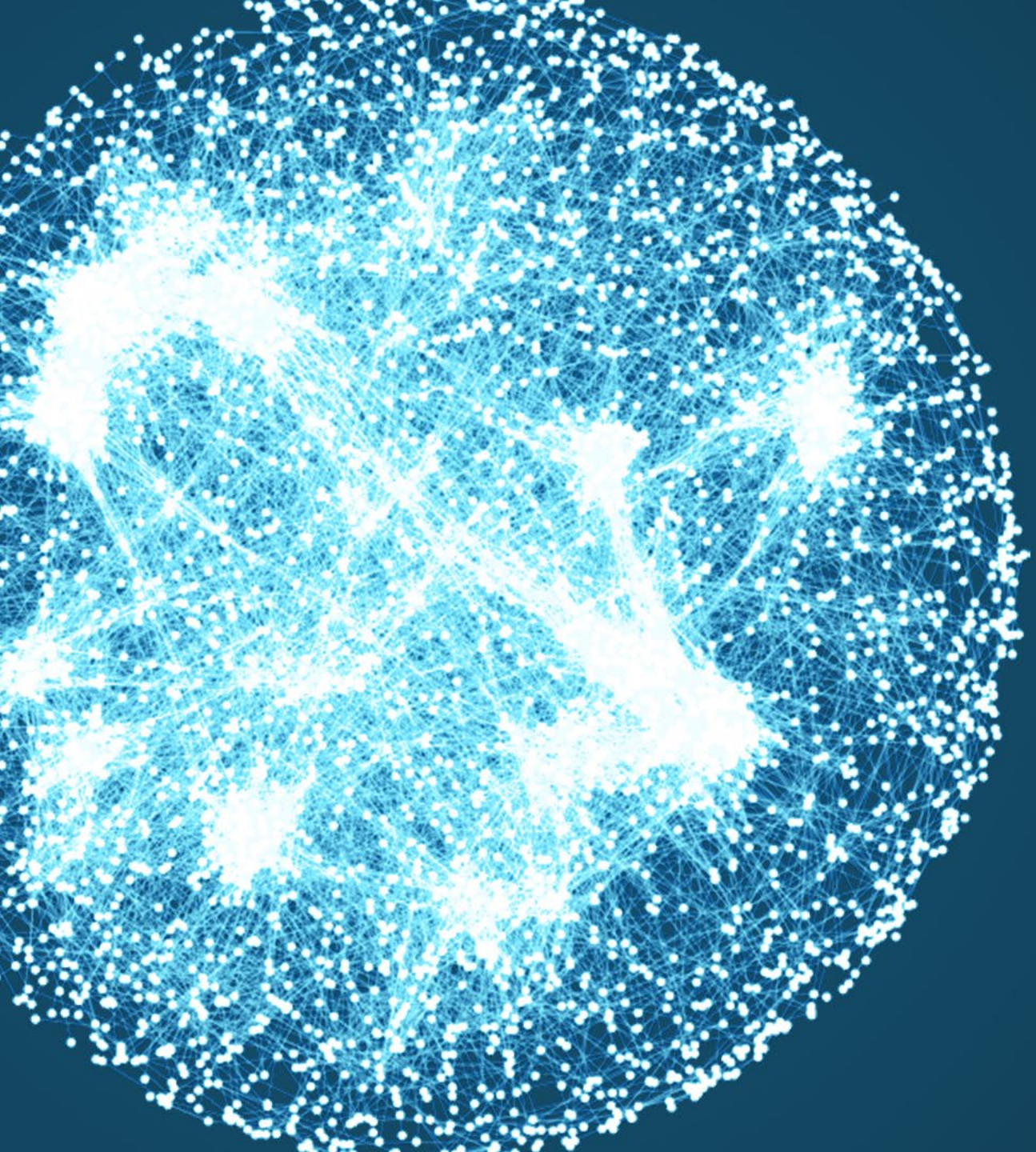


IDEAYA Investor R&D Day
December 4, 2023
NASDAQ: **IDYA**

IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicine

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 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; 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, 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, 2022, and any current and periodic reports filed thereafter. Except as required by law, the Company assumes no obligation and does not intend to update these forward-looking statements or to conform these statements to actual results or to changes in the Company's expectations.

This presentation concerns anticipated products that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). It is currently limited by Federal law to investigational use, and no representation is made as to its safety or effectiveness for the purposes for which it is being investigated.

IDEAYA Investor R&D Day

Welcome and Introduction

Yujiro S. Hata
IDEAYA Biosciences
President and Chief Executive Officer

IDEAYA Investor R&D Day

Welcome to our Participants and Guest Speakers

Timothy Yap, MBBS, FRCP, PhD, BSc (Hons), PgDip (Onc)

M.D. Anderson Cancer Center
Vice President, Head of Clinical Development, Therapeutics Discovery Division
Professor, Department of Investigational Cancer (Phase 1 Program)
Professor, Department of Thoracic/Head & Neck Medical Oncology
Associate Director of Translational Research, Khalifa Institute for Personalized Cancer Therapy

Ramon Kemp, Ph.D.

GSK
Vice President
Head, Oncology EDL/Interim Head, Oncology MDL

IDEAYA Investor R&D Day

Agenda Topics

The Synthetic Lethality Paradigm (Yujiro Hata, CEO)

IDEAYA Vision, Strategy and Pipeline

Computational Drug Discovery (Mike White, CSO)

Overview of Current Approach at IDEAYA

IDE161 Clinical Data and Program Updates (Tim Yap, MD Anderson)

Emerging Therapeutic Opportunities for MTAP-deletion (Mike White, CSO; Darrin Beaupre, CMO)

IDEAYA's multiple-pronged strategy

Dual Synthetic Lethal Strategy for MAT2A-PRMT5 Combination Therapy

IDE397-Trodelvy Clinical Combination

IDEAYA and GSK Partnership (Ramon Kemp, GSK)

Pol Theta Helicase and Werner Helicase Programs

Closing Remarks and Analyst Q&A (Yujiro Hata, CEO; Darrin Beaupre, CMO; Mike White, CSO)

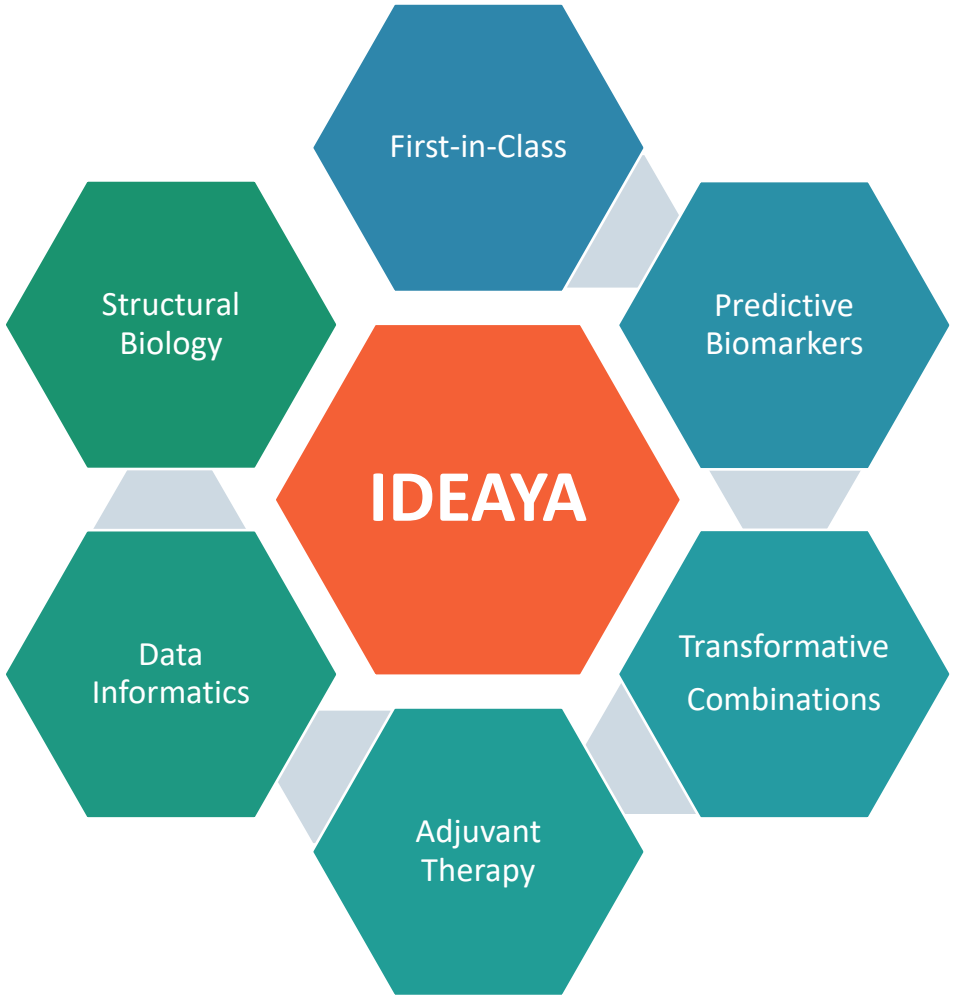
The Synthetic Lethality Paradigm

IDEAYA Vision, Strategy and Pipeline

Yujiro S. Hata
IDEAYA Biosciences
President and Chief Executive Officer

IDEAYA Vision & Strategy

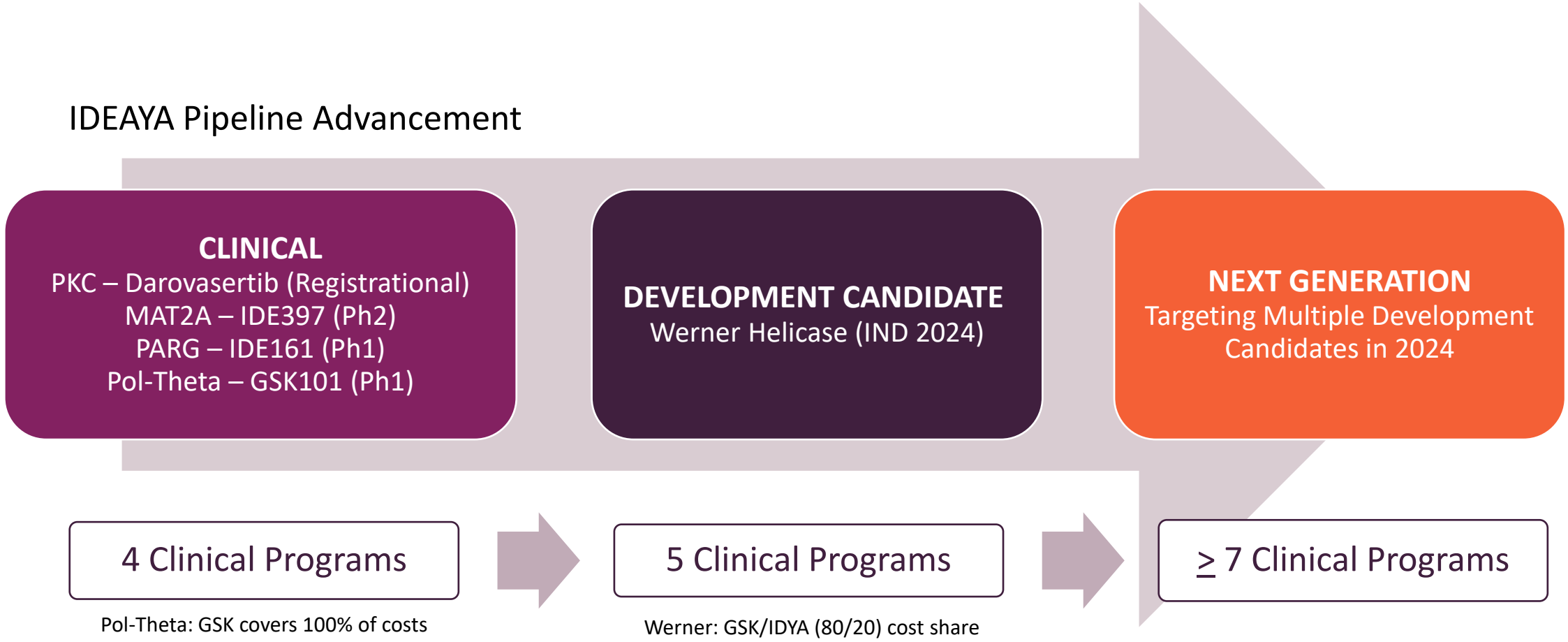
Improving Lives through Transformative Precision Medicines



Building the leading
Precision Medicine Oncology Company

IDEAYA Precision Medicine Oncology Pipeline

Targeting ≥7 First-in-Class Clinical Programs under our Cash Runway



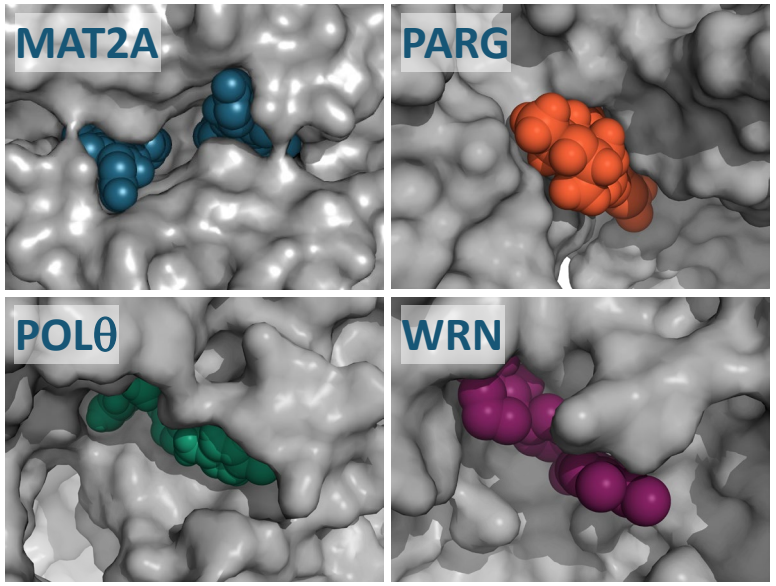
Computational Drug Discovery

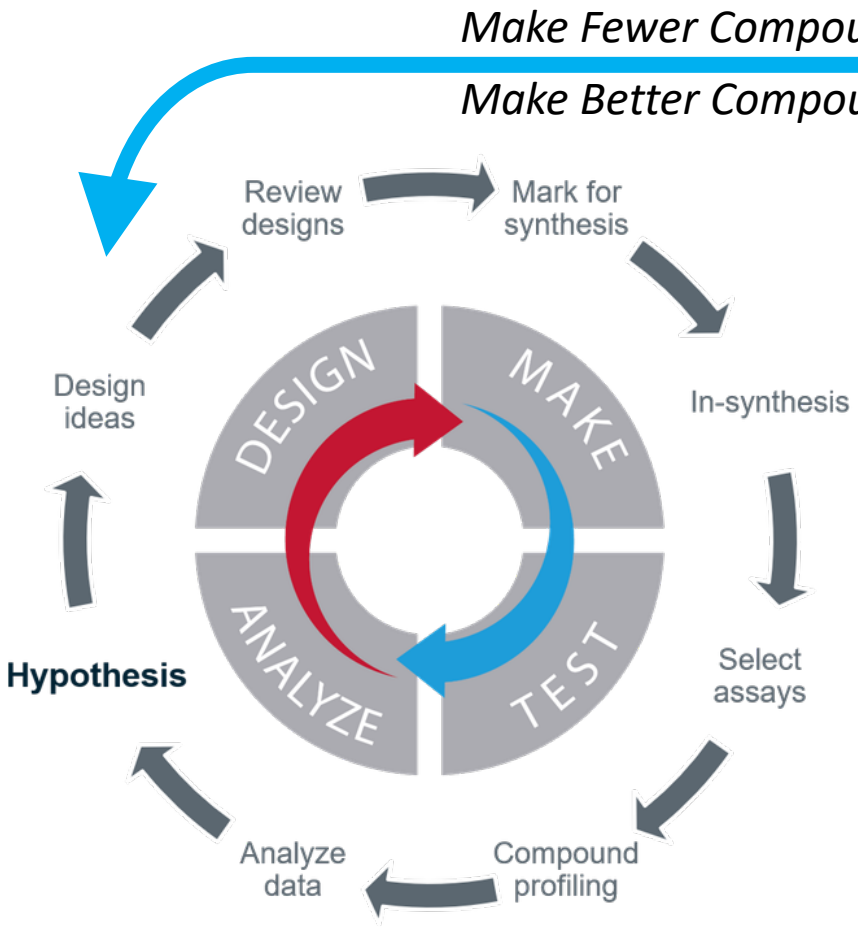
Maximizing efficiency and quality in pursuit of first-in-class NCEs

Michael White, Ph.D.
IDEAYA Biosciences
Chief Scientific Officer

Computer-assisted drug discovery at IDEAYA

Our focus is time to IND in the first-in-class arena





Accurate Predictive Models

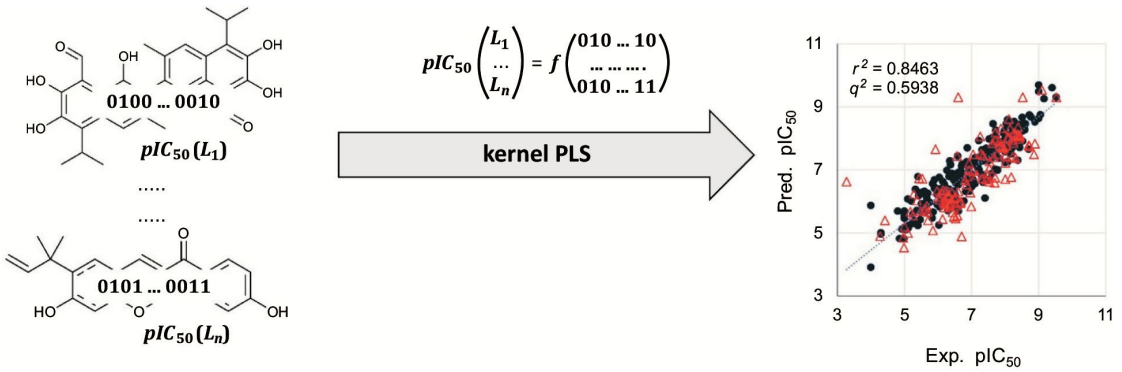
1. Solubility
2. Metabolic Stability
3. Activity

Enhance ROI by reducing time and increasing quality

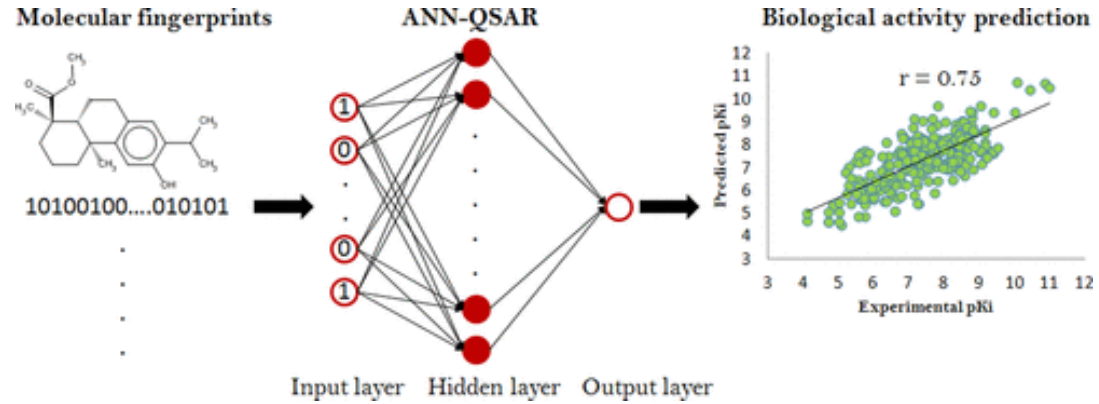
Drug-Like Property Predictions Enabled by HARMONY™ ML Drive Chemical Synthesis Prioritization

High Quality Compounds from fewer cycles

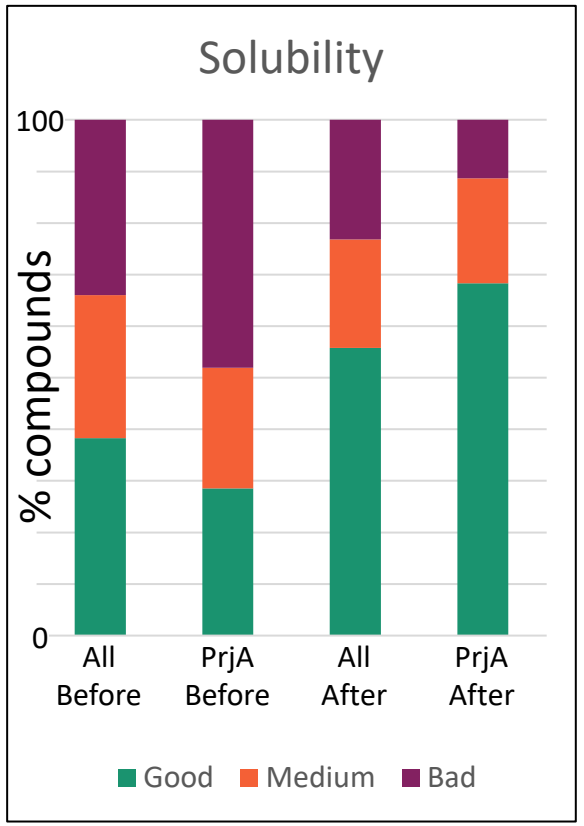
Partial least squares (then)

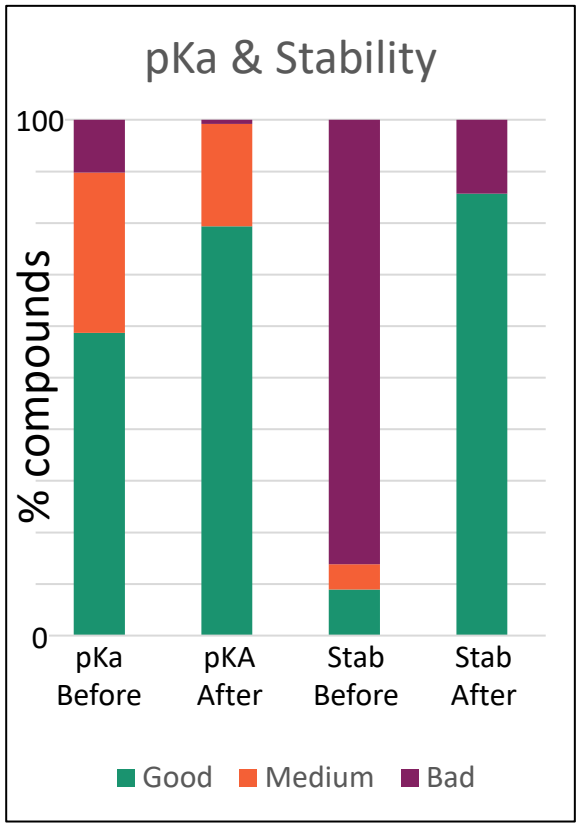


Deep neural network (now)



Impact on IDEAYA programs





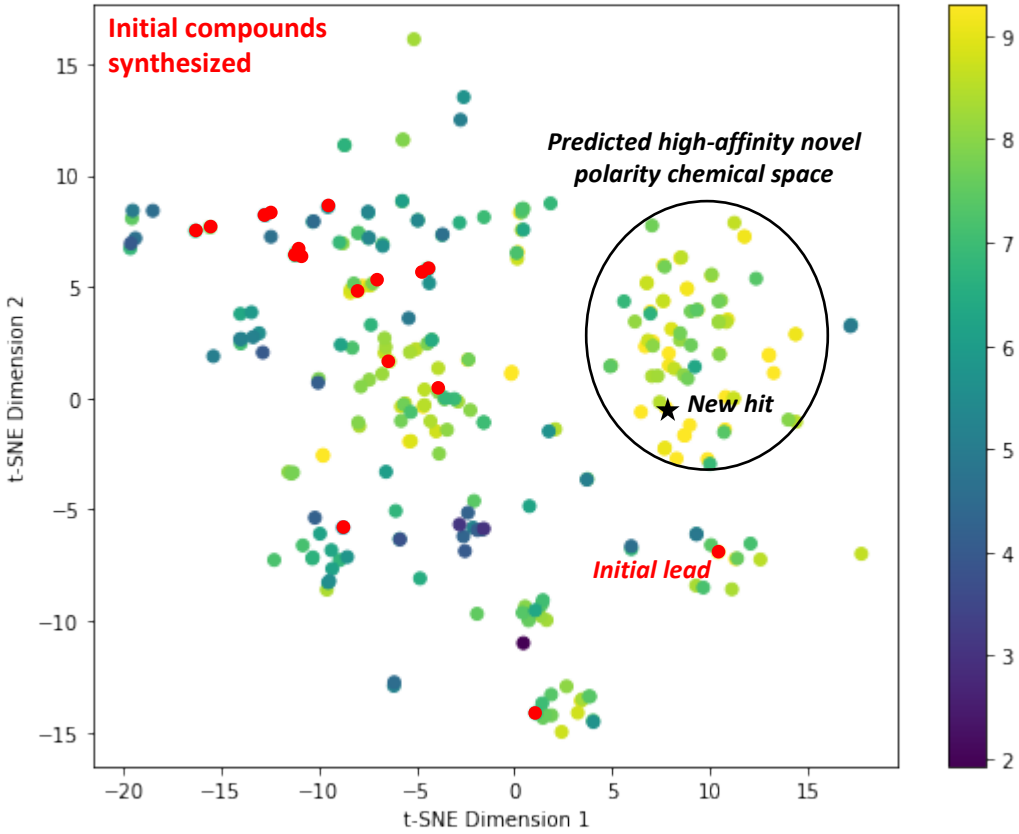
Lett. Drug Des. Discov. 17:1206–1215; *Mol. Pharmaceutics* 9:2912–2923

CONFIDENTIAL

At-Scale Free Energy Perturbation Opens New Windows in Chemical Space

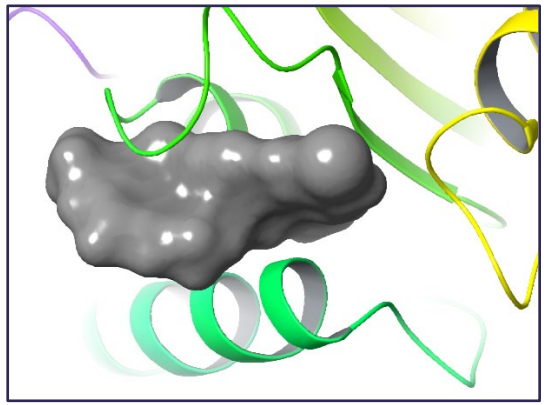
Fully leverage physics-based methods to enable creative design solutions

Exploration of diverse cores & R-groups



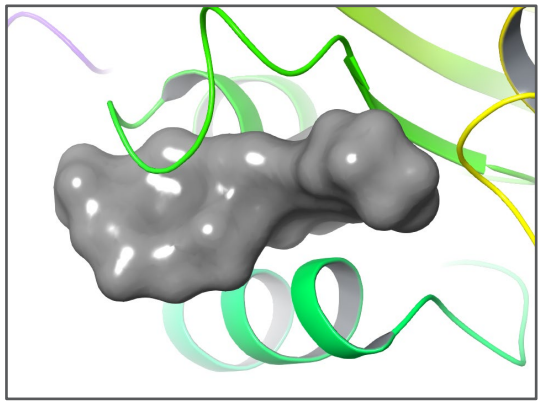
t-SNE dimensions 1 and 2 are dimensionality-reduced representations of the 2048-bit molecular fingerprint

Initial lead



- ✓ Maintains affinity
- ✓ Improves Phys-Chem
- ✓ Reduces PXR activation

New Hit

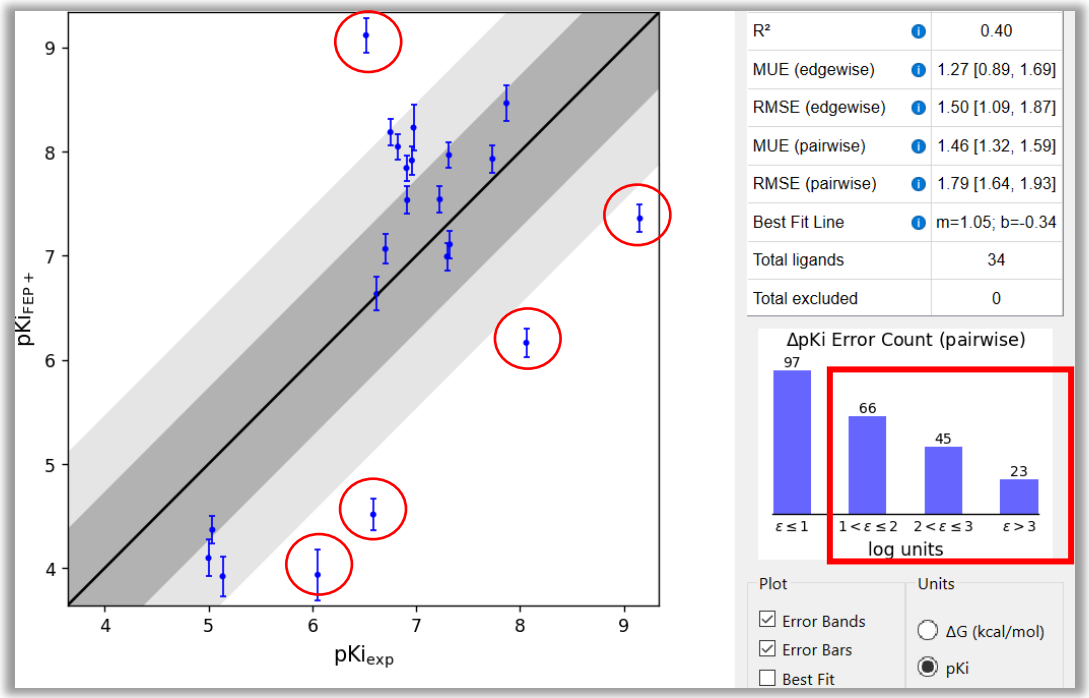


Compound	Target IC_{50} (nM)	Ksol (µM)	LM (ER%)	PXR (% activation at 10 µM)	LogD
IDC-A	1.4	9	61	616	2.7
IDC-B	24.2	260	<21	18	1.1
IDC-C	1	287	33	24	1.9

ML-Enabled FEP Parameter Optimization Can Solve Key Design Challenges

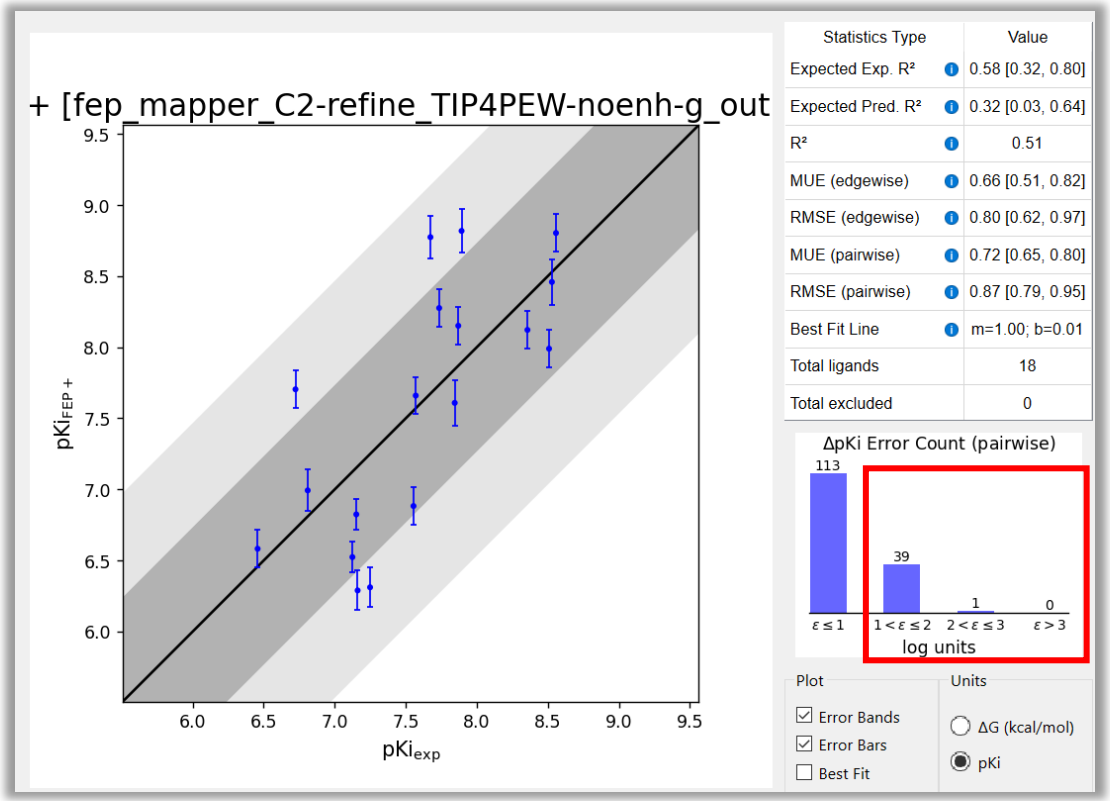
An example from our new MTAP program

Before



Many predictions off by 2 or more log units

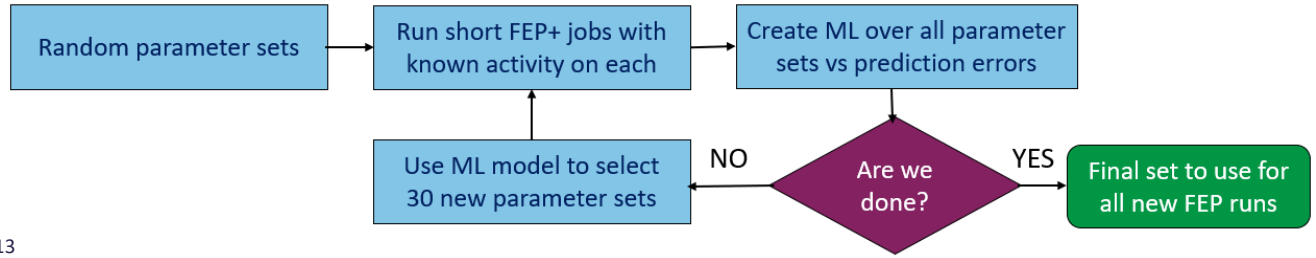
After



All predictions within 2 and most within 1 log unit

- water model
- important residues to enhance sampling (Heat)
- XRAY structures
- equilibration time (Molecular Dynamics)
- enhance sampling of dihedrals (or not)

Train FEP on the physics of the system



IDE161 Clinical Data and Program Update

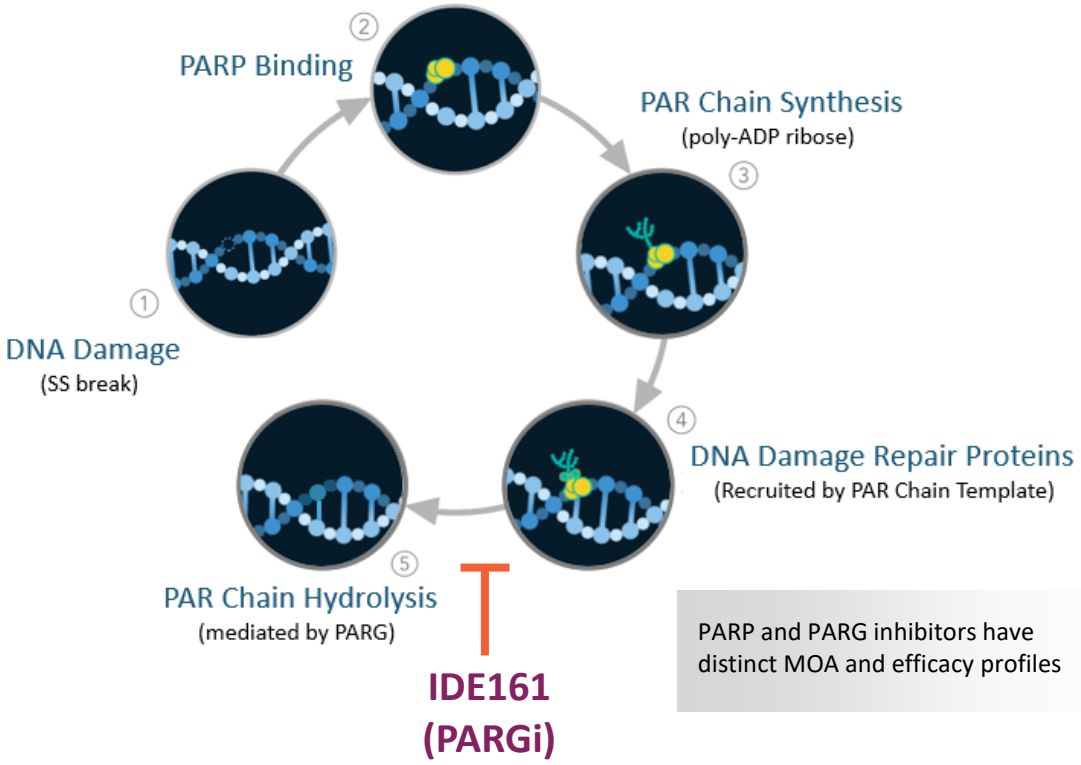
Timothy Yap, M.D.

M.D. Anderson Cancer Center
Vice President, Head of Clinical Development, Therapeutics Discovery Division
Professor, Department of Investigational Cancer (Phase 1 Program)
Professor, Department of Thoracic/Head & Neck Medical Oncology
Associate Director of Translational Research, Khalifa Institute for Personalized Cancer Therapy

Poly (ADP-ribose) Glycohydrolase (PARG)

Mechanistically-Differentiated Target in a Clinically Validated Pathway

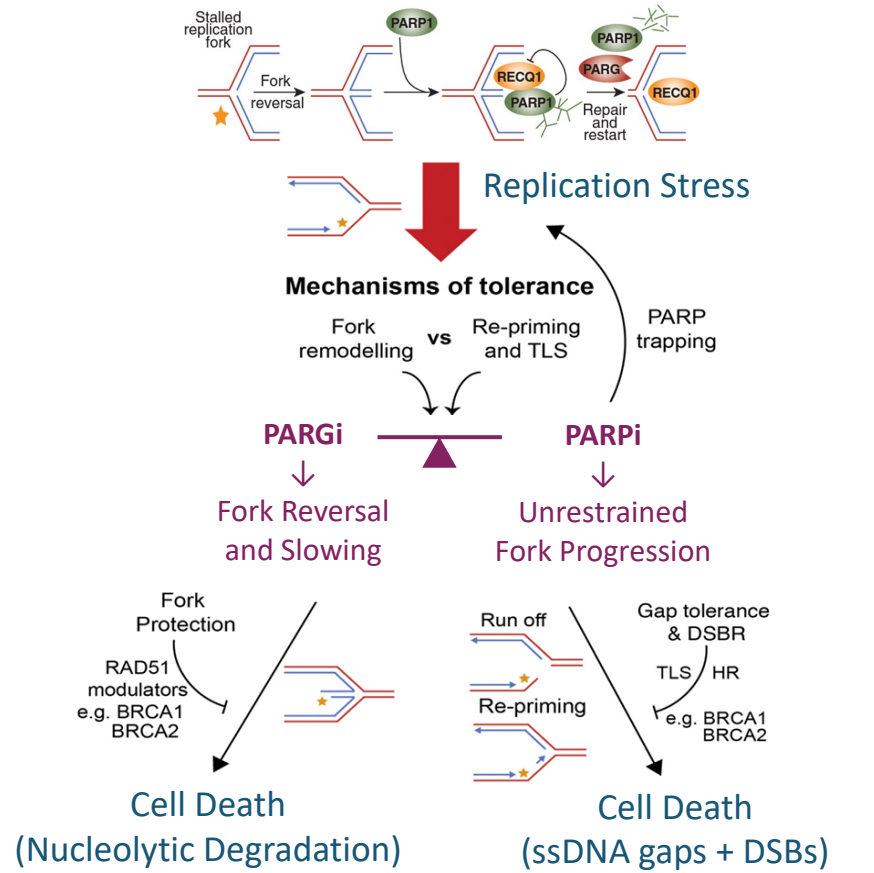
PARG Activity is required to resolve DNA Repair



PARP and PARG inhibitors have distinct MOA and efficacy profiles

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

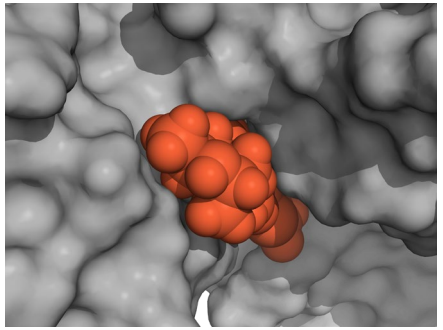
PARG Inhibition is Mechanistically Distinct from PARPi



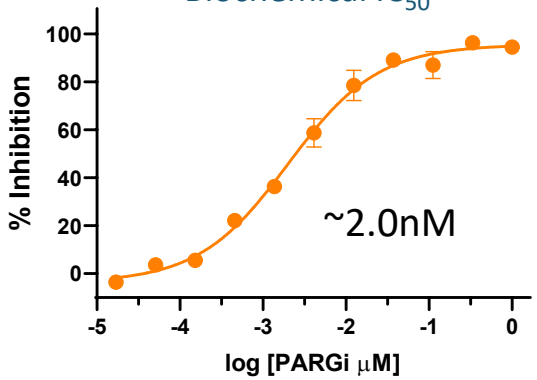
Pillay et al., Progress in Biophysics and Molecular Biology 2021; McDermott et al., Cancer Cell 2019; Zeman and Cimprich, Nature Cell Biology 2014

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

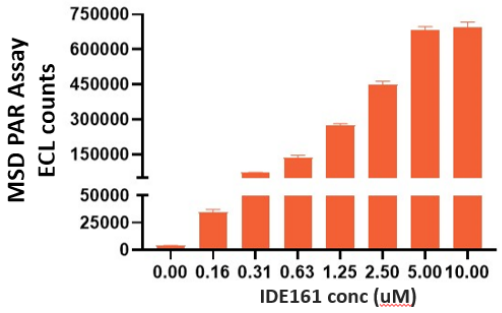
IDE161 Profile: Potent, Selective with Favorable Properties



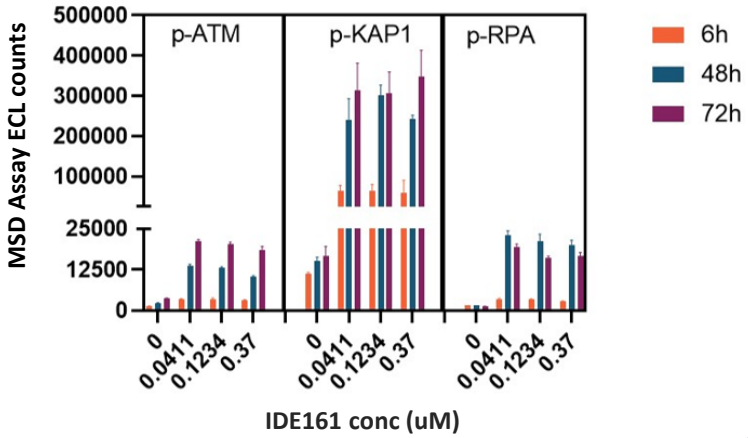
Biochemical IC_{50}



IDE161-induced Cellular PAR Accumulation



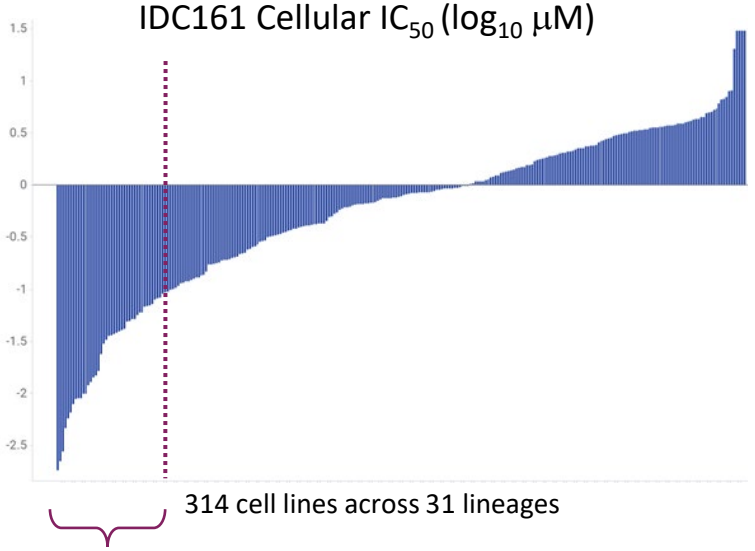
IDE161-induced DNA Damage Response



IDE161 Sensitivity Profile in Cell Panel

Cellular response profiles reveal mechanistic associations with PARGi sensitivity

IDC161 Cellular IC_{50} (log_{10} μM)



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

IDEAYA Data: AACR 2023 D. Munoz et al.

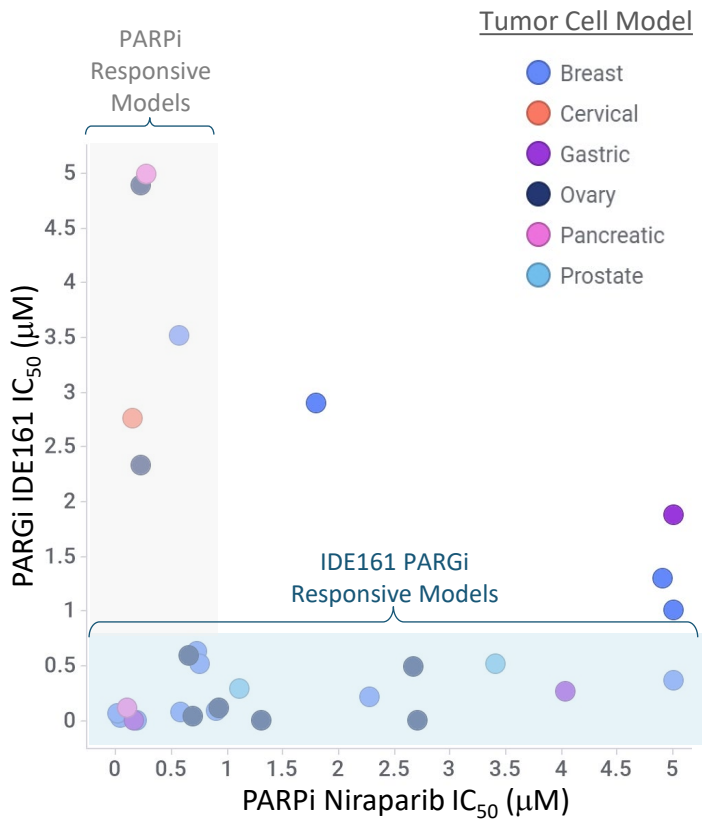
PARG = poly (ADP-ribose) glycohyrdolase; PAR = poly (ADP-ribose); DDR = DNA Damage Response; HRD = Homologous Recombination Deficiency; BER = Base Excision Repair

IDE161 is Active and Well-Tolerated in HRD ER+ HER2- Breast Cancer Models

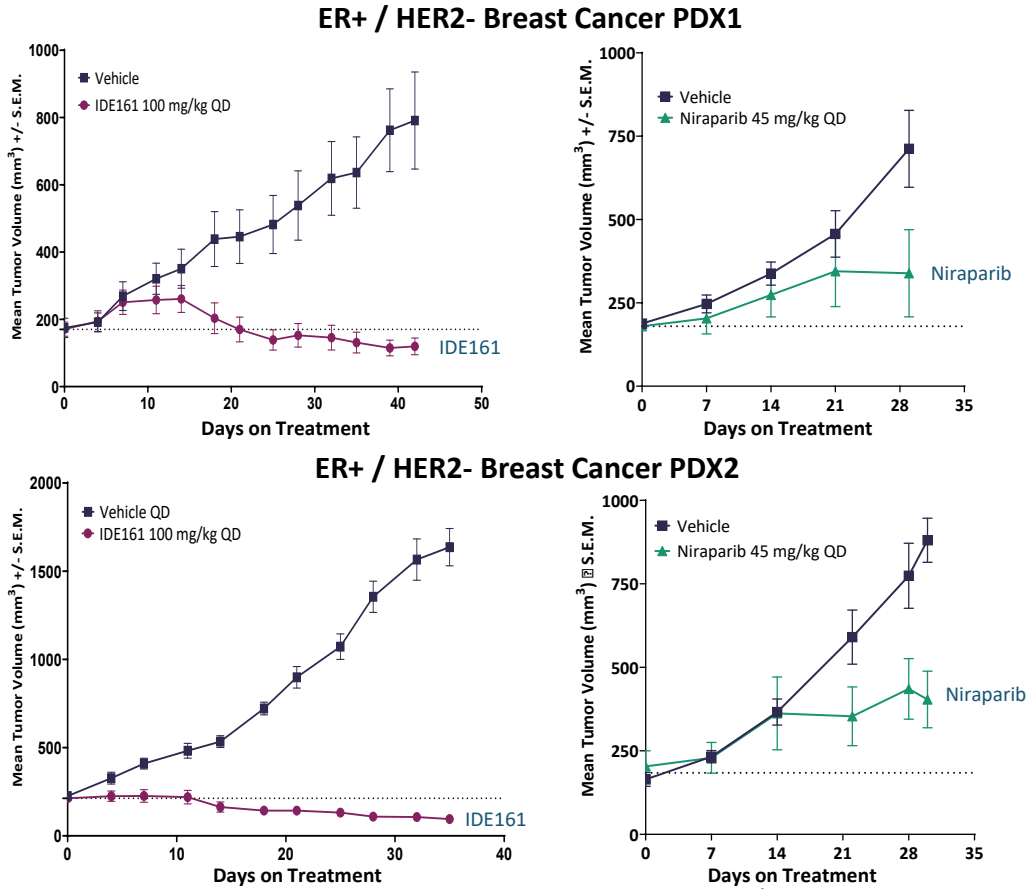
Observed PARG inhibitor Activity is Distinct from PARP Inhibition

IDE161 Selective Sensitivity vs PARPi

HRD cell lines are selectively sensitive to IDE161 versus PARPi



Regression in BRCA-altered Breast Cancer PDX Models



IDEAYA Data: 2023 AACR, D. Munoz et al.

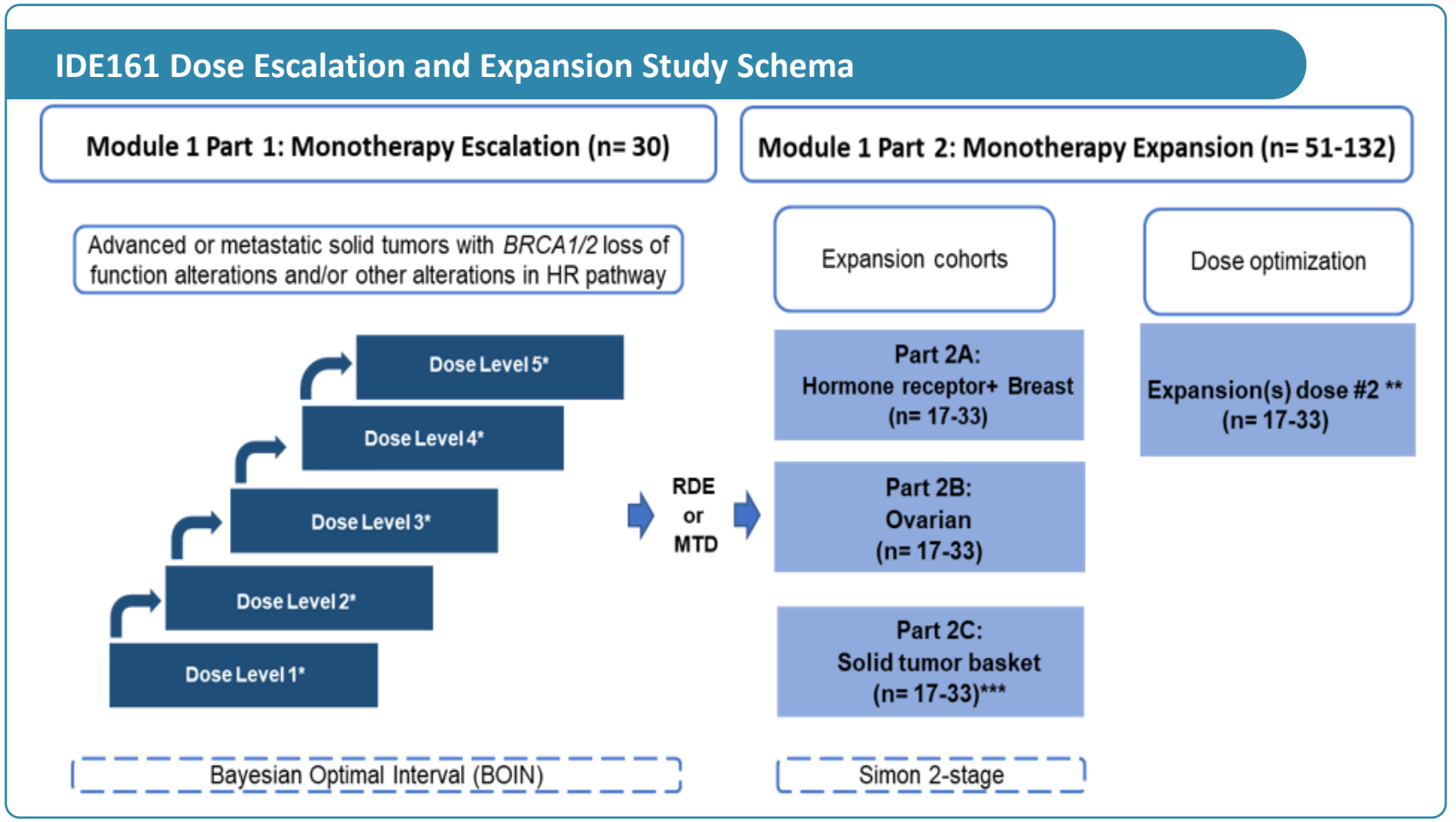
IDE161 Phase 1 FIH Study in HRD Solid Tumors

Expansion cohorts initiated in multiple priority solid tumor types

Selected back-fill priority tumors (with HRD):

- HR+ HER2- breast cancer
- Ovarian cancer
- Prostate cancer
- Colorectal cancer
- Gastric cancer
- Endometrial cancer

PARPi not approved in HRD CRC, gastric and endometrial cancer



IDE161 PK Predicts Therapeutic Exposure at Phase 1 Expansion Dose For Most Subjects Based On Pre-Clinical Models

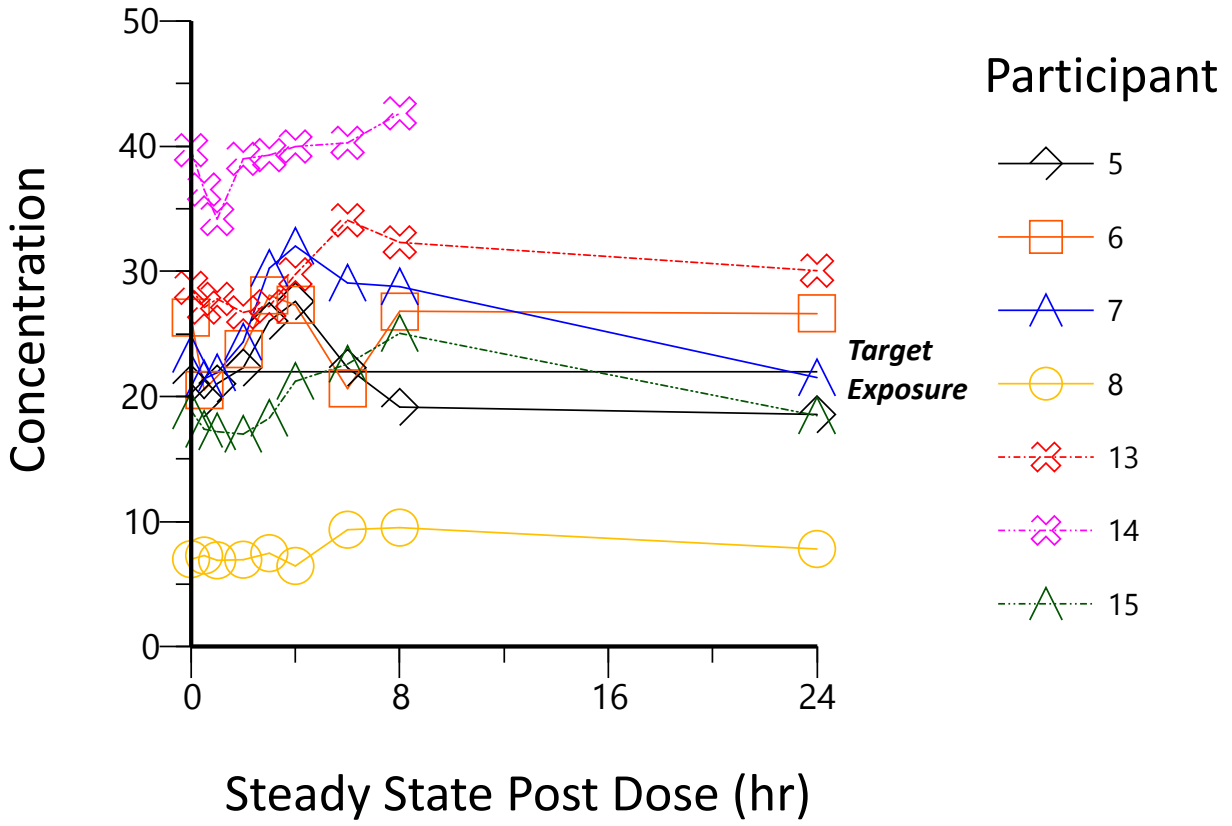
Preliminary C1D15 PK Analysis

Observed IDE161 human PK is in-line with pre-clinical predictions where tumor regressions observed

Based on Expansion Dose patients (n=7), six patients are within predicted therapeutic range

Patient #008 had plasma levels below predicted therapeutic range, but with radiographic partial response (31% tumor reduction at second scan)

C1D15 Pharmacokinetics at Expansion Dose



IDEAYA Data: preliminary analysis of unlocked database

PAR Accumulation in PBMCs Demonstrates On-Target Activity of IDE161

Preliminary Pharmacodynamic Analysis at Phase 1 Expansion Dose

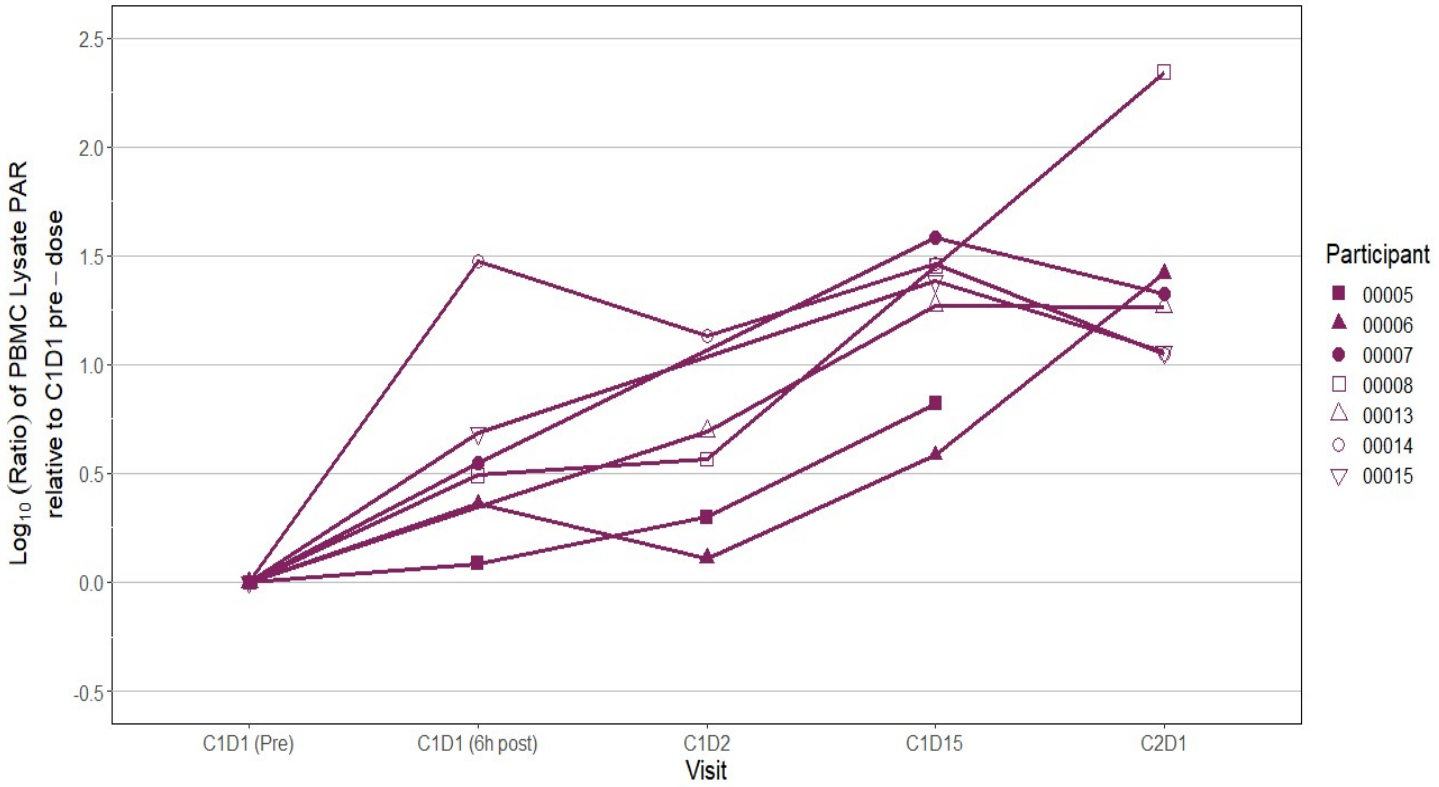
Data supports on-target activity of IDE161:

- Log-transformed PAR ratios are elevated relative to C1D1 pre-dose at all subsequent time points for all 7 patients at Expansion Dose

Potential emerging patterns:

- Preliminary Dose Response of PAR accumulation observed in dose escalation

PAR accumulation (Log_{10}[ratio] relative to C1D1 pre-dose)

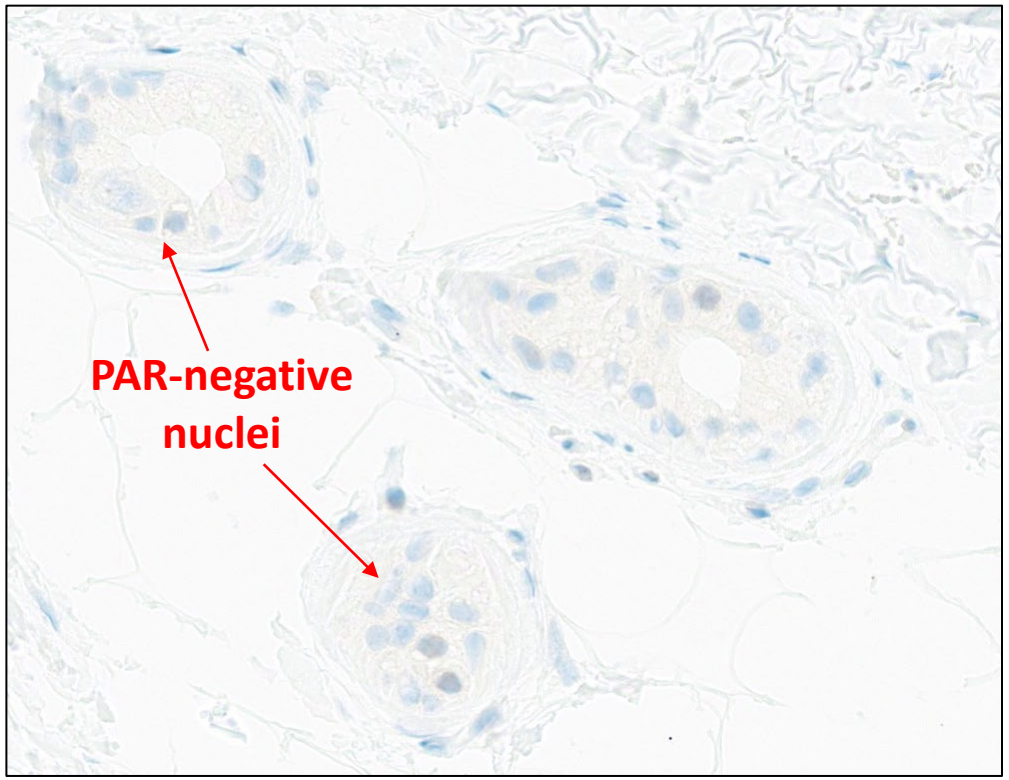


IDEAYA Data: preliminary analysis of unlocked database

IDE161 Phase 1 Pharmacodynamics: Paired Skin Biopsies of Nuclear PAR levels by Immunohistochemistry

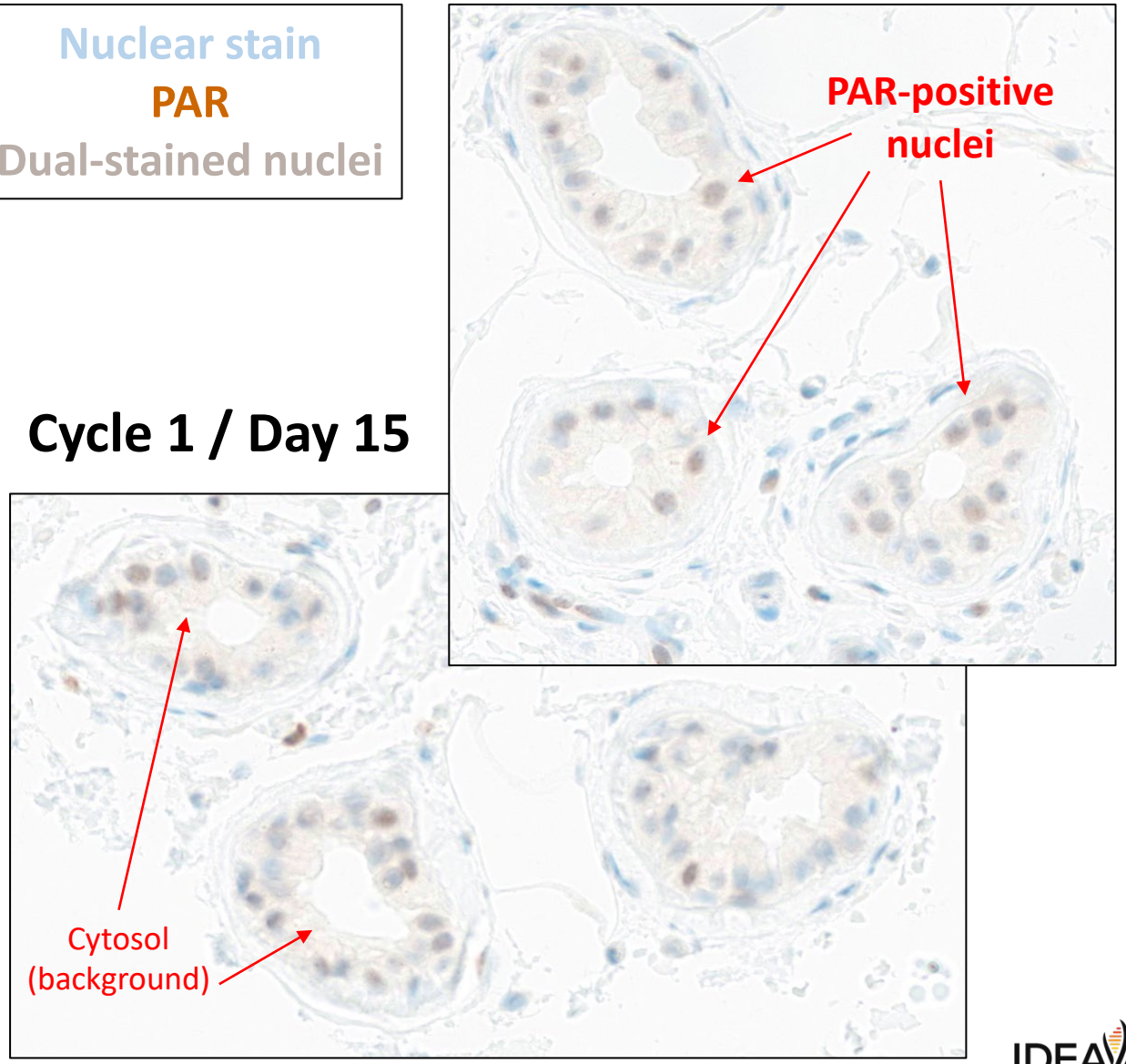
Nuclear stain
PAR
Dual-stained nuclei

Pre-Treatment



Patient Sample at Expansion Dose

Cycle 1 / Day 15



Transverse sections of glands in skin punch biopsies (@ 40X magnification)
Data are preliminary.

IDE161 Preliminary Safety Summary at Phase 1 Expansion Dose

- Preliminary experience shows manageable safety profile at expansion dose
- Majority of TEAEs were low grade
- No drug related discontinuations or treatment related SAEs reported
- Preliminary AE profile appears potentially favorable relative to PARPi therapy
- Dose Evaluation ongoing for determination of move forward Phase 2 expansion dose(s)
- Dose Expansion initiated in priority HRD solid tumor types:
  - HR+ HER2- breast cancer
  - Ovarian cancer
  - Prostate cancer
  - Colorectal cancer
  - Gastric cancer
  - Endometrial cancer

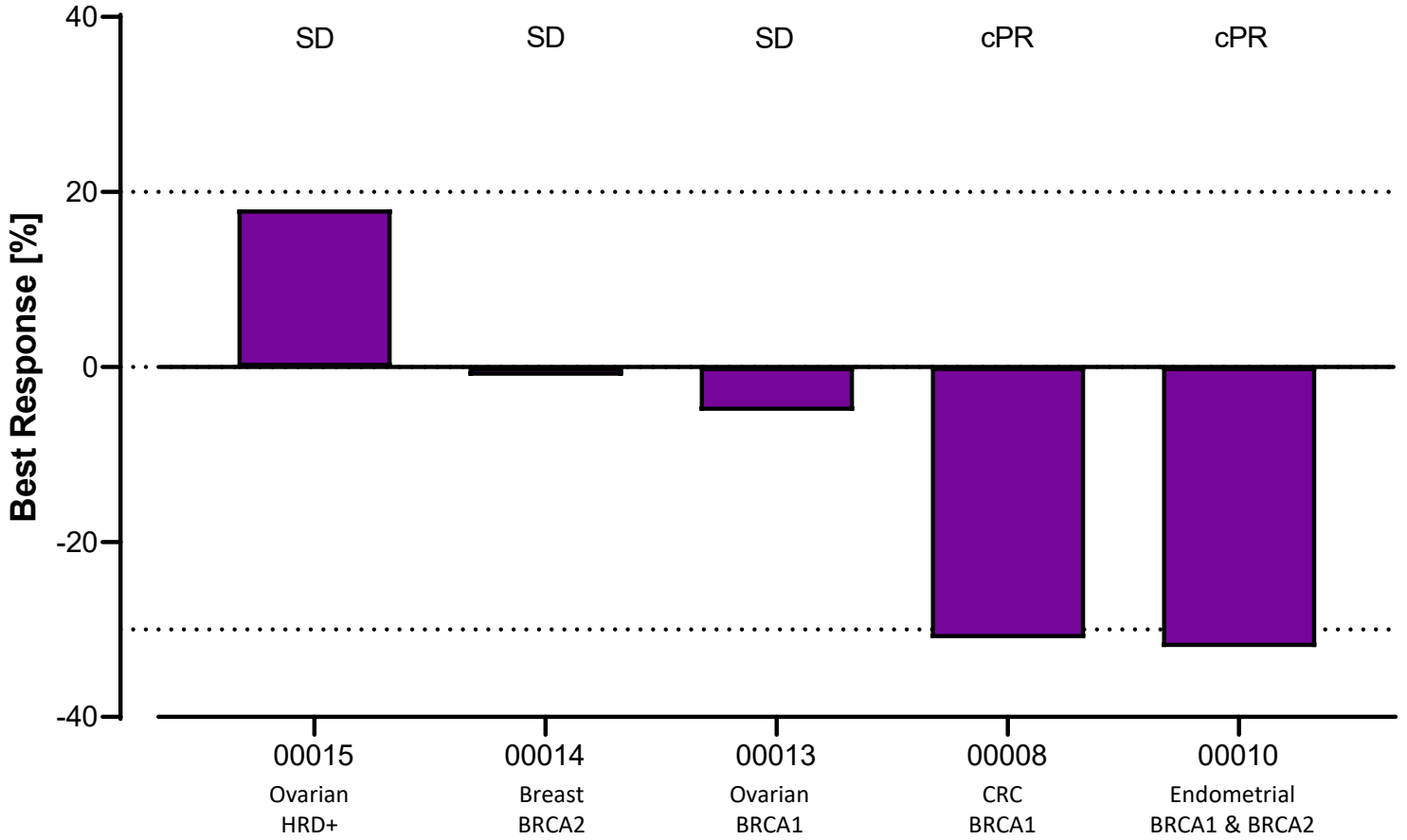
Preliminary IDE161 Clinical Efficacy at Phase 1 Expansion Dose

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 (00008) at second scan which was subsequently confirmed.
- Patient 00010 with EC 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



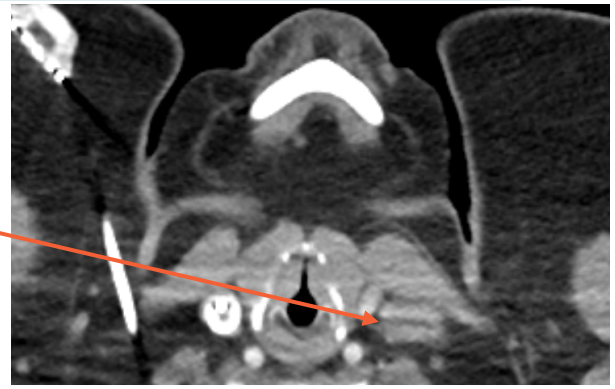
IDEAYA Data: preliminary analysis of unlocked database;
SD = Stable Disease, cPR = confirmed Partial Response

IDE161 Endometrial Cancer Patient: 31% Tumor Shrinkage (PR by RECIST 1.1)

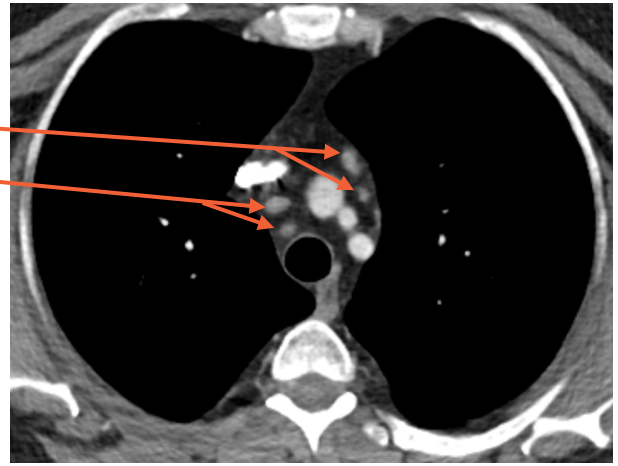
Complete Response in non-target lesions

Baseline Scan: Target & Non-Target Lesions

Target Lesion: Cervical Lymph Node



Non-Target Mediastinal Lesions*

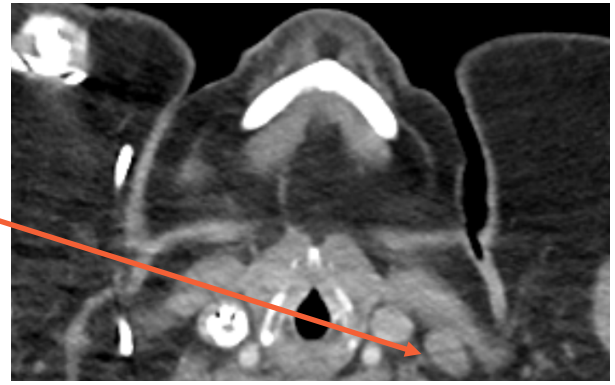


Prior Therapy
- CarboTaxol + Bev
- Taxol Maintenance
- Atezolizumab

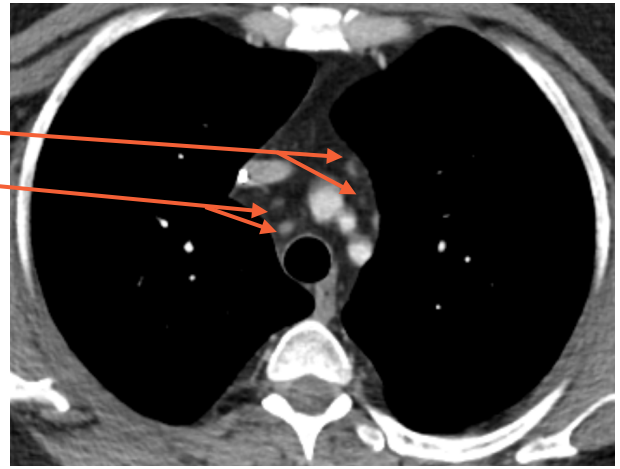
*Soft Tissue window view

Cervical Node Reduced by 31%

Target Lesion: Cervical Lymph Node



Non-Target Mediastinal Lesions*

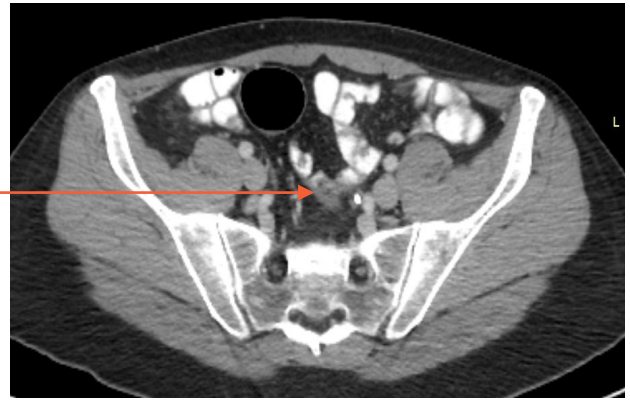


IDE161 Colon Cancer Patient: 31% Tumor Shrinkage (PR by RECIST 1.1)

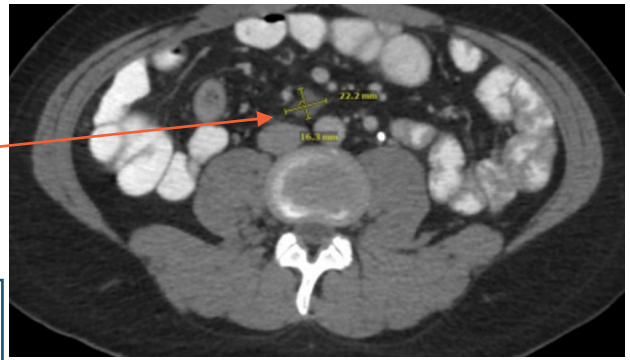
Complete Response in one target lesion

Baseline Scan

Pelvic Mesenteric Mass



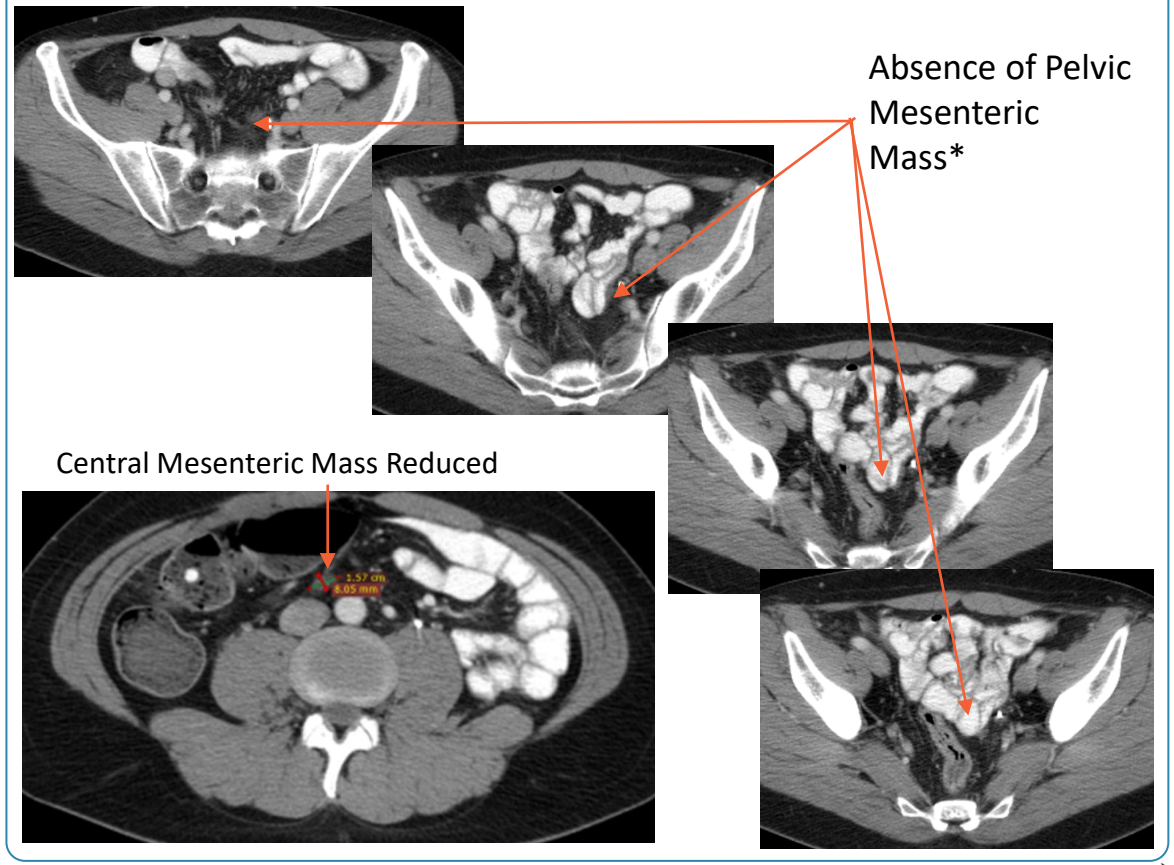
Central Mesenteric Mass



Prior Therapy:

- FOLFOXIRI

Complete Response of Pelvic Mesenteric Mass



* Image Slices 72,76-78 of the same timepoint

Emerging Therapeutic Opportunities for MTAP-deleted Cancers

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Chief Scientific Officer

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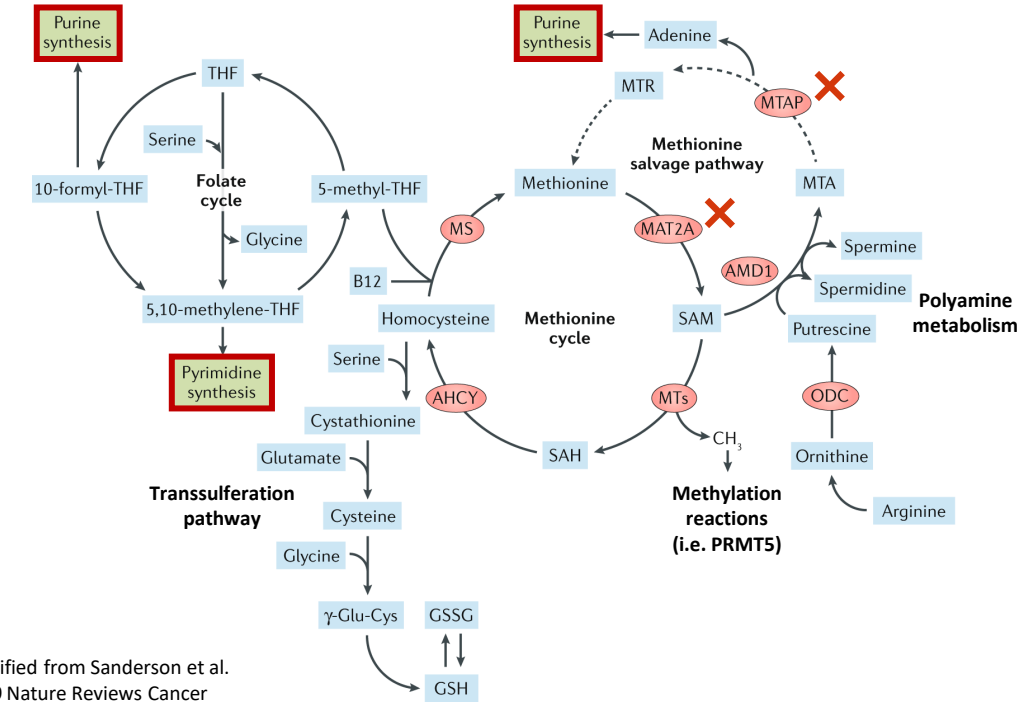
Chief Medical Officer

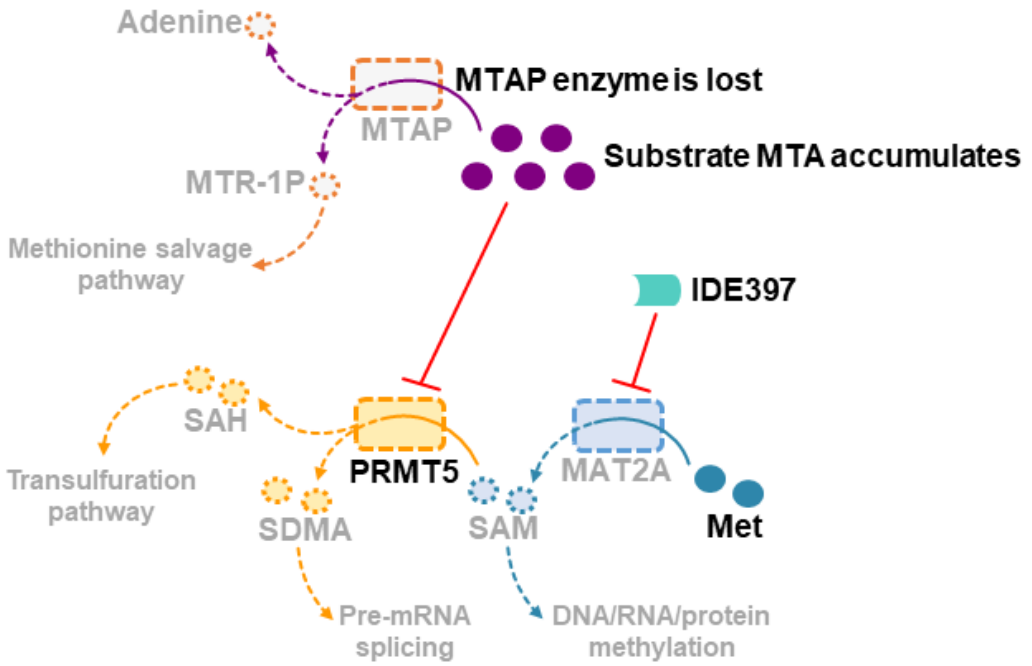
MTAP-Deletion Installs Two Distinct Mechanistic Liabilities That Define The IDE397 Therapeutic Opportunity Landscape

Perturbation of nucleotide pools



Modified from Sanderson et al. 2019 Nature Reviews Cancer

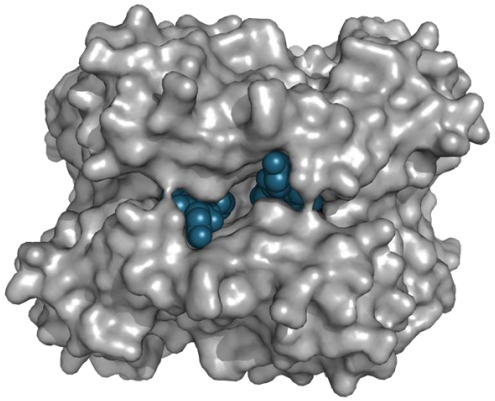
Perturbation of mRNA splicing



Modified from Marjon et al. 2016; Barriga et al. 2022

IDE397 selectively inhibits PRMT5 pathway activity in MTAP$^{-/-}$ cancer cells

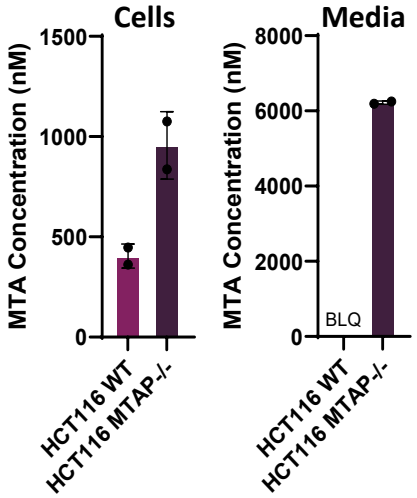
IDE397 selectively intercepts MTAP$^{-/-}$ vulnerabilities



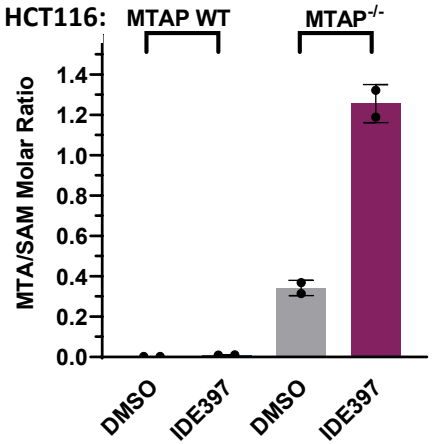
X-ray co-crystal structure of IDE397 bound to MAT2A dimer (1.25 Å)

	Viability		SDMA inhibition	
	EC50 (nM)	fold selectivity	EC50 (nM)	fold selectivity
HCT116 WT	>20000	>113	>5000	>1000
HCT116 MTAP$^{-/-}$	176		5	

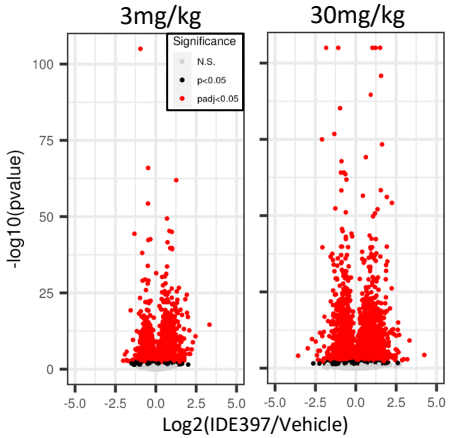
MTAP-dependent MTA accumulation



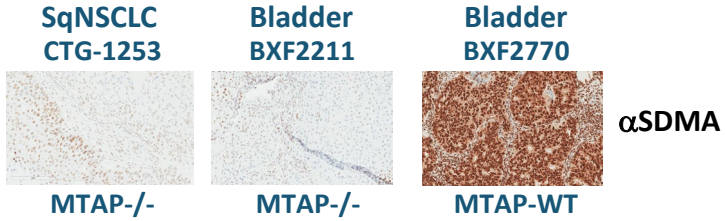
Robust modulation of MTA/SAM ratio by IDE397

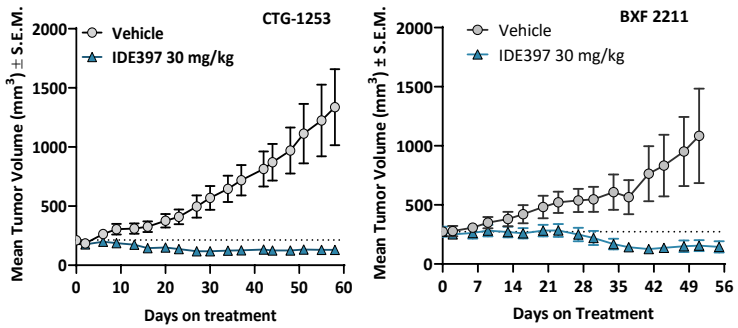


Dose-dependent perturbation of mRNA splicing (IR) *in vivo*

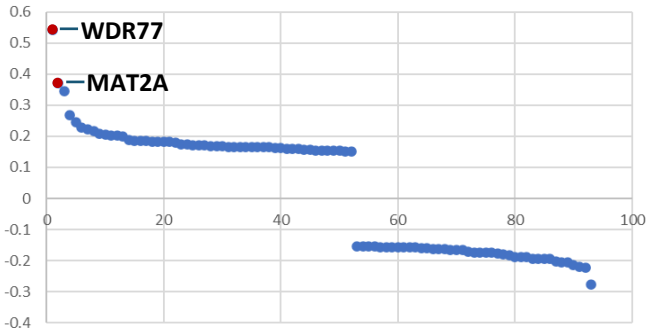


Low baseline PRMT5 activity is associated with robust anti-tumor response to monotherapy



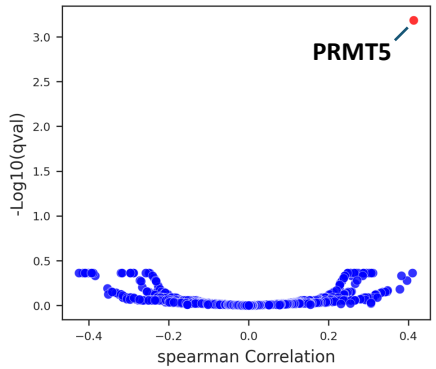


MAT2A and PRMT5 depletion show exceptional concordance across the CCLE



Top 100 genetic associations with PRMT5

IDE397 and PRMT5 depletion show exceptional concordance across the CCLE

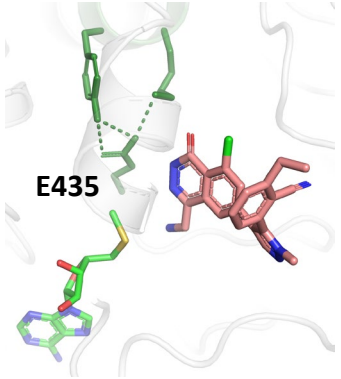


genetic correlations vs IDE397 Log10(IC50) across 263 cell lines

IDE397 Combination Benefit Observed with Clinically Validated MTA-PRMT5i

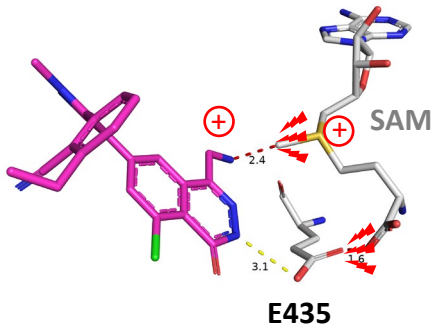
MTA-cooperative PRMT5 inhibitors share key target selectivity properties*

Feature 1: Reinforce inactive state



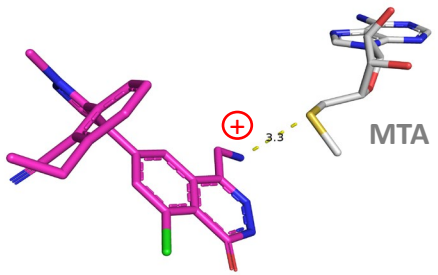
Compounds lock E435 rotamer in inactive state with MTA bound

Feature 2: SAM repulsion



Steric clash between amine and S-Me (SAM) occludes SAM binding

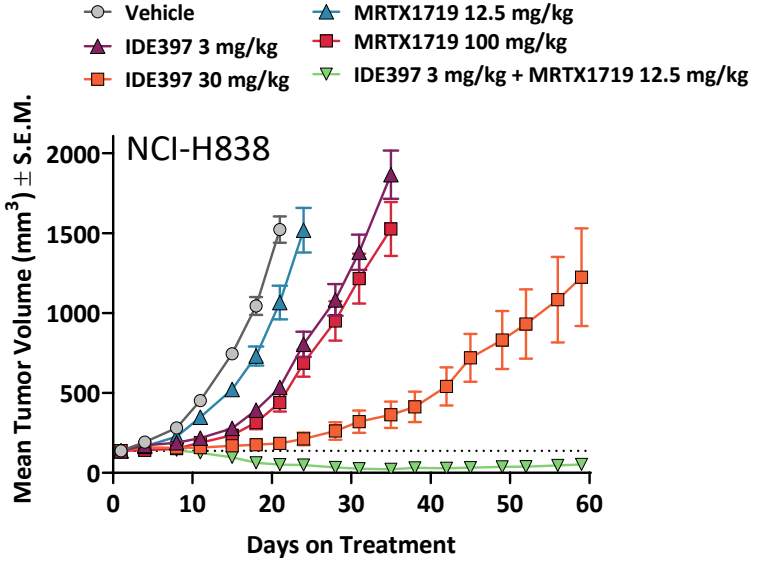
Feature 3: MTA "super-cooperativity"

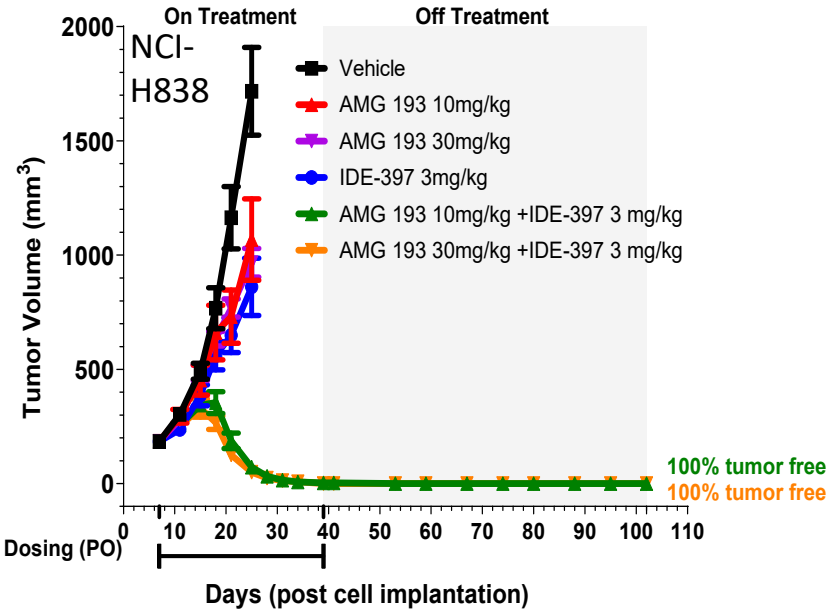


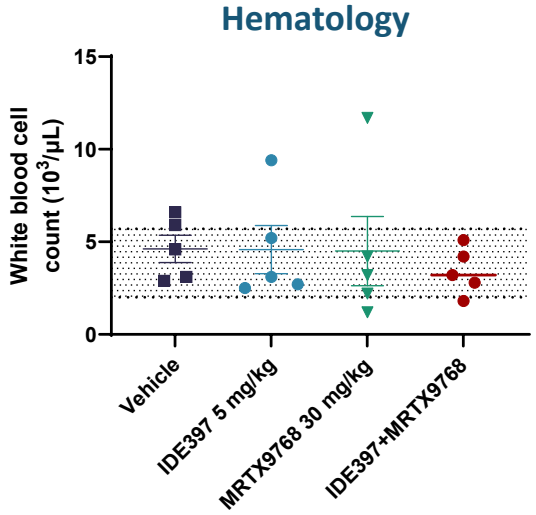
Attraction between charged amine and sulfur of MTA

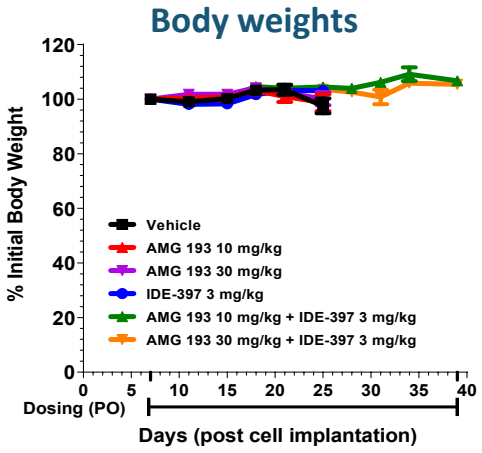
- **Feature 1**: shared (AMG193, TNG462, MRTX1719)
- **Feature 2**: shared (AMG193, TNG462, MRTX1719)
- **Feature 3**: MRTX1719 dominant

Reported HCT116 MTAP$^{-/-}$ vs. WT selectivity: AMG193 (43X), TNG462 (45X), MRTX1719 (74X)







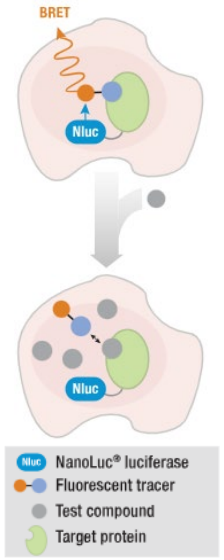


*Adapted from Mirati (Cancer Discovery), Tango (ACS, 2023) and Amgen (AACR/NCI/EORTC, 2023)

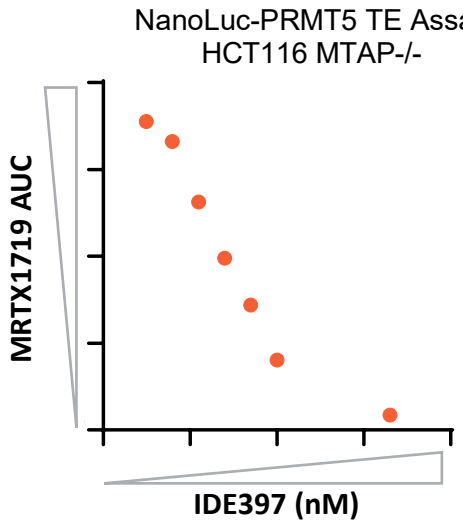
MAT2A/PRMT5 Combination Has Potential to Deliver Differentiated Efficacy

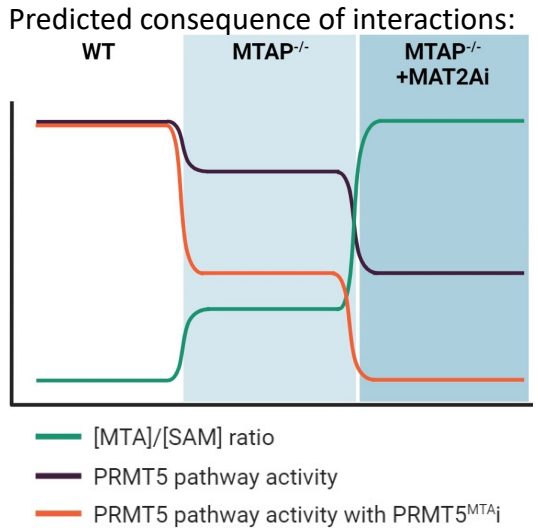
Combinatorial pathway inhibition is mechanistically distinct from monotherapy activity

IDE397 amplifies PRMT5 target engagement by MRTX1719

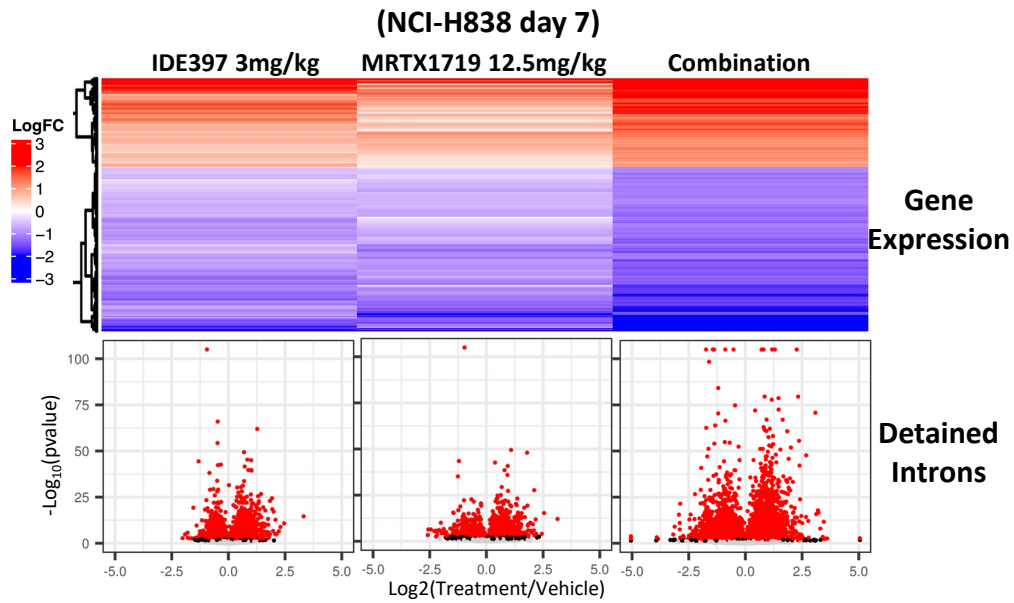


Promega

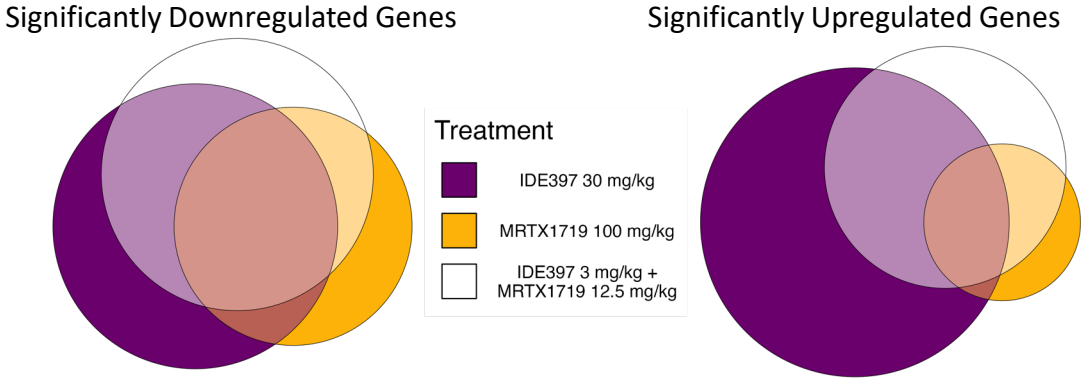




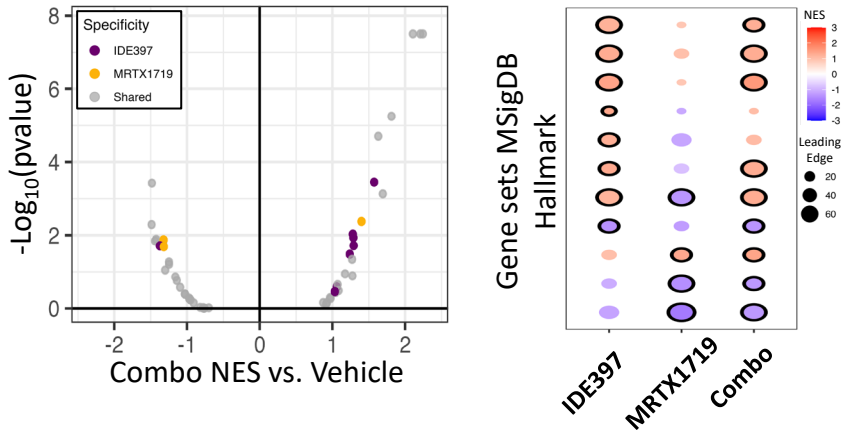
Amplified target engagement is recapitulated *in vivo*



Differential drug effects observed in tumors (NCI-H838)



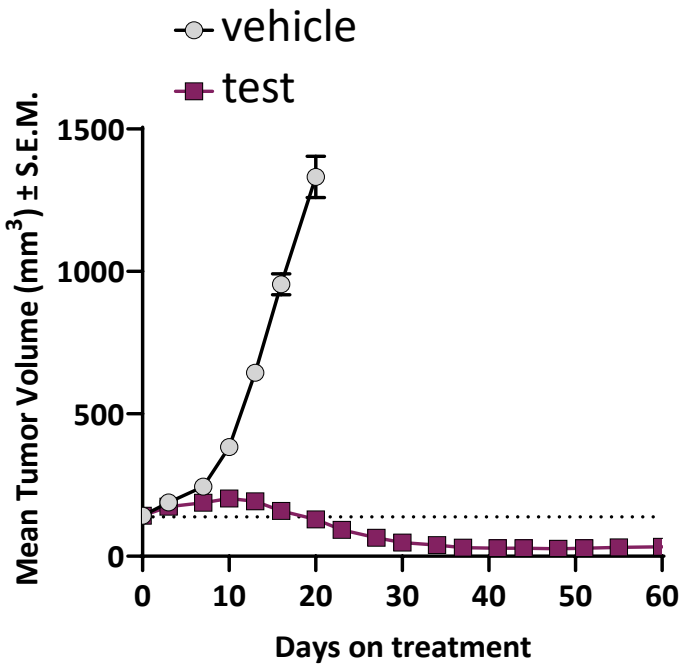
IDE397 perturbs distinct biology in tumors



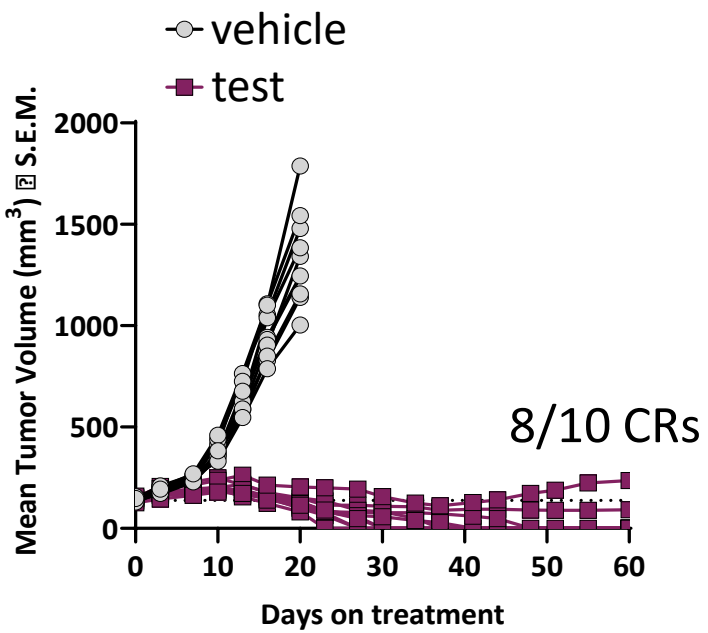
IDEAYA Pipeline: MTAP$^{-/-}$ New Target Opportunity

Mechanism-based activity distinct from PRMT5 pathway

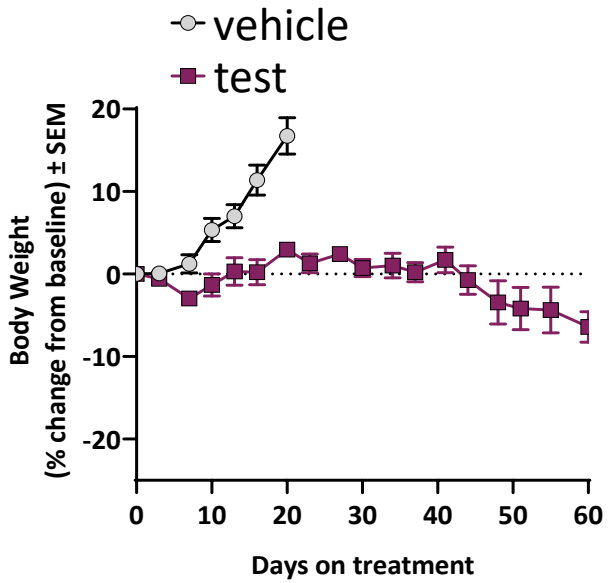
Mean Tumor Volume in NCI-H838



8 of 10 Complete Responses



Minimal Body Weight Change

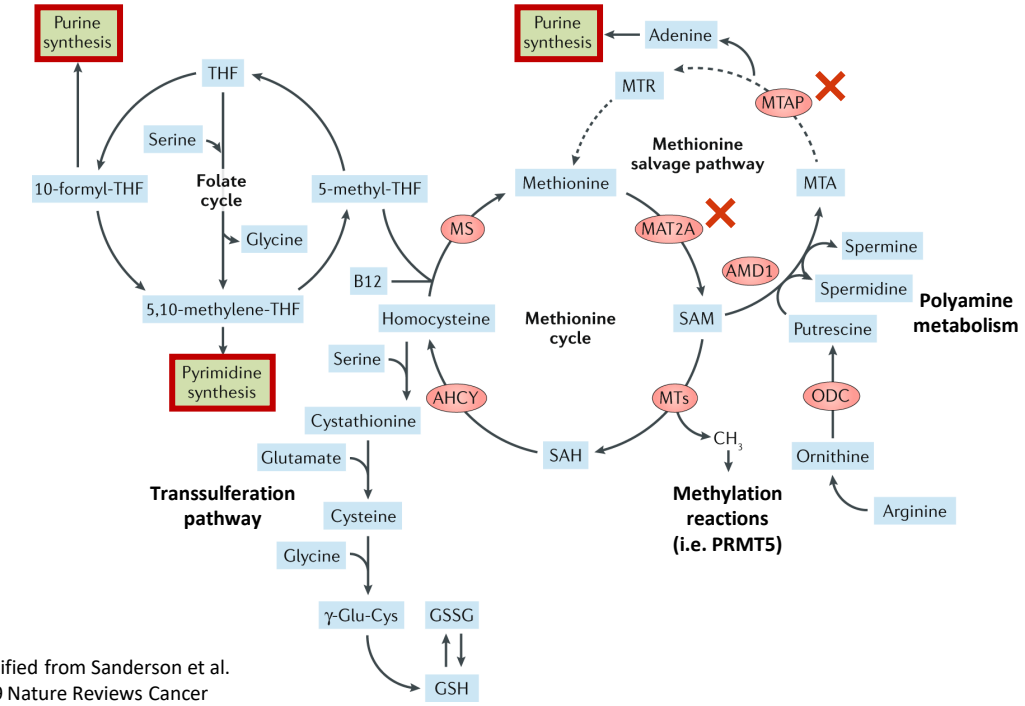


- First-in-class opportunity not yet evaluated in the clinic
- Cellular screens indicate potential for broad therapeutic benefit in MTAP$^{-/-}$ cancers
- Mechanism anticipated to combine well with MAT2A and PRMT5^{MTA} inhibitors

Sacituzumab–Govitecan (TRODELVY®)/IDE397 Combination in MTAP$^{-/-}$ Urothelial Cancer

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

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



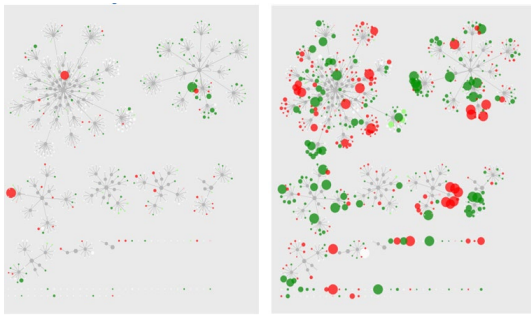
Modified from Sanderson et al. 2019 Nature Reviews Cancer

- De novo nucleotide synthesis is impaired upon loss of MTAP and MAT2A activity
- Depletion of nucleotide pools limits replication and repair capacity
- RNA splicing defects cause RNA polymerase stalling and R-loop accumulation
- R-loops must be resolved by TOP1 to prevent transcription / replication conflict and resulting mitotic catastrophe
- Resulting genome stability is vulnerable to further insult by tumor-selective TOP1 inhibition

Metabolic perturbation by IDE397 selectively interacts with MTAP

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

Metabolite Cytoscape



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

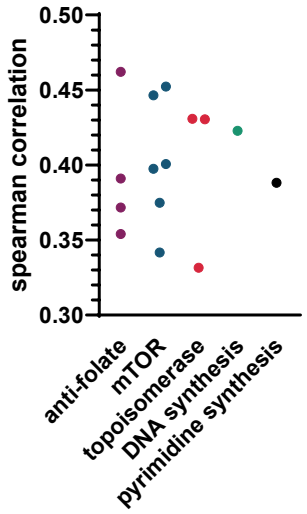
IDE397 effects on MTAP$^{-/-}$:

Pyrimidine Metabolism, Uracil containing	uracil	0.1
	uridine	0.37
	uridine 5'-monophosphate (UMP)	0.57
Purine Metabolism, (Hypo)Xanthine/Inosine containing	inosine	0.75
	inosine 5'-monophosphate (IMP)	1.29
	xanthine	0.45
	xanthosine 5'-monophosphate (xmp)	0.11
	xanthosine	0.36
Pyrimidine Metabolism, Thymine containing	thymidine	0.31
	thymine	0.45
Pyrimidine Metabolism, Cytidine containing	cytidine	0.56

Green shading indicates FDR< 0.05

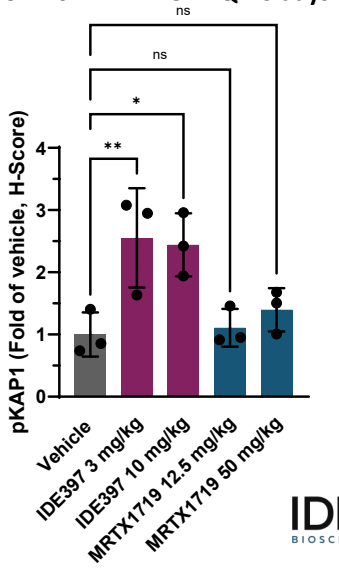
IDE397 sensitivity strongly correlates with response to DDR agents in MTAP$^{-/-}$ cells across the CCLE

1488 drugs across 737 cell lines



IDE397 provokes DDR response in vivo

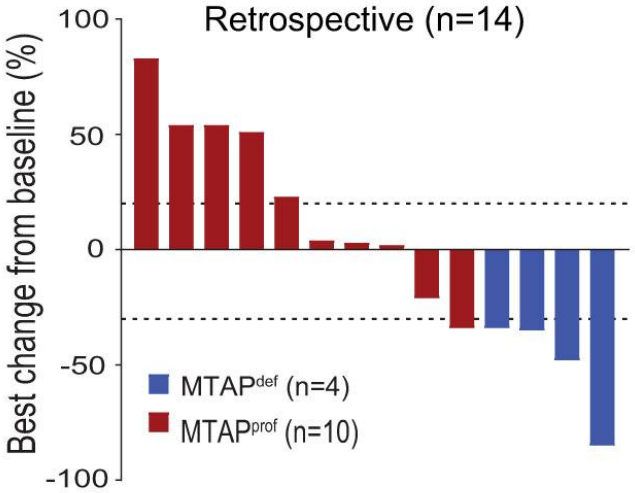
HCT116 MTAP$^{-/-}$ CDX QD 6 days



Urothelial Cancer is an Indication of Strategic Priority for IDE397

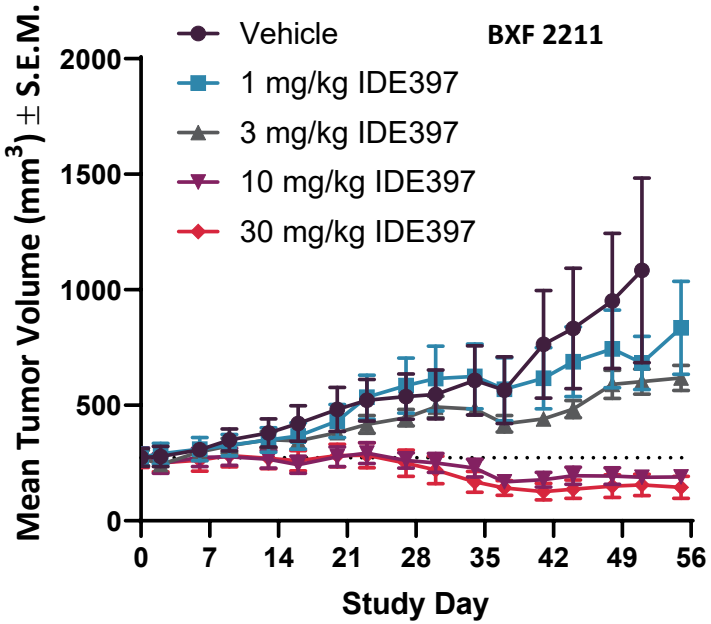
Nucleotide pool disruption may be a relevant therapy for MTAP$^{-/-}$ UC patients

- Alhalabi et al (2022) described improved response rate to pemetrexed in MTAP deficient UC patients
- With similar MOA to pemetrexed (depletion of nucleotide pools), a MAT2Ai may be effective in UC

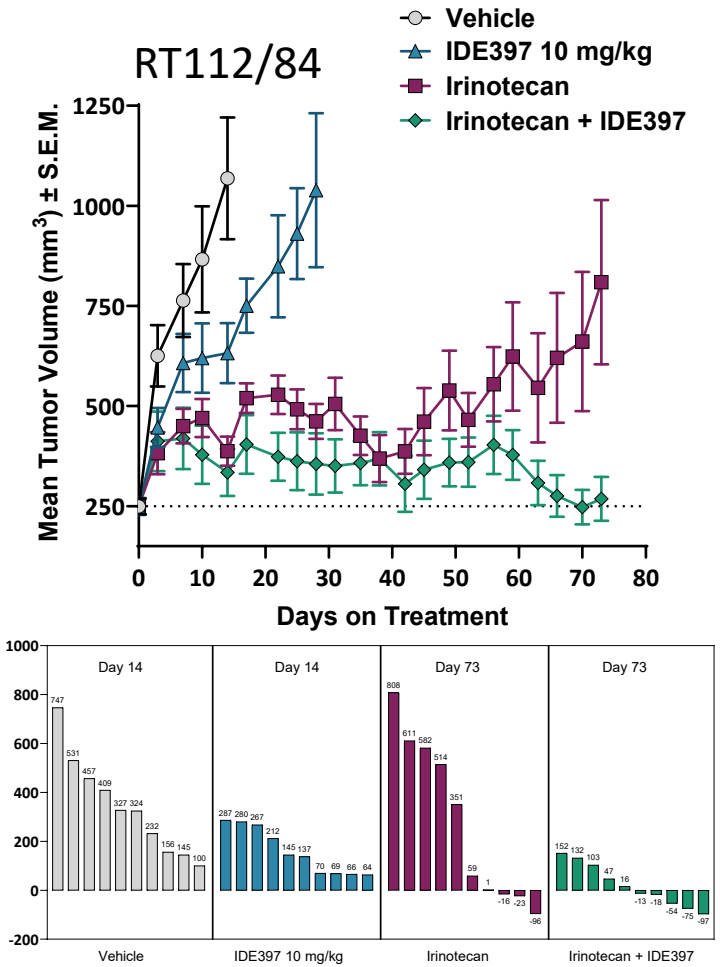


Alhalabi et al. Nature Communications, 2022

Regression observed in UC PDX with IDE397



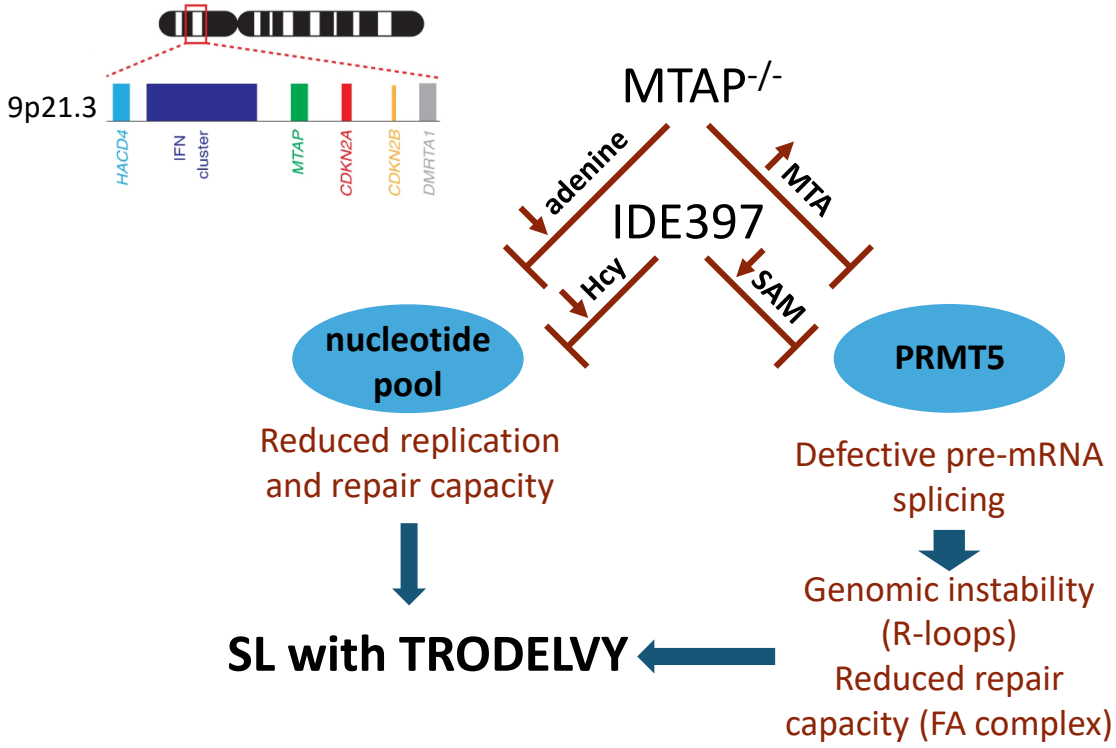
TOP1i combination delivers durable benefit in aggressive UC



IDE397 + Trodelvy® Combination in MTAP$^{-/-}$ Urothelial Cancers

Potential opportunity to favorably position IDE397 + TRODELVY® in an earlier line of therapy for MTAP$^{-/-}$ UC

Multiple lines of evidence support evaluation in the clinic



- IDE397 + TOP1 inhibitor has potential to create a synthetic lethal pair that fully capitalizes on mechanistic vulnerabilities (genomic instability, replication stress) associated with MTAP loss
- Tumor-selective delivery of TOP1 inhibitor would maximize therapeutic index
- Clinical correlates with TRODELVY® are consistent with this mechanistic rationale
- Early signs of clinical efficacy with IDE397 are also consistent with this mechanistic rationale

Rationale for Combination of IDE397 plus Trodelvy® in Urothelial Cancer

Trodelvy® appears preferentially active in MTAP deficient tumors where Enfortumab is less effective

MTAP-/- predicts for increased efficacy for Trodelvy® in UC

ORR to Trodelvy® based on genomic biomarkers

Biomarker	ORR (alteration present vs absent)	p-value
***MTAP* (n=8)**	**50% vs 19%**	**0.05**
ERBB2 (n=14)	22% vs 22%	0.98
FGFR3 (n=14)	15% vs 24%	0.49
BRCA2 (n=8)	38% vs 21%	0.28
DDR (n=15)	27% vs 22%	0.68
RB1 (n=11)	29% vs 22%	0.69
TP53/MDM2 (n=42)	18% vs 26%	0.41

Adapted from ASCO 2023 (#4572): Biomarkers of Response to Sacituzumab Govitecan and Efficacy After Treatment with Enfortumab Vedotin in Advanced Urothelial Carcinoma: Analysis of the UNITE Study; JCO.2023.41.16_suppl.4572

MTAP -/- predicts for worse outcomes with Enfortumab in UC

Comparison of PFS and OS among patients based on molecular biomarker status

Alteration	OS – HR; 95% CI	p-value	PFS – HR; 95% CI	p-value
***CDKN2A* (n=39)[1]**	1.5 (0.8 – 2.6)	0.16	1.7 (1.1 – 2.8)	**0.02**
***CDKN2B* (n=28) [1]**	1.6 (0.9 – 2.9)	0.11	2.0 (1.2 – 3.4)	**<0.01**
***MTAP* (n=20) [1]**	1.3 (0.7 – 2.6)	0.36	**1.7 (1.0 – 3.0)**	**0.05**
DDR[1]	0.9 (0.4-1.9)	0.82	0.9 (0.5 – 1.7)	0.78
***ERBB2* (n=19) [1]**	0.7 (0.3 – 1.6)	0.36	0.6 (0.3 – 1.3)	0.31
***TSC1* (n=15) [1]**	0.4 (0.1 – 1.5)	0.16	0.6 (0.2 – 1.5)	0.23
TMB High (≥10 Mut/Mb (n=34) [2]	0.4 (0.2 – 0.9)	**0.02**	0.7 (0.4 – 1.2)	0.14
***CDKN2A + CDKN2B* (n=28) [1]**	1.6 (0.9 – 2.9)	0.11	2.0 (1.2 – 3.3)	**<0.01**
***CDKN2B + MTAP* (n=14) [1]**	1.5 (0.7 – 3.2)	0.24	**2.4 (1.3 – 4.4)**	**<0.01**

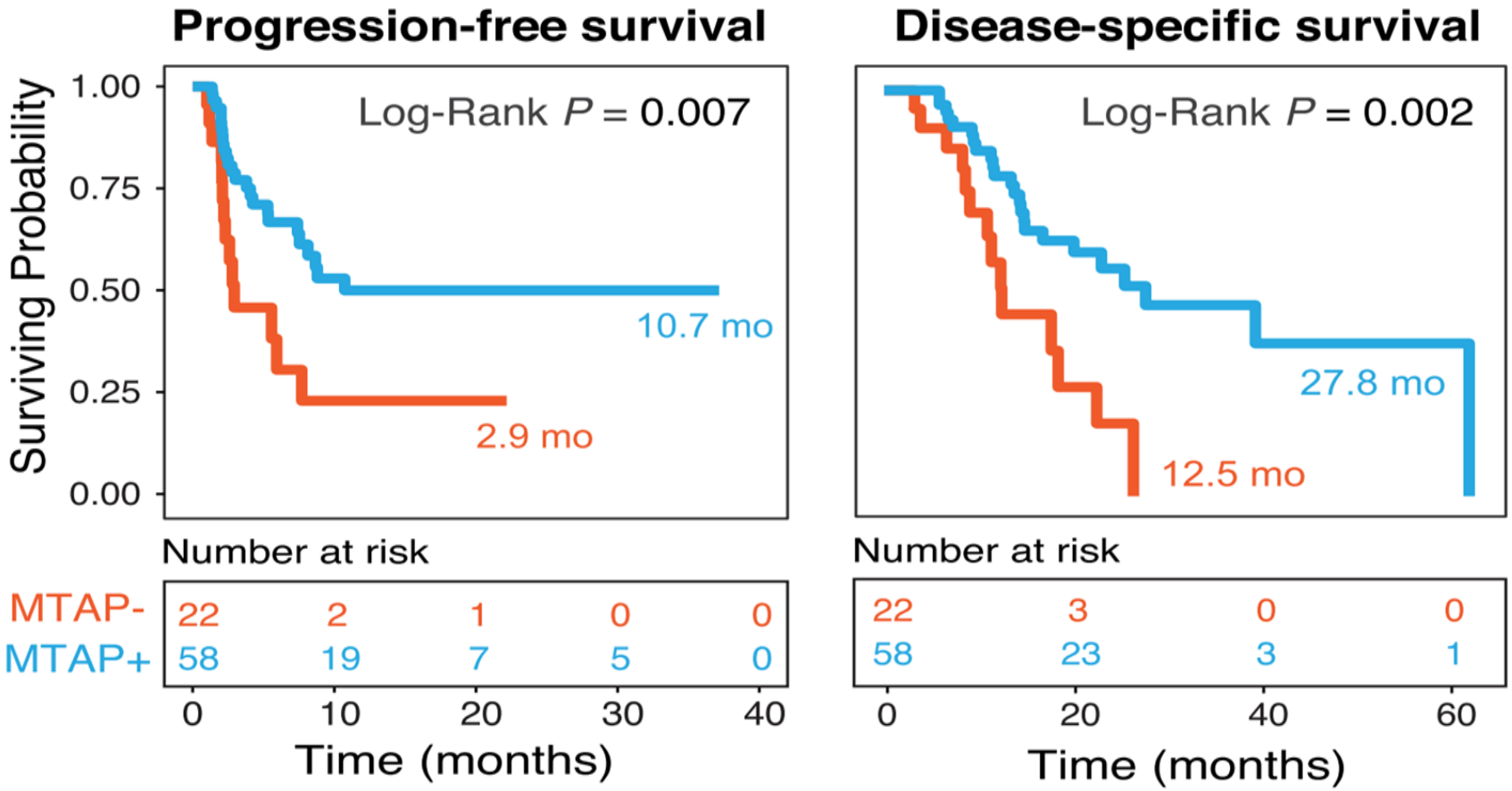
[1] 155 evaluable for OS and 135 evaluable for PFS
[2] 113 evaluable for OS and 98 evaluable for PFS

Adapted from ASCO GU 2023 (# 450)Biomarkers of response to enfortumab vedotin (EV) in patients (pts) with advanced urothelial carcinoma (aUC): Analysis of the UNITE study; JCO.2023.41.6_suppl.450

IDEAYA BIOSCIENCES

MTAP-/- Urothelial Cancer Patients Have Shorter PFS and Disease Specific Survival on PD1i or PDL1i

MTAP-/- subjects with UC treated with Pembrolizumab or Atezolizumab (n=80)



Source: Han et al, Nature Communications 2021

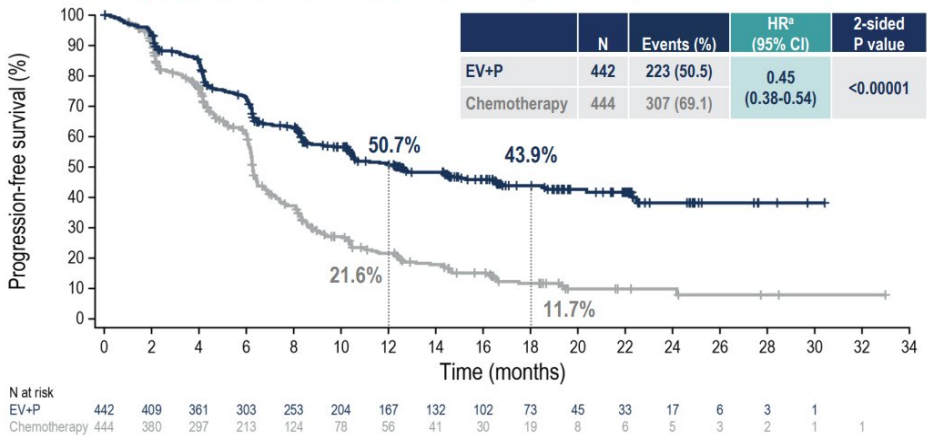
The Landscape in First Line UC is Changing: Enfortumab & Checkpoint Inhibitors Emerging

EV-302: Randomized trial of Enfortumab plus Pembrolizumab versus Cisplatin/Carboplatin + Gemcitabine in untreated advanced Urothelial cancers

Doubling of PFS with EV+P vs. SOC

Progression-Free Survival per BICR

Risk of progression or death was reduced by 55% in patients who received EV+P

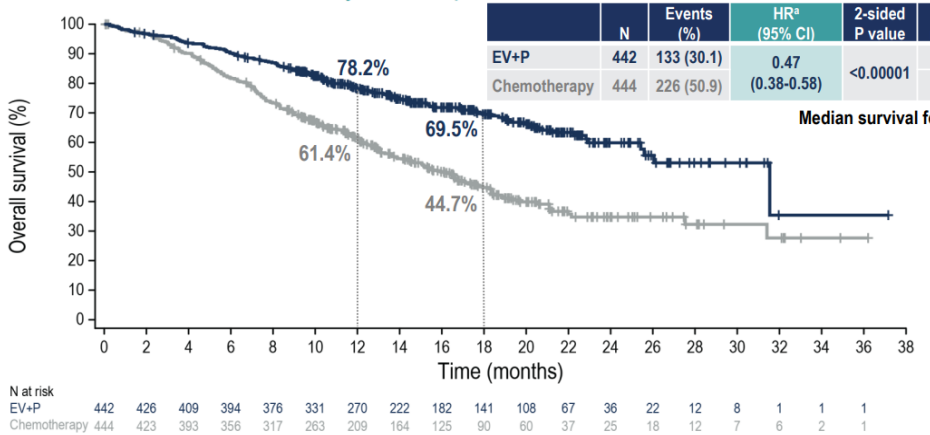


	N	Events (%)	HR[a] (95% CI)	2-sided P value	mPFS (95% CI), months
EV+P	442	223 (50.5)	0.45 (0.38-0.54)	<0.00001	12.5 (10.4-16.6)
Chemotherapy	444	307 (69.1)			6.3 (6.2-6.5)

Dual Primary Endpoint of OS also significantly improved

Overall Survival

Risk of death was reduced by 53% in patients who received EV+P



	N	Events (%)	HR[a] (95% CI)	2-sided P value	mOS (95% CI), months
EV+P	442	133 (30.1)	0.47 (0.38-0.58)	<0.00001	31.5 (25.4-NR)
Chemotherapy	444	226 (50.9)			16.1 (13.9-18.3)

Median survival follow-up: 17.2 months

Practice changing data: Significant improvement in PFS and OS noted for EV+P vs. Standard 1st line therapy. Trial Presented at ESMO

Potential opportunity to favorably position IDE397 + TRODELVY® as the treatment of choice for MTAP$^{-/-}$ UC

Source: Annals of Oncology (2023) 34 (suppl_2): S1254-S1335. Powles et al

MTAP-Deletion is Prevalent in ~26% of Bladder / Urothelial Cancer

MTAP-Deletion by Cancer Type

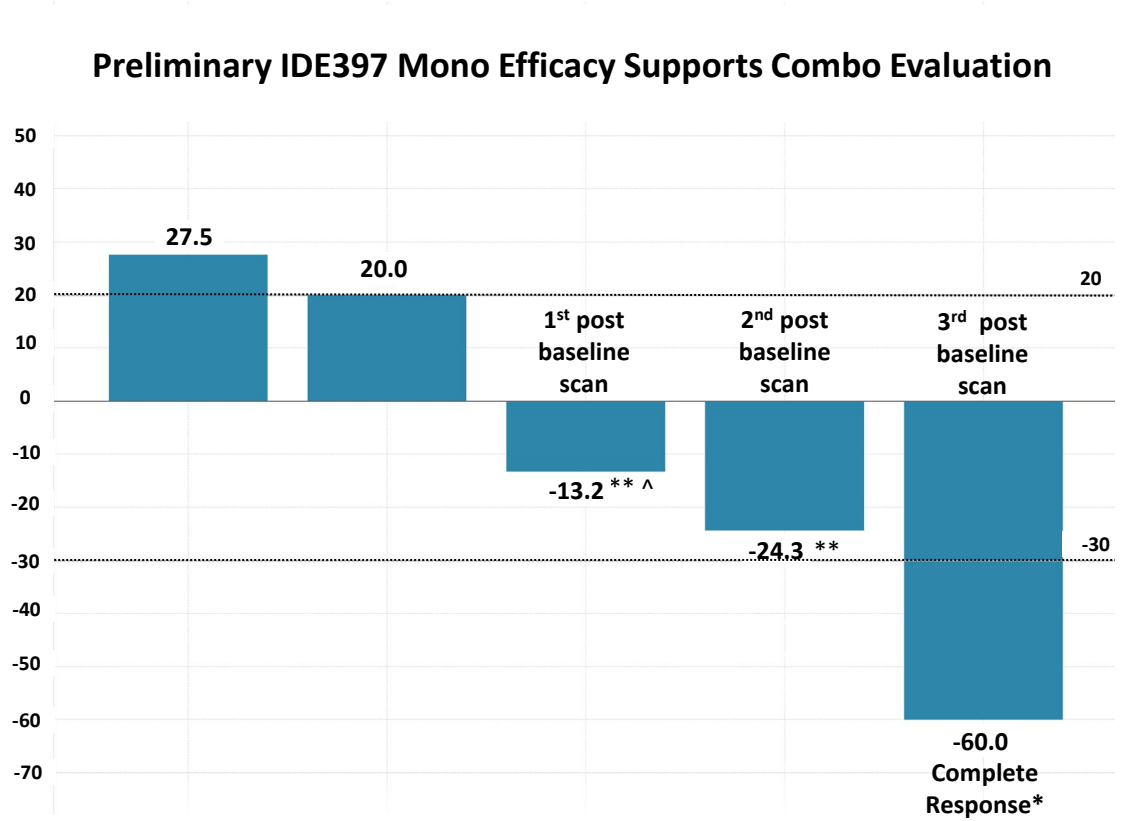
Cancer Type	U.S. Incidence	MTAP-deletion frequency
Bladder Urothelial Carcinoma	74,061	26%
Skin Cutaneous Melanoma	97,610	16%
Lung Squamous Cell Carcinoma	70,906	19%
Lung Adenocarcinoma	121,553	11%
Pancreatic Adenocarcinoma	57,645	21%
Breast Invasive Carcinoma	297,790	3%
Head and Neck Squamous Cell Carcinoma	66,920	14%
Glioblastoma Multiforme	12,430	41%
Esophageal Adenocarcinoma	17,248	21%
Prostate Adenocarcinoma	285,417	9%

* Source: Guggenheim Securities, LLC; TCGA PanCancer Atlas

IDE397 Phase 2 Monotherapy Expansion in MTAP$^{-/-}$ Urothelial Cancer

Robust Tumor Shrinkage by RECIST 1.1 and ctDNA Molecular Responses Observed

Best Overall Response by RECIST 1.1 in Urothelial / Bladder Cancer

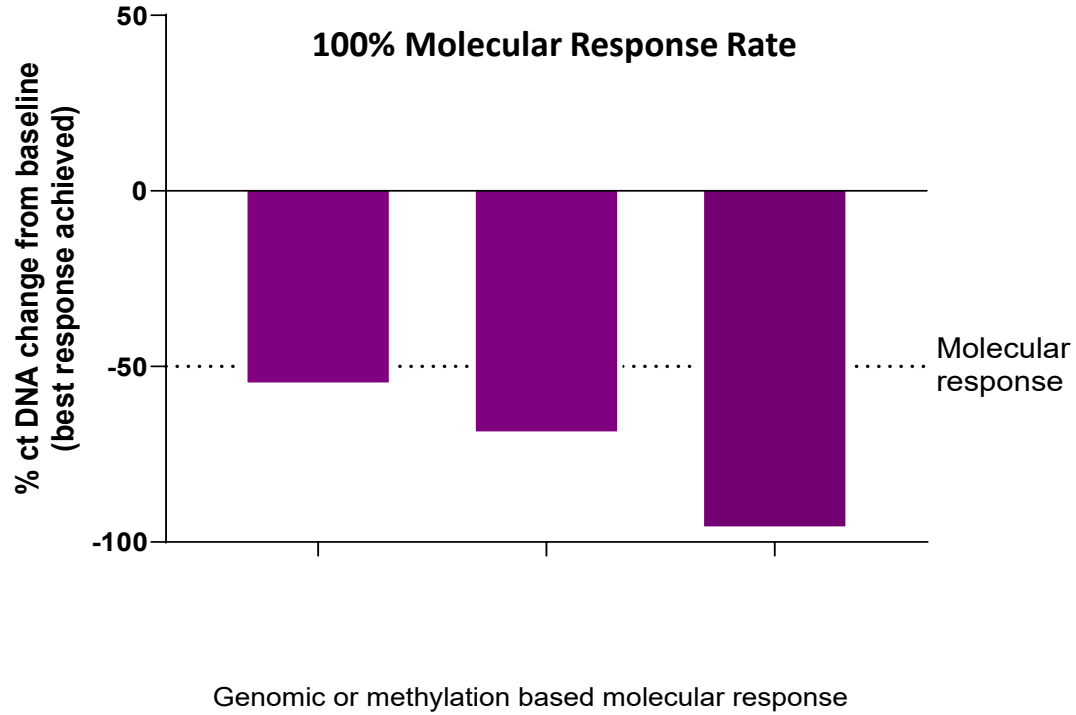


IDEAYA Data: preliminary analysis of unlocked database

* 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

Planned Clinical Testing of Trodelvy®+ IDE397 in *MTAP* -/- Urothelial Cancers

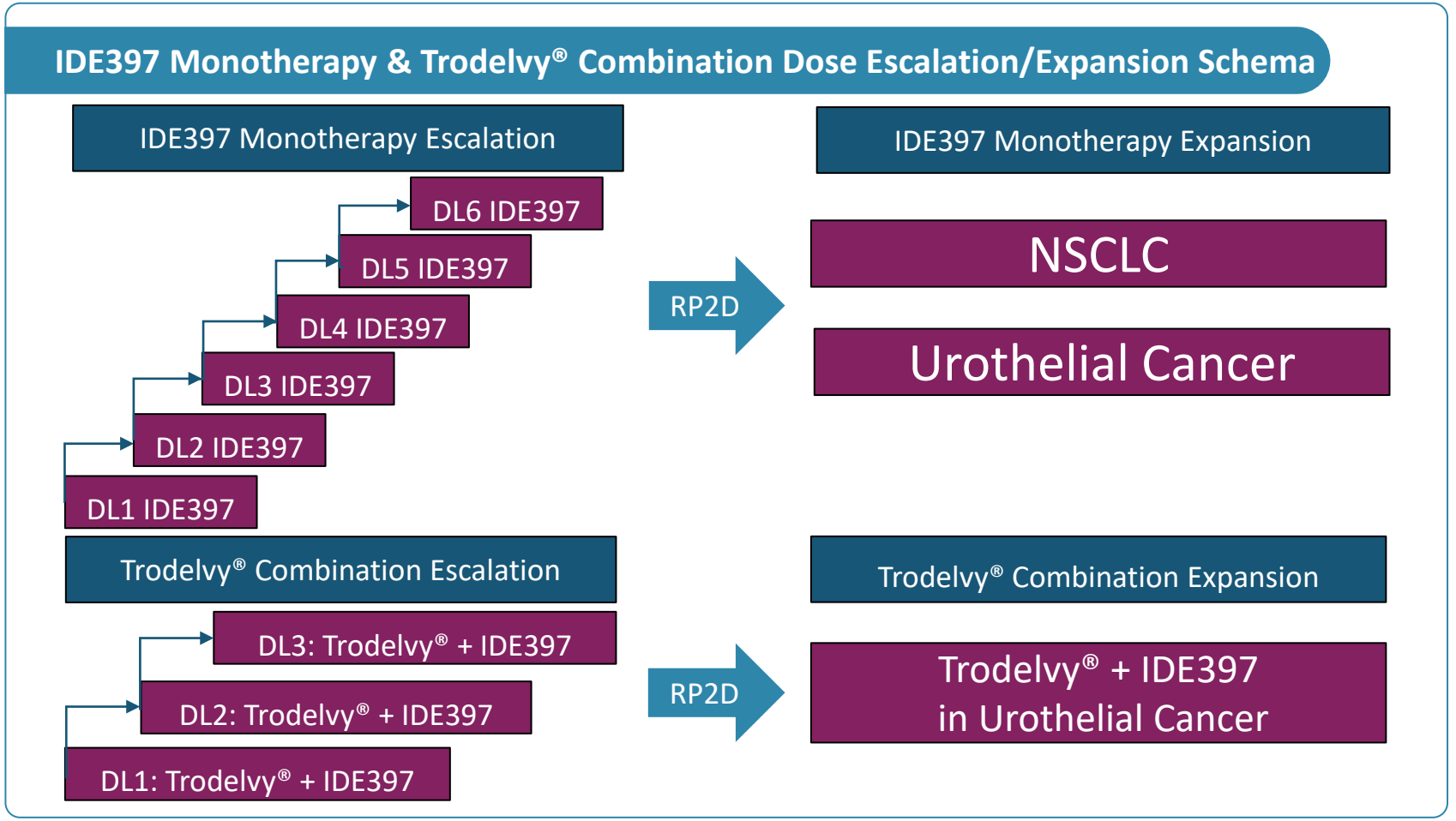
Opportunity to develop a novel combination regimen for subjects who may not benefit from EV+P or PD1/PD-L1 targeted therapy

Objective:
Demonstrate higher RR and DOR with the combination than seen with single agent Trodelvy® in this population

Target population: 2nd line + MTAP -/- UC

Trodelvy® benchmark in advanced pre-treated UC: ORR: 27%, median DOR: 7.2 months, median PFS: 5.4 months

Combination AE feasibility: Non-overlapping AE profile anticipated for IDE397 and Trodelvy®



GSK Partnership

Pol Theta and Werner Programs

Ramon Kemp, Ph.D.

GSK
Vice President
Head, Oncology EDL/Interim Head, Oncology MDL

GSK / IDEAYA Partnership: Potential First-in-Class Synthetic Lethality Programs

- Strong synergy and collaboration between GSK and IDEAYA
  - Discovery biology
  - Chemistry and CMC
  - Clinical strategy

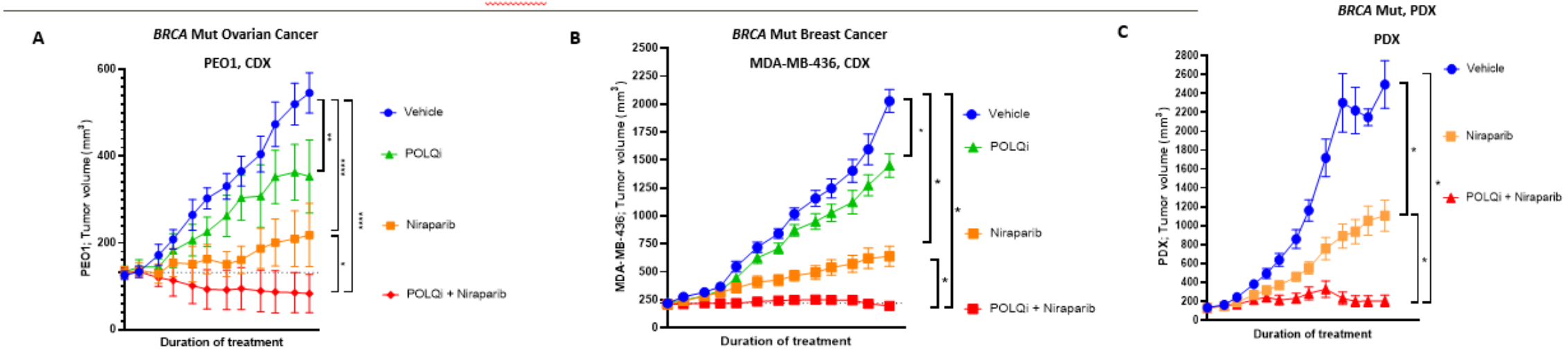
- Delivered back-to-back potential first-in-class helicase development candidates:
  - Pol Theta Helicase in Phase 1
  - Werner Helicase in IND-Enabling Studies

- Strategic Fit with GSK Commercial Portfolio:
  - Pol Theta Helicase / Niraparib Combo (HRD Solid Tumors)
  - Werner Helicase / Dostarlimab (MSI-High Solid Tumors)

POL Theta inhibitor, is Positioned as a Compelling Combination Partner for Niraparib

- Response to PARP inhibition is not curative and PARP inhibitor response inevitably leads to onset of resistance
- A key mechanism of PARP inhibitor resistance is reversion of BRCA mutation by Microhomology-Mediated End Joining (MMEJ) repair
- ~30% of PARPi progressors have MMEJ signatures at reversion sites (ASCO 2022)
- The POL Theta enzyme mediates the MMEJ repair function
- Inhibition of POL Theta may reduce PARP resistance and extend duration of PARPi response

- POL Theta inhibitor GSK4524101 significantly enhances the activity of niraparib in preclinical tumor models (shown below)
- POL Theta inhibitor GSK4524101 is positioned as a Niraparib combination partner for deeper, more efficacious responses

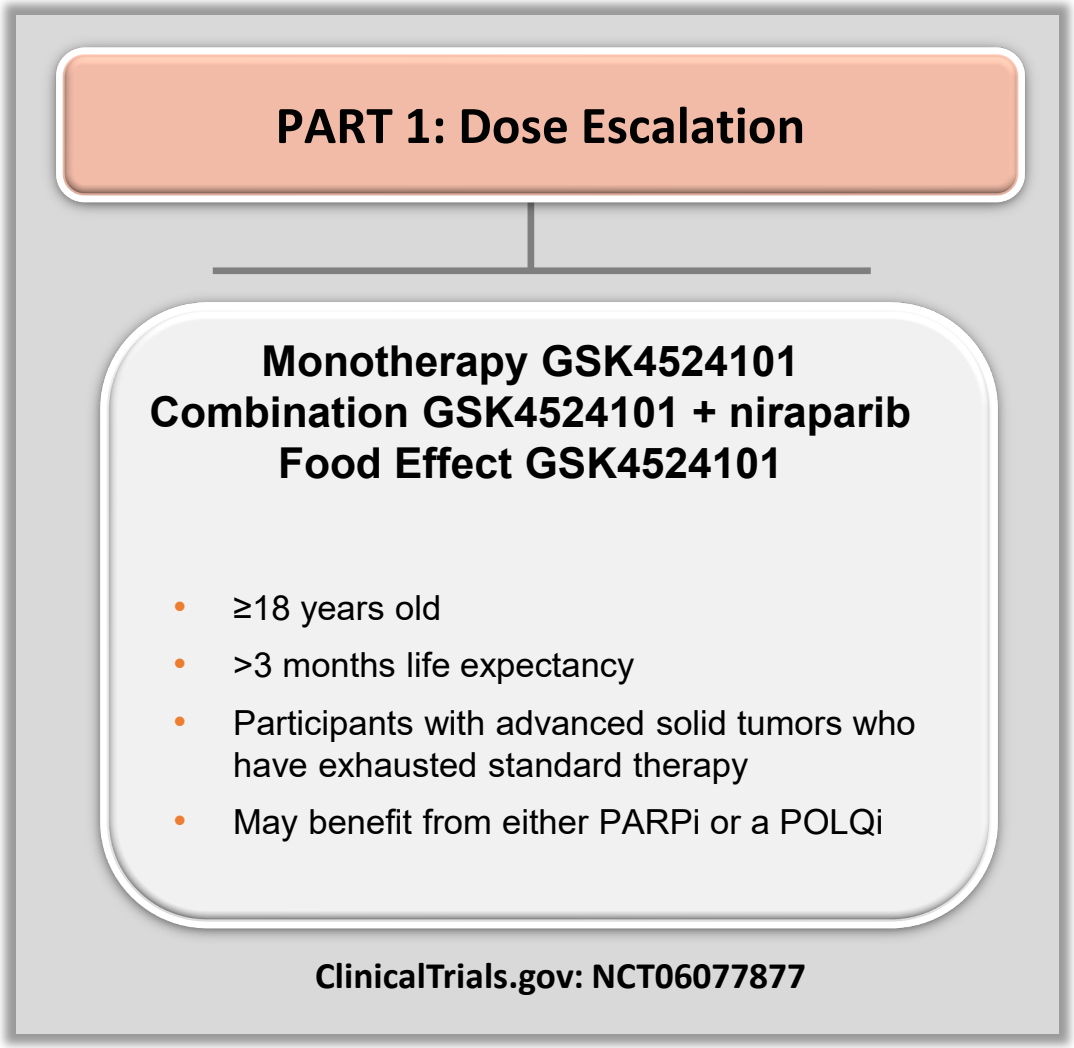


(A-C) Animals bearing (A) *BRCA* mutated (Mut) Ovarian Cancer, PEO1 CDX or (B) *BRCA* Mut Breast Cancer, MDA-MB-436 CDX, or (C) a *BRCA* Mut PDX were dosed with either vehicle or POLQi and Niraparib, as single agents or in combination. Mixed effects model with Tukey test was applied to calculate statistics at the end of the studies: *. $P < 0.05$: **. $P < 0.01$: ***. $P < 0.001$: ****. $P < 0.0001$.

Bononi et al., Keystone Conference 2023

Phase I : A Study to Investigate the Safety, Tolerability, Pharmacokinetics (PK), and Preliminary Anticancer Activity of GSK4524101 Alone or With Niraparib in Participants With Solid Tumors

- IND Active: August 2023
- Phase 1 FPI: Nov. 2023

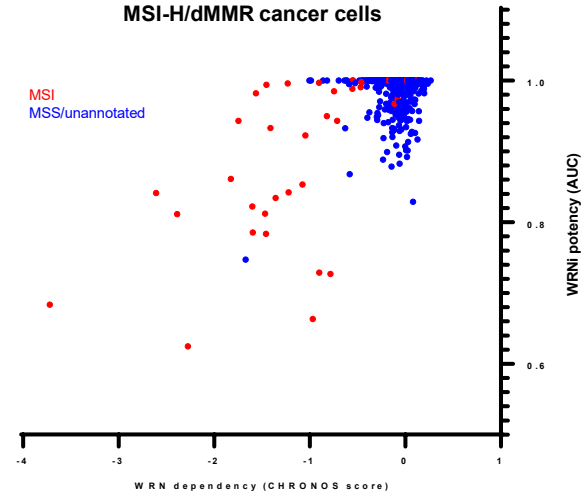


Werner helicase (WRN) Inhibitor Targets MSI-H/dMMR Cancers

- Standard of Care in MSI-H/dMMR CRC or EC includes checkpoint inhibitor(s) (CPI) and CPI+chemo, respectively.
- 30~50% MSI-H/dMMR CRC and EC patients will progress after CPI monotherapy. No effective treatment options available for these patients post Standard of Care
- WRN dependency in MSI-H cancer cells has been validated (left panel)
- Inhibition of helicase activity is sufficient to suppress MSI-H cancer (center panel)
- Robust tumor regression observed preclinical MSI-H/dMMR tumor models suggesting potential monotherapy efficacy (right panel)

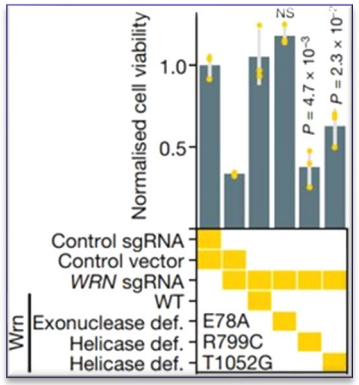
- WRN inhibition suppresses MSI-H/dMMR cancer via induction of DNA damage
- GSK/IDEAYA WRNi is a highly potent & selective small molecule helicase inhibitor of WRN

GSK/IDEAYA WRNi is potent & selective against MSI-H/dMMR cancer cells



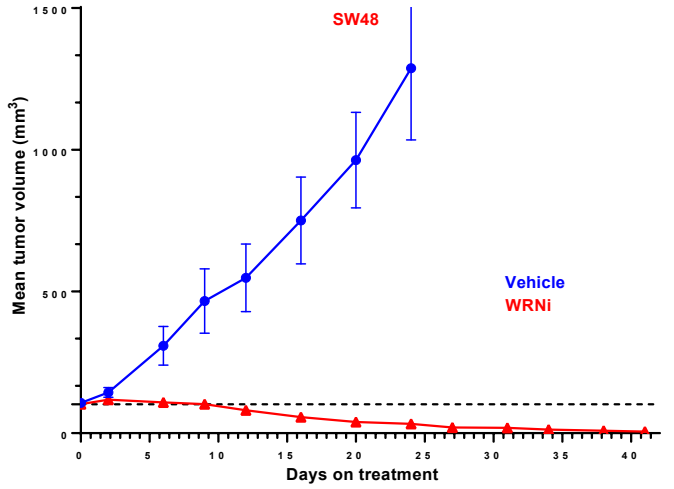
AACR 2023; Abstract 1628

Helicase domain (not exonuclease domain) is most critical for WRN activity



Behan et al., 2019, Nature

GSK/IDEAYA WRNi induced complete tumor regression *in vivo*

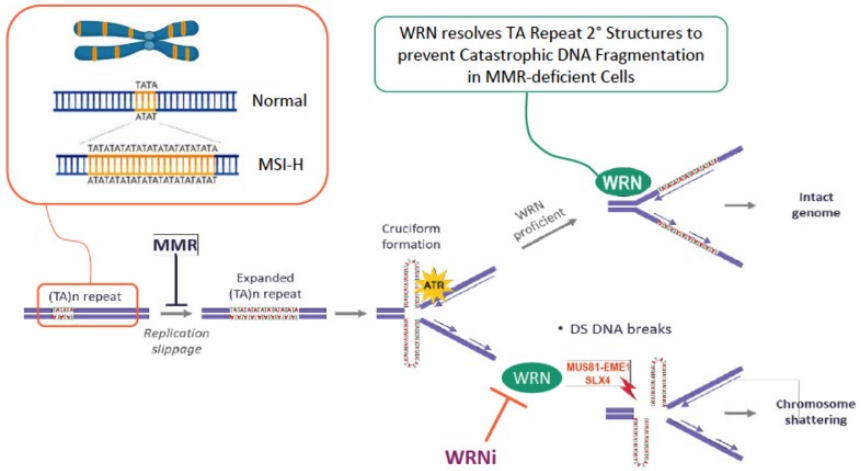


AACR 2023; Abstract 1628

GSK/IDEAYA WRNi Holds Potential as a Monotherapy and As a Combo Partner with GSK's Dostarlimab (PD1 inhibitor)

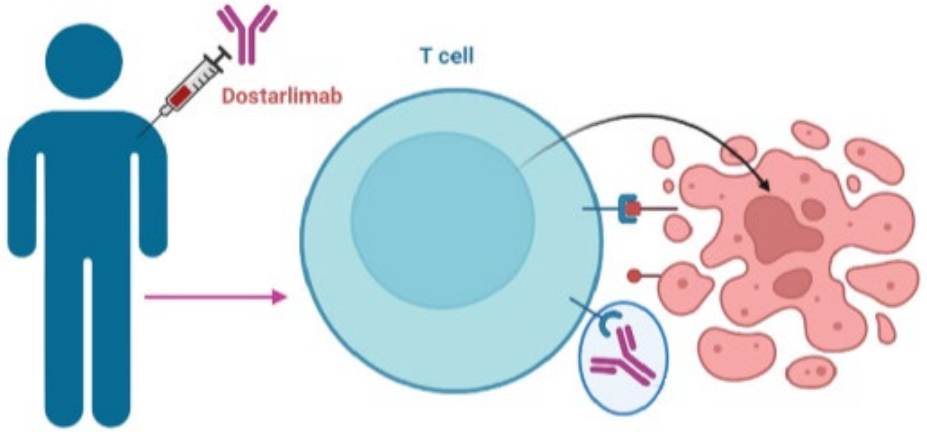
- Orthogonal MoAs of WRNi and PD1i (Dostarlimab) may present an opportunity for WRNi + Dostarlimab combinations to create potential added benefit in patients with MSI-H/dMMR solid tumors
  - WRN: Double Strand DNA breaks
  - PD1: Neoantigen processing / T-cell activation
- IND submission targeted in 2024 to enable First-in-Human study

WRNi: tumor intrinsic DNA damage



Modified based on Wietmarschen et al., 2020 Nature

PD1 / Dostarlimab: extrinsic immune/TME re-programming



Babar et al., Drug Discovery Today, 2023

IDEAYA Investor R&D Day

Closing Remarks

Industry Leading Potential First-in-Class Precision Medicine Oncology Pipeline

5 First-in-Class Clinical / IND-Enabling Stage Programs

- Darovasertib (PKC, Registrational), IDE397 (MAT2A, Ph2), IDE161 (PARG, Ph1), GSK101 (Pol Theta, Ph1), Werner (IND-Enabling)

Enabling First-in-Class Transformative Clinical Combinations

- Multi-pronged strategy in MTAP, including potentially first-in-class clinical combinations with PRMT5 (Amgen) and Topo-ADC (Gilead)
- Multiple potential transformative first-in-class clinical combination opportunities with IDEAYA pipeline, including with select ADCs

Next Generation Development Candidates (Targeting ≥ 7 clinical programs within cash runway)

- Targeting multiple development candidate nominations in 2024, including in MTAP-deletion

Investment Priorities to Enhance Leadership in Precision Medicine Oncology

Robust Data Informatics Capabilities - AI / Machine Learning to Reduce Time to IND

- Enhance leadership in computational drug, target, and biomarker discovery against First-in-Class opportunities

Industry Leading Structurally-Enabled Drug Discovery Platform to Unlock Challenging First-in-Class Targets

- Enhance drug discovery platform to enable challenging First-in-Class targets (DCs delivered for 2 helicases)

Pursue Breakthrough Neoadjuvant and Adjuvant Opportunities that Can Transform the Patient Journey

- Phase 2 advancement of first-in-class darovasertib in neoadjuvant / adjuvant uveal melanoma

Excellence in Translational Research to Discover Breakthrough Clinical Combos & Enrich Responder Population for Novel Targets

- First-in-Class Combos: PKC-cMET (Pfizer Registrational), MAT2A-PRMT5 (Amgen Ph1/2), MAT2A-Trop2ADC (Gilead Ph1), PARP-Pol Theta (GSK Ph1), Werner-PD1 (GSK Preclinical), Next Gen MTAP combos (IDYA Preclinical), IDYA-ADC combos
- First-in-Class Target Biomarkers: PKC-GNAQ/11, MAT2A-MTAP, PARG/Pol Theta-HRD, Werner-MSI, among others

IDEAYA BIOSCIENCES

IDEAYA Investor R&D Day

Analyst Q&A

Yujiro S. Hata
IDEAYA Biosciences
President and Chief Executive Officer