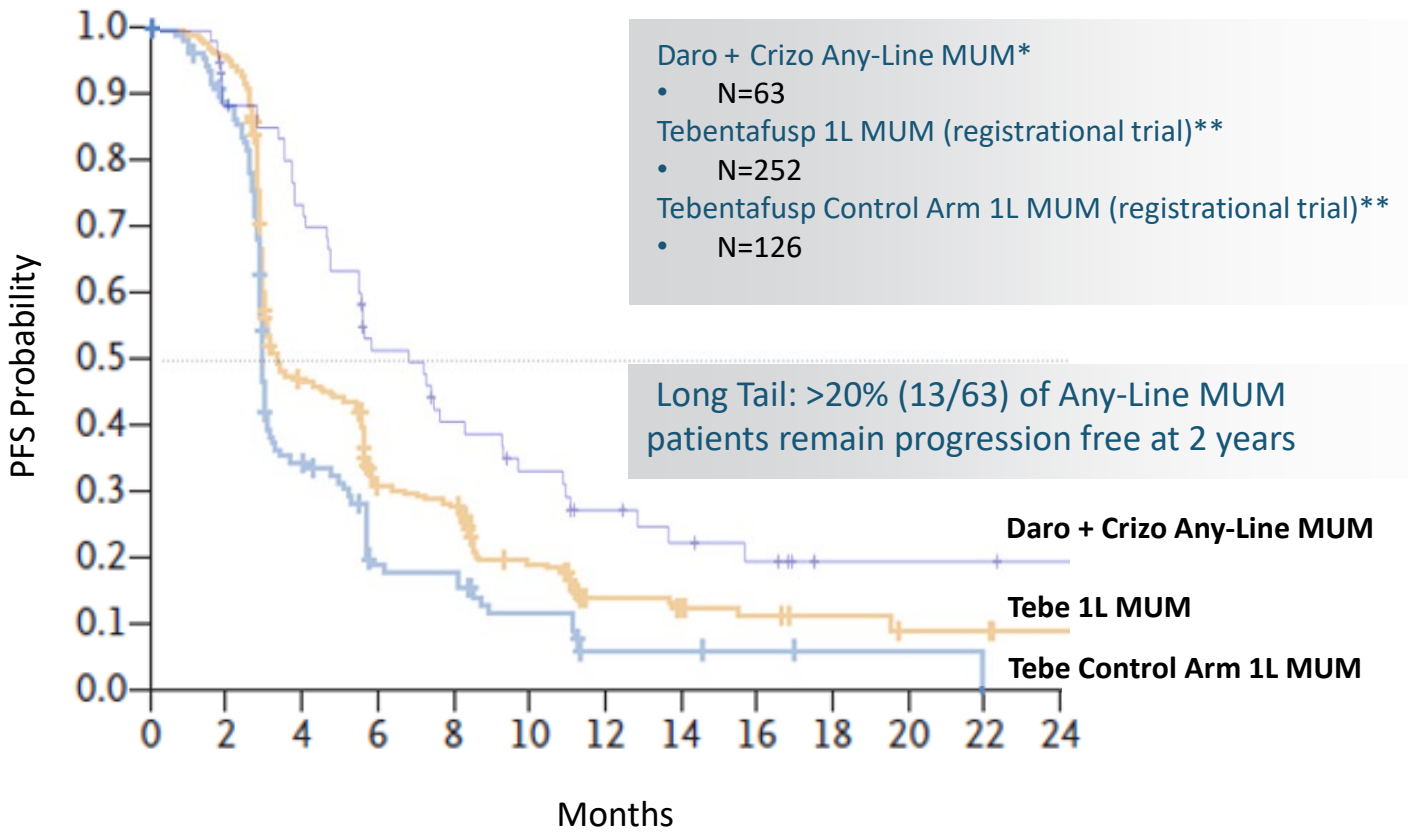
ESMO 2023 Proferred Presentation M McKean et al: Preliminary analysis of unlocked database as of 08/22/2023 by investigator review, C1D1 cutoff as of 9/22/2022, based on 63 evaluable Any-Line MUM patients

IDEAYA BIOSCIENCES

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

2-Year PFS Kaplan Meier Curves in MUM



Daro + Crizo Any-Line MUM*
- N=63

Tebentafusp 1L MUM (registrational trial)**
- N=252

Tebentafusp Control Arm 1L MUM (registrational trial)**
- N=126

Long Tail: >20% (13/63) of Any-Line MUM patients remain progression free at 2 years

* 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 Proferred 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

IDEAYA BIOSCIENCES

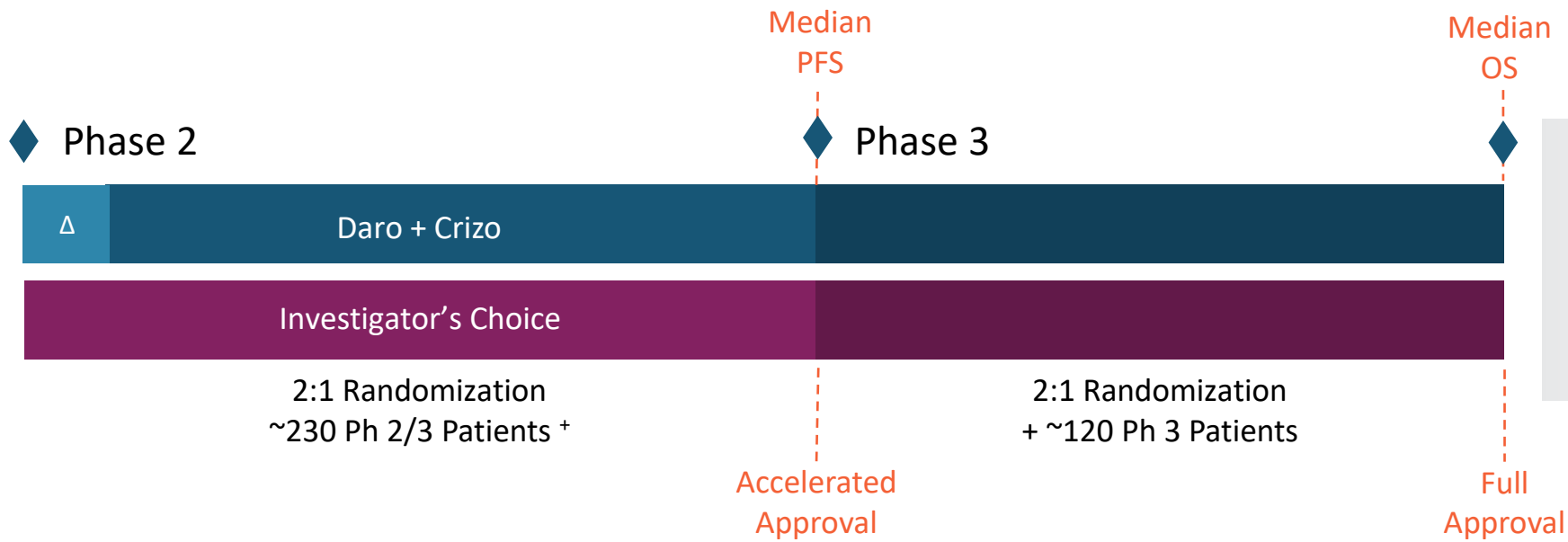
Accelerated Approval Trial Design in First-Line HLA-A2 Negative MUM

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



2:1 Randomization
Daro + Crizo vs Investigator's Choice
(IC = Ipi + Nivo, PD1, or DTIC)

Primary Endpoints (BICR)
Accelerated Approval: mPFS
Full Approval: mOS

FDA Fast Track Designation for Daro +Crizo in MUM

Δ 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

IDEAYA Phase 2 Darovasertib Neoadjuvant UM Company-Sponsored Study

Enucleation & Plaque Eligible Patients who Received ≥4 Months Treatment (n=8)

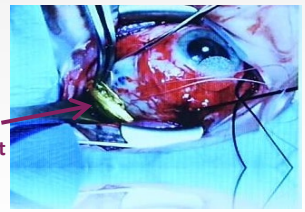
Preliminary data on 8 patients treated with neoadjuvant darovasertib for ≥ 4 months

Majority of enucleation patients eye preserved

Median % maximal tumor shrinkage by:

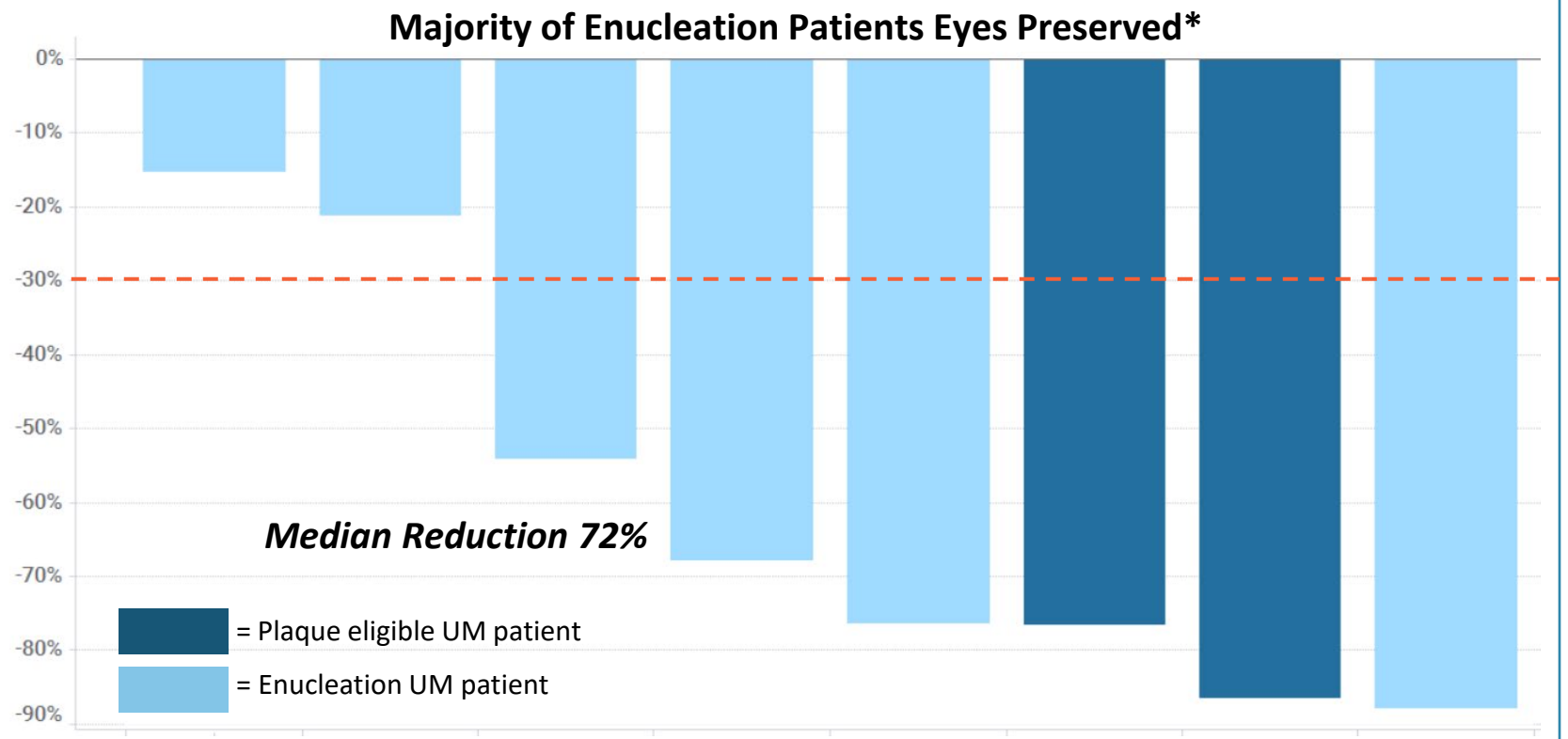
- Apical Height: -40%
- Basal Diameter: -25%
- Volume: -72%

Plaque Brachytherapy



Iodine-125 Plaque Surgery, UCLA

% Best Response for All Patients Treated w/Daro ≥ 4 Months By Tumor Volume^ (n=8)



^ Volumetric Calculation: 4/3 πa^2 b (tumour diameter divided by 2 = a; tumour height = b; π = 3.14) divided by 2; Richtig E, et al; Nature Eye 2004;18(6):619–623

* The majority of patients had reported Eye Saved (i.e., converted to plaque brachytherapy or EBRT eligible)

Preliminary data from unverified database as of 24May24; NCT#05907954 multi-centered global trial with over 14 enrolling sites.

IDEAYA Phase 2 Darovasertib Neoadjuvant UM Company-Sponsored Study

Case Study Examples in Enucleation and Plaque Eligible UM Patient

Plaque Patient: Maximal Change in Tumor Size

- 50+ year old plaque eligible UM patient who received at least 4 months of darovasertib treatment
- Dome-shaped tumor

	Baseline (mm)	Post Baseline (mm)	% Change From Baseline
Apical Height	4.9	1.9	-61%
Basal Diameter	14.7	8.7	-41%
By Volume	554.41	75.23	-86%

Enucleation Patient: Maximal Change in Tumor Size

- 60+ year old enucleation UM patient who received at least 4 months of darovasertib treatment
- Dome-shaped tumor

	Baseline (mm)	Post Baseline (mm)	% Change From Baseline
Apical Height	8.1	2.7	-67%
Basal Diameter	13.2	8	-39%
By Volume	738.98	90.48	-88%

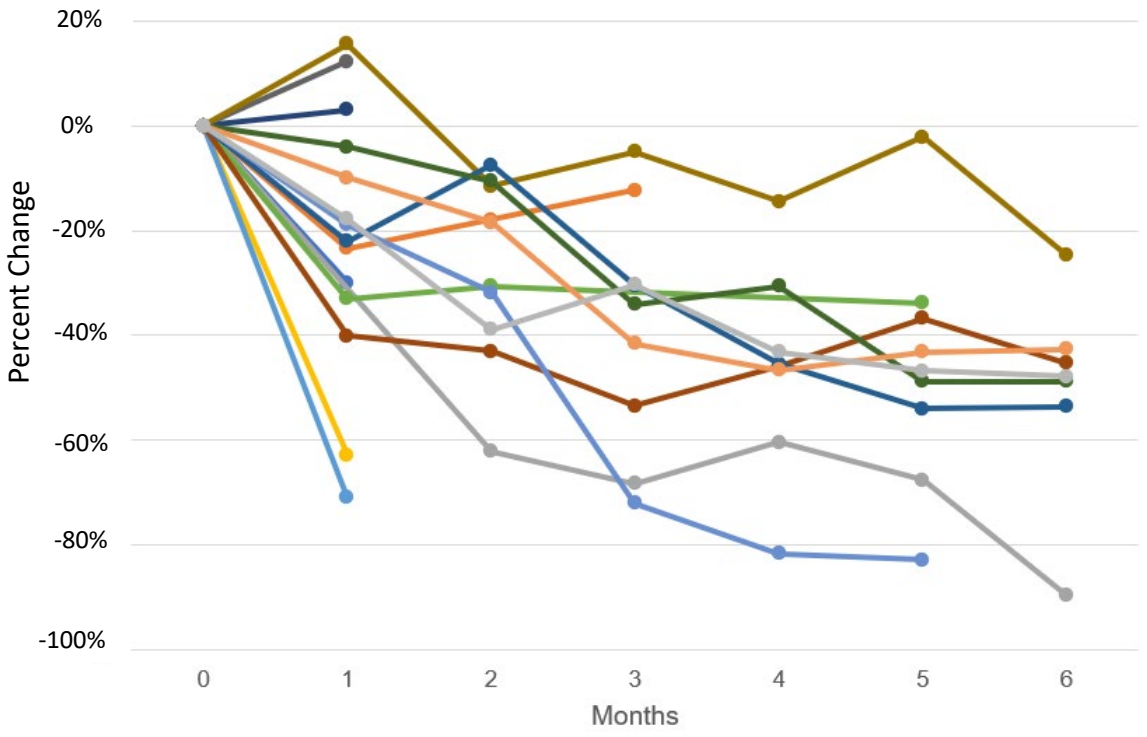
Preliminary data from an unverified database as of 24May24; NCT#05907954 multi-centered global trial with over 14 enrolling sites

2024 ASCO ANNUAL MEETING
Oral Presentation

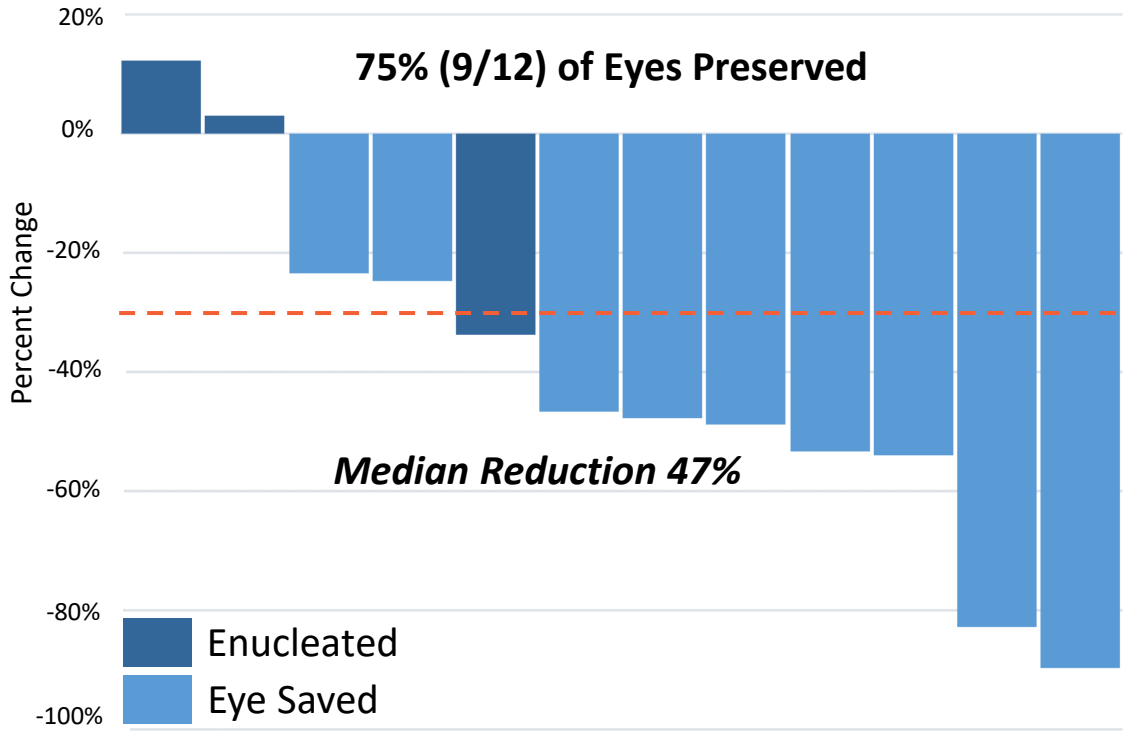
Phase 2 Darovasertib Neoadjuvant UM IST Results in Enucleation Patients

75% (9/12) of Eyes Preserved with Darovasertib Neoadjuvant Treatment up to 6 months

% Change in Tumor Volume^ Over Time For Each Patient (n=15#)



Best Response in Tumor Volume Post Darovasertib Treatment (n=12) – Median Reduction of 47%*



Adapted from A Joshua, ASCO 2024, NADOM Investigator Sponsored Trial (IST): NCT05187884; ^ Volumetric Calculation: 4/3 πa2 b (tumour diameter divided by 2 = a; tumour height = b; π = 3.14) Richtig E, et al; Nature Eye 2004;18(6):619–623

*Eyes preserved: 3 patients converted to Iodine plaque, 5 patients converted to Ruthenium plaque and 1 patient received external beam radiation therapy

#Thirteen patients completed allocated neoadjuvant treatment. One 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

IDEAYA BIOSCIENCES

2024 ASCO ANNUAL MEETING
Oral Presentation

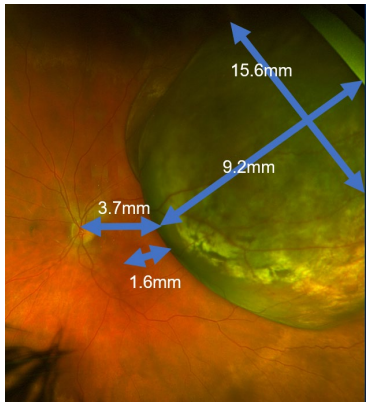
Phase 2 Darovasertib Neoadjuvant UM IST Results in Enucleation Patients

Pre & Post Darovasertib Treatment Radiation Plaque Planning and Vision Implications

Baseline & Post Baseline Measurements

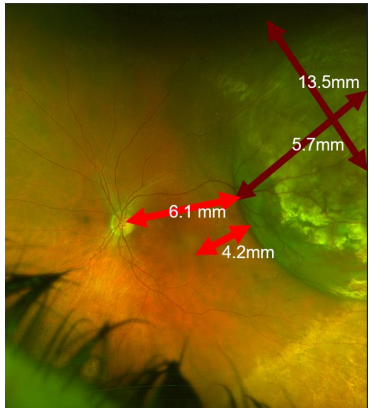
Baseline Tumor Size Measurements

- Distance of tumor to optic nerve and fovea are 3.7 mm and 1.6 mm respectively



Post Baseline Tumor Size Measurements

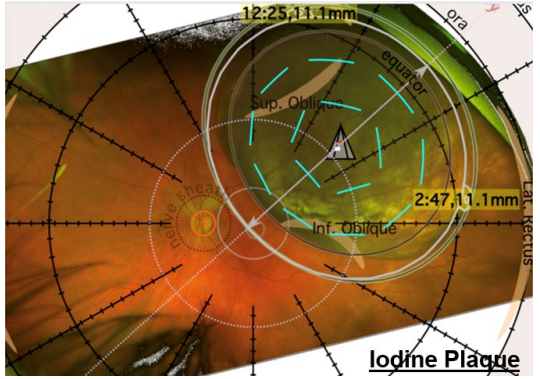
- Distance to tumor from optic nerve and fovea increased by ~65% and ~163% respectively



Plaque Treatment Plan

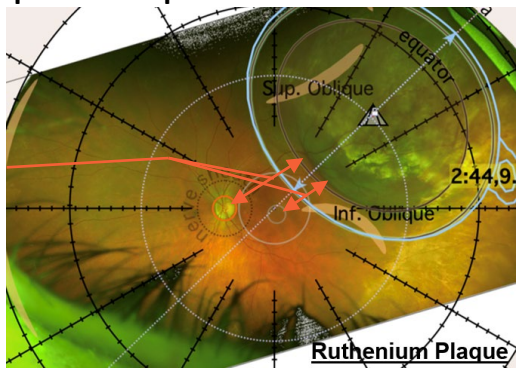
Baseline Plaque Size Requirements

Patient requires an Iodine plaque at Baseline



Post-Baseline Plaque Size Requirements

Increased distance to critical structures and tumor enables smaller Ruthenium plaque (less radiation)



Reduced Radiation to Critical Structures & Potential Improvement in Vision*

	Baseline	Post Baseline	Change
Dose to nerve	78 Gy	13 Gy	-83%
Dose to fovea	157 Gy	59 Gy	-62%
1-year probability of visual loss	~67%	~20%	-
3-year probability of visual loss	~95%	~43%	-

Adapted from A Joshua, ASCO 2024, NADOM Investigator Sponsored Trial (IST): NCT05187884
Slides courtesy of Dr Rod O'Day and Lotte Fog

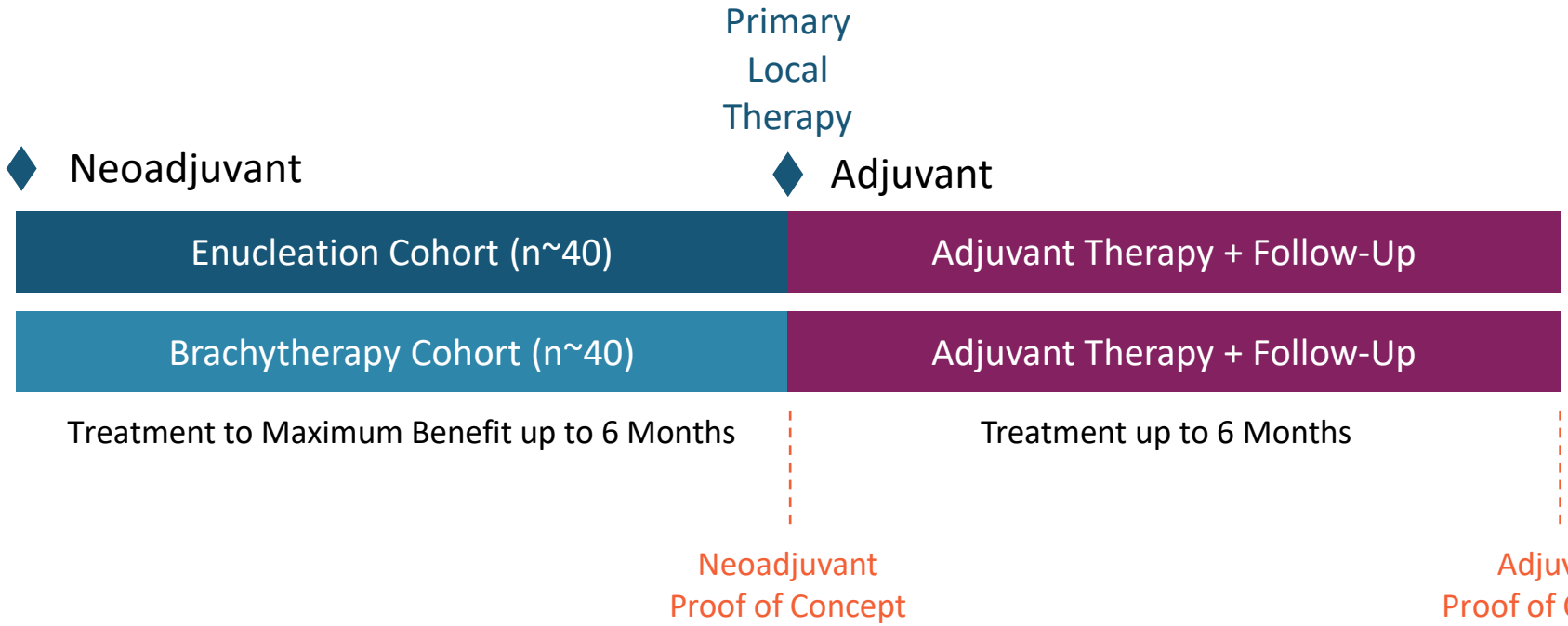
* Aziz et al., 2016 (Visual acuity of 20/200 or worse)

IDEAYA BIOSCIENCES

(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 ^



Primary Endpoints
- Safety
- Cohort 1: Eye Preservation
- Cohort 2: Decrease in Radiation Dose

Secondary Endpoints
- Useful Vision (1 yr)
- Relapse Free Survival (RFS)
  - Local (1 yr)
  - Distant (3 yr)

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

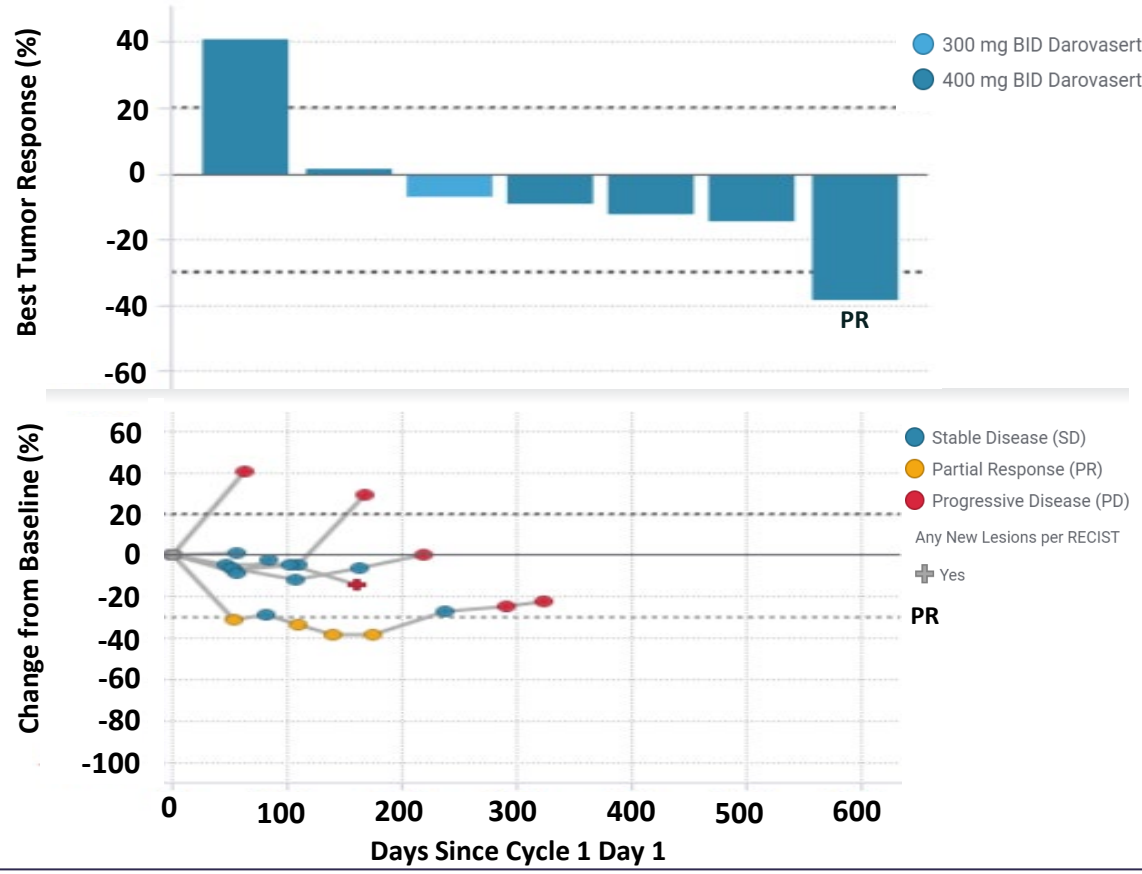
Enucleation Cohort → Save the Eye Brachytherapy Cohort → Protect Vision Adjuvant Therapy → Save Lives

^ Clinicaltrials.gov: NCT05907954

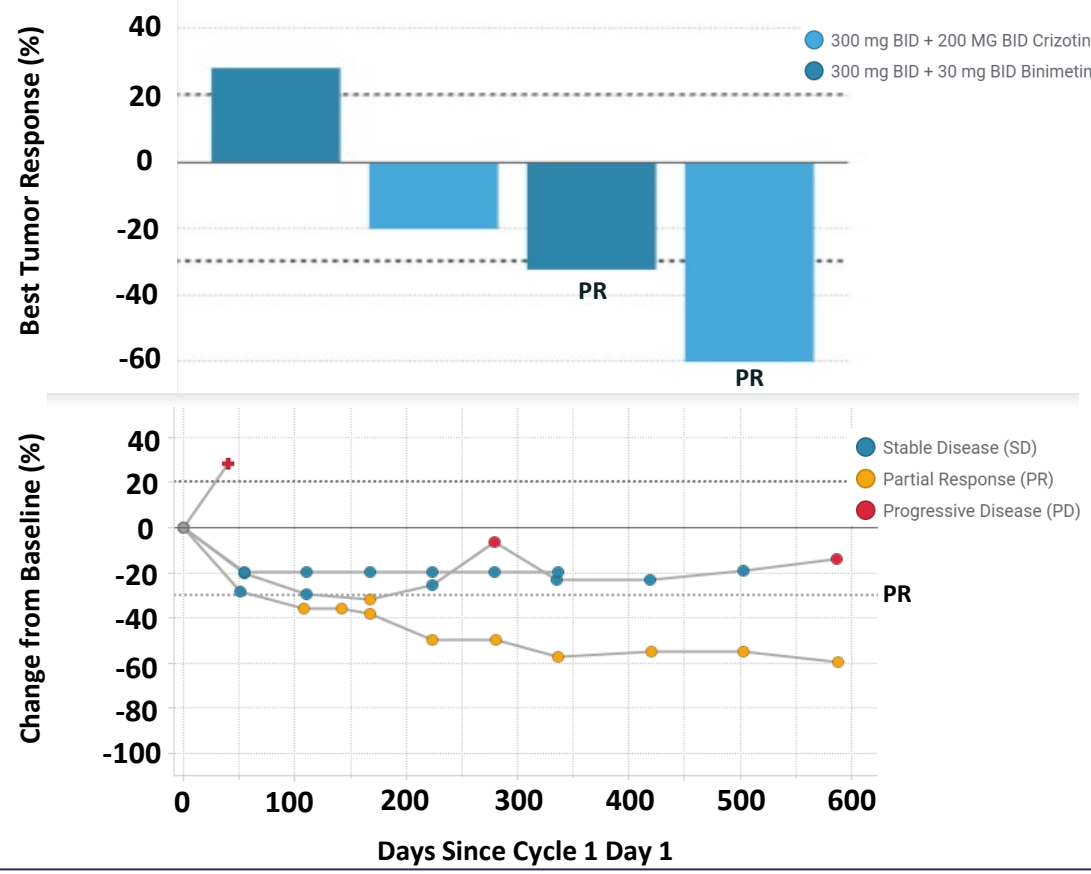
GNAQ/11 Cutaneous Melanoma Patients Treated With Darovasertib

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

Cutaneous Melanoma Patients Treated with Daro Mono (n=7)



Cutaneous Melanoma Patients Treated with Daro Combo (n=4)



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; **Daro** Phase 2 Radiation 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 + 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

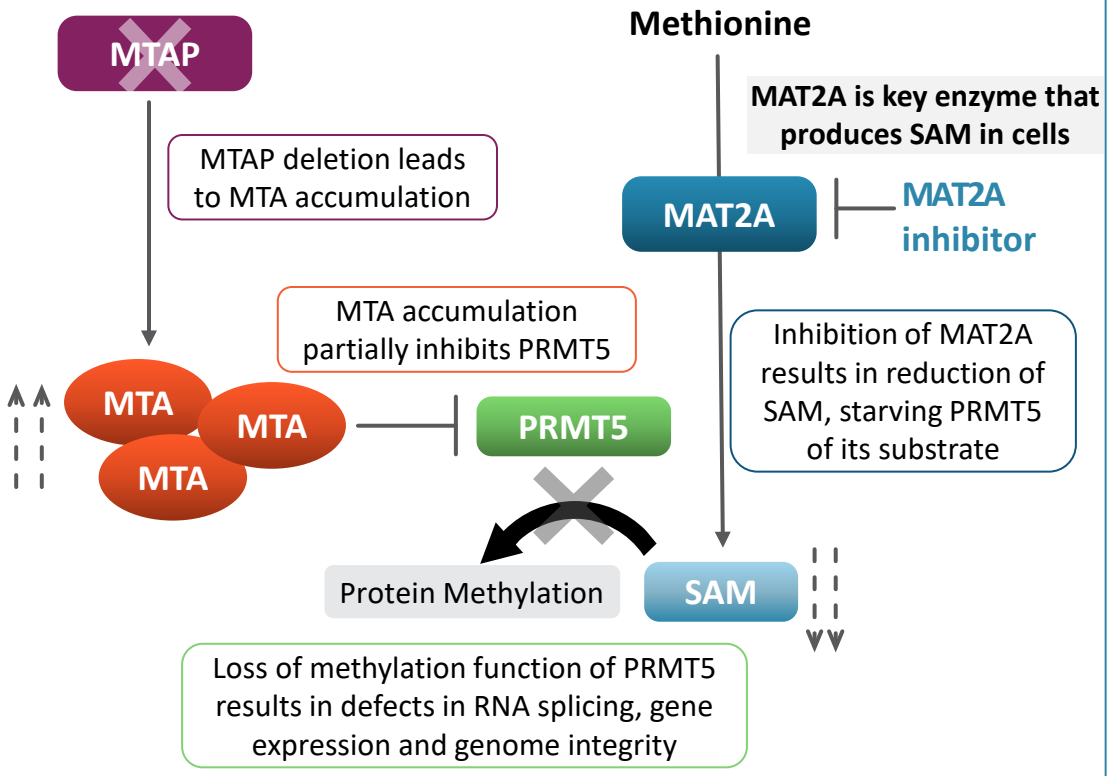
[1] GNAQ/11 cutaneous melanoma estimated annual incidence is approximately 5,000 patients in the US and 8,000 patients in the EU28. Based on several metastatic cancer patient databases, including Memorial Sloan Kettering Cancer Center (MSKCC) Impact, we project GNAQ/11 metastatic cutaneous melanoma has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

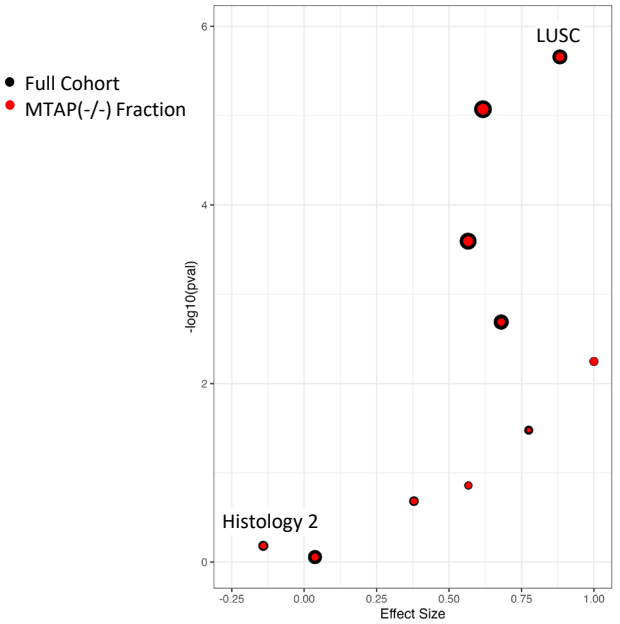
MTAP-MAT2A Synthetic Lethality Biology

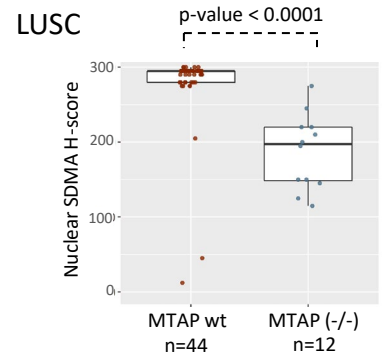


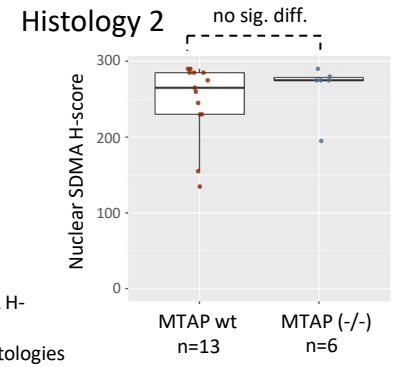
Endogenous Suppression in MTAP$^{-/-}$ PDX Models

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

SDMA Effect Size (PDX Tissue Microarray)







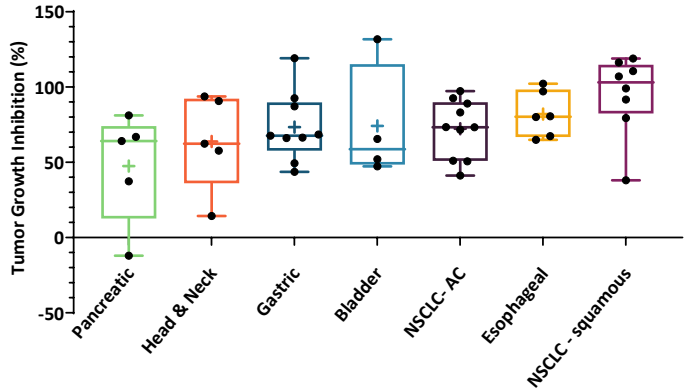
IDEAYA Data: AACR 2023 (M. Fischer et al.) – Volcano plot comparing nuclear SDMA H-Score by IHC in MTAP(-/-) relative to MTAP wt across tissue microarray (TMA) of treatment-naïve PDX models; LUSC shows most significance effect across tumor histologies

IDE397 Demonstrates Broad Efficacy across MTAP-Deletion PDX Models

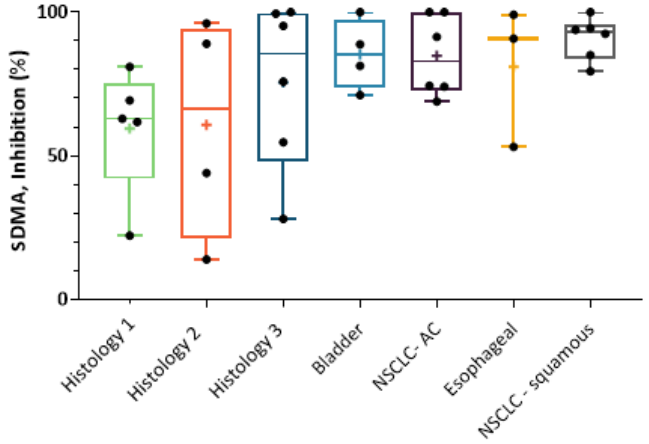
Deep Regressions observed in NSCLC-squamous (LUSC), Esophageal and Bladder Cancers

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

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



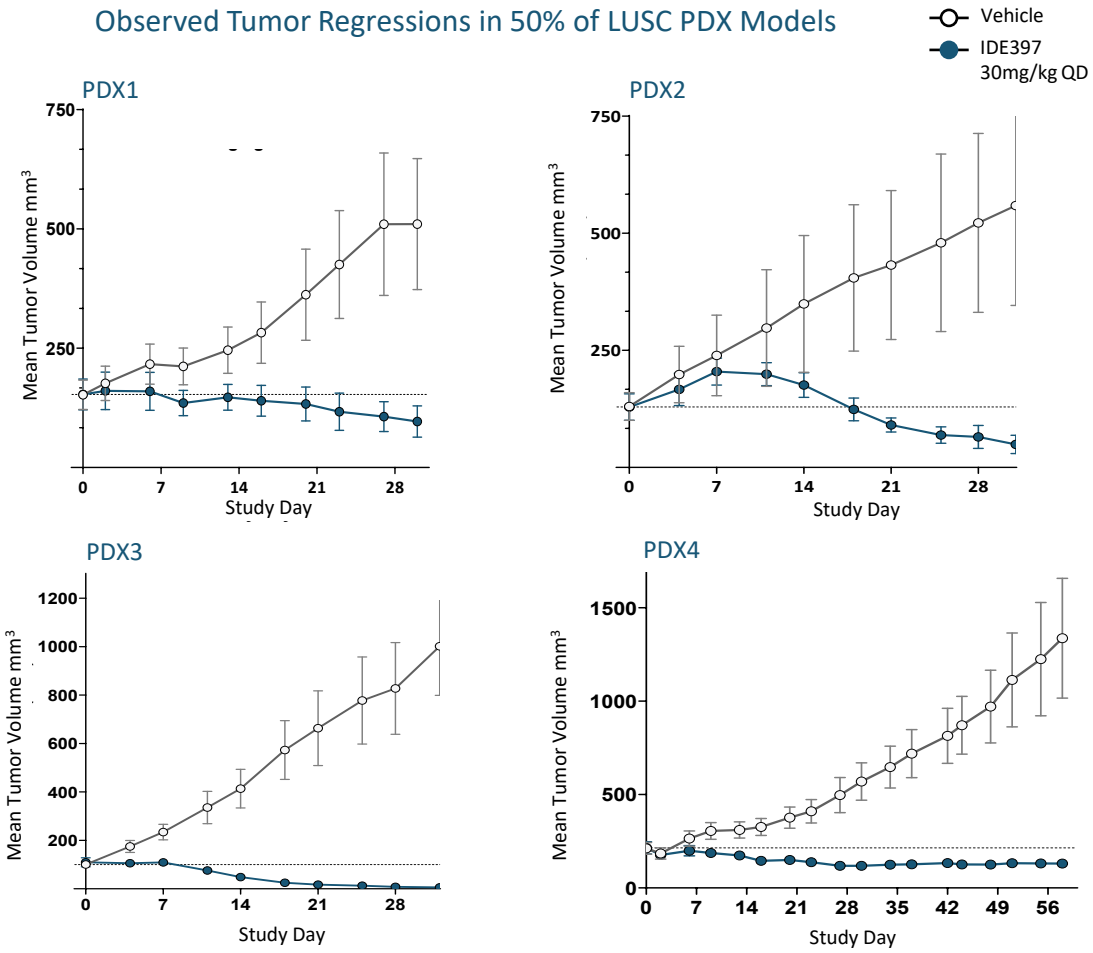
SDMA Suppression in Residual Tumors* at End of Study



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

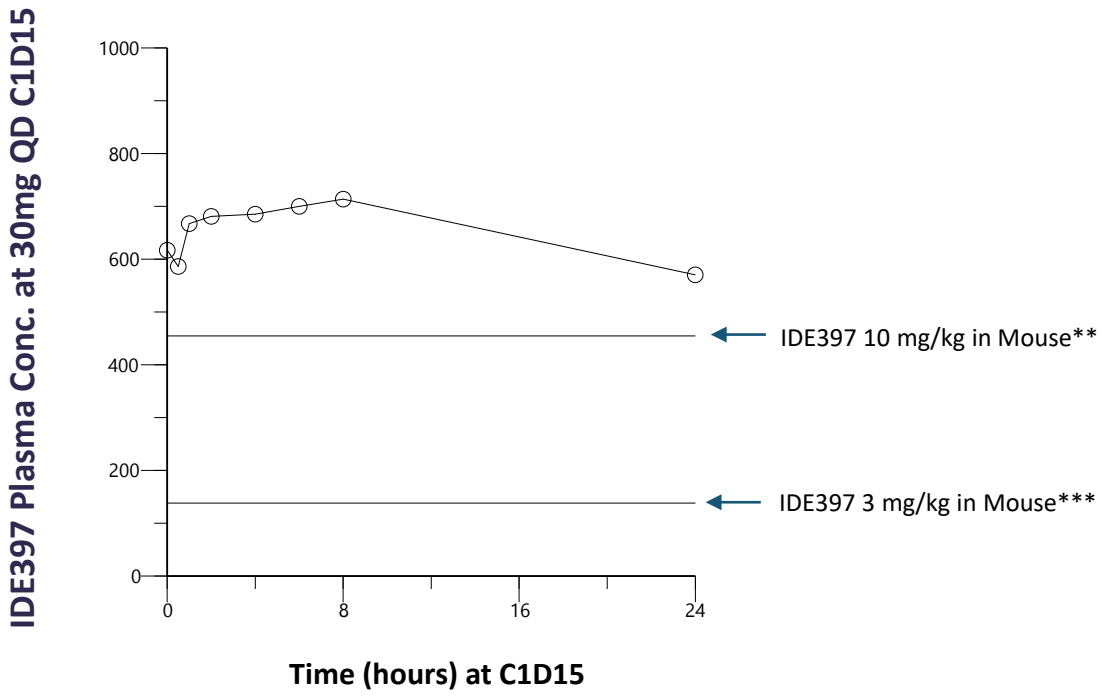


IDEAYA Data

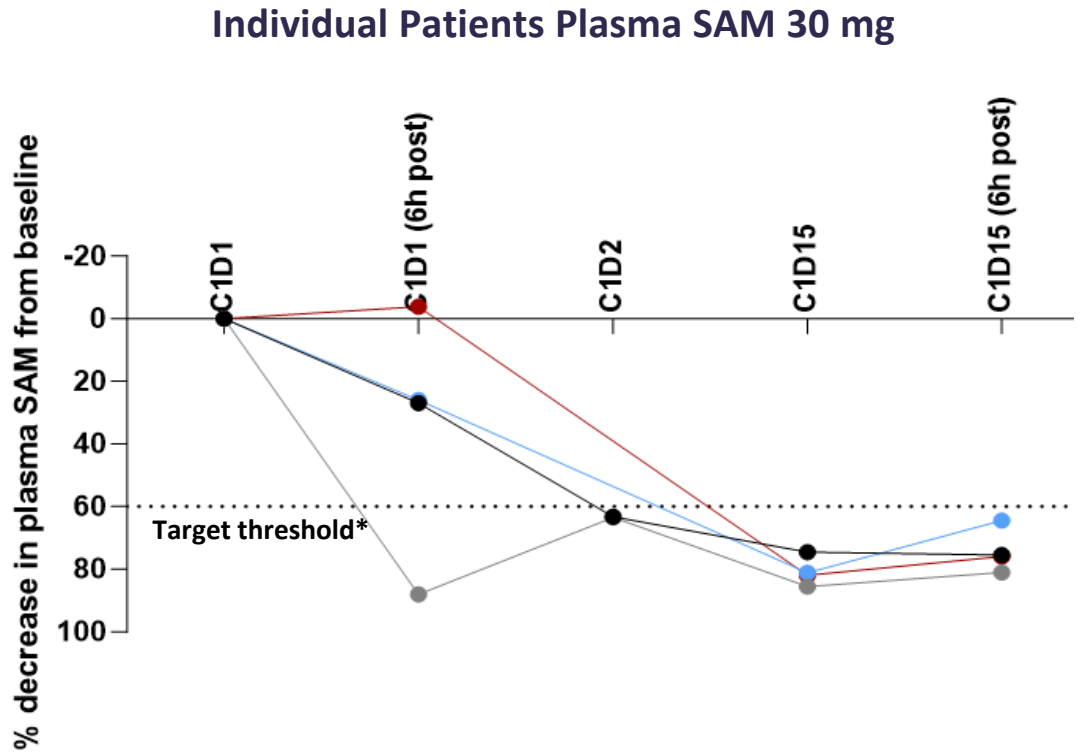
IDE397 Human Pharmacokinetics (PK) and Pharmacodynamics (PD)

30mg QD Expansion Dose Delivers Target Drug Coverage and Robust Plasma SAM PD

Human PK at 30 mg Expansion Dose (n=2)



Steady-State Plasma SAM PD at 30 mg Dose (n=4)



* IDEAYA Investigator's Brochure: Target threshold for human plasma SAM reduction determined based on anti-tumor response observed by IDE397 in MTAP-deletion xenograft preclinical models
** IDE397 at ≥10 mg/kg in mouse observes tumor regressions in MTAP-deletion xenograft models
*** IDE397 at 3 mg/kg in mouse observes tumor regressions in combination with clinical stage MTA-cooperative PRMT5 inhibitors in MTAP-deletion xenograft models

Preliminary IDE397 Adverse Event Profile of 30mg QD Ph2 Expansion Dose

MTAP-Deletion Solid Tumor Patients

- Favorable adverse event (AE) profile demonstrated for the 30 mg Phase 2 expansion dose (n=18)
- ~5.6% of grade ≥ 3 drug-related AEs
- No drug-related SAEs
- No discontinuations due to drug-related adverse events making long-term dosing feasible

Drug-Related Adverse Event Profile (>5%), n=18

	Drug Related AE		Drug Related Serious AE	
Preferred Term	**Grade >=3 n (%)**	**All Grade n (%)**	**Grade >=3 n (%)**	**All Grade n (%)**
Any Event	1 (5.6%)	11 (61.1%)	0 (0.0%)	0 (0.0%)
Nausea	0 (0.0%)	3 (16.7%)	0 (0.0%)	0 (0.0%)
Peripheral Neuropathy*	0 (0.0%)	3 (16.7%)	0 (0.0%)	0 (0.0%)
Blood Creatinine Increased	0 (0.0%)	2 (11.1%)	0 (0.0%)	0 (0.0%)
Alanine Aminotransferase Increased	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Anemia	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Aspartate Aminotransferase Increased	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Asthenia	1 (5.6%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Decreased Appetite	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Dehydration	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Dizziness	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Muscular Weakness	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
R/O Relative Adrenal Insufficiency	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)
Urethral Discharge	0 (0.0%)	1 (5.6%)	0 (0.0%)	0 (0.0%)

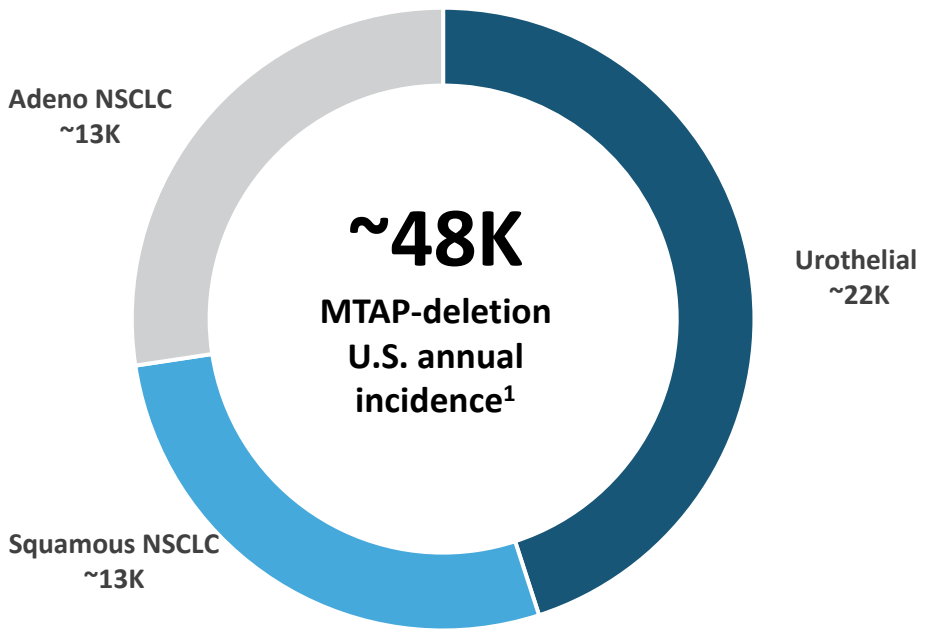
*All 3 patients reporting low grade Peripheral Neuropathy had prior platinum-containing chemotherapy regimens;
Data from an unlocked, unverified database as of June 12, 2024 data cut off; AE = Adverse Event

IDE397: Phase 2 Potential First-in-Class MAT2A Inhibitor

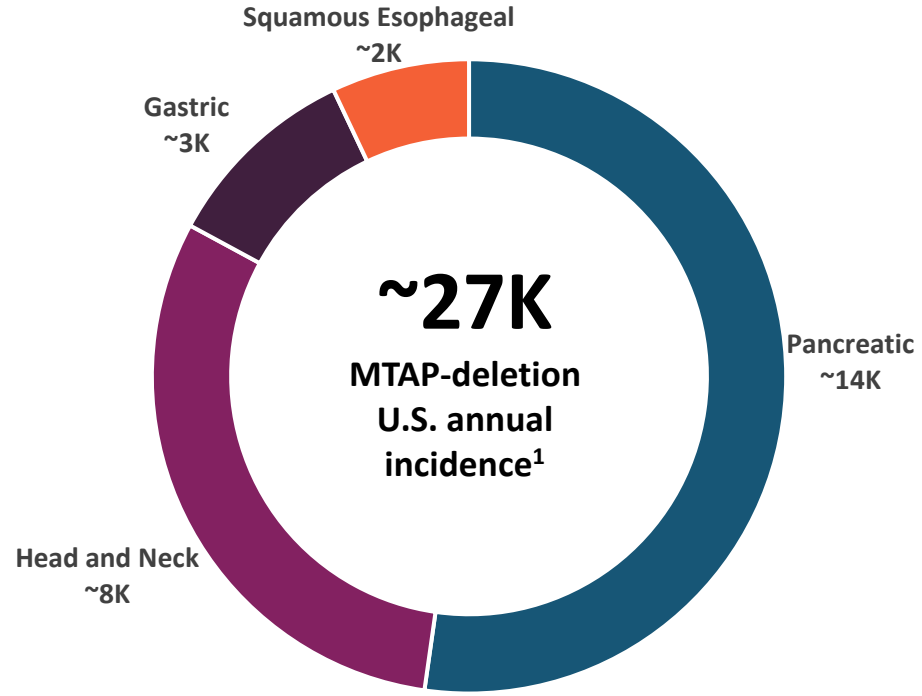
~48k U.S. Annual Incidence in MTAP-Deletion NSCLC and Urothelial Cancer

High Unmet Need: No FDA-Approved Therapies for MTAP-Deletion Solid Tumors

U.S. Annual Incidence in Priority Tumor Types



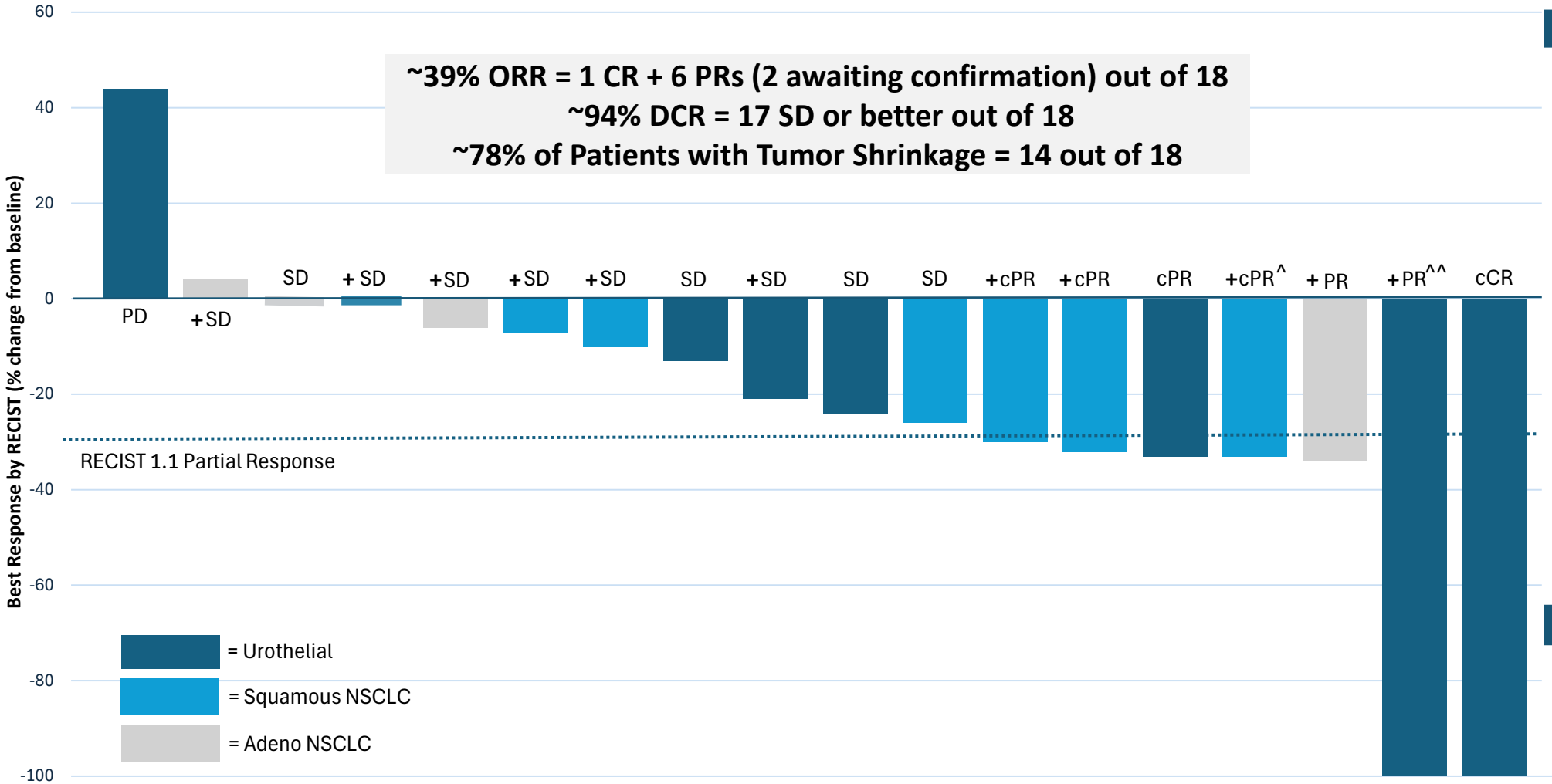
U.S. Annual Incidence in Potential Expansion Tumor Types



[1] Estimated addressable patient population based on SEER 2024 incidence and MTAP-deletion frequency from TCGA PanCancer Atlas, including frequency of 26% in urothelial, 19% in squamous NSCLC, 11% in adeno NSCLC, 21% pancreatic, 14% head and neck, 10% gastric, and 28% squamous esophageal cancers.

Preliminary IDE397 Efficacy Evaluation of 30 mg Phase 2 Expansion Dose

ORR by RECIST 1.1: 18 Evaluable NSCLC & Urothelial Cancer MTAP-Deletion Patients*



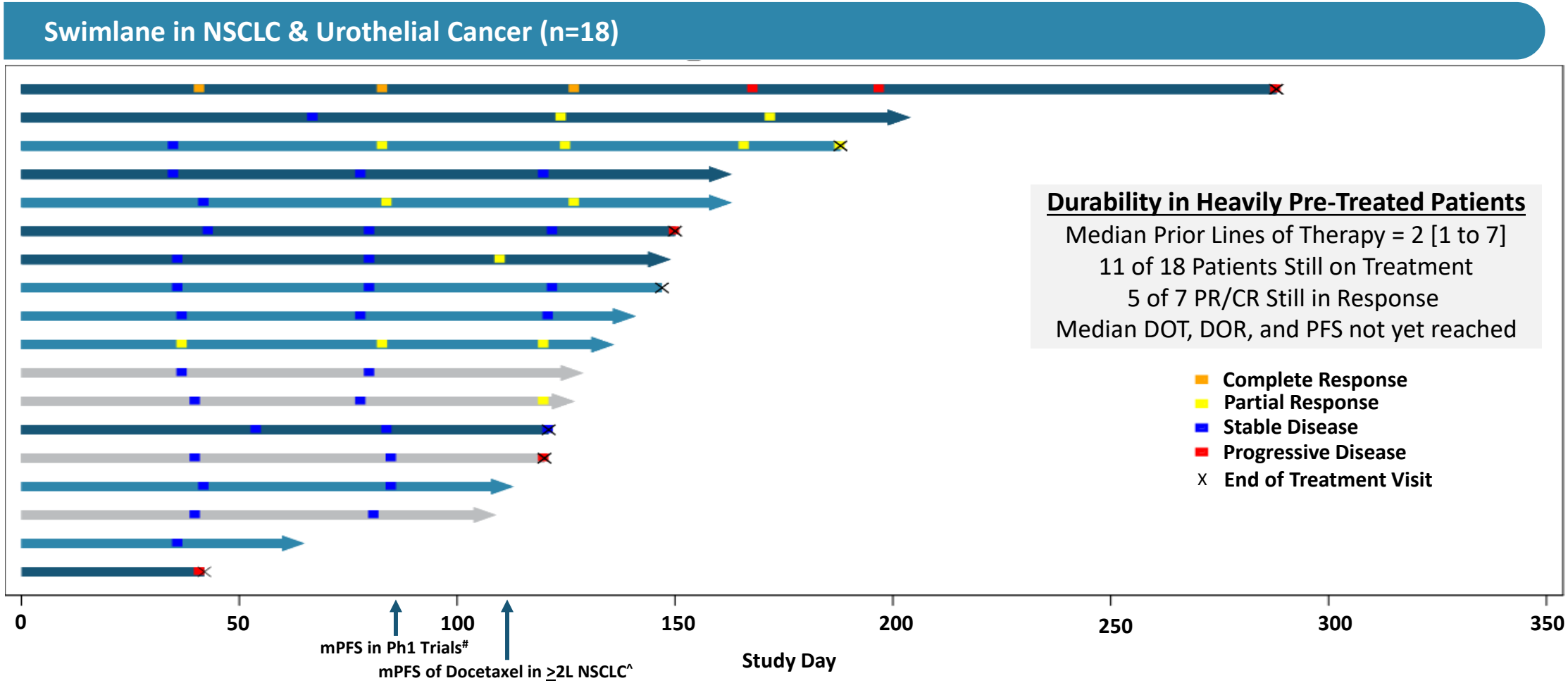
IDE397 Efficacy by RECIST 1.1*	
Evaluable Patients	18
Best Overall Response, n (%)	
Complete Response	1 (6)
Partial Response	6 (33)
Stable Disease	10 (56)
Progressive Disease	1 (6)
ORR, n (%)	7 (39)
Confirmed, n	5
Awaiting confirmation, n	2
ORR, n (%), by Tumor Type (n)	
Squamous NSCLC (7)	3 (43)
Adeno NSCLC (4)	1 (25)
Urothelial (7)	3 (43)
DCR (CR+PR+SD), n (%)	17 (94)

SoC Benchmark in NSCLC#	
Docetaxel, ORR (%)	(13)
DCR (%)	(60)

* Evaluable Patients: Treated with ≥1 cycle (21 days) of IDE397 at 30 mg expansion dose and with ≥1 post-baseline scan(s); One non-evaluable patient who discontinued due to rapid clinical progression of cancer fatigue and drug-unrelated AEs in cycle 1
^ Response evaluation by central review; ^^ Urothelial cancer patient that had a -100% tumor reduction in the target lesion at the last CT-scan assessment; + patient still on treatment as of cut-off date;
Data from an unlocked, unverified database as of June 21, 2024 data cut off; CR = Complete Response, PR = Partial Response; SD = Stable Disease; ORR = Overall Response Rate; DCR = Disease Control Rate; c = confirmed response
SoC = Standard of Care. Docetaxel ORR and DCR efficacy benchmark data in NSCLC from CodeBreaK 200, Lancet (2023) 401: 733-746; ESMO 2023: TROPION-Lung01 reported 12.8% ORR for Docetaxel in ≥2L NSCLC (n=305)

Preliminary IDE397 Efficacy Evaluation of 30 mg Phase 2 Expansion Dose

Swimlane: 18 Evaluable NSCLC and Urothelial Cancer MTAP-Deletion Patients*



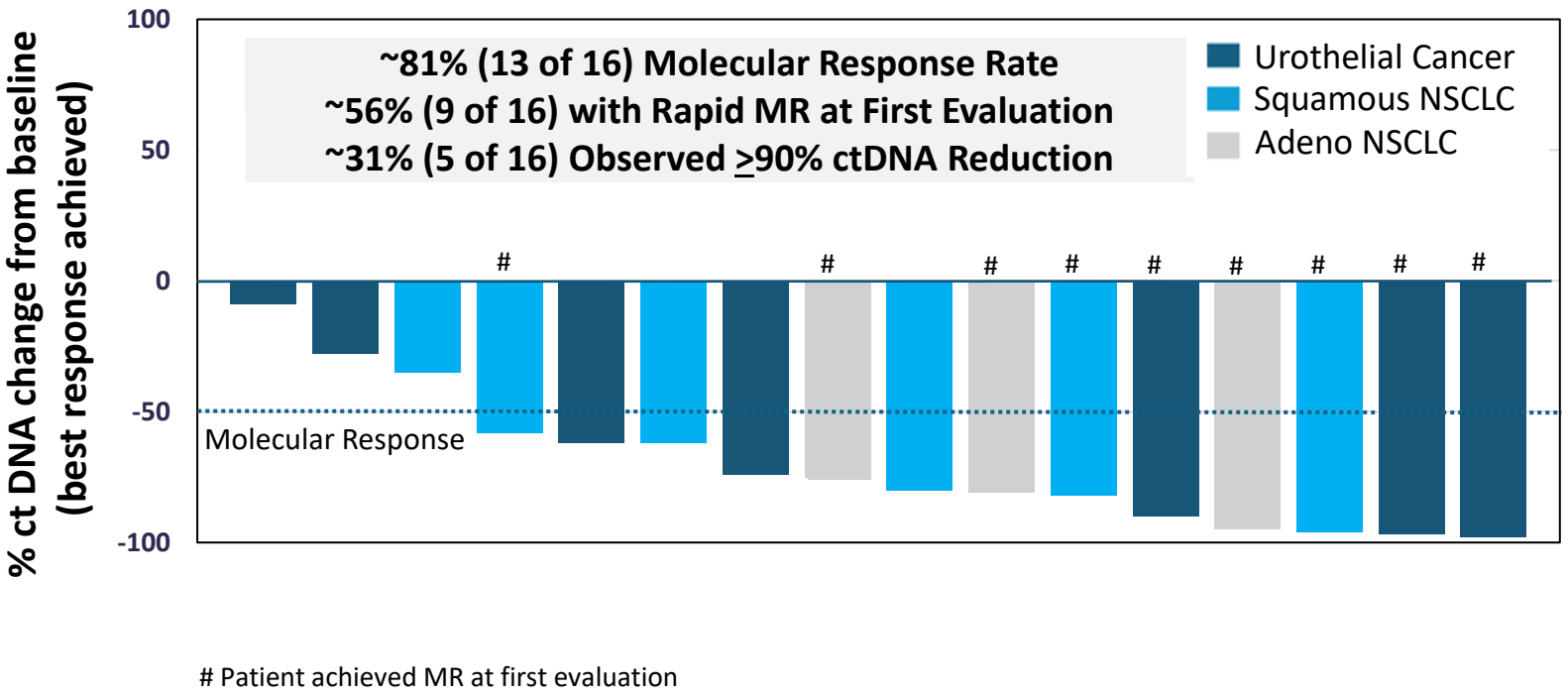
* Evaluable Patients: Treated with ≥1 cycle (21 days) of IDE397 at 30 mg expansion dose and with ≥1 post-baseline scan(s); One non-evaluable patient who discontinued due to rapid clinical progression of cancer fatigue and drug-unrelated AEs in cycle 1
Data from an unlocked, unverified database as of June 21, 2024 data cut off; CR = Complete Response, PR = Partial Response; SD = Stable Disease; ORR = Overall Response Rate; DCR = Disease Control Rate; DOT = Duration of Treatment; DOR = Duration of Response; PFS = Progression Free Survival; # Median PFS in Ph1 oncology trials ~3 months, Reference: Arkenau, HT., Olmos, D., Ang, J. et al. Clinical outcome and prognostic factors for patients treated within the context of a phase I study: the Royal Marsden Hospital experience. Br J Cancer 98, 1029–1033 (2008). The confirmed complete response urothelial patient progressed after the week 18 scan due to a drug-unrelated AE dose holiday and then restarted treatment
^ESMO 2023: TROPION-Lung01 reported mPFS of 3.7 months for Docetaxel in ≥2L NSCLC (n=305)

Preliminary IDE397 Efficacy Evaluation of 30 mg Phase 2 Expansion Dose

~81% ctDNA Molecular Response Rate in 16 NSCLC & Urothelial MTAP-Deletion Patients*

- Molecular Response (MR) analysis of 16 MTAP-deletion patients (3 adeno NSCLC, 7 urothelial, and 6 squamous NSCLC) at 30mg QD expansion dose
- ctDNA reduction observed in all subjects evaluated, including ~56% (9 of 16) with rapid MR at first evaluation and ~31% (5 of 16) with ≥90% ctDNA reduction

ctDNA Molecular Response (MR) Analysis (n=16)



Patient achieved MR at first evaluation

*Guardant Health ctDNA Infinity Platform; Molecular Response (MR): >= 50% reduction; There were several Quality Control (QC) failures of patient samples; which are not included in waterfall

IDE397 Confirmed PR by RECIST 1.1 in NSCLC at 30mg Expansion Dose

Case Report and CT-Scan Images

Baseline Characteristics:

60+ year old male with squamous NSCLC

Treatment History:

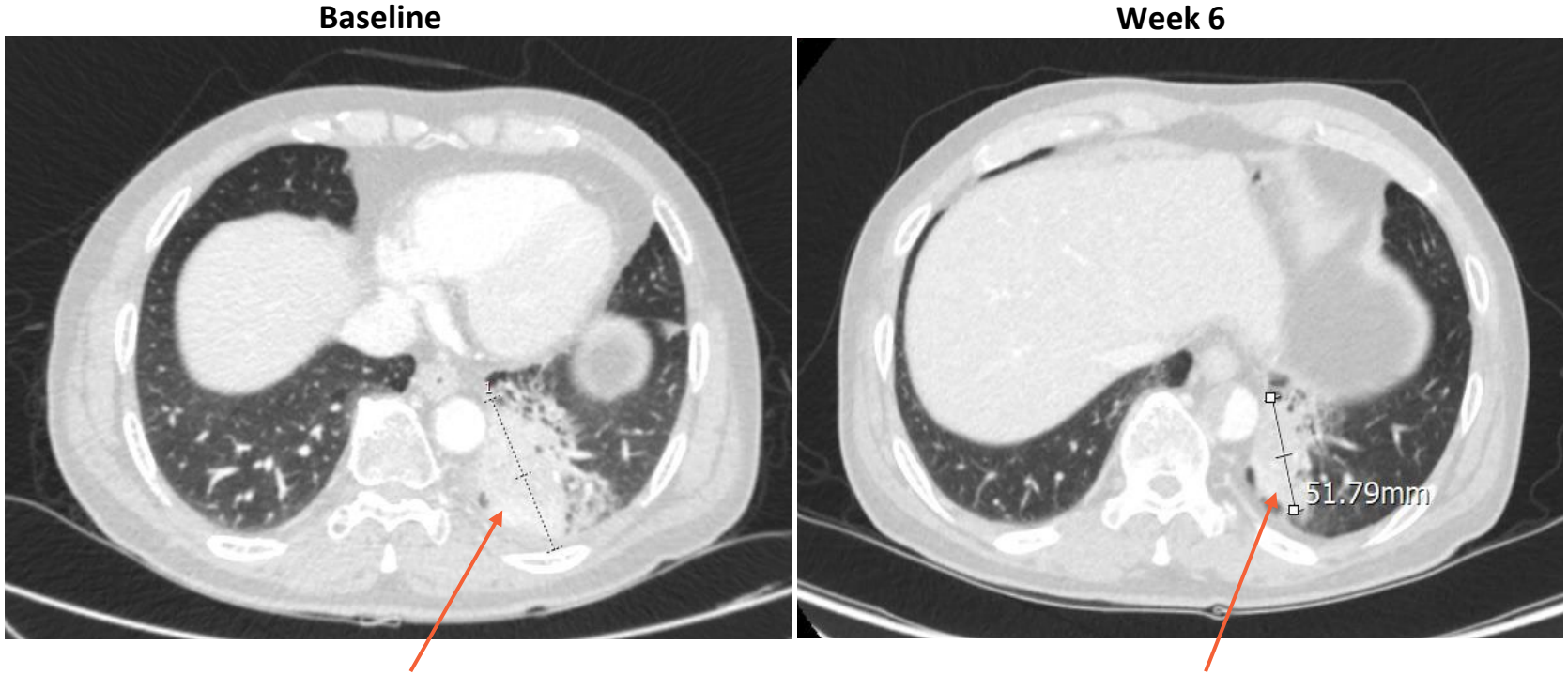
2 prior lines of therapy:

- Necitumumab + Carboplatin + Paclitaxel followed by
- Gemzar.
- Received palliative radiation therapy

RECIST 1.1 Evaluation:

Unconfirmed Partial Response by RECIST 1.1 at week 6 with -30% reduction and confirmed at week 12

NSCLC MTAP-Deletion Patient: Partial Response at Week 6 CT-Scan



IDEAYA Data (based on preliminary analysis of investigator provided images); tumor lesion reductions by investigator review, from an unlocked unverified database

IDE397 Confirmed CR by RECIST 1.1 in Urothelial at 30mg Expansion Dose

Case Report and CT-Scan Images

Baseline Characteristics:

60+ year old male with high grade urothelial carcinoma of the renal pelvis

Treatment History:

Prior therapy:

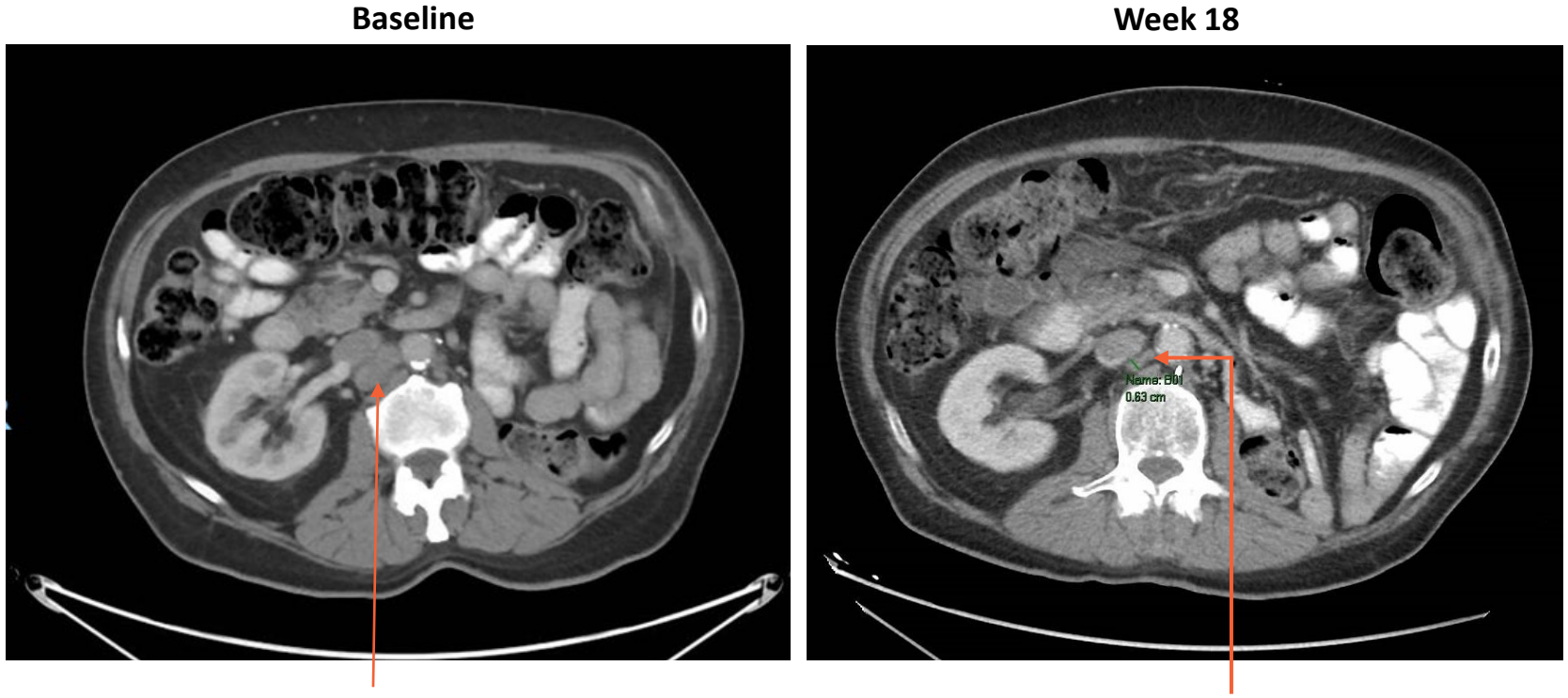
- Neo-adjuvant Gemzar/Cisplatin,
- Left Nephro-ureterectomy.
- Adjuvant Nivolumab

Recurrent disease after treatment, including immunotherapy

RECIST 1.1 Evaluation:

Unconfirmed Complete Response by RECIST 1.1 at week 6 and confirmed at week 12

Urothelial MTAP-Deletion Patient: Complete Response at Week 18 CT-Scan



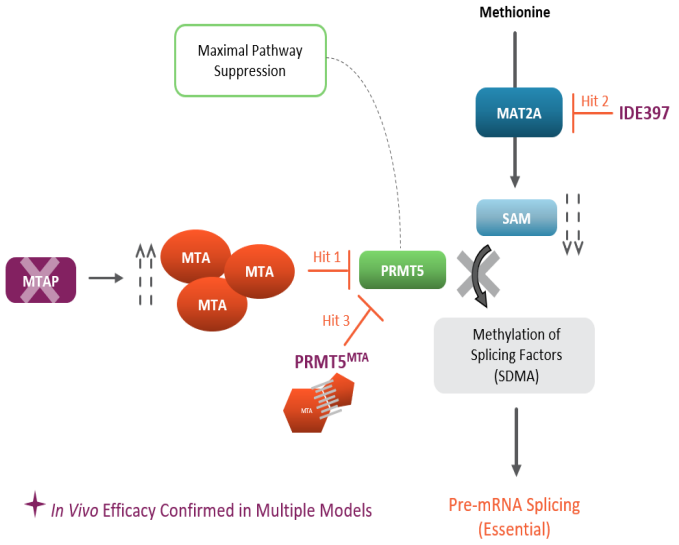
IDEAYA Data (based on preliminary analysis of investigator provided images); tumor lesion reductions by investigator review, from an unlocked unverified database

IDE397 Clinical Combination Strategy in MTAP-Deletion NSCLC

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

IDE397 + MTA-Cooperative PRMT5i

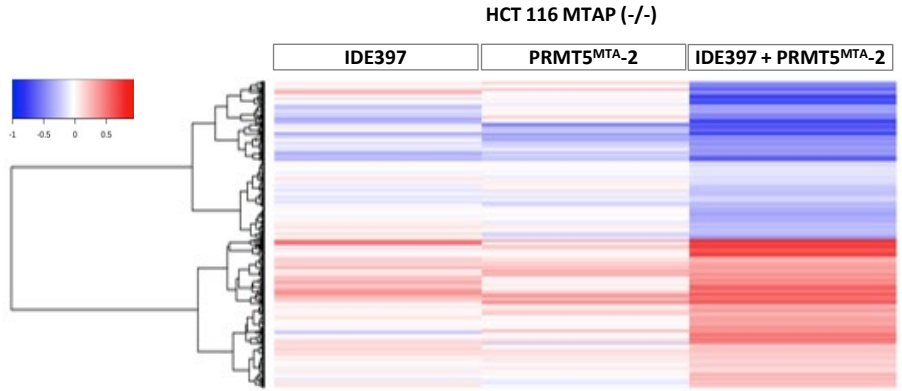
IDE397 + MTA-Cooperative PRMT5 Inhibitor enables Maximal Pathway Suppression



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

Alternative mRNA Splicing Analysis

Combination Highly Perturbs Splicing Fidelity



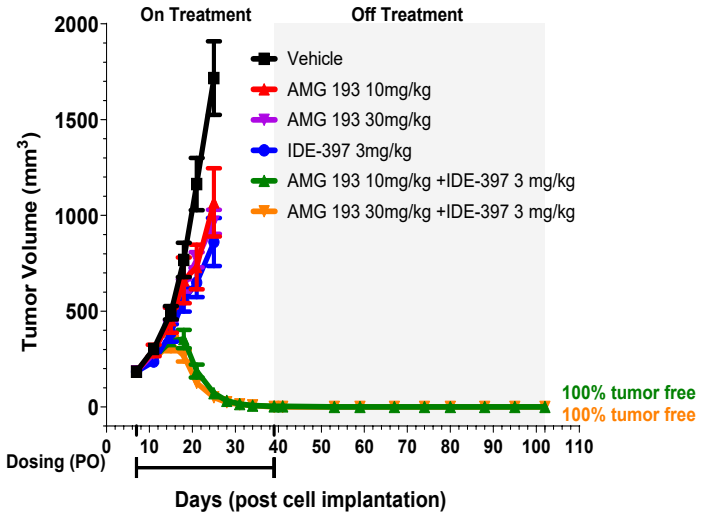
Quantitative Assessment of IDE397 / PMRT5i Effect on pre-mRNA Splicing

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

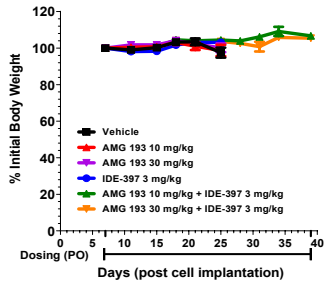
Identified as novel splice junctions or as not meeting significance criteria in monotherapy arms
Color = heatmap of Z-scored TMM-normalized counts per million

Preclinical Efficacy

Observed Durable Complete Responses



No Body Weight Loss

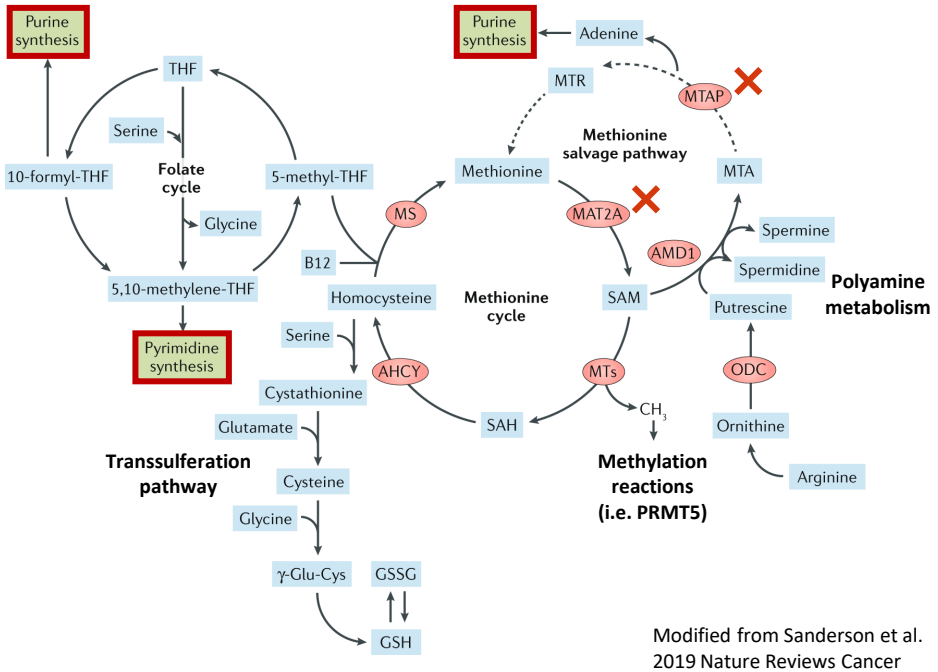


IDEAYA / Amgen Data: AACR 2023, M. Fischer et al.

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

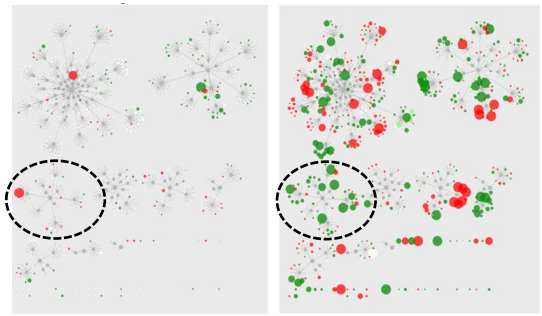


Modified from Sanderson et al. 2019 Nature Reviews Cancer

Metabolic perturbation by IDE397 selectively interacts with MTAP

Metabolite Cytoscape

Global (untargeted) metabolic profiling of MTAP^{wt} vs MTAP$^{-/-}$ +/- IDE397

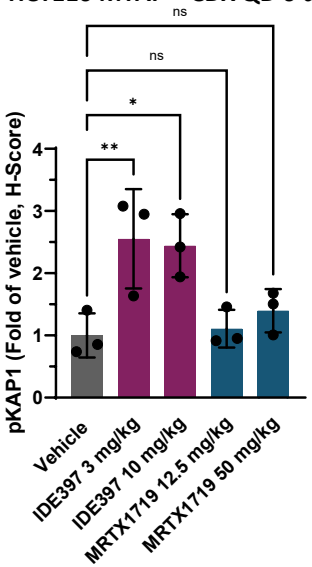


MTAP WT +/- IDE397 **MTAP$^{-/-}$ +/- IDE397**

Ovals indicate nucleotide subcluster (purine/pyrimidine); green-decrease, red-increase FDR< 0.05

IDE397 provokes DDR response in vivo

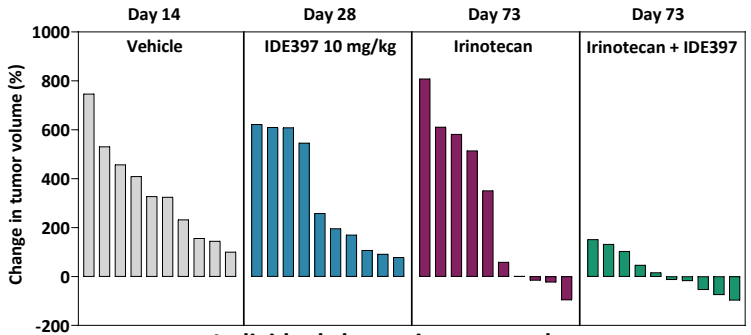
HCT116 MTAP$^{-/-}$ CDX QD 6 days



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 demonstrated monotherapy efficacy in MTAP$^{-/-}$ UC (CR observed in a patient with short DFI post platinum and CPI, other tumor reductions and molecular responses seen)

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



Individual change in tumor volume

Individual tumors measured on day of study group termination as indicated; termination timing was based on endpoint criteria for tumor volume

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 demonstrated 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

IDE397 Monotherapy Expansion in Select MTAP-Deletion Solid Tumor Types

- IDE397 RDE Monotherapy Expansion: Squamous NSCLC and Urothelial Cancer
- Focus or Additional Indication Expansion

PRMT5 Combination – Targeting Clinical PoC in MTAP-Deletion NSCLC

AMGEN

- IDE397 + AMG 193 MTA-Cooperative PRMT5i#^[1]: Expansion Focus in NSCLC
- Other Potential Indications and/or Combinations

IDE397 + AMG 193 Enrollment Ongoing

Trop2-ADC Combination – Targeting Clinical PoC in MTAP-Deletion Urothelial Cancer

GILEAD

- IDE397 + Trodelvy®*: Urothelial Cancer

IDE397 + Trodelvy® Enrollment Ongoing

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

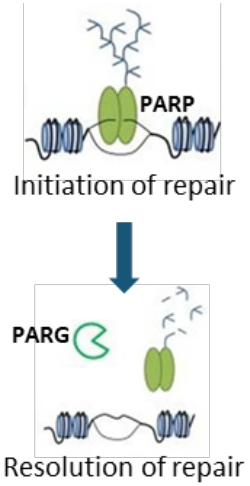
IDEAYA BIOSCIENCES

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

PARG inhibition is synthetic lethal with HRD/replication stress

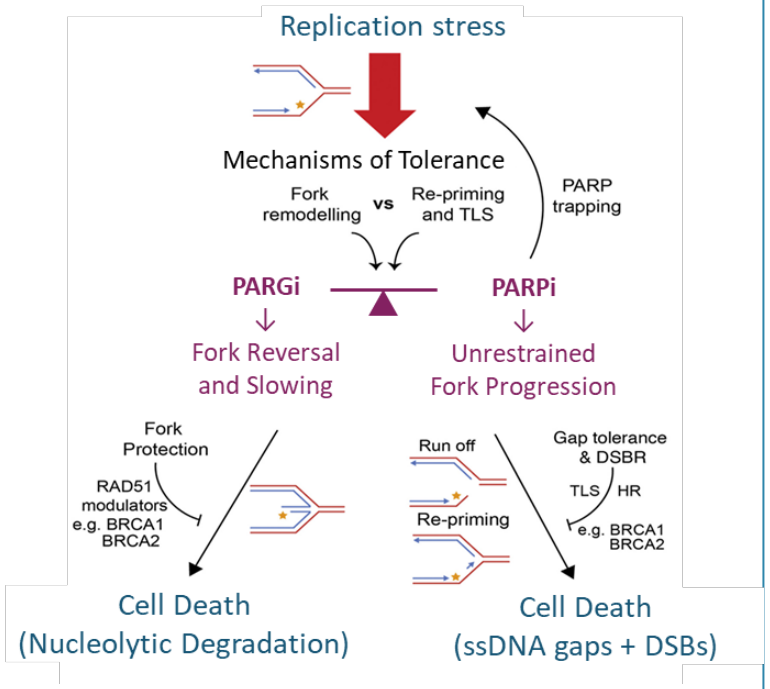
PARG Inhibition is Mechanistically Distinct from PARPi

PARG hydrolyzes PAR chains to resolve DNA repair events



Modified from James et al., ACS Chem. Biol. 2016

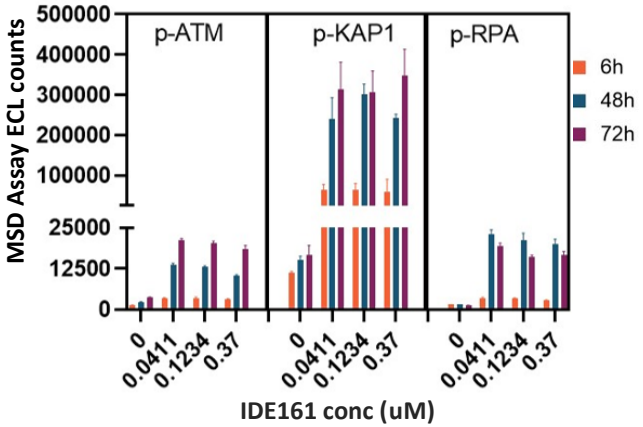
PARG activity is selectively required for tolerance to replication stress

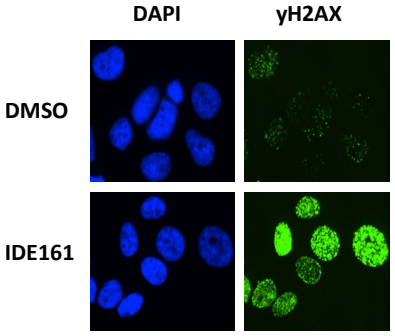


Modified from Pillay et al., Progress in Biophysics and Molecular Biology 2021

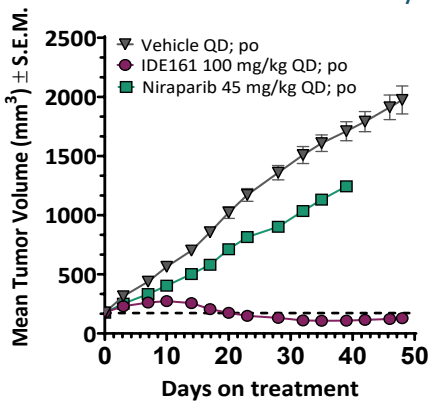
IDE161 is a potent and selective PARG inhibitor

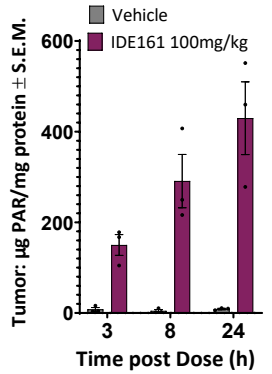
Induction of DNA damage, persistent replication stress and checkpoint activation





Robust anti-tumor activity in PARPi-refractory HRD models





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]

- Dose Escalation
- Expansion Cohort: ER+, Her2-, HRD Breast Cancer
- Expansion Cohort: HRD Tumors (EC, CRC, Prostate Cancer)
- Expansion Opportunities beyond HRD Tumors

IDE161 + KEYTRUDA® (pembrolizumab) in Endometrial Cancer

- MERCK (2) — IDE161+ KEYTRUDA® in Endometrial Cancer – Targeting H2 2024 FPI

IDE161 Combination Opportunities Validated Preclinically

- IDE161+ Rational Combination Assets

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) glycohyrdolase; PAR = poly (ADP-ribose; PBMC = peripheral blood mononuclear cells, PSA = prostate specific antigen, EC = endometrial cancer, CRC = colorectal cancer
[1] Clinicaltrials.gov: NCT05787587
[2] 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

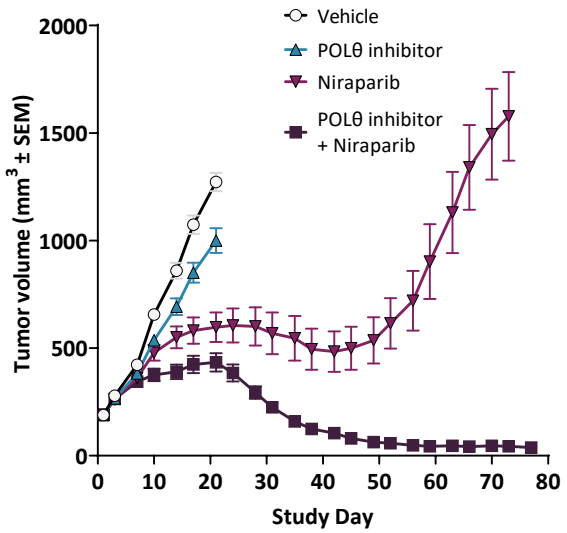
IDEAYA BIOSCIENCES

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

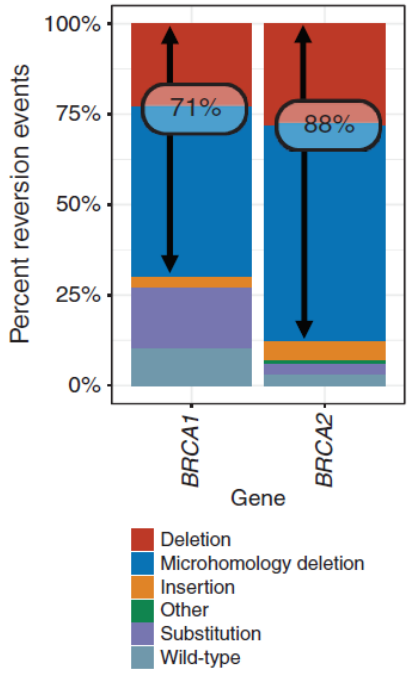


Observed Deep and Durable Responses in Multiple Xenograft Models

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 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	Prevent PARPi Resistance	Overcome PARPi Resistance

Potential Clinical Opportunities

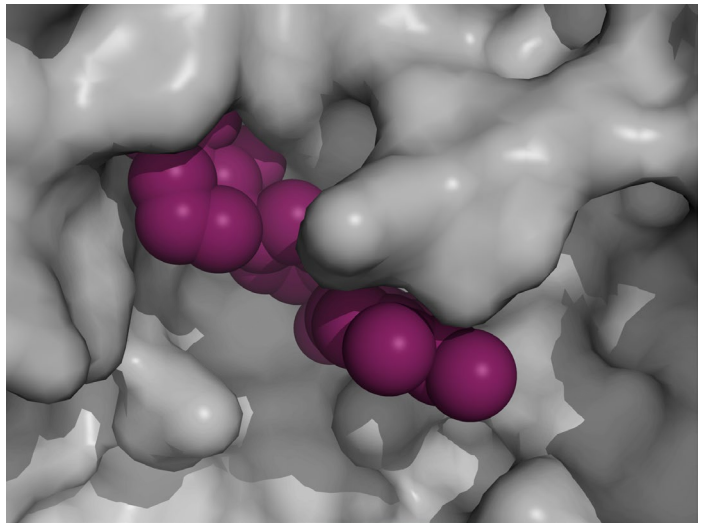
GSK Strategic Partnership: Global Royalties with GSK covering all Costs, ~$1B Milestones, incl up to $20M Preclinical / Ph1 Clinical Potential Combination with GSK's Zejula™, a PARP Inhibitor

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

IND-Filing and Multiple Potential First-in-Class Development Candidates (DCs) Targeted in H2 2024

WRN Helicase

Nominated Werner Helicase Development Candidate

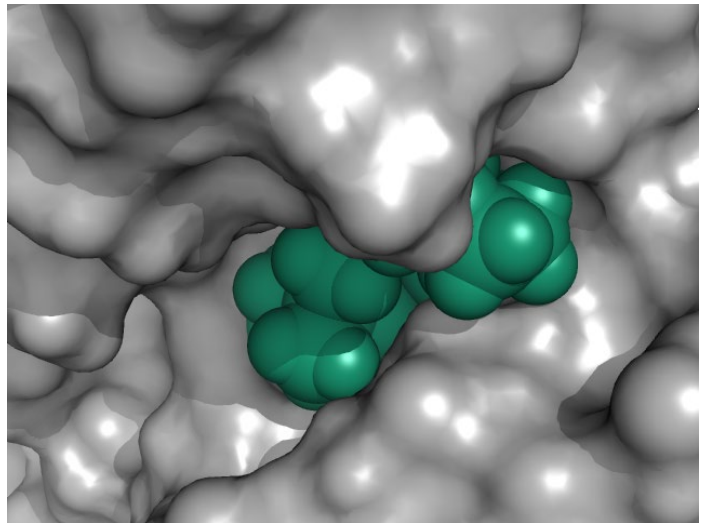


Targeting IND Submission in H2 2024*
MSI-High Tumor Agnostic

*Pursuant to GSK Collaboration

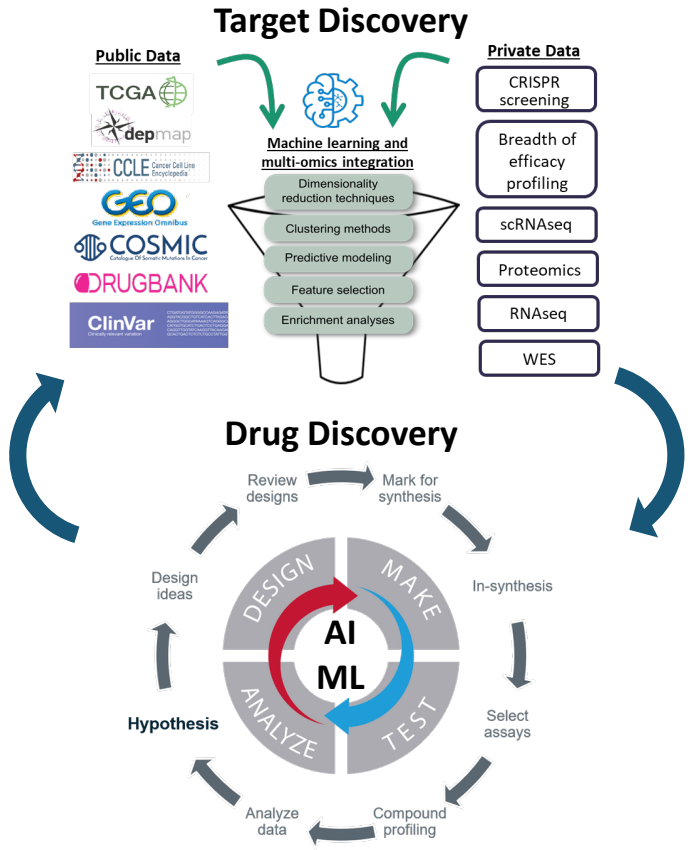
Multi-Pronged Strategy in MTAP$^{-/-}$

Next Generation Programs



Enabling wholly-owned rational combination with IDE397

AI/ML-Enabled IND-Engine



Targeting multiple DCs in H2 2024

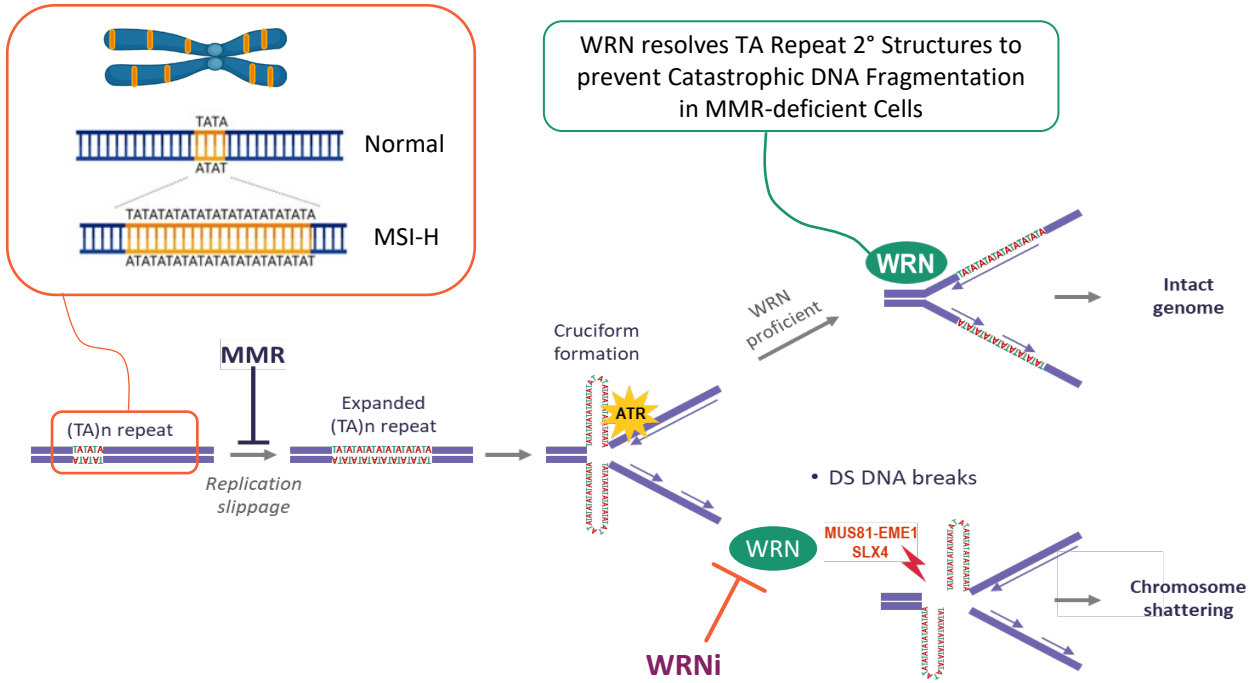
Werner Helicase is Synthetic Lethal with Microsatellite Instability

Targeting IND Submission in H2 2024

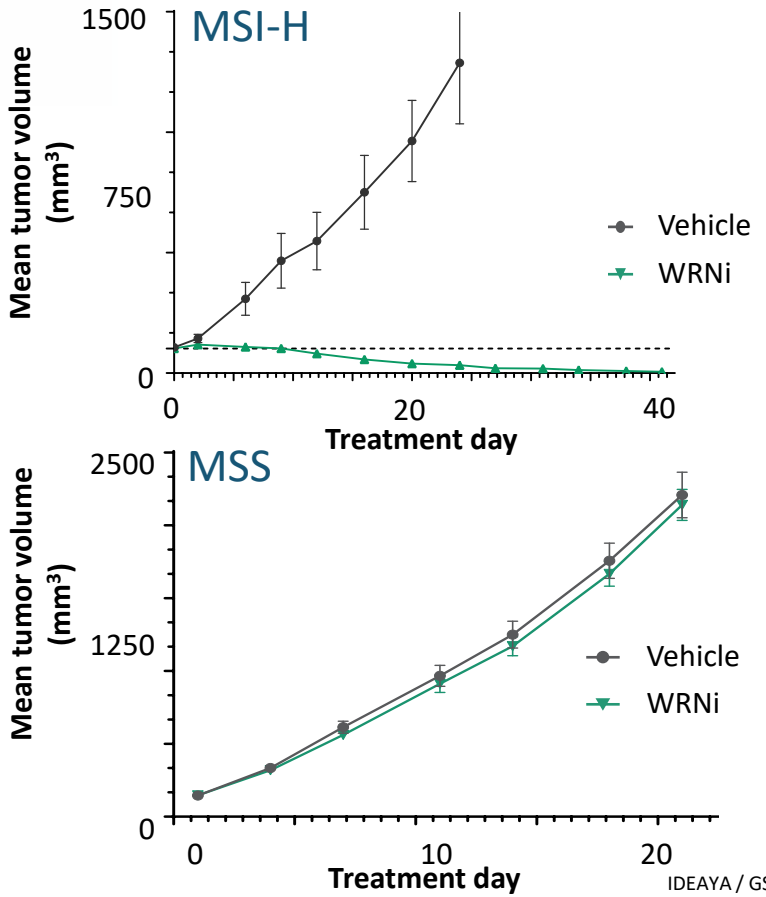
Werner Helicase Inhibitors Phenocopy Genetic SL in MSI-High Cancers

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

Building a Fully-Integrated Biotech in Precision Medicine Oncology

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

CLINICAL PROGRAMS	DEVELOPMENT CANDIDATES	PRECLINICAL
Ph 2/3 – Darovasertib [1] Ph 2 – IDE397 (MAT2A) [1] Ph 1 – IDE161 (PARG) [1] Ph 1 – GSK101 (Pol Theta Helicase) [2]	Werner DC – Targeting H2 2024 IND [2]	Targeting Multiple DCs in H2 2024, including in MTAP and potential first-in-class in KAT6 pathway
4 Clinical Programs	5 Clinical Programs	≥7 Clinical Programs

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 H2 2024, including in MTAP and KAT6 pathway

Strong Balance Sheet with ~$978M[3] and opportunity for milestones with cash runway to 2028

Pharma Collaborations include combinations with Pfizer, Amgen, Gilead, Merck, and GSK partnership with ~$2 billion[2] in potential milestones

(1) Clinical Trial Collaboration and Supply Agreements, independently with Pfizer (Darovasertib + Crizotinib), Amgen (IDE397 + AMG193), Gilead (IDE397 + Trodelvy®), 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 $941.4M cash, cash equivalents and marketable securities as of March 31, 2024, plus pro forma $36.5M estimated net proceeds from sales of common stock through at-the-market offerings in April 2024