



July 2021

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 any expectations regarding the Company’s target discovery platform or new target validation efforts as creating opportunities for research and development initiatives; any projections of financial information, market opportunities, cash runway or profitability; any statements about historical results that may suggest trends for the Company’s business; any statements of the plans, strategies, and objectives of management for development programs or future operations; any statements about the timing of preclinical research, clinical development, regulatory filings, manufacturing or release of data; any statements of expectation or belief regarding future events, potential markets or market size, technology developments, or receipt of cash milestones, option exercise fees or royalties; and any statements of assumptions underlying any of the items mentioned. The Company has based these forward-looking statements on its current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company’s control. These and other important factors may cause actual results, performance or achievements to differ materially from those expressed or implied by these forward-looking statements. The forward-looking statements in this presentation are made only as of the date hereof. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see the Company’s periodic filings with the Securities and Exchange Commission (the “SEC”), including its Quarterly Report on Form 10Q for the quarter ended March 31, 2021 and any current and periodic reports filed thereafter. Except as required by law, the Company assumes no obligation and does not intend to update these forward-looking statements or to conform these statements to actual results or to changes in the Company’s expectations.

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

# IDEAYA Biosciences Highlights

**Leading Synthetic Lethality (SL) focused biotechnology company** advancing transformative precision medicine therapies for cancer patients

- **Broad Pipeline for Key Emerging Targets** including clinical stage IDE397 (MAT2A) and IDE196 (PKC), and development candidate selection stage programs PARG & Pol Theta
- **Pharma Collaborations** with GSK (over ~\$3 billion in potential milestones) and Pfizer
- **Strong Balance Sheet** with ~\$400 M in cash anticipated to fund operations into 2024<sup>1, 2</sup>
- **NASDAQ:** IDYA

- **Target Catalysts – 2021**

- IDE397 Phase 1
  - Clinical Pharmacodynamic Data (Tumor PD - Q4)
- Select PARG Development Candidate
- Select Pol Theta Development Candidate
- Darovasertib (IDE196) Phase 1/2
  - Clinical Data Update for Combination(s)
  - Regulatory Guidance Monotherapy and/or
  - Regulatory Guidance Combinations (H1 2022)

(1) IDEAYA Form 10Q and Q1 2021 Financials filed with the U.S. Securities and Exchange Commission on May 10, 2021

(2) Estimated, including cash, cash equivalents and marketable securities as of March 31, 2021, and subsequent proceeds from issuance of shares under an at-the-market (ATM) facility and from issuance of shares under an underwritten public offering, pursuant to IDEAYA Form 10Q and Q1 2021 Financials (May 10, 2021), IDEAYA Prospectus Supplement (July 8, 2021) and IDEAYA Form 8K (July 12, 2021)

# Synthetic Lethality

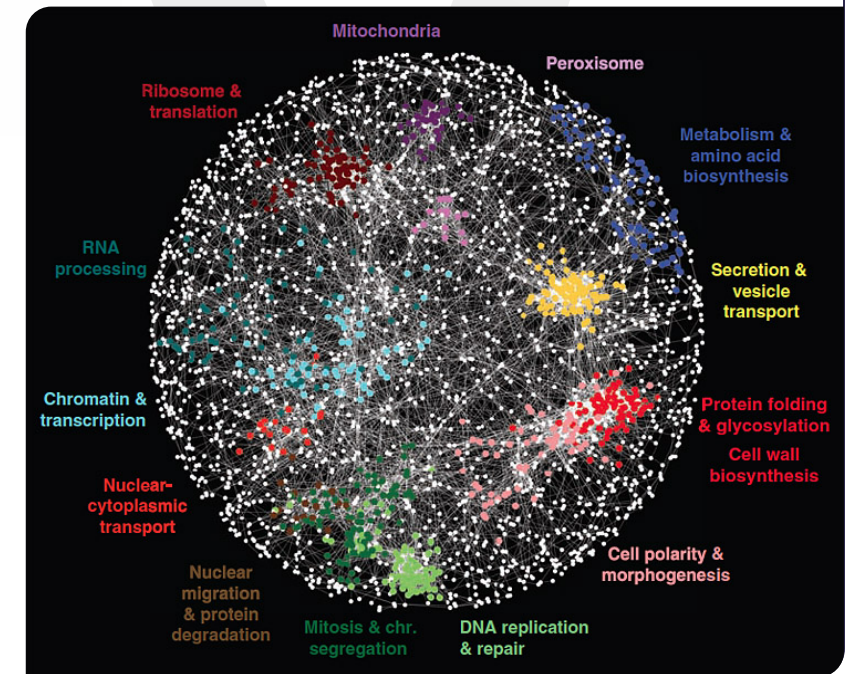
## The Next Frontier in Precision Medicine Oncology

**Synthetic Lethality** provides a powerful approach to discover novel precision medicine therapies with patient biomarkers, including MTAP-deletion (~15% of solid tumors), BRCA/HRD (Breast, Prostate, Ovarian), and high-MSI (15% GI Cancers)



- **Synthetic lethality** occurs when the simultaneous perturbation of two genes results in cell death
- Synthetic lethal interactions with tumor-specific mutations (biomarker) may be exploited to develop anticancer therapies
- Large-scale screening for synthetic lethal targets has progressed through advances in molecular biology (e.g., RNA interference, CRISPR-Cas9 editing) and bioinformatics

Nature Reviews Genetics, Vol. 18, 2017, Hieter, et al



Reference: Charles Boone

# IDEAYA's Precision Medicine Oncology Pipeline

Building the Industry Leading Synthetic Lethality Focused Biotechnology Company

## Precision Medicine Pipeline

|                     |                     | Modality/Indication                 | Biomarker            | Preclinical | IND Enabling | Phase 1 | Phase 2 | 2021 Goals                                                                       | Collaborations                                                                            | Commercial (IDEAYA)                      |
|---------------------|---------------------|-------------------------------------|----------------------|-------------|--------------|---------|---------|----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|------------------------------------------|
| Synthetic Lethality | IDE397<br>MAT2A     | Monotherapy<br>Solid Tumors         | MTAP                 |             |              |         |         | Clinical Pharmacodynamic Data (PD)<br>Tumor PD Q4 2021                           |  (1)   | US 50/50 Profit Share<br>Ex-US Royalties |
|                     |                     | Combinations<br>Solid Tumors        | MTAP                 |             |              |         |         | Preclinical Data to enable Combos<br>(Taxanes, PRMTi, Others)                    |                                                                                           |                                          |
|                     | PARG                | Ovarian, Gastric,<br>Breast Cancers | HRD                  |             |              |         |         | Select Development Candidate H2 2021                                             |  (2)   | WW Commercial Rights                     |
|                     | Pol Theta           | Small Molecule<br>Protein Degraders | HRD                  |             |              |         |         | Select Development Candidate H2 2021                                             |  (1)   | Global Royalties                         |
|                     | WRN                 | GI Cancers                          | High-MSI             |             |              |         |         | Chemistry Lead Optimization                                                      |  (1)   | US 50/50 Profit Share<br>Ex-US Royalties |
|                     | MTAP-SL             | Solid Tumors                        | MTAP                 |             |              |         |         | Lead Series                                                                      |                                                                                           | WW Commercial Rights                     |
|                     | Platform            | Solid Tumors                        | Defined<br>Biomarker |             |              |         |         | Lead Series (DNA Damage Targets)<br>New Target / Biomarker Validation            |                                                                                           | WW Commercial Rights                     |
| Kinase              | Darovasertib<br>PKC | Monotherapy<br>MUM, Skin Melanoma   | GNAQ/11              |             |              |         |         | Regulatory Guidance in MUM H2 2021<br>(Monotherapy) and/or H1 2022 (Combination) |  (3) | WW Commercial Rights                     |
|                     |                     | +MEK, +cMET<br>Combinations, MUM    | GNAQ/11              |             |              |         |         | Clinical Data Update - Combination(s) H2 2021                                    |                                                                                           |                                          |

- (1) Pursuant to GSK Collaboration, Option and License Agreement: MAT2A and WRN: 50/50 US Profits + ex-US Royalties; Polθ: Global Royalties  
 (2) Pursuant to CRUK Evaluation, Option and License Agreement, with ongoing Collaborative Research; IDEAYA controls all Commercial Rights  
 (3) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreement for MEK and cMET Combinations; IDEAYA retains all IDE196 Commercial Rights

MAT2A=methionine adenosyltransferase 2a, MTAP=methylthioadenosine phosphorylase, PARG= poly (ADP-ribose) glycohydrolase  
 DDT = DNA Damage Target, WRN = Werner Helicase, Polθ = DNA Polymerase Theta, HRD = homologous recombination deficiency, MSI = microsatellite instability  
 PKC = protein kinase C, MUM = metastatic uveal melanoma, MEK = binimetinib, cMET = crizotinib, WW = worldwide

 = Target Program Milestone through 2021

# IDEAYA Leadership Team and Scientific Advisory Board

## Experienced Team & Scientific Thought Leaders in Precision Medicine Oncology

### IDEAYA Executives & R&D Leadership



**Yujiro Hata, M.B.A.**  
President, Chief Executive Officer, Director



**Michael Dillon, Ph.D.**  
SVP, Chief Scientific Officer  
Head of Research



**Paul Stone, J.D.**  
SVP, Chief Financial Officer



**Mark Lackner, Ph.D.**  
SVP, Head of Biology &  
Translational Sciences



**Matthew Maurer, M.D.**  
VP, Head of Clinical Oncology &  
Medical Affairs



**Mick O'Quigley, M.B.A.**  
VP, Development Operations



**Paul Barsanti, Ph.D.**  
SVP, Head of Drug Discovery



**Jason Throne, J.D.**  
SVP, General Counsel



### IDEAYA Scientific Advisory Board



**Alan D'Andrea, M.D.**  
**IDEAYA SAB Chair**  
Harvard Medical School, Professor  
Director, Center of DNA Damage and Repair, Dana Farber



**William Sellers, M.D.**  
Broad Institute, Dana Farber, and Harvard, Professor  
Novartis, Former Head Oncology Research,  
SL Project Drive initiative



**Frank McCormick, Ph.D.**  
UCSF, Professor and former Director,  
Helen Diller Cancer Center  
Former President AACR; Founder and CSO, Onyx



**Trey Ideker, Ph.D.**  
UCSD, Professor, Co-Director Cancer Genomes & Networks  
Program, Research in Dual-CRISPR and SL interaction maps



**Brian Daniels, M.D.**  
Bristol Myers Squibb, Former SVP Global Development  
& Medical Affairs



**Elizabeth Swisher, M.D.**  
University of Washington, Professor; Co-Leader, Breast and  
Ovarian Cancer Research Program, Seattle Cancer Care Alliance  
Principal Investigator on multiple PARP inhibitor trials



**Jeffrey Hager, Ph.D.**  
Former Chief Technology Officer, IDEAYA

# IDEAYA and GSK Strategic Partnership

## Landmark Partnership in Synthetic Lethality



### Transformative Strategic Partnership

- Validates IDEAYA Synthetic Lethality platform
- Creates strategic combination opportunities
- Advancing small molecules and protein degraders

### Key Partnership Terms

- \$100M cash upfront
- \$20M equity investment as direct private placement
- \$50M option exercise fee for MAT2A
- Over \$3 billion in potential Milestone Payments, including approximately \$1 billion per program
- 50/50 US profit share for MAT2A and Werner Helicase
- 20% cost share allocated to IDEAYA for MAT2A, Werner
- Royalties tiered high single-digit to sub-teen double digit %

### MAT2A (MTAP Deletion)

- \$50M Option Fee, 50/50 US Profit Share & ex-US Royalties
- Option Data Package based on Clinical Dose Escalation Data
- ~\$1B potential Milestone Payments
- Evaluating multiple clinical combination opportunities

### Werner Helicase (MSI High)

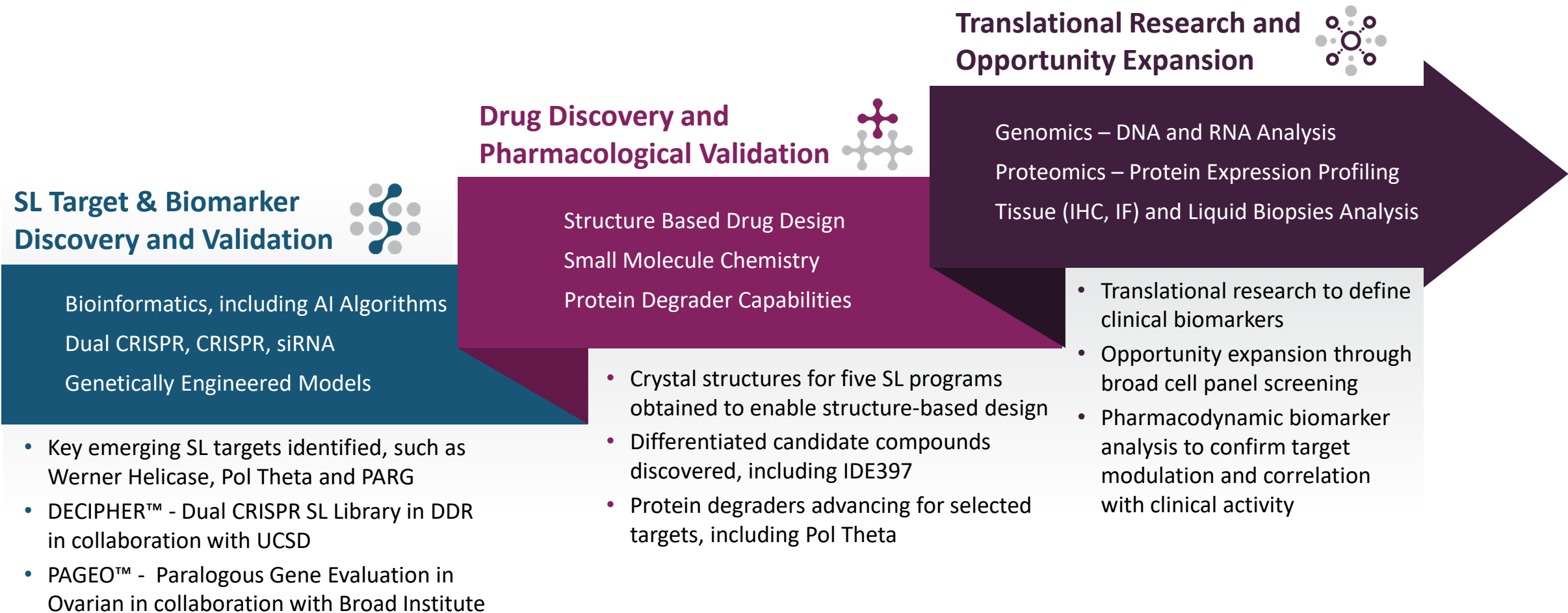
- 50/50 US Profit Share and ex-US Royalties
- ~\$1B potential Milestone Payments
- Potential Combination with GSK's Dostarlimab, a PD-1 IO Agent

### Pol Theta (BRCA/HRD)

- GSK covers all Costs
- Global Royalties and ~\$1B potential Milestone Payments
- Potential Combination with GSK's Zejula™, a PARP Inhibitor

# IDEAYA Synthetic Lethality Platform

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



# IDEAYA Synthetic Lethality Platform

## Synthetic Lethality Target and Biomarker Discovery and Validation



### Synthetic Lethality Target Discovery & Validation Platform

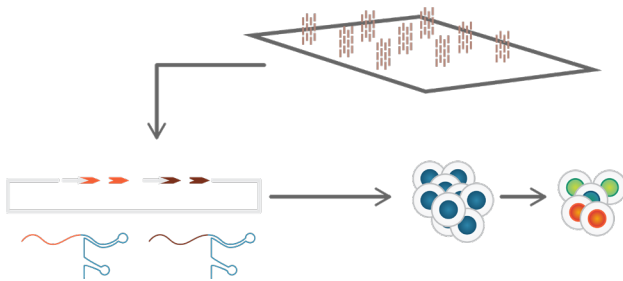
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

Bioinformatic analysis enables identification and validation of synthetic lethal target / biomarker interactions across vast datasets

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

#### DECIPHER™

##### Dual CRISPR SL Library in DNA Damage Repair <sup>(2)</sup>

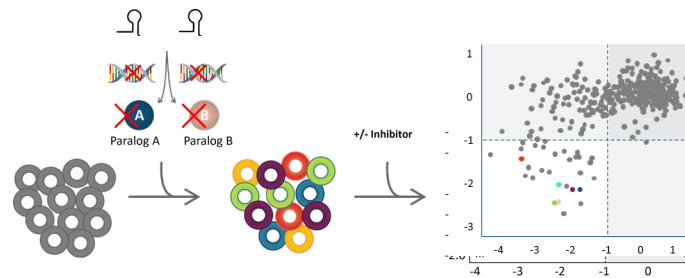


Evaluation of DNA Damage Targets synthetic lethal with tumor suppressor or oncogenes

>20 Novel Drug Targets Identified  
Target Validation Ongoing

#### PAGEO™

##### Paralogous Gene Evaluation in Ovarian Cancer <sup>(1)</sup>



Evaluation of SL targets in context of functionally redundant paralogous genes in ovarian cancer

#### Partnership Datasets

Cancer Dependency Map – Broad Institute  
Foundation Insights™ – Foundation Medicine



#### Public Databases

IDEAYA data mining and analysis across data sets



# IDEAYA is Advancing the Next Generation of Synthetic Lethality Programs

## IDEAYA Synthetic Lethality Pipeline

### IDE397 (MAT2A/MTAP) in Phase 1 to treat MTAP-deletion Solid Tumors

Differentiated clinical candidate advancing in-clinic; observed early clinical PD modulation of plasma SAM  
Potential to evaluate in major indications, including in NSCLC, Pancreatic, Gastric, Esophageal, Bladder, H&N

### Targeting PARG and Pol Theta Development Candidates in H2 2021

PARG monotherapy efficacy in multiple tumor types; Pol Theta + PARPi combination regressions in BRCA2-/- xenograft

### Advancing Werner Helicase, MTAP-SL and Synthetic Lethality Platform Programs

Robust pipeline of next generation of synthetic lethality programs, including WRN, MTAP-SL and DDT Targets

**IDE397 (MAT2A)**

MTAP Deletion

**Pol Theta**

HRD

**MTAP-SL**

MTAP Deletion

**PARG**

HRD

**WRN**

High-MSI

**SL Platform**

SL Targets

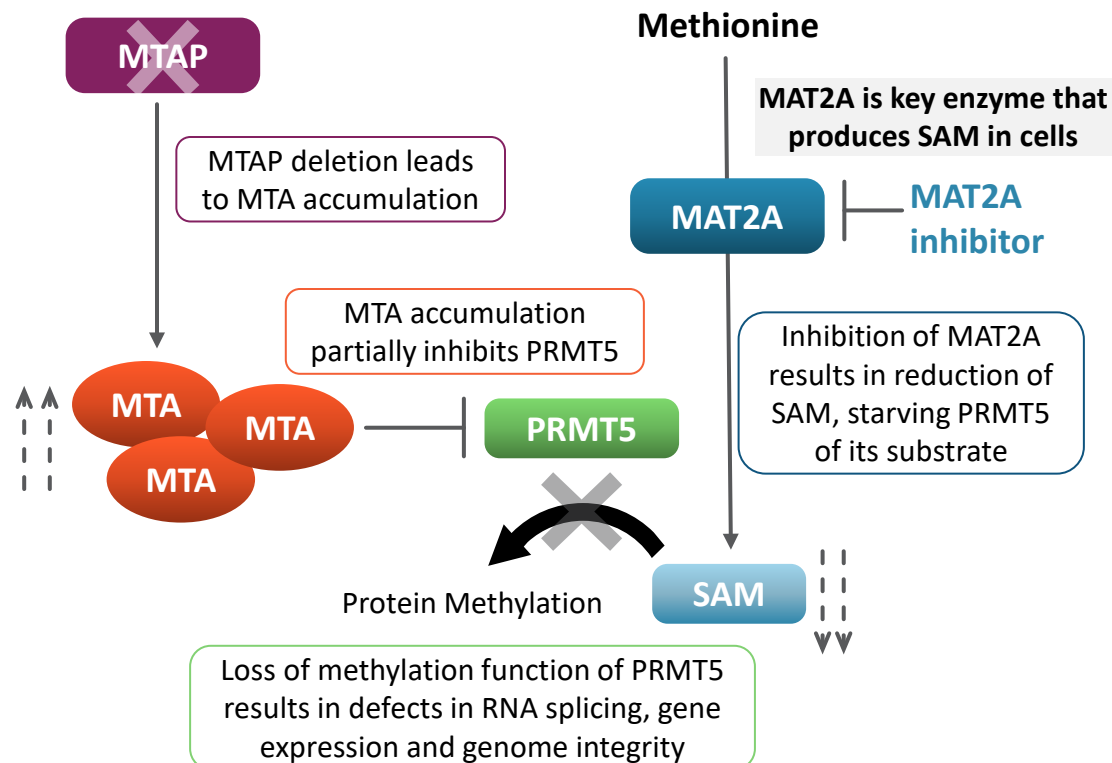
HRD = Homologous Recombination Deficiency, MSI = Microsatellite Instability



# MAT2A Inhibition is Synthetic Lethal with MTAP Deletion

MTAP Deletion Prevalence ~15% of all Solid Tumors

## MTAP-MAT2A Synthetic Lethality Biology



## MTAP Deletion Prevalence

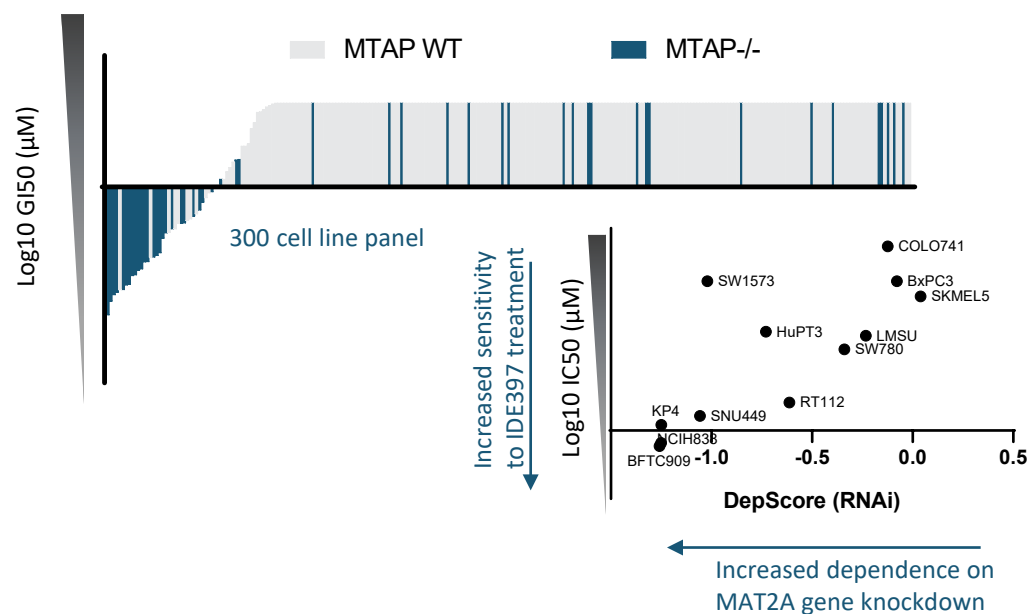
| Cancer Type          | N    | MTAP Deletions (%) |
|----------------------|------|--------------------|
| Glioblastoma         | 592  | 41                 |
| Mesothelioma         | 87   | 32                 |
| Esophageal           | 95   | 28                 |
| Bladder              | 411  | 26                 |
| Pancreatic           | 184  | 22                 |
| Melanoma             | 448  | 16                 |
| Lung Cancer (NSCLC)  | 1053 | 15                 |
| Head and Neck        | 523  | 14                 |
| Sarcoma              | 255  | 10                 |
| Esophagogastric      | 514  | 10                 |
| Diffuse Glioma       | 513  | 9                  |
| Breast               | 1084 | 3                  |
| Ovarian              | 585  | 3                  |
| Adrenocortical       | 92   | 3                  |
| Thymic               | 123  | 3                  |
| Hepatocellular       | 369  | 3                  |
| Renal non-clear cell | 348  | 2                  |

Data from The Cancer Genome Atlas in cBioPortal

# IDE397: MAT2A Development Candidate *in vitro* Profile

IDE397 is selective for MTAP-/- Cell Lines

## IDE397 is Selective for MTAP-/- Cell Lines

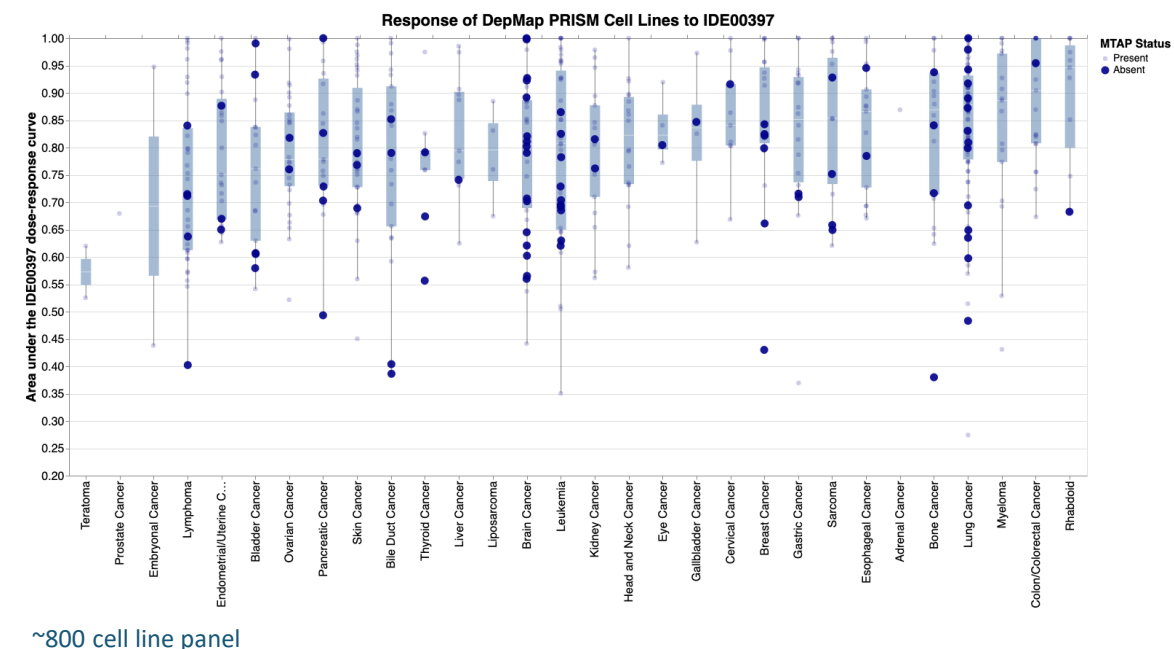


MTAP-/- cell lines are sensitive to IDE397

MTAP WT cell lines are generally insensitive

Pharmacological inhibition correlates with MAT2A genetic knockdown

## IDE397 has Broad Activity across Tumor Types



Differential sensitivity across tumor types; potential for discovery of additional predictive biomarkers

MTAP gene expression and copy number loss emerge as top predictors of sensitivity across cell lines

# IDE397: MAT2A Inhibitor

## Preclinical Evaluation of IDE397 – Differentiated Profile and Selective for MTAP-/- Cell Lines

### IDE397 Target Product Profile

**IDE397 demonstrates superior cellular potency and selectivity compared to AG-270**

**IDE397 has not caused preclinical liver injury or increased bilirubin**

- Not an inhibitor of UGT1A1 (AG-270 noted to inhibit UGT1A1)<sup>1</sup> or BSEP transporters at relevant concentrations
- Liver injury not observed in preclinical tox studies

**IDE397 has favorable physical properties, including solubility**

- AG-270 observed non-linear exposure >200mg QD (GI absorption)

**IDE397 demonstrates *in vivo* efficacy and PD modulation at 5 to 30mg/kg**

- AG-270 published preclinical dose typically 200mg/kg QD <sup>1</sup>

### Biochemical and *in vitro* Potency and Selectivity

|                                                         | IDE397 | AG-270 |
|---------------------------------------------------------|--------|--------|
| MAT2A biochemical IC <sub>50</sub> (nM)                 | 7      | 12     |
| KP4 EC <sub>50</sub> cellular (nM) MAT2A dependent      | 15     | 731    |
| BXPC3 cellular EC <sub>50</sub> (nM) MAT2A independent  | 13200  | 1630   |
| HuCCT1 cellular EC <sub>50</sub> (nM) MAT2A independent | >20000 | 1400   |

### Differentiating ADME/Physicochemical Properties

|                           | IDE397 | AG-270 |
|---------------------------|--------|--------|
| BSEP inhibition @10μM (%) | 1      | 25.2   |
| UGT1A1 inhibition (%)     | 34     | 83     |
| PXR Emax @30 μM (%)       | 9      | 35     |
| Solubility @pH 7.4 (μM)   | >100μM | BLOQ*  |

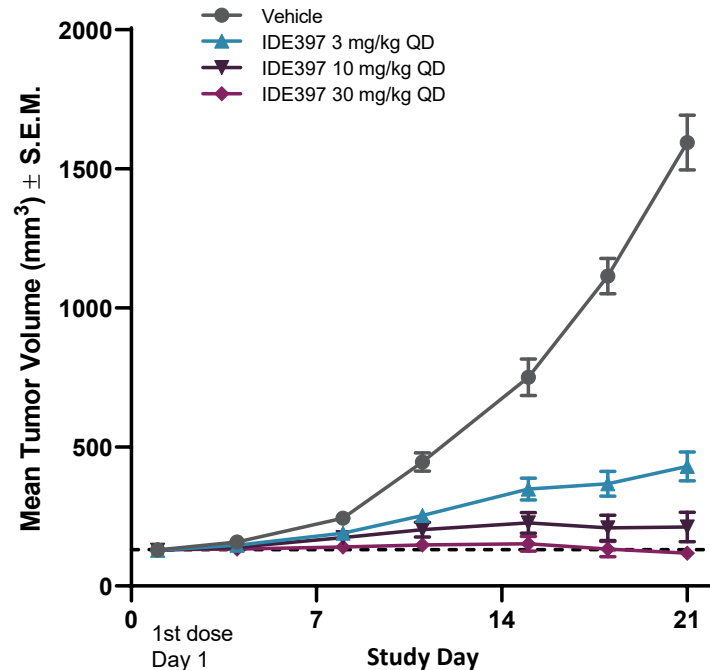
IDEAYA Data

\*BLOQ = below limit of quantitation

(1) Agios, AACR 2019, Keystone 2019, Triple Meeting 2019 (Webcast Call Q&A), J Med Chem 2021

# IDE397 Monotherapy Demonstrates Tumor Regressions and Robust PD Modulation in CDX Xenograft models

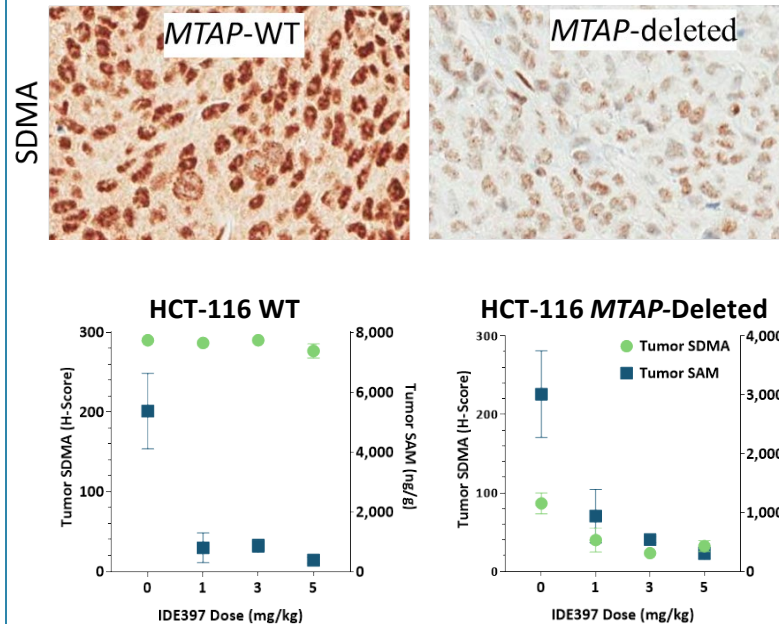
## NSCLC Endogenous MTAP-/- CDX Model



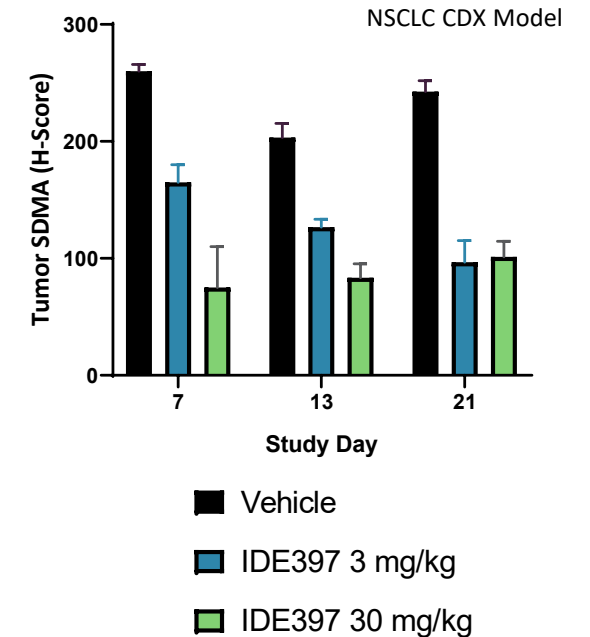
IDEAYA Data

## SDMA and SAM are Proximal PD Biomarkers of MAT2A inhibition

SDMA and SAM are modulated in a dose dependent manner



IDEAYA Data: Fischer et. al., AACR 2021



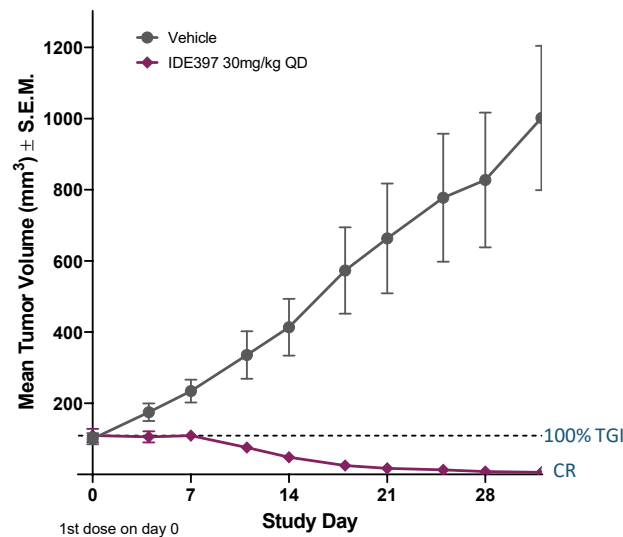
Robust dose-dependent efficacy and PD modulation observed in NSCLC CDX Model

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

## Monotherapy Tumor Regressions & Significant TGI Across Multiple Solid Tumor Types

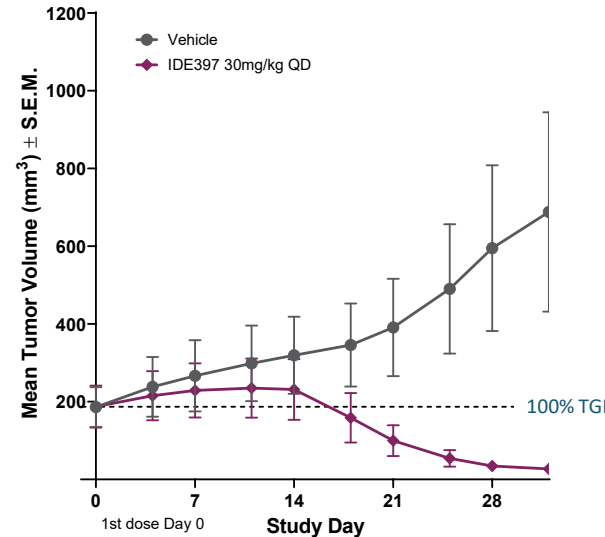
### NSCLC and Bladder Cancer MTAP-/- PDX Models

NSCLC PDX Model

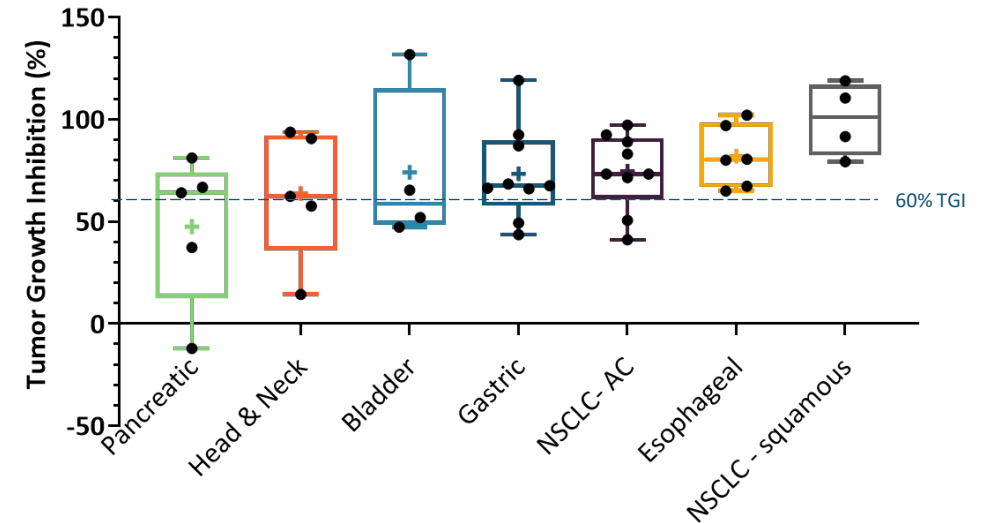


IDEAYA Data

Bladder PDX Model



### Panel Study of >40 MTAP-/- PDX Models



IDEAYA Data: Fischer et. al., AACR 2021

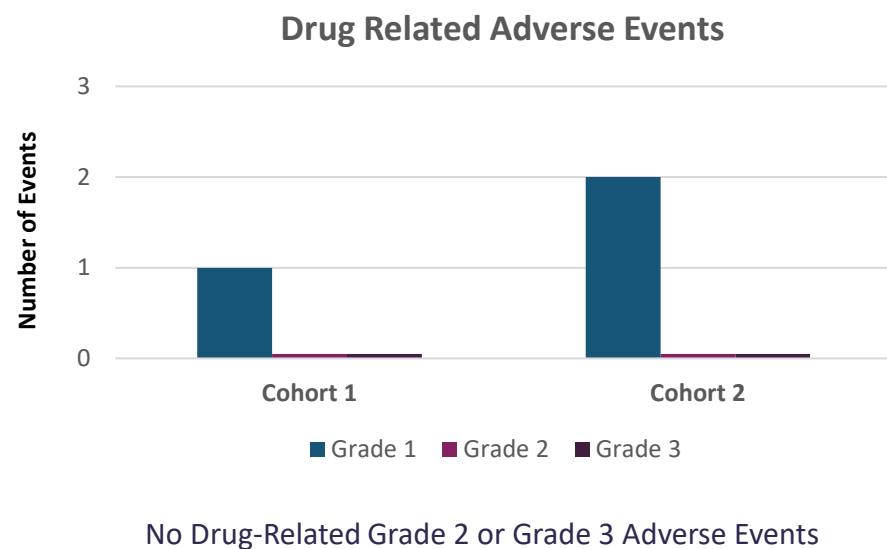
### IDE397 evaluation in Patient Derived Xenograft (PDX) models with homozygous MTAP deletions in Solid Tumors

- Tumor Regressions ( $\geq 100\%$  TGI) observed in multiple PDX models / indications, including in 2 of 4 NSCLC squamous models, with 1 CR
- Observed  $> 60\%$  TGI in 11 of 13 NSCLC PDX models, including in 7 of 9 adenocarcinoma and in 4 of 4 squamous carcinoma PDX models

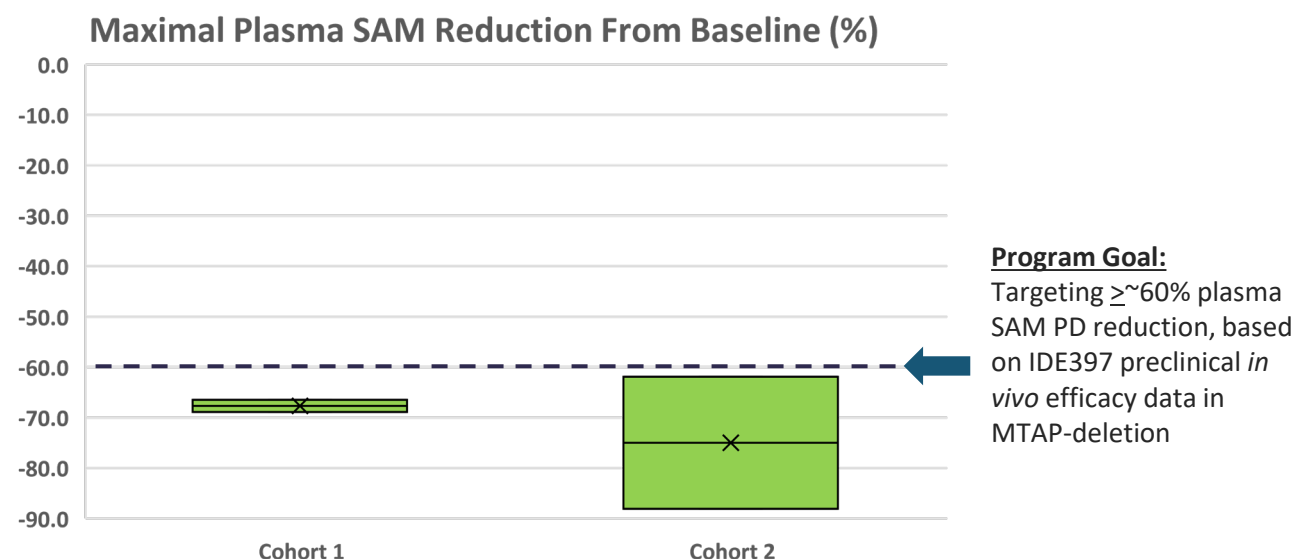
# IDE397 Phase 1 Pharmacodynamic (PD) & Safety / Tolerability Data

## Observed Early Robust Plasma SAM PD Reduction with no Drug-Related SAEs

### IDE397 Safety / Tolerability – Ph1 Cohorts 1 & 2



### IDE397 Plasma SAM PD – Ph1 Cohorts 1 & 2



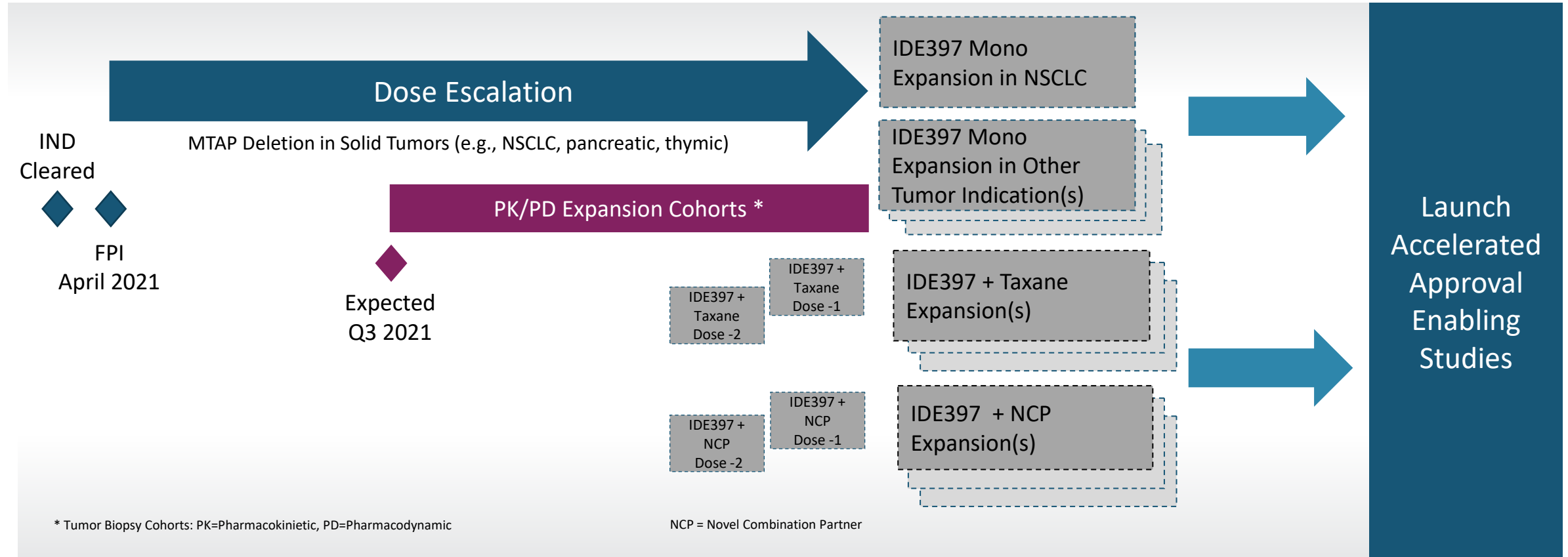
### Preliminary Phase 1 Dose Escalation Data Shows early robust IDE397 Target Engagement in MTAP-deleted Patients with no related SAEs

- Observed early and robust plasma SAM PD reduction in first two cohorts of Phase 1 dose escalation and achieved target clinical protocol threshold of ~60% or greater plasma SAM reduction to initiate tumor biopsy cohort for evaluating tumor PD markers, including SAM and SDMA
- All drug-related adverse events have been Grade 1 (no drug-related serious adverse events), including constipation, nausea and fatigue, and no reported myelosuppression, or changes to bilirubin or AST/ALT enzymes
- IDE397 demonstrates clinical protocol target of ~60% or greater plasma SAM PD reduction at a fraction of the clinical dose reported for AG270\*

# IDE397 Phase 1 Clinical Trial

## Comprehensive Approach for Concurrent Evaluation of Monotherapy and Combinations

### Phase 1 Dose Escalation and Expansion Strategy



Addressable Patient Population of ~75,000 estimated in US, EU5 and JP across six indications, including NSCLC, head and neck, bladder, gastric, pancreatic and esophageal cancers

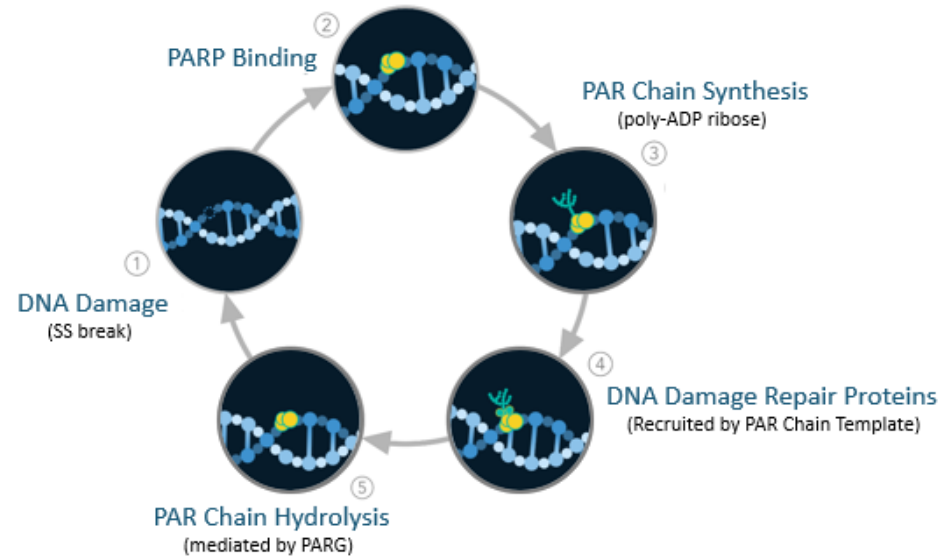
# PARG Synthetic Lethality Program

## Targeting Development Candidate in H2 2021

### PARG Biology

#### Novel target in Clinically Validated Pathway

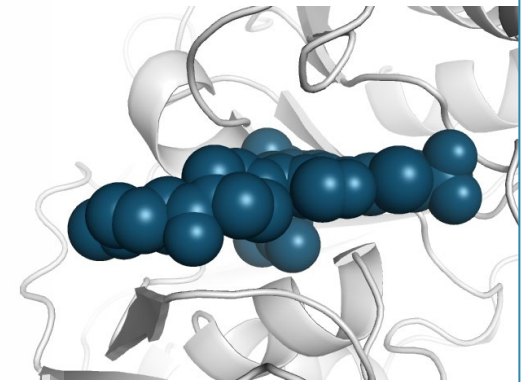
Poly(ADP-ribose) glycohydrolase (PARG) regulates DNA repair by hydrolyzing PAR chains in final step of DDR cycle



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

### PARG Drug Discovery Program

**Key Emerging Target with lead optimization program guided by structure-based drug design to identify potent, selective candidates**



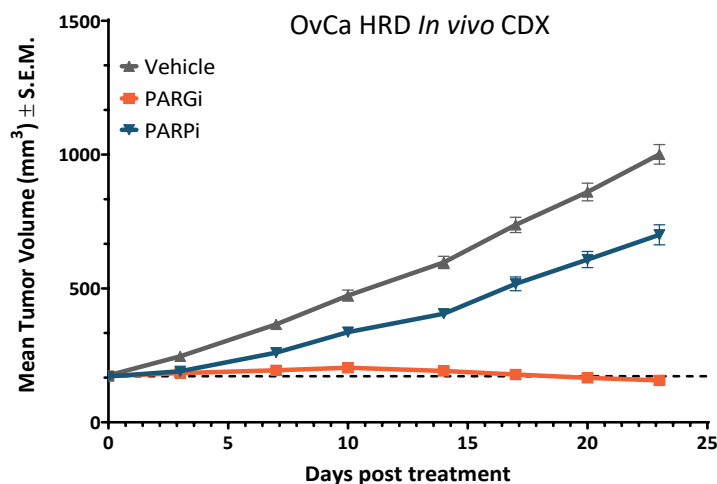
- Multiple potent cellularly active compounds demonstrate *in vitro* and *in vivo* PAR accumulation (PD) and *in vivo* efficacy in defined biomarker setting
- Collaboration with Bill Sellers lab (Broad) established to identify additional genetic sensitizers to PARGi

IDEAYA Data

# Biomarker Selected *in vitro* & *in vivo* Models are Sensitive to IDEAYA PARGi

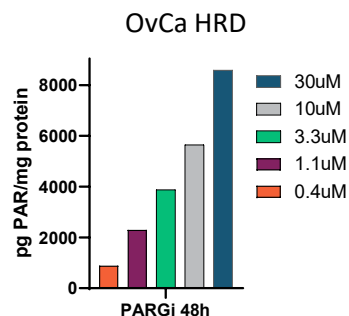
## Differentiated Activity to PARP inhibition in Ovarian, Gastric and Breast Cancer Models

### Ovarian Cancer HRD Cell Line Models

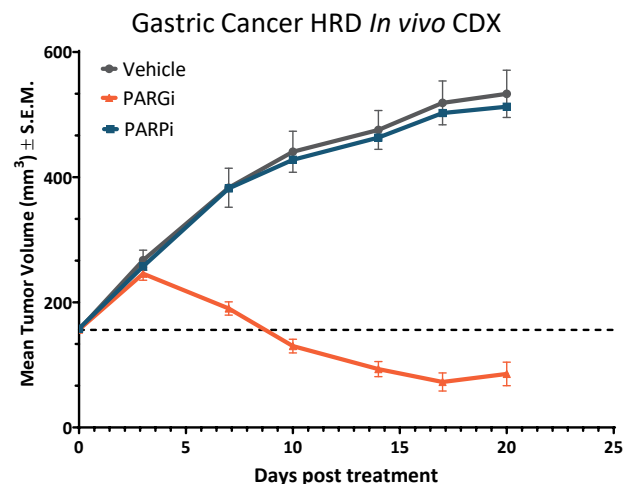


PARGi Tumor Regression  
and enhanced TGI  
relative to PARPi

Dose-dependent poly-  
PAR (PD) accumulation

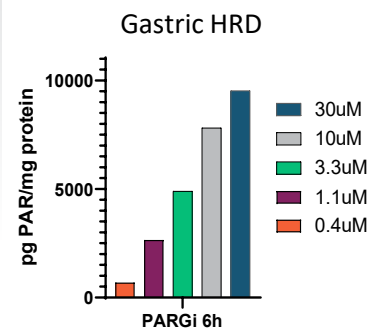


### Gastric Cancer HRD Cell Line Models

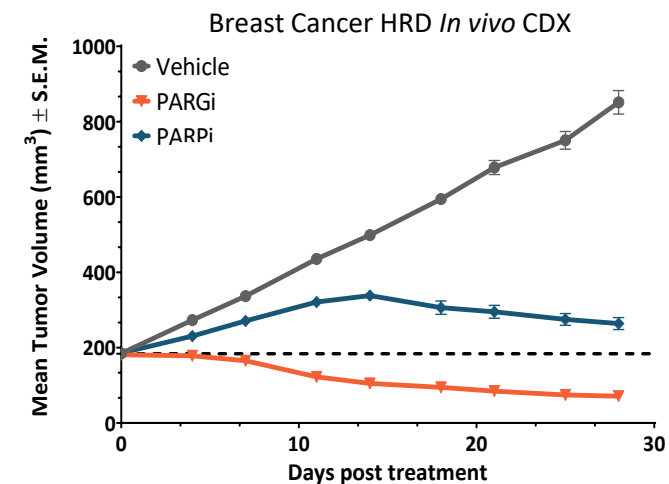


PARGi Tumor Regression  
in PARPi Refractory  
Setting

Dose-dependent poly-  
PAR (PD) accumulation

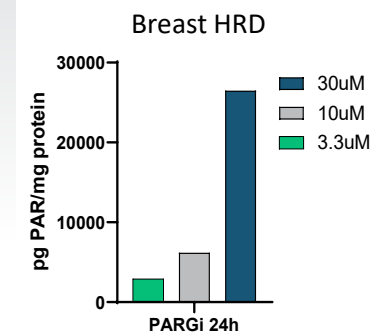


### Breast Cancer HRD Cell Line Models



PARGi Tumor Regression  
and enhanced TGI  
relative to PARPi

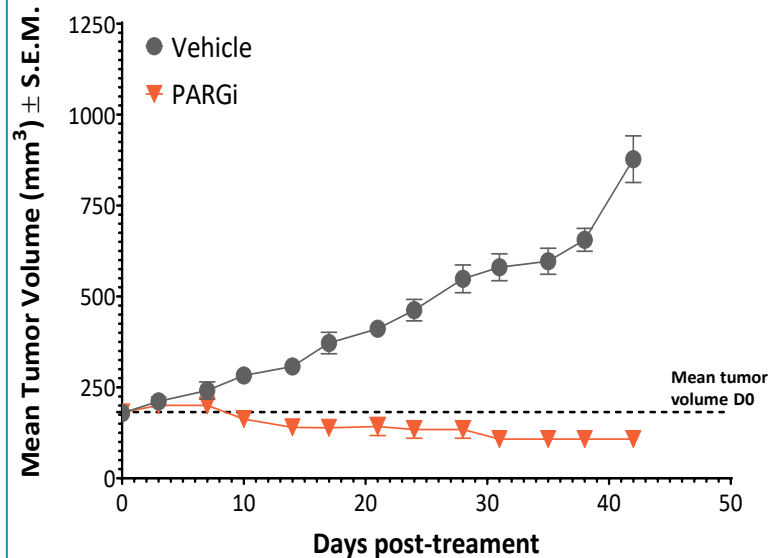
Dose-dependent poly-  
PAR (PD) accumulation



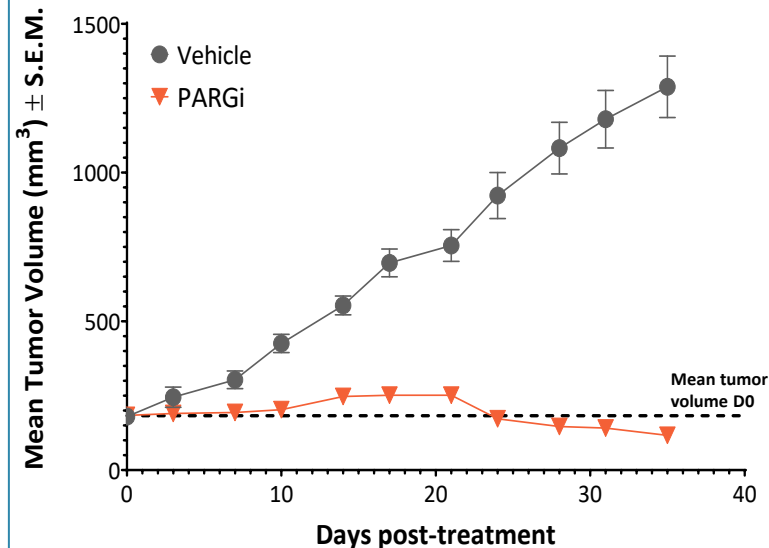
# IDEAYA PARGi shows Robust TGI in Breast PDX Models

Monotherapy Tumor Regressions observed across Multiple Breast PDX Models

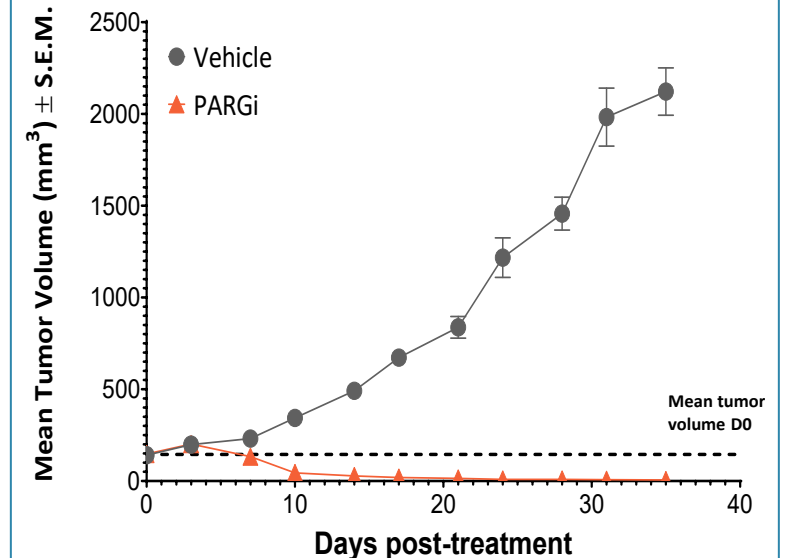
Breast Cancer PDX Model 1



Breast Cancer PDX Model 2



Breast Cancer PDX Model 3



## Evaluation of IDB-PARG in Patient Derived Xenograft (PDX) models in Breast Cancer

- Tumor Regressions ( $\geq 100\%$  TGI) observed in multiple PDX models with defined genetic and subtyping profiles
- Enhanced Tumor Growth Inhibition (TGI) relative to Niraparib (PARPi) observed in some models



# Pol Theta Synthetic Lethality Program

## Targeting Development Candidate in H2 2021

### Pol Theta Synthetic Lethality with BRCA/HRD

DNA polymerase theta (Pol Theta) promotes DNA repair by Microhomology-Mediated End-Joining (MMEJ) an error-prone mutagenic DNA repair pathway

MMEJ is active, and Pol Theta is overexpressed, in HRD cancer cells (e.g. BRCA1/2) making Pol Theta a SL target in HRD cancers

PARP1 & Pol Theta are both involved in MMEJ mediated DNA repair supporting a synergistic effect

IDEAYA Pol Theta inhibitors show selective cell viability effects in DLD1 BRCA2<sup>-/-</sup> vs. wildtype cell lines

Advancing both small molecule inhibitors and protein degraders

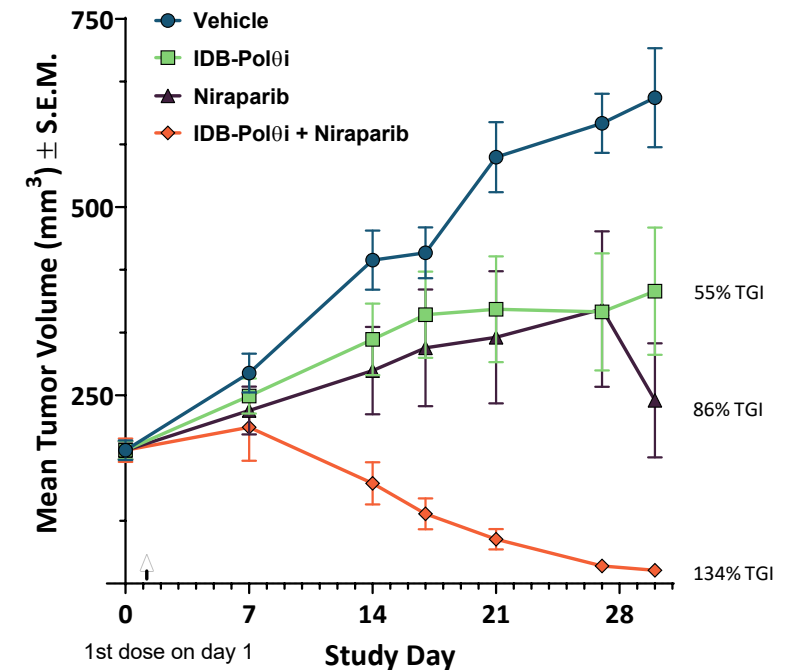
IDEAYA Data

### Pol Theta ATPase inhibitor *In Vivo* Activity

**Pol Theta inhibitor in combination with niraparib demonstrates significant tumor regression in DLD1 BRCA2<sup>-/-</sup> xenograft model**

Regressions observed for all animals dosed within combination study

IDEAYA Data





# Werner Helicase Synthetic Lethality Program

Candidate Biomarker: High-MSI (15% GI Cancers and 16% CRC)<sup>1</sup>

## Werner Helicase Synthetic Lethal with High-MSI

**CellPress**

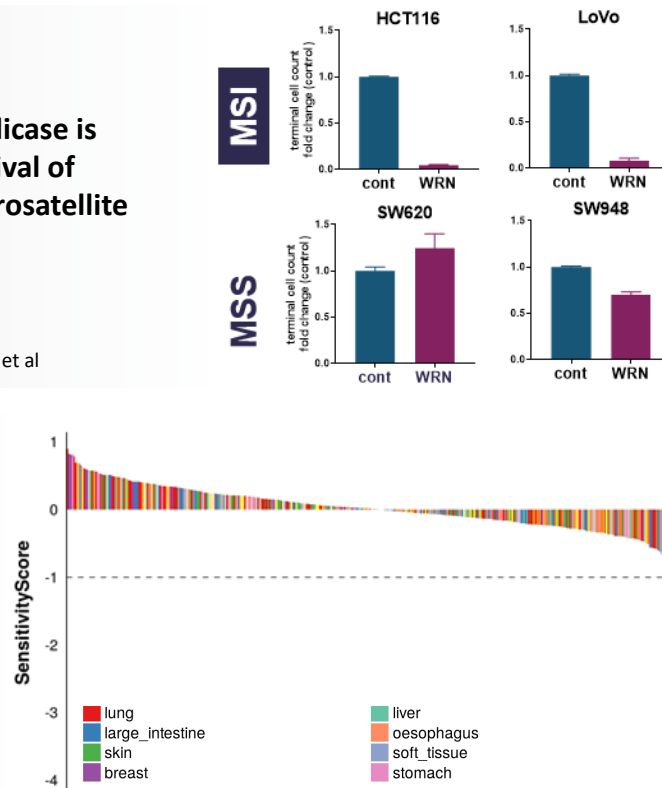
**Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability**

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al

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

Project Drive

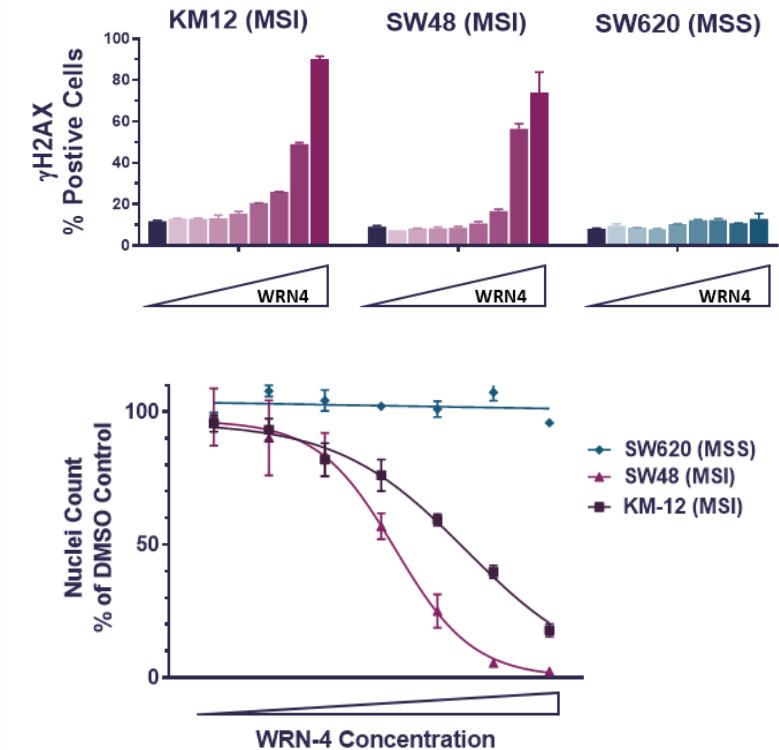


## Werner Inhibitor Cellular PD and Viability

**PD-marker:** dose dependent increase of DNA damage marker  $\gamma$ H2AX

**Cell viability:** MSI-high specific cell viability effect; no effect in MSS cell lines

**In vivo efficacy:** Preliminary WRN inhibitor *in vivo* PD and efficacy



IDEAYA Data

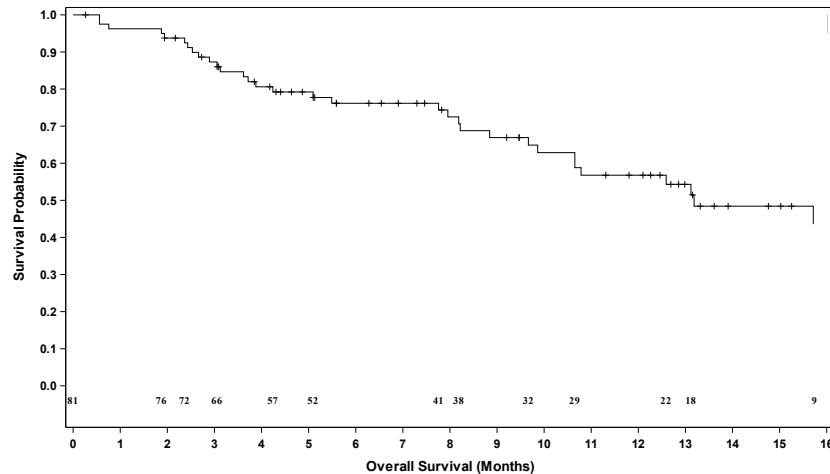
# Darovasertib Phase 1/2 Clinical Trial in GNAQ/11 Patients

## Robust Mono 1-Year Overall Survival Data and Early Partial Responses in Combinations

### Darovasertib Monotherapy Overall Survival in MUM<sup>1</sup>

#### Monotherapy

n=81 (predominantly 2L/3L and heavily pre-treated to 7L/8L)

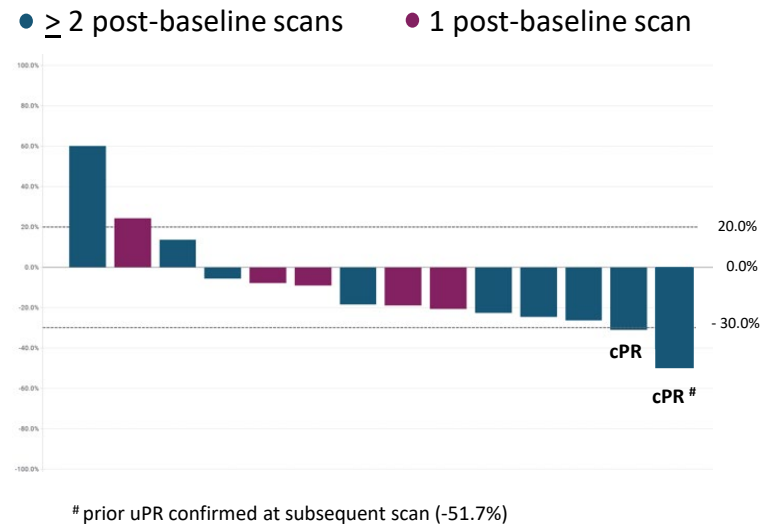


- 57% 1-Year Overall Survival with 95% CI (44%, 69%)
- 13.2 mo Median OS with 95% CI (10.7 mo, Not Reached)
- Historical 1-Year OS = 37% and Median OS = 7mo<sup>2</sup> in similar predominantly 2L/3L+ patient population

### Darovasertib Combination Activity in MUM<sup>1</sup>

#### Darovasertib + Binimetinib

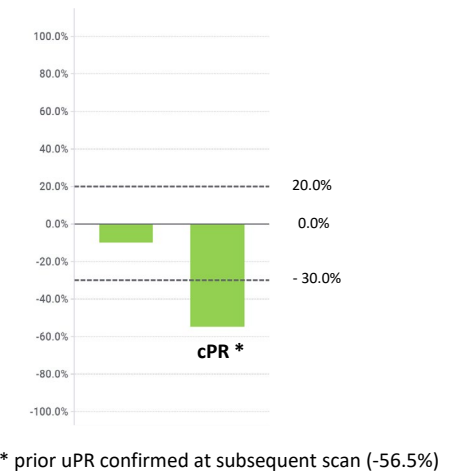
n=24 with 14 evaluable patients



- Daro/Bini: tumor reduction observed in 11 of 14 (79%) evaluable patients, with 2 partial responses out of nine patients with >2 post-baseline scans (22%)
- Daro/Crizo: one partial response observed in first cohort
- Historical response in MUM = zero to low/mid-single-digit %

#### Darovasertib + Crizotinib

n=4 with 2 evaluable patients



<sup>1</sup> IDEAYA Data (based on preliminary analysis of unlocked database, including: pooled IDEAYA and Novartis BID monotherapy clinical data as of Apr 13, 2021; and IDEAYA darovasertib + binimetinib as of Apr 13, 2021 and darovasertib + crizotinib as of May 5, 2021)

<sup>2</sup> Rantala 2019 (meta-analysis of overall survival of patients with metastatic uveal melanoma over 1980 to 2017 evaluated by treatment modality and lines of treatment)

# Crizotinib Combination – Confirmed Partial Response

Patient has Deepest Response observed to Date (-56.5%)

## Patient Profile

56 year old woman

GNAQ mutant MUM

Elevated baseline LDH

2 prior therapies:

- immunoembolization
- chemoembolization

Significant tumor burden

- multiple liver and lung lesions
- axillary adenopathy

## Patient Experience

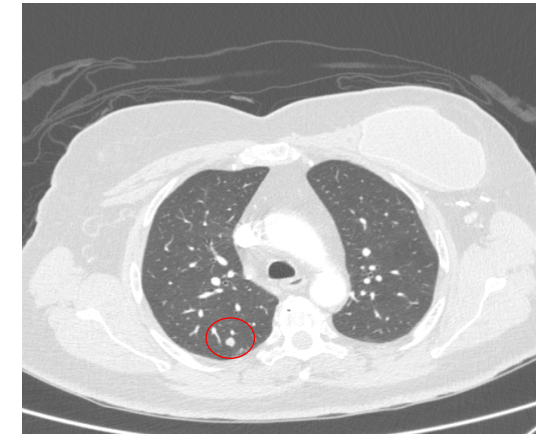
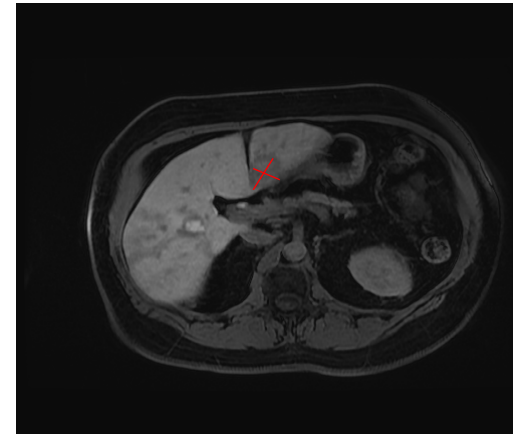
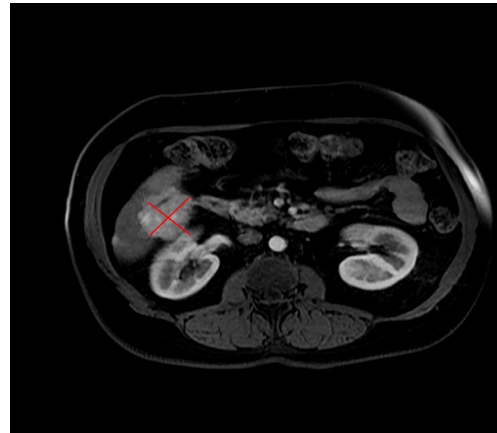
Tolerating treatment well

Initial response at 4 months and confirmed response at 6 months

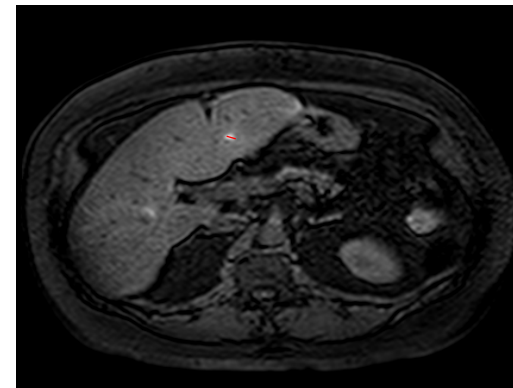
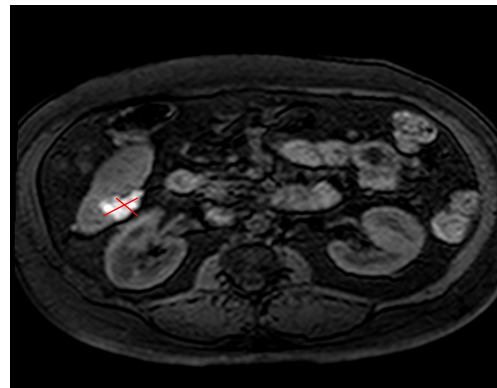
56.5% reduction in target lesions  
6 months into therapy

## Patient Response

Baseline



4 Months



# Darovasertib (IDE196) Phase 1/2 Clinical Program Overview

## Clinical Data Supports Potential Registrational Strategies

### Metastatic Uveal Melanoma <sup>1, 2</sup>



#### Darovasertib Monotherapy – Phase 2

- Potential registrational approach: randomized, OS endpoint in 1L or 2L/3L

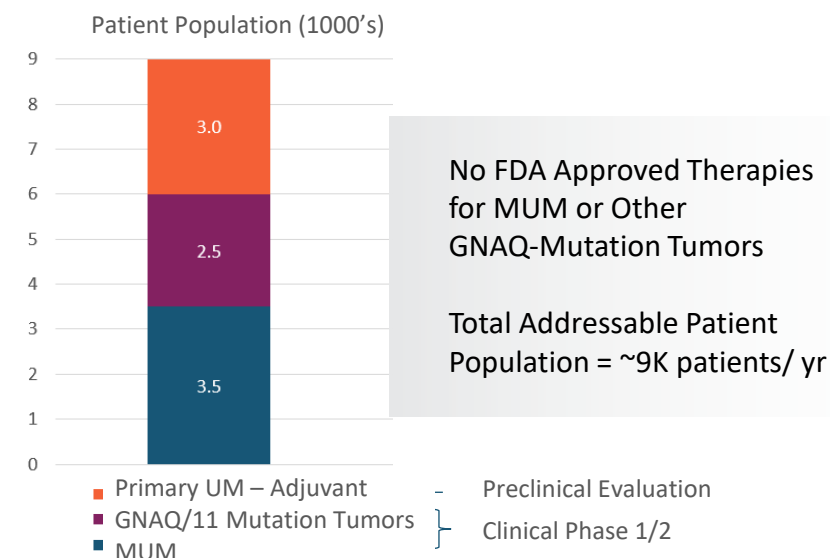
#### Darovasertib Combination Therapies – Phase 2

- Program goal for darovasertib combination therapies (+ binimetinib, + crizotinib) of >20% ORR and enhance overall survival
- Potential registrational approach: single arm, ORR endpoint with in 1L or 2L/3L with potential Accelerated Approval pathway

#### Clinical and Regulatory Strategy to Define Registrational Path

- Continue combination studies (+ Bini, +Crizo) with data maturing
- Obtain regulatory guidance on potential registrational path in MUM – targeting feedback for monotherapy (H2 2021) and/or combination therapy (H1 2022)
- Advance to registrational trial based on monotherapy (current OS data) or combination therapy (maturing ORR data) with potential accelerated pathway
- Evaluate optionality for 1L or 2L/3L+, e.g., considering HLA status and ORR

### Addressable GNAQ/11 Patients (US/EU5)



<sup>1</sup> IDEAYA clinical data based on preliminary analysis of unlocked database, including: pooled IDEAYA and Novartis BID monotherapy clinical data as of Apr 13, 2021; IDEAYA darovasertib + binimetinib data as of Apr 13, 2021; IDEAYA darovasertib + crizotinib data as of May 5, 2021; and IDEAYA GNAQ skin melanoma data as of April 13, 2021

<sup>2</sup> Preclinical rationale and synergy demonstrated for darovasertib combinations IDE196+MEKi Combination Preclinical Data AACR 2020; IDE196+cMET Preclinical Combination Data AACR 2021

# Building a Premier Synthetic Lethality Focused Precision Medicine Oncology Biotech in 2021 and Beyond

## Focus on Potential *First-in-Class* Synthetic Lethality Programs to Deliver Patient Breakthroughs

Patient Impact: Large addressable patient populations in major solid tumor types

Potential First-in-Class / Best-in-Class: Optimized small molecule and protein degrader development candidates

Precision Medicine: Compelling biomarker hypotheses for patient selection and pharmacodynamic

Synthetic Lethality Platform: Deep and rich target pipeline with ongoing target identification and validation

### MTAP-Deletion

#### IDE397 (MAT2A)

Phase 1 Pharmacodynamic Data  
Tumor PD Q4 2021

#### MTAP-SL Target

Lead Series ID

### HRD/BRCA

#### PARG

Development Candidate Nomination  
H2 2021

#### Pol Theta

Development Candidate Nomination  
H2 2021

#### DNA Damage Target

Lead Series ID

### MSI-High

#### Werner Helicase

Lead Optimization

***2021 Target Catalysts to Build Industry Leading Synthetic Lethality Pipeline***