NASDAQ: IDYA



# **IDEAYA Biosciences**

Improving Lives
Through Transformative
Precision Medicines



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Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future financial performance of IDEAYA Biosciences, Inc. (the "Company") and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as "may," "will," "could," "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, assumptions, estimates or projections that are subject to change, 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; 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 2029; 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, regulatory approvals, manufacturing or release of data; any statements of expectation or belief regarding future events, potential markets dynamics, 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 the Company'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 the manufacturing and/or commercialization; timing of product launches, potential pricing and reimbursement; potential revenue, expected breakthrough, best or first-in-class or blockbuster status, regulatory landscape, economic conditions, competitive landscape, the Company'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, 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 or any other country regulatory authority. 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.

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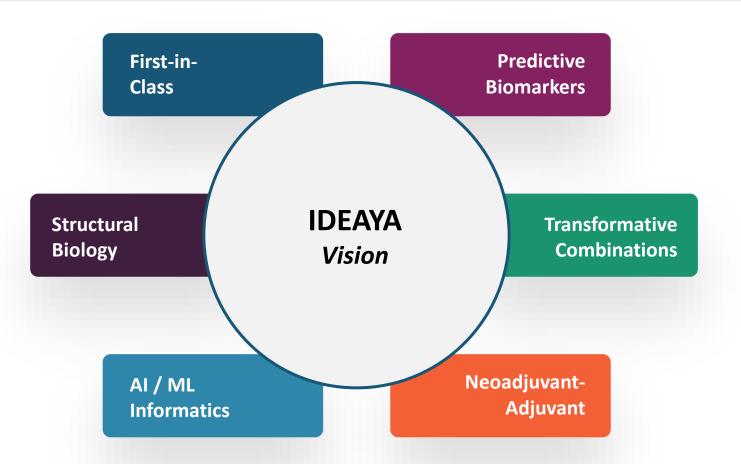
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## **IDEAYA Vision to Build Industry Leading Precision Medicine Oncology Company**

Improving Lives through Transformative Precision Medicines

Our mission is to advance the discovery, development, and commercialization of transformative precision medicines to address unmet medical needs in cancer



#### **Potential First-in-Class Pipeline**

6 Clinical Stage (5 SM & 1 ADC) 3 IND-Enabling (2 SM & 1 ADC)

#### **Biomarker Populations**

GNAQ/GNA11 DLL3

MTAP-Deletion B7H3/PTK7

HRD/BRCA 8P11

MSI-High

#### **Potential First-in-Class Combos**

PKC-cMET WRN-PD1

MAT2A-PRMT5 PARG-TOP1

POLQ-PARP MAT2A-TOP1



## **IDEAYA Precision Medicine Oncology Platform to Deliver First-in-Class Therapies**

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

Drug Discovery and Pharmacological Validation



Genomics – DNA and RNA Analysis

Proteomics – Protein Expression Profiling

Tissue (IHC, IF) and Liquid Biopsies Analysis

**Translational Research and** 

**Opportunity Expansion** 

**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, PARG and Pol Theta Helicase
- DECIPHER™ Dual CRISPR SL Library in DDR
   Cell Lines in collaboration with UCSD
- PAGEO<sup>™</sup> Paralogous Gene Evaluation in Ovarian in collaboration with Broad Institute
- Machine Learning and Multi-Omics platform

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, IDE275 (GSK959), IDE161, and IDE705 (GSK101)

- 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 Biosciences Highlights**

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

#### Target Milestone Guidance on Broad Pipeline of 6 Clinical & 3 Preclinical (IND-enabling) Programs:

PHASE 2/3	РНА	PRECLINICAL		
<ul> <li>DAROVASERTIB (PKC)</li> <li>Daro + Crizo 1L HLA-A2(-) MUM potential registrational Ph2/3 median PFS readout – by YE 2025</li> <li>Daro + Crizo Ph2 1L MUM median OS readout at medical conference – H2 2025</li> <li>Daro Ph2 Neoadjuvant UM clinical data update at medical conferences – mid-2025 and H2 2025</li> <li>Daro Ph3 Neoadjuvant UM registrational trial initiation – H1 2025</li> </ul>	<ul> <li>IDE397 (MAT2A)</li> <li>Phase 1/2 mono expansion ongoing IDE397 + Trodelvy® (Trop2-ADC)</li> <li>Expansion into NSCLC IDE397 + PRMT5</li> <li>Wholly-owned clinical combo with IDE892 (IDEAYA PRMT5) – H2 2025</li> <li>IDE849 / SHR-4849 (DLL3 ADC)</li> <li>Clinical data update at medical conference by Hengrui – Q3 2025</li> <li>Combo initiation with IDE161 – H2 2025</li> </ul>	<ul> <li>IDE275 / GSK959 (WERNER)</li> <li>Ongoing Phase 1 dose escalation</li> <li>IDE161 (PARG)</li> <li>Phase 1 mono dose optimization</li> <li>IDE161 + Merck's anti-PD-1, KEYTRUDA® (pembrolizumab)</li> <li>Phase 1 enrollment ongoing</li> <li>IDE161 + Topo1i-ADC</li> <li>Enable clinical combo with IDE849 – H2 2</li> <li>IDE705 / GSK101 (POL THETA)</li> <li>Phase 2 expansion (\$10M Milestone)</li> </ul>	<ul> <li>NEXT GEN PROGRAMS</li> <li>IDE892 DC (MTA-cooperative PRMT5) IND submission – Mid-2025</li> <li>IDE034 DC (B7H3/PTK7 Bi-Specific ADC) IND submission – H2 2025</li> <li>IDE574 DC (KAT6/7) IND submission – H2 2025</li> </ul>	

#### **Pharma Collaborations**











~\$2B in potential milestones

#### **Financials and Investor Relations**

~\$1.05B to fund operations into 2029 1, 2

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- (1) Includes aggregate of approximately \$1.05 billion of cash, cash equivalents and marketable securities as of March 31, 2025
- (2) IDEAYA's Form 10-Q dated May 6, 2025, as filed with the U.S. Securities and Exchange Commission
- KEYTRUDA® is a registered trademark of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co, Inc, Rahway NJ, USA



## **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)
	+cMET <sup>1</sup> Combination 1L HLA-A2(-) MUM	GNAQ/11						Ph 2 (AA) / Ph 3 registrational trial <sup>1</sup> – targeting median PFS readout by YE'25	Pfizer (4)	
<b>Darovasertib</b> <i>PKC</i>	(Neo)Adjuvant UM	GNAQ/11						Ph 2 clinical data update(s) – targeting mid'25 & H2'25 Ph3 Neoadj. UM registrational trial initiation <sup>2</sup> – H1'25		WW Commercial Rights
	cMET <sup>1</sup> Combination MUM	GNAQ/11						Ph 2 OS 1L MUM readout – targeting H2'25 HLA-A2(+) Phase 2 clinical trial <sup>3</sup>	Pfizer (4)	
IDE397	Monotherapy Solid Tumors	MTAP						Ongoing Phase 2 expansion in MTAP urothelial and lung cancer		WW Commercial
MAT2A	Combination UC and NSCLC	MTAP						Targeting Phase 1/2 IDE397 + Trodelvy® expansion into NSCLC	GILEAD (5)	Rights
<b>IDE849 (SHR-4849)</b> DLL3 ADC	SCLC, Neuroendocrine Tumors	DLL3						Clinical data update at medical conference – Q3'25 Combination initiation with IDE161 – H2'25	HENGRUI (6)	Worldwide Rights Outside of Greater China
IDE275 (GSK959) Werner Helicase	Solid Tumors	High-MSI						Ongoing Phase 1 Trial in MSI-High Solid Tumors	<b>GSK</b> (7)	50% US Profits and 20% costs
IDE161	Monotherapy Solid Tumors	HRD						Ongoing Phase 1 monotherapy dose optimization		WW Commercial
PARG	Combination Endometrial Cancer	High-MSI, MSS						Ongoing Phase 1 IDE161 + KEYTRUDA®	MERCK (8)	Rights
IDE705 (GSK101) Pol Theta Helicase	+Niraparib Combo Solid Tumors	HR Mutations						Targeting Phase 2 Expansion (\$10M Milestone)	GSK (7)	Global Royalties
IDE892 PRMT5 <sup>MTA</sup>	Combination Solid Tumors	МТАР						Targeting IND Submission – Mid-Year 2025 Enable wholly-owned combination with IDE397 – H2'2025		WW Commercial Rights
IDE034 B7H3/PTK7 BsADC	Solid Tumors	В7Н3/РТК7						Targeting IND Submission – H2'25	BIOCYTOGEN (9)	WW Commercial Rights
I <b>DE574</b> KAT6/7	Solid Tumors	8p11						Targeting IND Submission – H2'25		WW Commercial Rights
Platform	Solid Tumors	Defined Biomarkers						Multiple Potential First-in-Class Programs Advancing		WW Commercial Rights

<sup>(1)</sup> 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



<sup>(2)</sup> Phase 3 randomized registrational trial enables potential approval based on FDA Type C Meeting Q3 2024

<sup>(3)</sup> Targeting enrollment of additional HLA-A2(+) patients in ongoing IDE196-001 Phase 2 clinical trial

<sup>(4)</sup> Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreements for Darovasertib/Crizotinib Combination; IDEAYA retains all Darovasertib Commercial Rights

<sup>(5)</sup> 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. Gilead retains all commercial rights to Trodelvy.

<sup>(6)</sup> Pursuant to exclusive license agreement with Jiangsu Hengrui Pharmaceuticals Co., Ltd for worldwide rights outside of Greater China

<sup>(7)</sup> Pursuant to GSK Collaboration, Option and License Agreement: Polθ: Global Royalties; WRN: 50/50 US Profits + ex-US Royalties

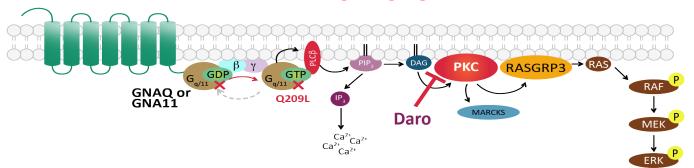
<sup>(8)</sup> Pursuant to Merck Clinical Trial Collaboration and Supply Agreement for IDE161 + Keytruda\*, an anti-PD-1 therapy; the Company will sponsor the study and Merck will provide Keytruda at no cost

<sup>(9)</sup> Pursuant to exclusive worldwide licensing and option agreement with Biocytogen

MAT2A = Methionine Adenosyltransferase 2a, MTAP = Methylthioadenosine Phosphorylase, MTA = Methylthioadenosine Phosphor PKC = Protein Kinase C, MUM = Metastatic Uveal Melanoma, Crizo = Crizotinib, UC = Urothelial Cancer, NSCLC = Non-Small Cell Lung Cancer, WW = Worldwide, HLA-A2(+) = HLA-A2\*02:01 Positive, DC = Development Candidate, TOP1i = Topo-I-Payload, BsADC = Bispecific Antibody Drug Conjugate

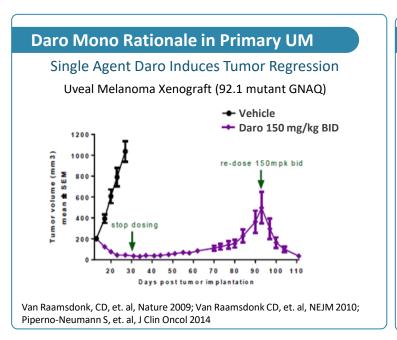
# Darovasertib: Potential to Broadly Impact Uveal Melanoma (UM) Potential First-in-Class and Best-in-Class in (Neo)adjuvant UM and Metastatic UM (MUM)

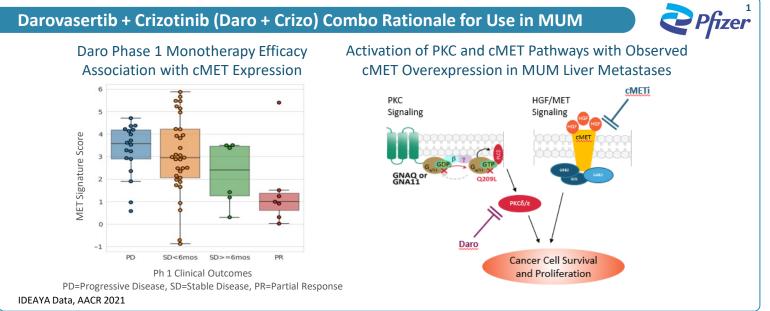
Mutations in GNAQ / GNA11 activate PKC Signaling, a genetic driver of Uveal Melanoma



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





## **Darovasertib and Uveal Melanoma Patient Journey**

## High Unmet Need and Multiple First-Line Opportunities in UM and MUM<sup>1</sup>

+95% of UM patients harbor GNAQ/GNA11 mutation

#### **Uveal Melanoma Patient Journey**

	Neoadjuvant UM		
HLA-A2-Negative <sup>2</sup>	No Approved Therapies  Daro: Phase 3  Enucleation Cohort		
HLA-A2-Positive <sup>2</sup>	Daro: Phase 3 Plaque Brachytherapy Cohort		
Target Treatment Duration	6 months		
Target Clinical Endpoints	Eye Preservation, Proportion of patients with BCVA 15-letter loss, No detriment to EFS		
Annual Incidence <sup>3</sup>	~12K		

Adjuvant UM
No Approved Therapies Daro: Phase 2
≥6 months
Relapse Free Survival
~12K

мим
No Approved Therapies Daro + Crizo (HLA A2-) Phase 2/3 Registrational Trial
Daro + Crizo (HLA A2+) Target NCCN / Compendia Listing
mPFS + ~3 months
ORR, mPFS, mOS
~4-5k



<sup>(1)</sup> No approved systemic therapies in multiple UM and MUM indications across the patient journey

<sup>(2) ~70%</sup> HLA-A\*02:01-negative and ~30% HLA-A\*02:01-positive frequency observed based on IDEAYA Clinical Study Data (n=170)

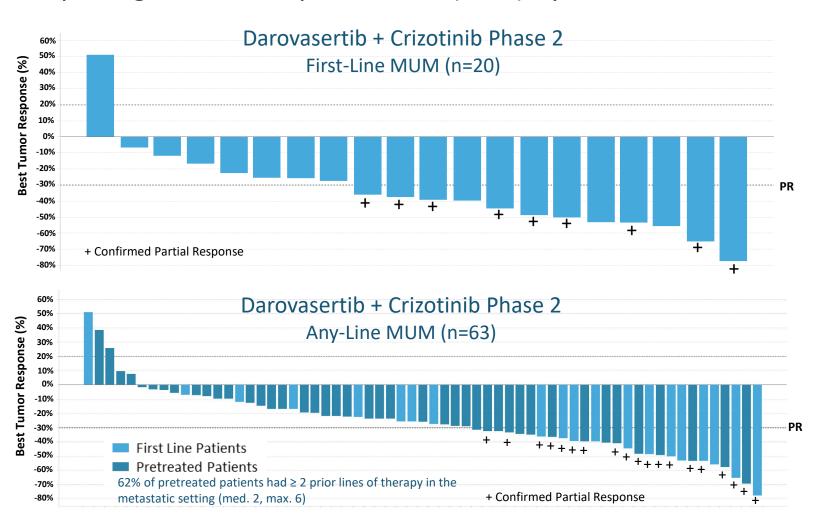
<sup>(3)</sup> Annual incidence for North America, Europe and Australia ( as applicable), based on market research analysis

UM = Uveal Melanoma, MUM = Metastatic Uveal Melanoma, BCVA = Best Corrected Visual Acuity ORR = Overall Response Rate, mPFS = Median Progression Free Survival, mOS = Median Overall Survival



## 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

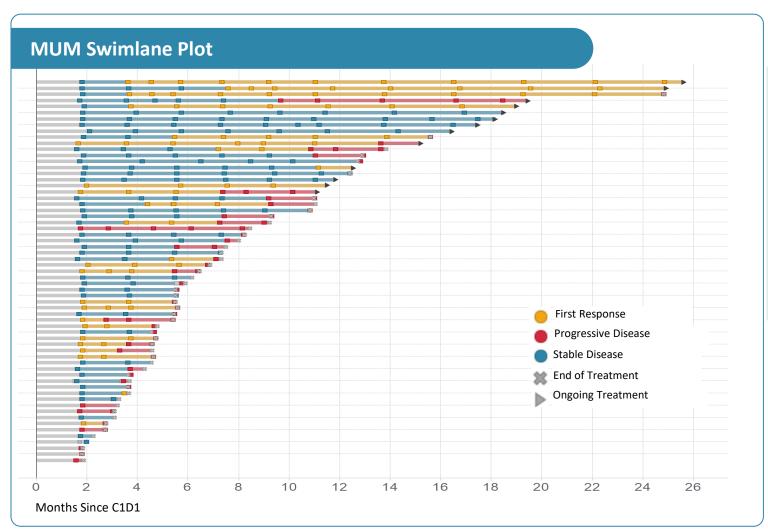
Response by RECIST 1.1 Any-Line MUM	Evaluable (N=63)
Confirmed ORR (19/63)	30%
Tumor Shrinkage (58/63)	92%
>30% Tumor Shrinkage (27/63)	43%
Best Overall Response	
cPR (19/63)	30%
SD (37/63)	59%
DCR (56/63)	89%





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

## Observed Compelling Median Progression Free Survival with Encouraging Trend



#### Darovasertib + Crizotinib Phase 2

#### Median Progression Free Survival

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

#### Treatment Duration – Observations

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



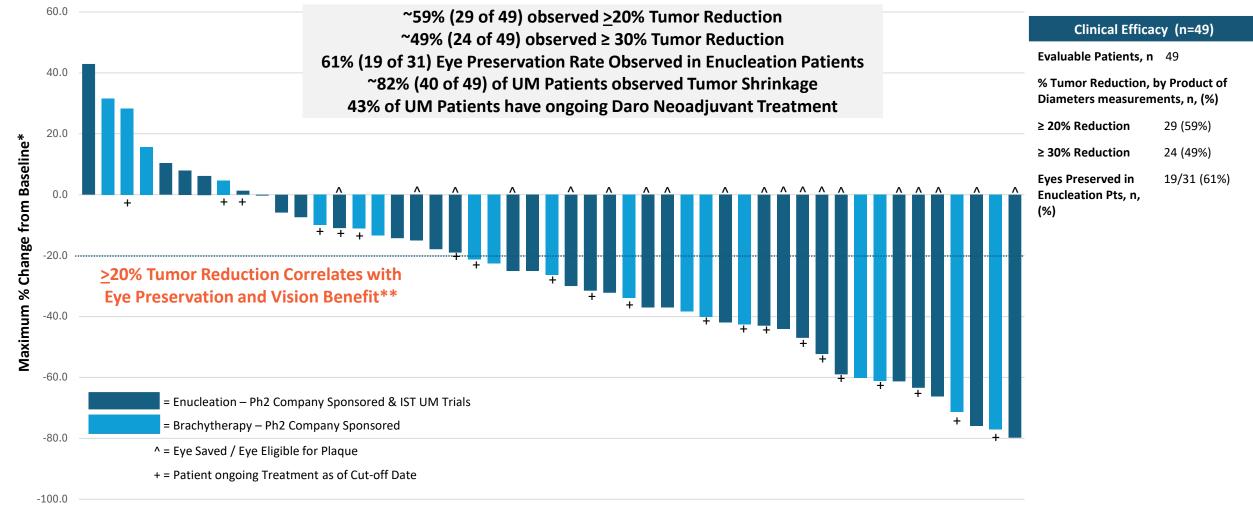
## **Review of Published Clinical Data in MUM**

	Darovasertib + Crizotinib	Cabozantinib Mono / Crizotinib Mono	Selumetinib + DTIC	lpi + Nivo	Tebentafusp
Target / Mechanism	PKC + cMET	сМЕТ	MEK + Chemotherapy	CTLA4 + PD-1	HLA-A2-0201 Bi-Specific
Study Name(s)	NCT03947385	A091201 <sup>1</sup> / NCT05063058 <sup>2</sup>	NCT01974752 <sup>3</sup>	NCT02626962 <sup>4</sup>	IMCgp100-102 <sup>5</sup>
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% <sup>6</sup>	23% <sup>7</sup> / NA	35% <sup>7</sup>	27% <sup>7</sup>	44% <sup>7</sup>
Confirmed ORR% (by RECIST 1.1)	First-Line = 45% / Any-Line = 30% / Hepatic Only = 37% <sup>6</sup>	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 <sup>6</sup>	2 months / NA	2.8 months	3 months	2.8 months

Note: these data are derived from different clinical studies, with differences in study design and patient populations. No head-to-head studies have been conducted. (1) 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 (2) European Journal of Cancer, Leyraz, et. al, 2022; 146-155 (3) Journal of Clinical Oncology, Carjaval, et. al, 2018; 1232-1239 (4) ASCO 2021, Piulats, J, et. al, Ipi = Ipilimumab, Nivo = Nivolumab, ORR% did not require PR/CR confirmation (5) Based on Immunocore reported 2L+ study data (to reflect comparative patient population) and by independent review and ORR% was with confirmed PRs (6) ESMO 2023 Proffered Presentation McKean, M, 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 (7) Estimated from Waterfall plot



# Darovasertib Neoadjuvant Therapy: Ph2 Company Sponsored & Ph2 IST UM Trials 61% (19 of 31) Observed Eye Preservation and 49% (24 of 49) with >30% Tumor Reduction\*

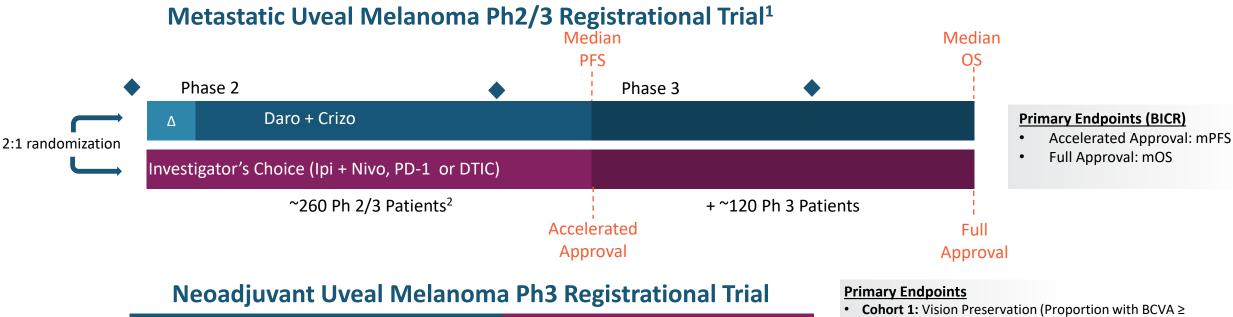


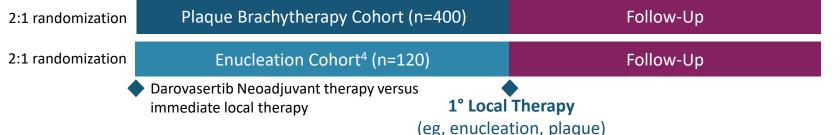


IST = Investigator Sponsored Trial

## Darovasertib Ph2/3 Registrational Trial Designs in MUM & Neoadjuvant UM

Broad opportunity to address unmet need in MUM and Save the Eye and Protect Vision in Neoadjuvant UM





- Cohort 1: Vision Preservation (Proportion with BCVA ≥ 15 letters loss)
- Cohort 2: Eye Preservation Rate

#### **Secondary Endpoints**

- Cohort 1: Proportion with clinically significant macular edema;
   Proportion with VA 20/200 or worse; Radiation reduction
- Cohorts 1 & 2: ORR (≥20% ocular tumor shrinkage by product of diameters); No detriment to Event Free Survival (EFS)

FDA ▶ Orphan Drug Designation in UM³; Fast Track Designation in MUM; Breakthrough Therapy Designation⁴

(1) Clinicaltrials.gov: NCT05987332



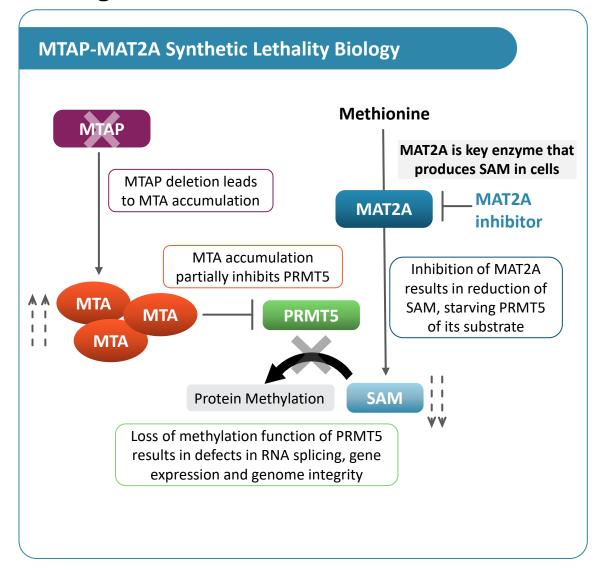
<sup>(2)</sup> Phase 2 study contemplates data set of n=200 patients randomized 2:1 with treatment arm at move forward dose in support of potential accelerated approval based on mPFS

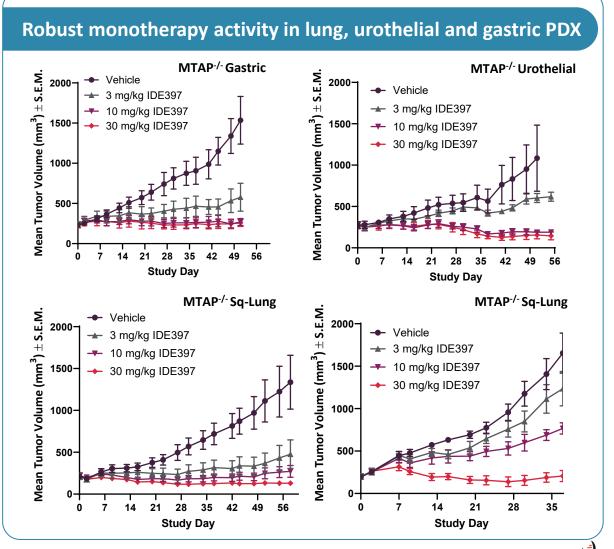
<sup>(3)</sup> Orphan Drugs benefit from certain tax credits and may be excluded from certain mandatory price negotiation provisions of the 2022 Inflation Reduction Act

<sup>(4)</sup> Breakthrough therapy designation for the neoadjuvant treatment of adult patients with primary uveal melanoma (UM) for whom enucleation has been recommended 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

## MAT2A Inhibition is Synthetic Lethal with MTAP-Deletion

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



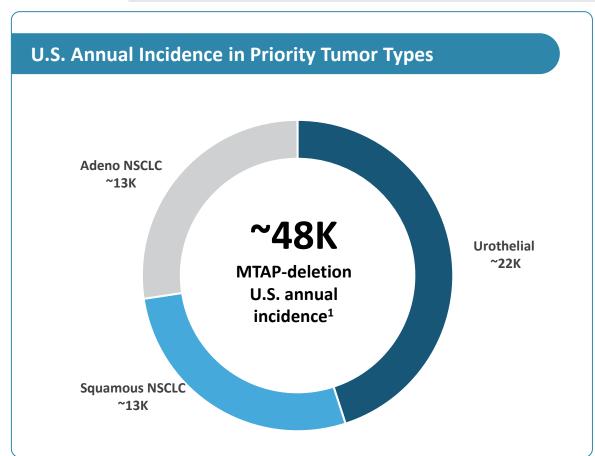


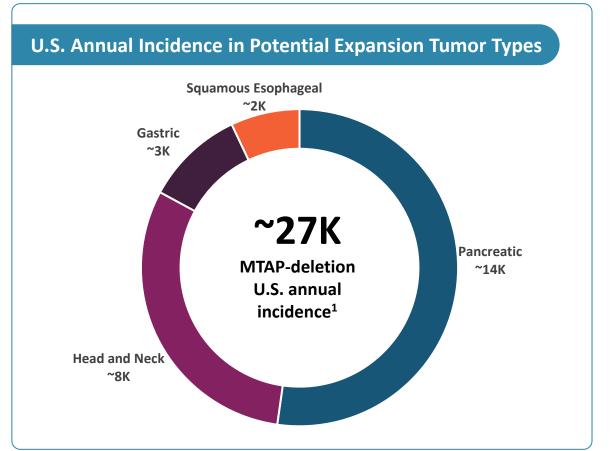


### **IDE397: Phase 2 Potential First-in-Class MAT2A Inhibitor**

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

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



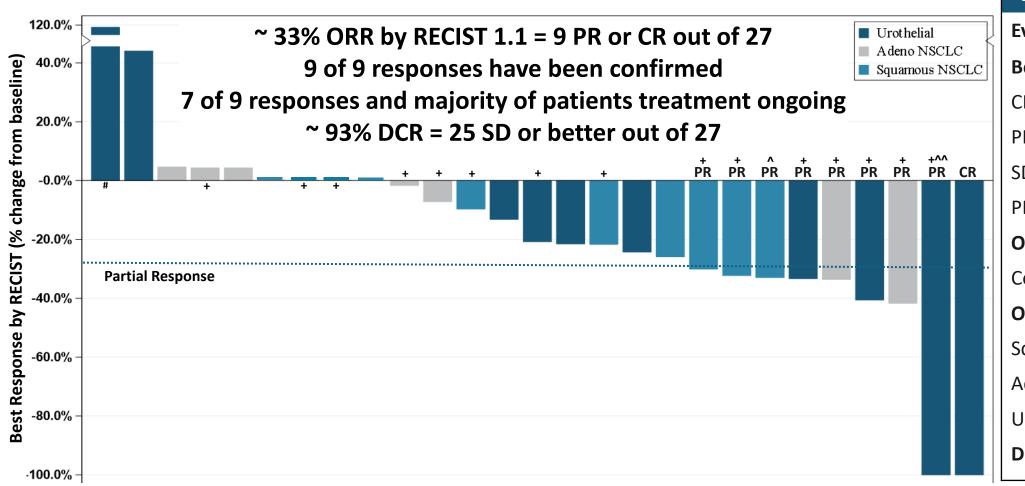






## IDE397 Phase 1 Clinical Efficacy in MTAP-Deletion NSCLC & UC

Best Response by RECIST 1.1 at 30mg QD Phase 2 expansion dose<sup>1</sup>



Efficacy by RECI	ST 1.1 <sup>1</sup>			
Evaluable Pts	27			
Best Response, n (9	%)			
CR	1 (4)			
PR	8 (30)			
SD	16 (59)			
PD	2 (7)			
ORR, n (%)	9 (33)			
Confirmed, n^^	9			
ORR, n (%), by Tumor (n)				
Squam NSCLC (8)	3 (38)			
Adeno NSCLC (9)	2 (22)			
Urothelial (10)	4 (40)			
DCR, n (%)	25 (93)			



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

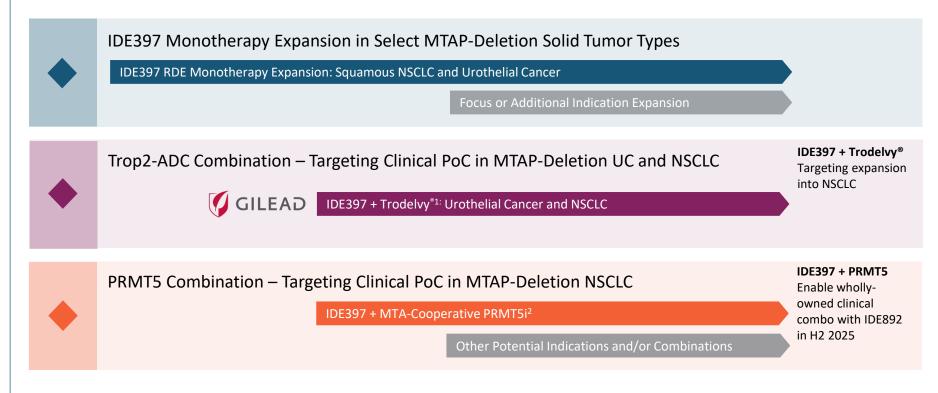
Clinical Strategic Focus on High Conviction Rational Combinations

#### **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





<sup>(1)</sup> Trodelvy® = Gilead's Trop-2 directed ADC

<sup>2)</sup> UC = Urothelial Cancer, NSCLC = Non-Small Cell Lung Cancer

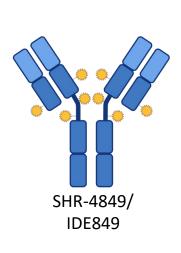
<sup>(3)</sup> IDE892, IDEAYA PRMT5 inhibitor in IND-enabling studies

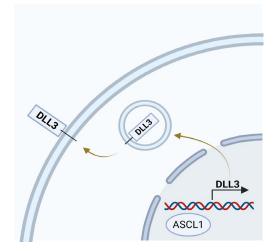
## IDE849 (SHR-4849): Phase 1 DLL3 TOP1i ADC

## First-in-Class Potential and Targeting Lineage Survival Oncogene Activity

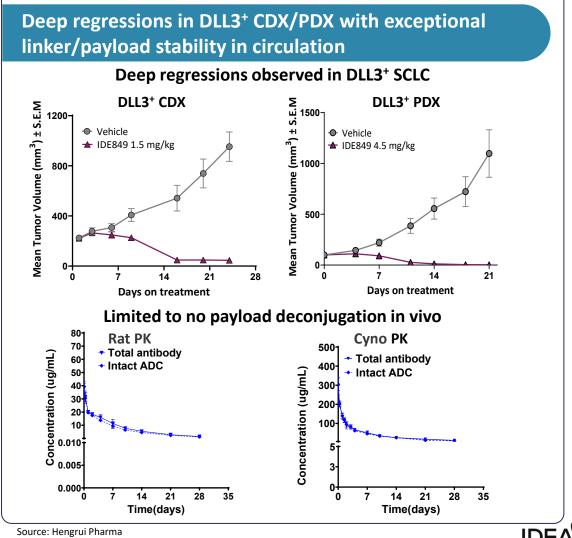
#### IDE849 (SHR-4849) potential first-in-class/best-in-class

The SCLC lineage survival oncogene, ASCL1, directly promotes DLL3 expression





- > DLL3 expression driven by the tumor-essential ASCL1 TF
- Humanized antibody with strong affinity and high selectivity
- Proprietary TOP1i payload (~4,000 patients treated)
- Internalization-dependent cleavable linker
- Optimized DAR value of 8
- High plasma stability
- Estimated high therapeutic index

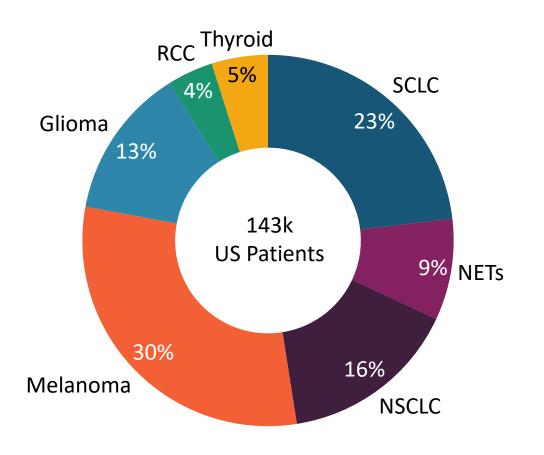


# DLL3 Expression is Upregulated in a Broad Range of Solid Tumor Types >100k Potential Addressable Population in the US Alone

#### **Table of DLL3 Upregulated Expression Solid Tumors**

Tumor Type	US Incidence (2024), 000	DLL3 Expressed, %	Addressable US Population, 000
SCLC	33	85%	33.0 <sup>1</sup>
NETs	37	34.1%	12.6
NSCLC	202	11%	22.2
Melanoma	101	43%	43.4
Glioma	25	72-78%	18.8
RCC	82	7%	5.7
Thyroid	44	16%	7.0

#### Addressable US Population: SCLC and NETs only 32%



Source: SEER, Rojo, F., at al., Lung Cancer. 2020;147:237–243; Tanaka, K., at al., Lung Cancer. 2018 Jan:115:116-120; Yao, J., at al., The Oncologist, 2022, 27, 940–951; Ali, G., at al., Front. Oncol. 11:729765; Song, H., at al., Exp Ther Med 16: 53-60, 2018. Lozada JR, et al. Expression Patterns of DLL3 across Neuroendocrine and Non-neuroendocrine Neoplasms Reveal Broad Opportunities for Therapeutic Targeting. Cancer Res Commun. 2025 Feb 1;5(2):318-326. doi: 10.1158/2767-9764.CRC-24-0501



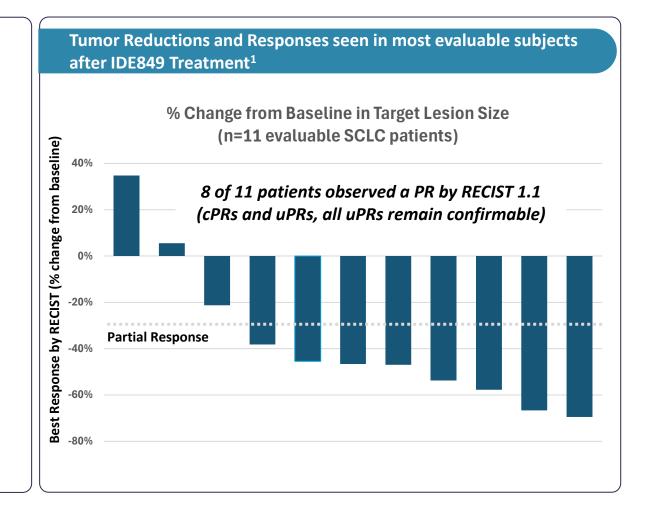
<sup>&</sup>lt;sup>1</sup>Based on 100% as no need to stratify SCLC population

## IDE849 (SHR-4849): Potential First-in-Class with Preliminary Ph1 Clinical PoC

Phase 1 FIH Study of DLL3 Topo-1-Payload ADC in Pre-Treated SCLC Patients

#### Phase 1 Dose Escalation in China in Pre-Treated SCLC Patients<sup>1</sup>

- Preliminary Clinical PK Summary
  - Dose dependent increase in exposure
  - Promising T-Ab to ADC ratio
- Preliminary Clinical Efficacy Summary<sup>2</sup>
  - 8 of 11 evaluable SCLC patients observed a partial response by RECIST 1.1, resulting in a ~73% ORR (confirmed and unconfirmed, all unconfirmed PRs remain confirmable)
- Preliminary Clinical Safety Summary
  - TRAEs were largely Grade 1 or 2
  - No AE leading to discontinuation (related or unrelated)
  - Maximum tolerated dose has not yet been reached
  - Most commonly observed TRAEs: white blood cell count decreased, anemia, neutrophil count decreased, nausea and platelet count decreased



<sup>(1)</sup> All unconfirmed responses pending further evaluation

<sup>(2)</sup> Clinical efficacy summary at therapeutic dose levels

## IDE849 (SHR-4849): Potential First-in-Class with Preliminary Ph1 Clinical PoC

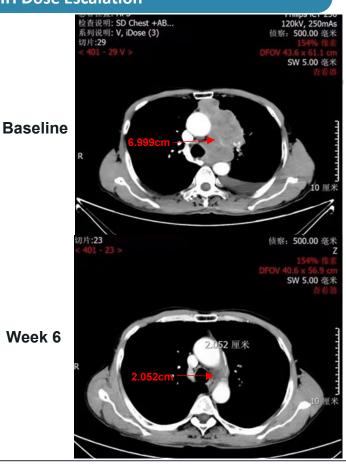
Pre-Treated SCLC Patient Case Study and Preliminary IDEAYA Clinical Development Plan

#### **Case Example in Phase 1 FIH Dose Escalation**

Week 6

A 70-year-old male with extensive stage SCIC who had failed prior PD-L1 and platinum doublet treatment

The subject was treated with IDF849 and achieved PR at Week 6 with a 70.6% reduction in the large mediastinal tumor mass



IDE849 Phase 1/2 Clinical Development Plan

IDE849 Monotherapy Dose Escalation and Expansion



IDE849 Combination with IDE161/PARG



#### **Preliminary Clinical Strategy:**

- Potential monotherapy path in 2L plus SCLC
- Evaluate clinical combinations, including with SOC, in 1L SCLC
- Evaluate NETs as monotherapy, including potential basket trial
- Target to enhance durability with IDE849 + IDE161/PARG combo



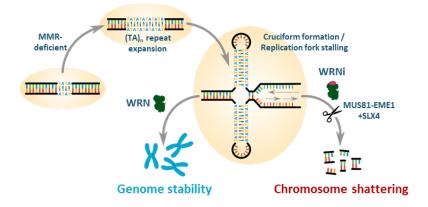


## IDE275 (GSK959): Phase 1 Werner Helicase Non-Covalent Inhibitor

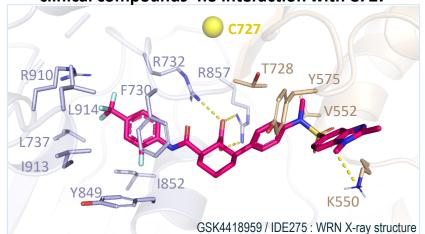
# New Drugs on the Horizon AACR 2025, Chicago, IL Oral Presentation

## Potential Best-in-Class Profile with Distinct Binding Mode

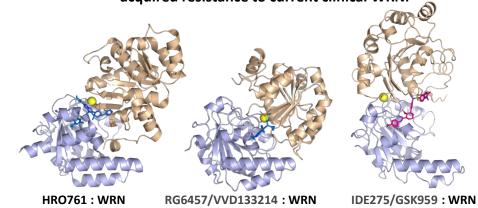
WRN Helicase Activity is Essential for Survival of MSI-high/dMMR Cancer Cells



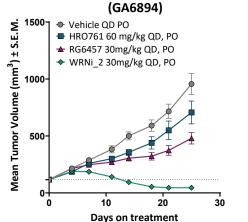
IDE275 (GSK959) has distinct binding mode vs current clinical compounds- no interaction with C727



Unique IDE275/GSK959-bound helicase conformation can overcome intrinsic and acquired resistance to current clinical WRNi

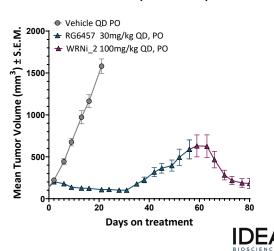


### MSI-H Chemo Refractory Gastric Cancer PDX (GA6894)



WRNi 2 = in vivo tool analog of IDE275/GSK959

#### SW48 (MSI-H CRC)



## IDE275 (GSK959): Phase 1 Werner Helicase Non-Covalent Inhibitor



## Phase 1 Clinical Development Plan in MSI-High Solid Tumors

## IDE275 (GSK959) Werner Helicase Inhibitor

- IDE275 (GSK959) has demonstrated robust and selective synthetic lethality preclinically in the high microsatellite instability (MSI-High) biomarker setting
- Phase 1 clinical trial enrolling patients having tumors characterized by MSI-High (NCT06710847)

#### **Werner Clinical Development Plan**

## PART 1: Monotherapy Dose Escalation

#### **Monotherapy IDE275 (GSK959)**

- ≥18 years old
- >3 months life expectancy
- dMMR/MSI-H tumor
- Advanced (unresectable/metastatic or recurrent)
- Must have exhausted SOC

## PART 2: Monotherapy Dose Expansion

Histological diagnosis of CRC or ECH

## PART 3: Combination Dose Escalation

#### Combo IDE275 (GSK959) + PD-1

- ≥18 years old
- >3 months life expectancy
- dMMR/MSI-H tumor
- Advanced (unresectable/metastatic or recurrent)
- Must have exhausted SOC



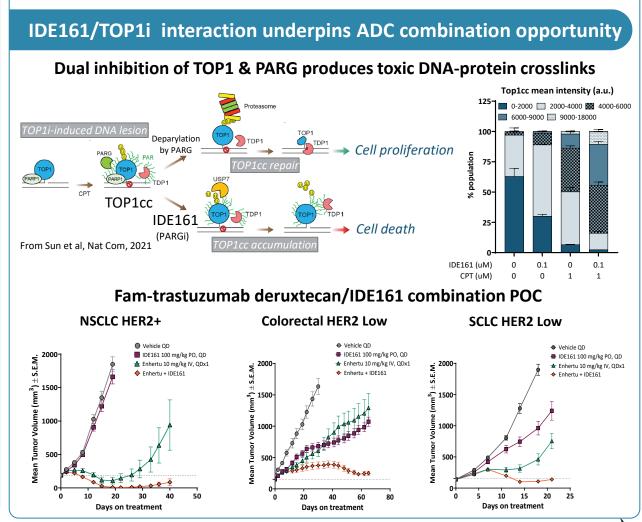
GSK Strategic Partnership: 50/50% US Profit Share and ex-US Royalties, ~\$1B Milestones, incl. up to \$20M Preclinical / Ph1 Clinical; Cost Share 80% (GSK) / 20% (IDEAYA); Potential Combination with GSK's Jemperli™, a PD-1 IO Agent



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

SL with replication stress; broad potential in combination with TOP1i-ADCs

#### PARGi disrupts DDR and replication fork fidelity PARG inhibition is synthetic-lethal with oncogene-induced replication stress PARP1 initiates > PARG inhibition promotes **DDR** death by mitotic catastrophe Damaged DNA Recruitment of DNA damage repair proteins ▼ Vehicle QD; po ● IDE161 100 mg/kg QD Poly (ADP-ribose) PARG resolves ■ Niraparib 45 mg/kg QD Volume (mm³) 2000-**DDR** 1500-PARG hydrolyzes Poly 1000 (ADP-ribose) 500· Release of DNA 10 20 30 40 50 Days on treatment Replication stress triggers replication fork reversal PARG is required for replication fork restart Adapted from Pillay et al. Cancer Cell, 2019

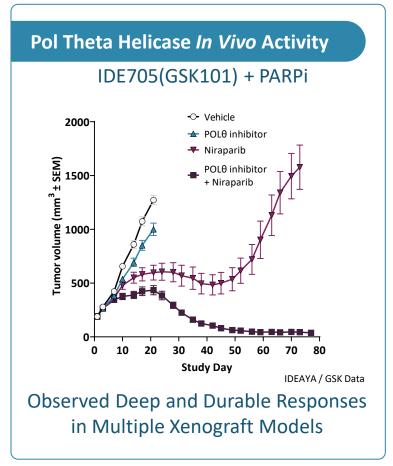


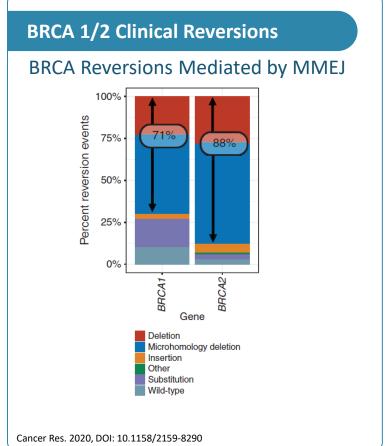


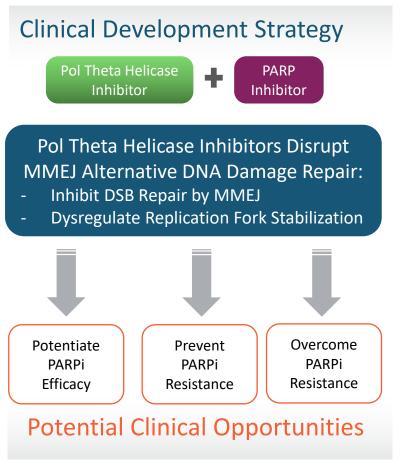
GSK

## IDE705 (GSK101): Potential First-in-Class Ph1 Pol Theta Helicase Inhibitor

Phase 1 in Combination with Niraparib (PARPi)



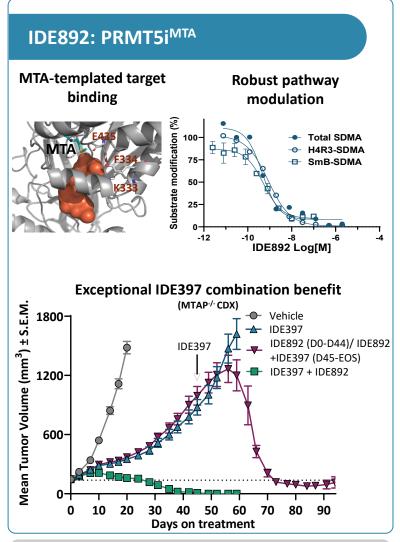




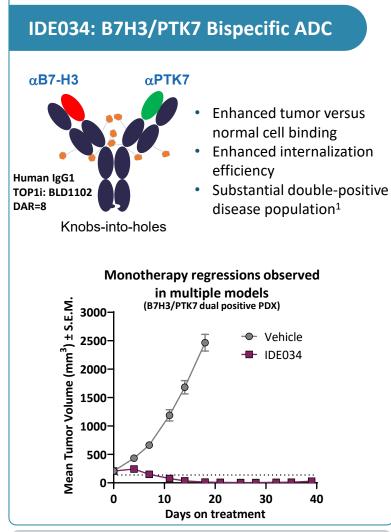
GSK Strategic Partnership: Global Royalties with GSK covering all Costs, ~\$1B Milestones, incl. up to \$20M Preclinical / Ph1 Clinical Potential Combination with GSK's Zejula™, a PARP Inhibitor



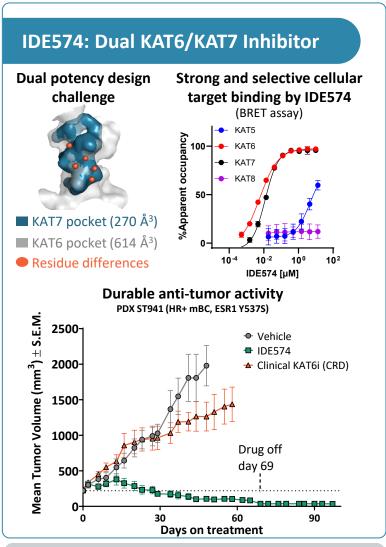
## **Development Candidates: Targeting INDs Mid-2025 to H2-2025**



Wholly-owned MAT2a/PRMT5 combination for MTAP-deletion



Dual tumor-antigen targeting to maximize SM combination benefit (IDE161)



Potent pathway modulation delivers broad opportunity to drug lineage-addiction

## **Building a Fully-Integrated Biotech in Precision Medicine Oncology**

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

#### **CLINICAL PROGRAMS**

Ph 2/3 – Darovasertib (PKC) <sup>1</sup>
Ph 2 – IDE397 (MAT2A) <sup>1</sup>
Ph 1 – IDE849 (DLL3 ADC) <sup>2</sup>
Ph 1 – IDE275 (Werner Helicase) <sup>3</sup>
Ph 1 – IDE161 (PARG) <sup>1</sup>
Ph 1 – IDE705 (Pol Theta Helicase) <sup>3</sup>

#### **DEVELOPMENT CANDIDATES**

IDE892 (PRMT5) – Targeting IND Mid-2025 IDE034 (B7H3/PTK7 Bi-Specific ADC <sup>4</sup>) – Targeting IND H2 2025 IDE574 (KAT6/7) – Targeting IND H2 2025

#### PRECLINICAL PROGRAMS

Multiple Potential First-in-Class
Programs Advancing

#### **6 Clinical Programs**

**Targeting 3 IND Filings** 

Darovasertib Registration-Enabling Trial with Potential Accelerated Approval in HLA-A2(-) MUM and Ph3 registrational trial targeted in Neoadjuvant UM 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), IDE849 (Ph1), IDE275 / GSK959 (Ph 1), IDE161 (Ph 1), IDE705 / GSK101 (Ph 1), IDE892 (IND-enabling), IDE034 (IND-enabling), and IDE574 (IND-enabling)

Strong Balance Sheet with ~\$1.05B<sup>5</sup> and opportunity for milestone payments with cash runway into 2029

**Pharma Collaborations** including Pfizer, Gilead, Merck, Hengrui, and GSK partnership with ~\$2 billion<sup>3</sup> in potential milestones



<sup>(1)</sup> Clinical Trial Collaboration and Supply Agreements, independently with Pfizer (Darovasertib + Crizotinib), Gilead (IDE397 + Trodelvy®), and Merck (IDE161 + KEYTRUDA®); IDEAYA retains all commercial rights to its products

<sup>2)</sup> IDE849 (SHR-4849): DLL3 Top1i Antibody Drug Conjugate. Exclusive license agreement with Jiangsu Hengrui Pharmaceuticals Co., Ltd for worldwide rights outside of Greater China

<sup>(3)</sup> IDE705 (GSK101) Pol Theta Program Cost Share = 100% GSK with ~\$1B Milestones and WW Royalties; IDE275 (GSK959) Werner Helicase Program Cost Share = 80% GSK / 20% IDEAYA with ~\$1B Milestones, 50/50 US Profit Share and Ex-US Royalties

<sup>4)</sup> IDE034: B7H3/PTK7Top1i Bispecific ADC development candidate. Exclusive worldwide licensing and option agreement with Biocytogen

Includes aggregate of approximately \$1.05 billion of cash, cash equivalents and marketable securities as of March 31, 2025