JP Morgan Healthcare Conference
January 10, 2023

NASDAQ: **IDYA**

# IDEAYA Biosciences

## Improving Lives Through Transformative Precision Medicines

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

# IDEAYA Biosciences Highlights

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

- **Broad Pipeline of Key Emerging Targets**
  - Clinical Ph2: Darovasertib (PKC)
  - Clinical Ph 2: IDE397 (MAT2A)
  - Clinical Ph 1: IDE161 (PARG)
  - DC-Stage: Pol Theta Helicase Dev Candidate
  - Preclinical Lead Optimization: Werner Helicase
- **Pharma Collaborations** with GSK (over ~$2 billion in potential milestones), Amgen and Pfizer
- **Balance Sheet** of ~$394M anticipated to fund operations into 2026 [1, 2]
- **NASDAQ**: IDYA

- **2023 Target Catalysts**
  - Darovasertib (PKC) – Phase 2
    - Daro/Crizo MUM Registrational Trial – Q1 2023
    - Daro Neoadjuvant UM Phase 2 – Q1 2023
  - IDE397 (MAT2A) – Phase 1/2
    - Mono Expansion Phase 2, Combo Cohorts Ph 1/2
  - IDE161 (PARG)
    - IND Effective / Received FDA Clearance
    - Phase 1 First-in-Human – Q1 2023
  - Pol Theta Helicase Development Candidate
    - Phase 1 First-in-Human – H1 2023
  - Werner Helicase
    - Development Candidate – 2023

(1) Includes aggregate of ~$393.9M cash, cash equivalents and marketable securities as of September 30, 2022
(2) IDEAYA Form 10-Q dated November 8, 2022, as filed with the U.S. Securities and Exchange Commission
IND = Investigational New Drug, DC = Development Candidate

# Synthetic Lethality

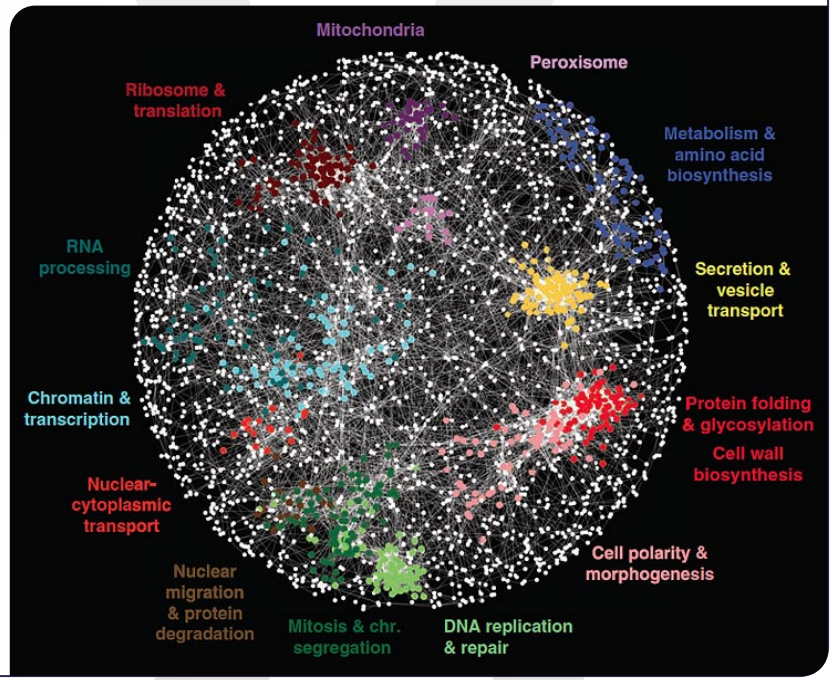
## The Next Frontier in Precision Medicine Oncology

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

nature REVIEWS GENETICS

- **Synthetic lethality** occurs when the simultaneous perturbation of two genes results in cell death
- Synthetic lethality provides a novel approach to target several historically undruggable loss of function mutations
- 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. , as edited by IDEAYA




Reference: Charles Boone



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# 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
FLEXUS BIOSCIENCES · Bristol-Myers Squibb · ONYX PHARMACEUTICALS · ENANTA Pharmaceuticals · AMGEN

**Darrin Beaupre, M.D., Ph.D.**
SVP, Chief Medical Officer
Pfizer · pharmacyclics · AMGEN

**Michael White, Ph.D.**
SVP, Chief Scientific Officer, Head of Research
Pfizer · UTSouthwestern Medical Center

**Paul Stone, J.D.**
SVP, Chief Financial Officer
5AM VENTURES · ILYPSA · AMGEN

**Matthew Maurer, M.D.**
VP, Head of Clinical Oncology & Medical Affairs
Bristol-Myers Squibb · COLUMBIA

**Mick O'Quigley, M.B.A.**
SVP, Development Operations
Genentech · AMGEN

**Paul Barsanti, Ph.D.**
SVP, Head of Drug Discovery
5AM VENTURES · nurix · NOVARTIS · CHIRON

**Jason Throne, J.D.**
SVP, General Counsel
neotract · THORATEC CORPORATION

### IDEAYA Scientific Advisory Board

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

**Karlene Cimprich, Ph.D.**
Professor, Chemical and Systems Biology and (by courtesy) Biochemistry, Member, Stanford Cancer Institute, Stanford University

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

**Kornelia Polyak, M.D., Ph.D.**
Professor of Medicine at Dana-Farber Cancer Institute, Harvard Medical School, and a co-leader of the Dana-Farber Harvard Cancer Center Cancer Cell Biology Program

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

**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



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# IDEAYA Synthetic Lethality Platform

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

### SL Target & Biomarker Discovery and Validation

Bioinformatics, including AI Algorithms

Dual CRISPR, CRISPR, siRNA

Genetically Engineered Models

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

### Drug Discovery and Pharmacological Validation

Structure Based Drug Design

Small Molecule Chemistry

Protein Degrader Capabilities

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

### Translational Research and Opportunity Expansion

Genomics – DNA and RNA Analysis

Proteomics – Protein Expression Profiling

Tissue (IHC, IF) and Liquid Biopsies Analysis

- Translational research to define clinical biomarkers
- Opportunity expansion through broad cell panel screening
- Pharmacodynamic biomarker analysis to confirm target modulation and correlation with clinical activity

# IDEAYA Synthetic Lethality Platform

## Synthetic Lethality Target and Biomarker Discovery and Validation

### Synthetic Lethality Target Discovery & Validation Platform

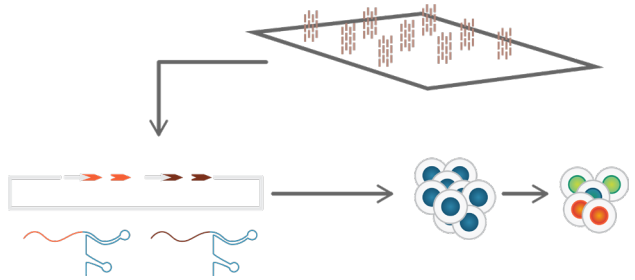
IDEAYA SL Platform integrates extensive proprietary and public data sets with orthogonal and complementary content

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 and *in vivo*

**DECIPHER™**

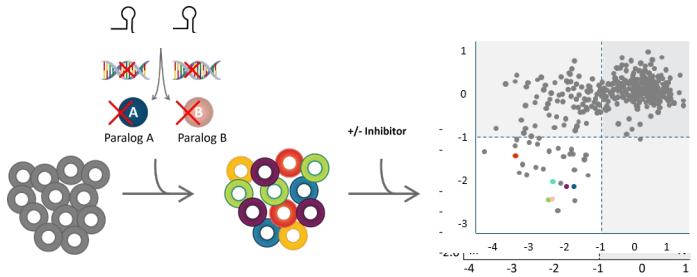
**Dual CRISPR SL Library in DNA Damage Repair [2]**



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

**PAGEO™**

**Paralogous Gene Evaluation in Ovarian Cancer [1]**




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

**Partnership Datasets**

Cancer Dependency Map – Broad Institute

Foundation Insights™ – Foundation Medicine

depmap portal | FOUNDATIONINSIGHTS™

**Public Databases**

IDEAYA data mining and analysis across data sets

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

>20 Novel Drug Targets Identified
Target Validation Ongoing



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

# IDEAYA Synthetic Lethality Drug Discovery Platform

## Structure-Based Drug Design & Proprietary Chemical Library Enable “Hard to Drug” Targets

### Structural Biology & Structure Based Drug Design

Full suite of capabilities in structural biology, biophysics, & computational chemistry

Ligand bound co-crystal structures resolved to enable Structure Based Drug Design for each of the Synthetic Lethality drug-discovery programs

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

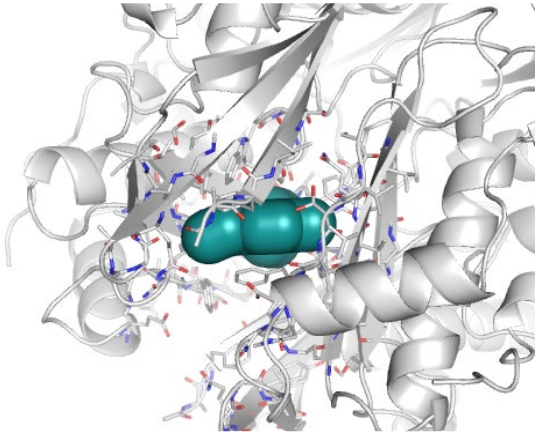
### HARMONY™ Proprietary Machine-Learning

Internal Machine-Learning engine empowers discovery platform through effective prioritization leading to efficient SAR cycles

### INQUIRE™ Proprietary Chemical Library

Expert-curated HTS library to enhance hit discovery capabilities against novel SL targets classes, such as helicases and endonucleases

Enhances IDEAYA’s SL Drug Discovery Platform and competitive differentiation



# IDEAYA's Precision Medicine Oncology Pipeline

## Building the Industry Leading Synthetic Lethality Focused Biotechnology Company

### Precision Medicine Pipeline

| | Modality/Indication | Biomarker | Pre-clinical / IND Enabling / Phase 1 / Phase 2 / Potential Registrational | Program Goals | Collaborations | Commercial (IDEAYA) |
|---|---|---|---|---|---|---|
| **Darovasertib** *PKC* | +cMET[1] Combination MUM, Basket | GNAQ/11 | | Daro + Crizo Reg Trial in MUM Q1 2023 | Pfizer (1) | WW Commercial Rights |
| | (Neo)Adjuvant UM | GNAQ/11 | | Neoadjuvant UM – Phase 2 Q1 2023 | | |
| **IDE397** *MAT2A* | Monotherapy NSCLC, Esophagogastric | MTAP | | Mono Expansion Phase 2 | | WW Commercial Rights |
| | Combinations Solid Tumors | MTAP | | Combination Cohorts Ph1 Initiation +Pemetrexed √ +PRMT5i$^{MTA}$ (AMG 193) | AMGEN (2) | |
| **IDE161** *PARG* | Breast, Ovarian Cancers | HRD | | Phase 1 First-in-Human Q1 2023 | CANCER RESEARCH UK (3) | WW Commercial Rights |
| **Pol Theta** | Small Molecule Helicase Inhibitor | HRD | | Phase 1 First-in-Human H1 2023 | GSK (4) | Global Royalties |
| **WRN** | GI Cancers | High-MSI | | Development Candidate 2023 | GSK (4) | US 50/50 Profit Share Ex-US Royalties |
| **Next-Gen SL** | Solid Tumors | Multiple Biomarkers | | Lead Series across Multiple Targets | | WW Commercial Rights |
| **SL Platform** | Solid Tumors | Defined Biomarkers | | New Target / Biomarker Validation | | WW Commercial Rights |

(1) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreements for Darovasertib/Crizotinib Combination in MUM; IDEAYA retains all Darovasertib Commercial Rights
(2) Pursuant to Amgen Clinical Trial Collaboration and Supply Agreement for IDE397 + AMG 193, an investigational MTA-cooperative PRMT5 inhibitor; Amgen will sponsor the study and the parties will jointly share external costs of the study
(3) Pursuant to CRUK Evaluation, Option and License Agreement; IDEAYA controls all PARG Commercial Rights
(4) Pursuant to GSK Collaboration, Option and License Agreement: Polθ: Global Royalties; WRN: 50/50 US Profits + ex-US Royalties

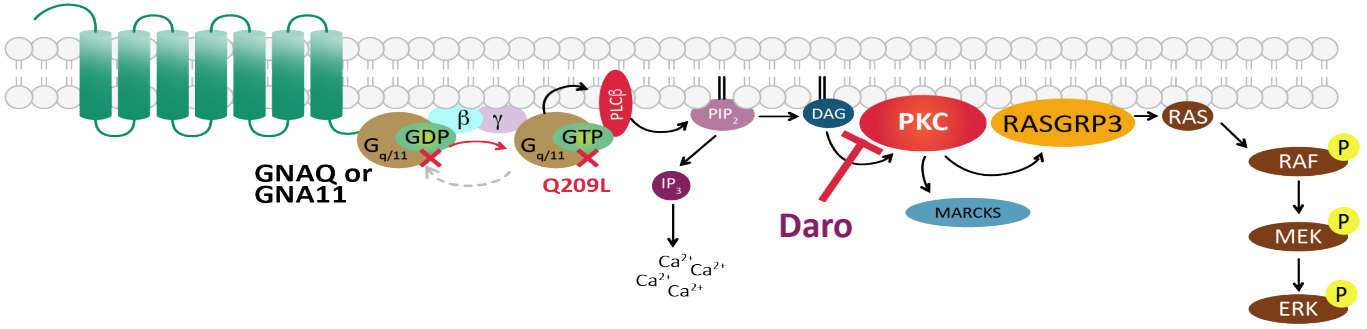
= Target Program Milestones

MAT2A=methionine adenosyltransferase 2a, MTAP=methylthioadenosine phosphorylase, MTA=methylthioadenosine, PRMT5=protein arginine methyltransferase 5 (PRMT5), 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, Crizo = crizotinib, NSCLC = non-small cell lung cancer, WW = worldwide

# Darovasertib – Potential to Broadly Impact Uveal Melanoma

## Potential First-in-Class and Best-in-Class in Neoadjuvant UM and Metastatic UM

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




Darovasertib is an oral, potent and selective PKC inhibitor

GNAQ or GNA11 (~95%) and other upstream mutations activate PKC signaling in UM and MUM patients

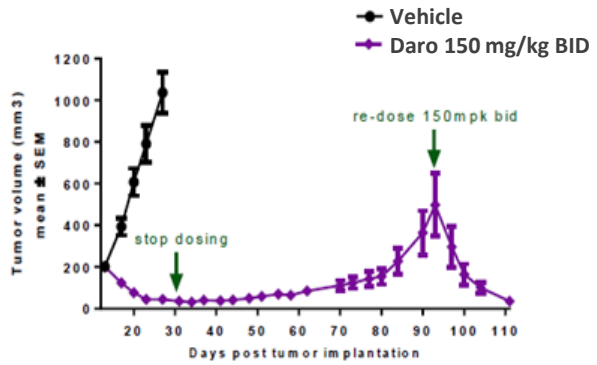
UM is typically treated with radiation and/or enucleation, with no approved systemic therapies for Neoadjuvant UM

MUM occurs in approximately 50% of UM patients and predominantly as liver metastasis in ~90% of MUM patients, with no approved therapies for HLA-A*02:01 negative MUM

## Daro Mono Rationale in Primary UM

### Single Agent Daro Induces Tumor Regression

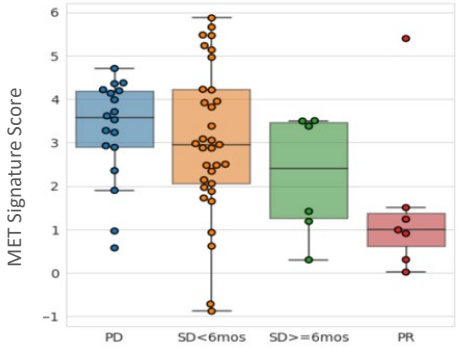
Uveal Melanoma Xenograft (92.1 mutant GNAQ)




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

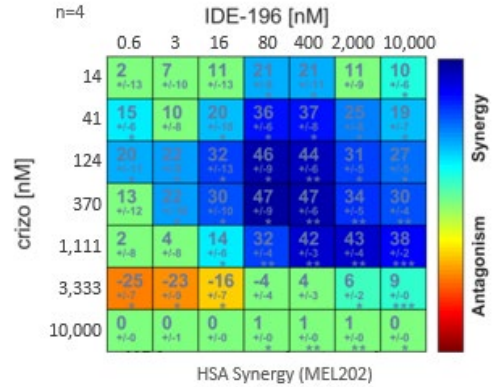
## Daro + Crizo Combo Rationale for Use in Metastatic Uveal Melanoma (MUM)

### Daro Ph1 Efficacy Association with cMET Expression




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

### Darovasertib + Crizotinib Synergy in cMET High Cells




HSA Synergy (MEL202)

IDEAYA Data, AACR 2021

# Darovasertib Monotherapy in Neoadjuvant Primary Uveal Melanoma

## High Unmet Need with Opportunity to Improve Patient Outcomes

**Current Treatment Approach** following diagnosis of UM depends on tumor size and location:

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

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

**Neoadjuvant or Adjuvant Systemic Therapy** might reduce or prevent Micro-Metastases and Save Lives:

- Save the Eye by avoiding enucleation
- Reduce the Tumor Thickness in the Eye enabling less radiation and improved vision
- Reduce occurrence of metastasis, which currently occurs in 50% of patients with UM after 1$^{o}$ treatment

**Paradigm Shifting Opportunity:** Darovasertib monotherapy treatment could potentially:

- Preserve the Eye
- Protect Vision
- Save Lives

**Potential to Broadly Impact** UM, a disease with annual incidence of ~8,000 – 9,000 patients in US and Europe

**Phase 2 Study for (Neo)Adjuvant UM [1]**

Primary Uveal Melanoma Patients

Cohort 1: Tumors require Enucleation

Cohort 2: Tumors require Plaque Brachytherapy

↓

**Neoadjuvant Therapy**

Darovasertib Monotherapy

Treat Until Maximum Benefit

↓

**Primary Therapy**

Clinical Objective to Evaluate

Vision / Organ Preservation

↓

**Adjuvant Therapy**

Clinical Objective to Evaluate

Relapse Free Survival and Useful Vision

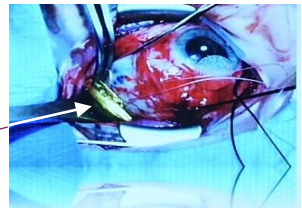
[1] Preliminary Phase 2 study plan, pending investigator and regulatory guidance

### Neoadjuvant Endpoints

Cohort 1: Eye Preservation (e.g., ↓ in % of Patients undergoing Enucleation)

Cohort 2: Preserve / Protect Vision (e.g., ↓ in radiation dose during Brachytherapy or other Radiotherapy)

### Plaque Brachytherapy



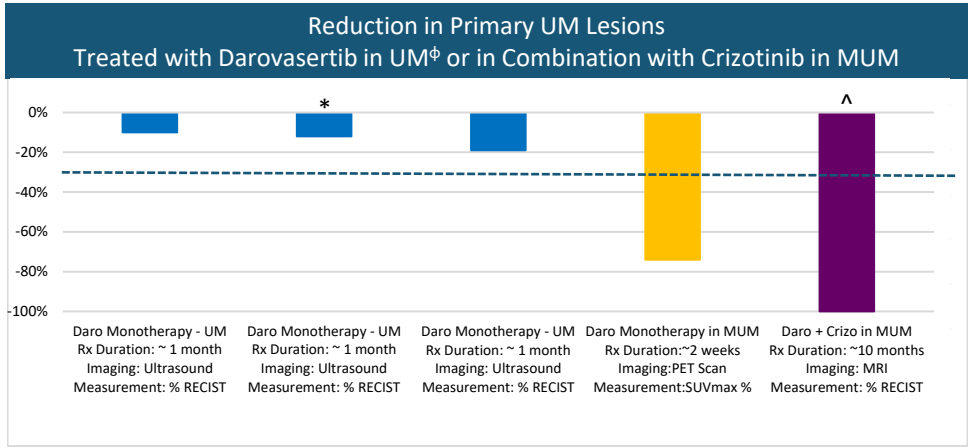

Iodine-125 Plaque Surgery, UCLA

# Preliminary Clinical Proof-of-Concept for Darovasertib in (Neo)Adjuvant UM

## Observed 100% Tumor Reduction by RECIST in Primary Eye Lesion ^

### Darovasertib Neoadjuvant Uveal Melanoma

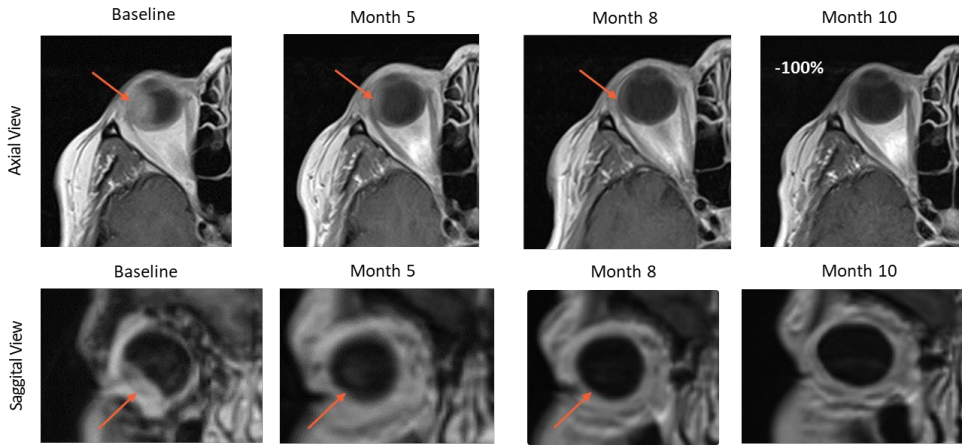
- All primary ocular tumor lesions have responded to darovasertib
- Consistent and clear evidence of response with 1 month of darovasertib monotherapy in NADOM IST per protocol design
- Provides rationale to treat to maximal response for clinically meaningful improvement in primary therapies
- Well tolerated oral treatment




Each Reported Case has shown a Reduction in Size of Primary Eye Lesion with Darovasertib Treatment #

### Daro + Crizo Combination Therapy in MUM Patient With Intact Primary

- Case Study: 50+ Yr Old First-Line MUM Pt
- Intact $1^{o}$ Lesion
- Treated with Darovasertib + Crizotinib
- Observed 100% Tumor Reduction in Ocular Lesion by MRI (RECIST, v1.1)
- Visual Symptoms Resolved
- Confirmed PR




Images (MRI) courtesy of Marcus Butler, MD

Patient Remains on Treatment at ~ 11 mo

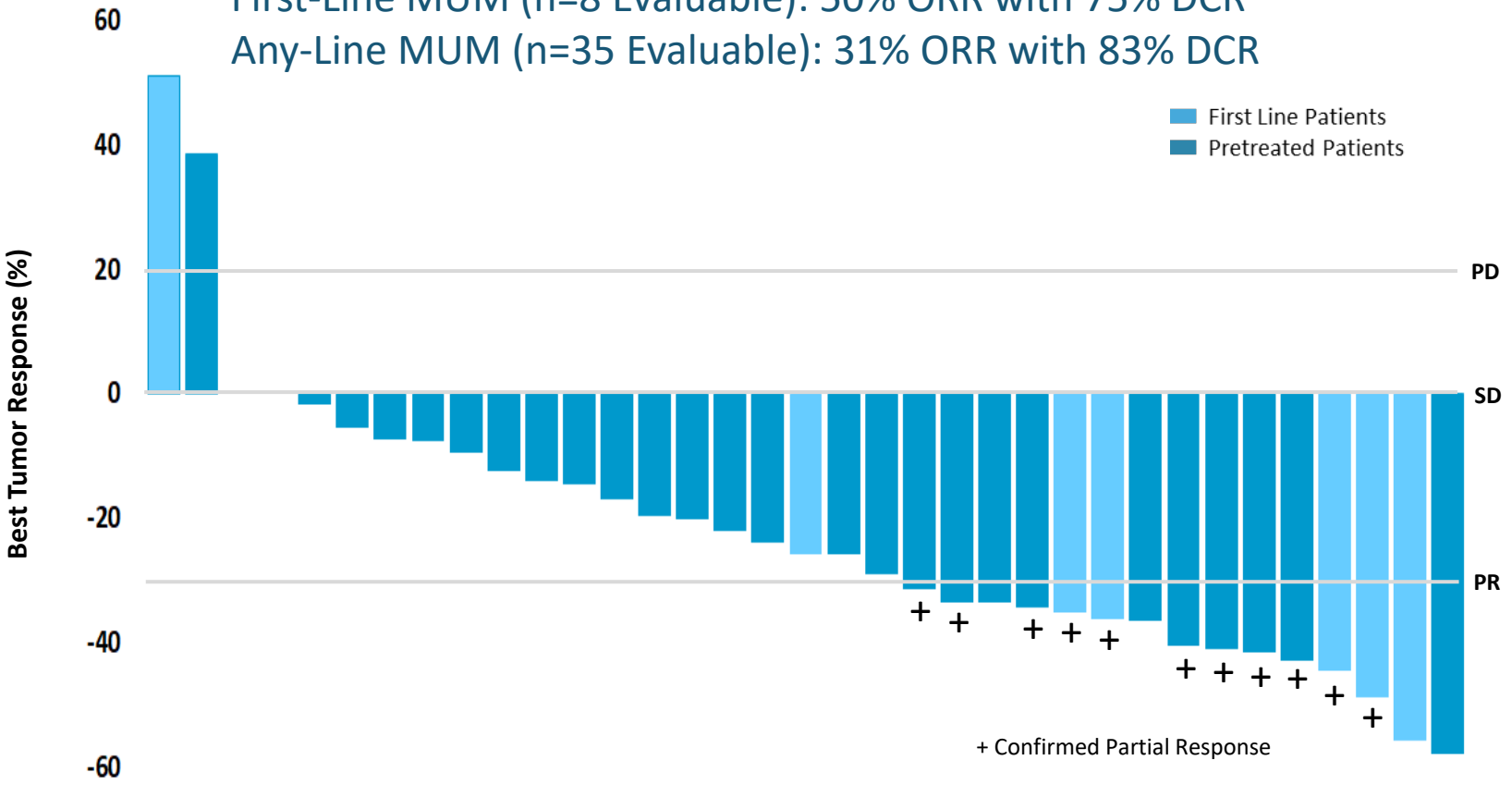
# Data for each reported case based on investigator assessment
Φ Data from NADOM IST courtesy of Professor Anthony Joshua, MBBS, PhD, FRACP, St. Vincent's Hospital
* Patient showed ~42% SUVmax reduction by PET scan after 1 month
^ Patient's non-target ocular lesion scored by investigator as "Absent" by MRI RECIST, with an observed ~81% reduction of apical tumor height by ultrasound relative to baseline intact primary lesion with 10 months of treatment

# Darovasertib + Crizotinib – Clinical Experience in Heavily Pretreated MUM

## Observed Unprecedented ORR% and DCR% with Potential First-Line Differentiation

First-Line MUM (n=8 Evaluable): 50% ORR with 75% DCR

Any-Line MUM (n=35 Evaluable): 31% ORR with 83% DCR




| First-Line MUM * | Evaluable (n=8) |
|---|---|
| ORR (4/8) | 50% |
| Tumor Shrinkage (6/8) | 75% |
| >30% Tumor Shrinkage (5/8) | 63% |
| cPR (4/8) | 50% |
| DCR (6/8) | 75% |

| Any-Line MUM * | Evaluable (n=35) |
|---|---|
| ORR(11/35) | 31% |
| Tumor Shrinkage (31/35) | 89% |
| >30% Tumor Shrinkage (15/35) | 43% |
| cPR (11/35) | 31% |
| DCR (29/35) | 83% |

* Response by RECIST 1.1

Manageable Side Effect Profile with No Drug Related Grade 4/5 AEs

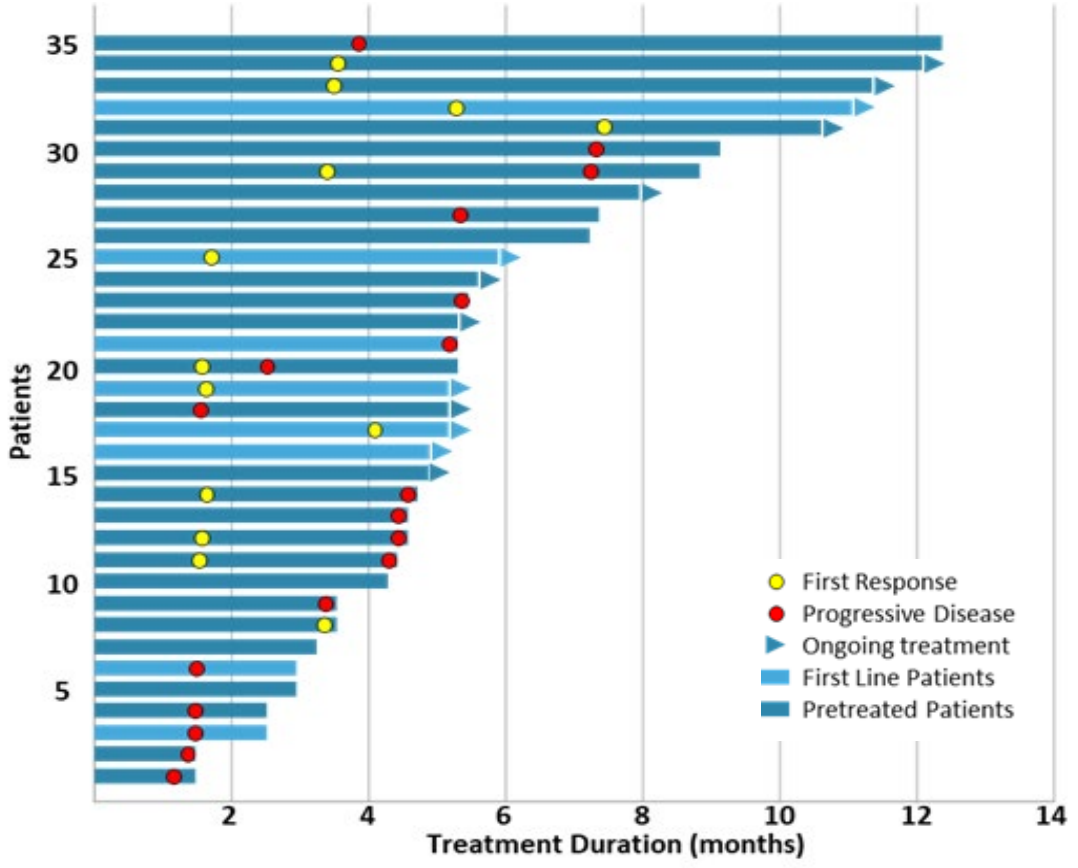
IDEAYA Data: preliminary analysis of unlocked database as of 06/26/2022 by investigator review (n=37); efficacy based on evaluable patients (n=35 for all lines; n=8 for first line), including one PR confirmed after cutoff date; two non-evaluable patients, both pretreated, did not progress due to disease: one (1) patient withdrew consent and one (1) patient discontinued early due to fatigue

ORR = Overall Response Rate by RECIST 1.1; DCR = Disease Control Rate, including cPR, uPR or SD as best overall response; cPR = Confirmed Partial Response; uPR = Unconfirmed Partial Response; SD = Stable Disease

# Darovasertib + Crizotinib Combo Phase 2 Clinical Efficacy

## Encouraging mPFS and mDOR in 1L and Any-Line MUM versus historical data in MUM

### Darovasertib + Crizozotinib Any-Line MUM (n=35)




### Clinical Efficacy Summary in Any-Line and First-Line MUM

**Median Study Follow-Up ***

- Any-Line: 7.8 months
- First-Line: 6.5 months

**Median Duration-of-Response**

- not reached in Any-Line or in First-Line
- 7 of 11 cPRs in Any-Line MUM remain in response
- 4 of 4 cPRs in First-Line MUM remain in response

**Median Progression Free Survival ^**

- Any-Line: ~5 months
- First-Line: Not yet reached and >5 months

IDEAYA Data: preliminary analysis of unlocked database as of 06/26/2022 by investigator review
* Median Study Follow-up: Cycle 1 Day 1 to data cut-off date (n=37)
^ mPFS Analysis: median assessment estimated, based on efficacy-evaluable patients (n=35)

# Darovasertib + Crizotinib Synthetic Lethality Combination Therapy

## Differentiated Clinical Efficacy in MUM+

**ESMO 2022**: IPI + Nivo Combo in HLA-A2-0201 MUM reports ~6% ORR (2 PRs out of 33 patients)++

| | Darovasertib + Crizotinib | Cabozantinib | Selumetinib + Dacarbazine | Tebentafusp |
|---|---|---|---|---|
| **Target / Mechanism** | PKC + cMET | cMET | MEK + Chemotherapy | HLA-A2-0201 Bi-Specific Ab |
| **Study Name** | NCT03947385 | Alliance A091201^ | SUMIT (NCT01974752) | IMCgp100-102 |
| **Population** | 1L/2L/3L+ MUM (n=35 eval) | 1L+ MUM (n=31 eval) | 1L+ MUM (n=97) | 2L+ MUM (n=127) |
| **Patient Selection** | N/A (100% of MUM) | N/A (100% of MUM) | N/A (100% of MUM) | HLA-A2-0201 (~40-45% of MUM) |
| **Drug Form** | Oral Tablets (BID) | Oral Capsules (QD) | Oral Capsules (BID) plus chemo | IV Infusion (Weekly) |
| **Tolerability (Grade ≥3 Drug-Related AE)** | **24%** | **51.6%** | **63% ^^^ (All Cause)** | **46.5%** |
| **% of Pts with Tumor Shrinkage** | **89%*** | **23% ^^** | **35%^^** | **44%#** |
| **Overall Response Rate (ORR%, by RECIST 1.1)** | **All-Line = 31% / First-Line = 50%* (confirmed PRs only)** | **0%** | **3% ^^^** | **4.7%#** |
| **Progression Free Survival (mPFS)** | **All-Line: ~5 months / First-Line: >5 months** | **2 months** | **2.8 months ^^^** | **2.8 months#** |

\+ Cross-trial comparisons are not based on head-to-head studies and are presented for informational purposes; no direct comparisons are being made
++ ESMO 2022: F. Dimitriou, et.al
* IDEAYA Data: preliminary analysis of unlocked database as of 06/26/2022 by investigator review
# Based on Immunocore reported 2L+ study data (to reflect comparative patient population) and by independent review
^ Randomized Phase II Trial and Tumor Mutational Spectrum Analysis from Cabozantinib versus Chemotherapy in Metastatic Uveal Melanoma (Alliance A091201); Clin Cancer Res 2020;26:804–11
^^ Estimated from Waterfall plot
^^^ Journal of Clinical Oncology, Carjaval, et. al, 2018; 1232-1239

# Darovasertib + Crizotinib Clinical Development Plan in First-Line MUM

## Targeting Potential Registration Enabling Trial Initiation in Q1 2023[1]

### Clinical Development Approach

- Strategic Objectives
  - Optimize Probability of Success and Timing to Potential Approval
  - Efficient Design to Capture Commercial Opportunity in MUM
- Randomized Phase 2/3 in 1st Line MUM
  - Unmet Need – No Approved Therapies in HLA-A*02:01 Neg
  - Better Assessment of Patient Response to Treatment
  - Regulatory – Project Frontrunner, Approval Data for FDA and EMEA
  - Phase 2 Endpoints for Accelerated Approval – ORR, PFS
  - Phase 3 Endpoints for Confirmatory Trial – PFS, OS
- HLA-A*02:01 Serotype
  - Negative:
    - Randomized Integrated Ph 2/3 in 1L HLA-A Negative
    - → Approved Label (55-60% of MUM Patients)
  - Positive:
    - Randomized Study in 1L HLA-A Positive to Support Publication
    - → Potential for NCCN Guidelines (40-45% of MUM Patients)

**Randomized Integrated Phase 2/3**

**Randomized Integrated Phase 2/3 Trial in 1L Patients**


Phase 2 Endpoints – ORR, PFS
ORR Target ≥20%, PFS Target ≥ 5-6 months
Phase 2 Data → Accelerated Approval

Expand within same Study Protocol
→ Phase 3 Confirmation

Phase 3 Endpoints – PFS, OS
PFS Target ≥ 5-6 months

Daroavasertib received U.S. FDA Orphan Drug Designation and Fast Track Designation in MUM

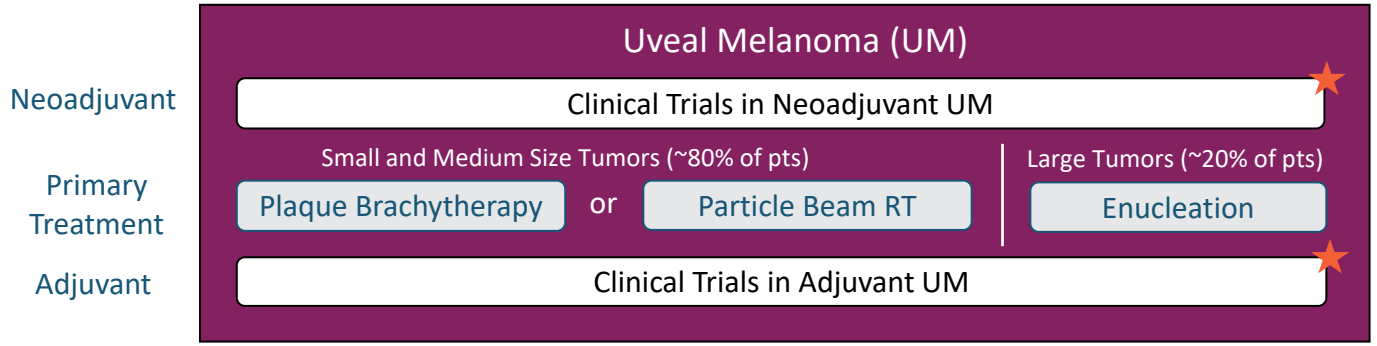


[1] Scenarios for potential accelerated approval, including randomized integrated Phase 2/3, are subject to clinical investigator and regulatory guidance

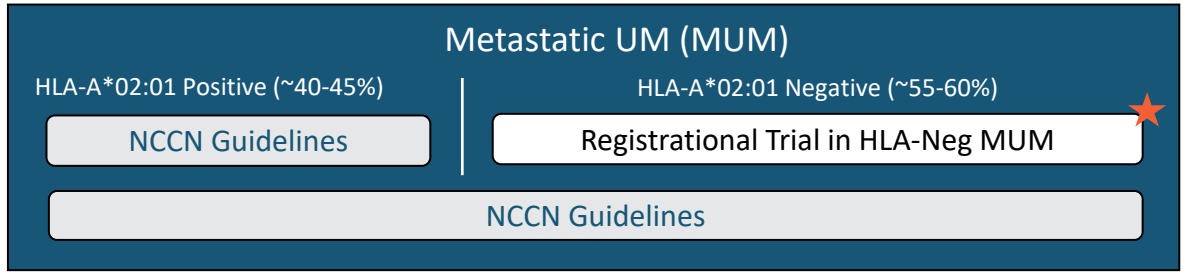
# Market Opportunity: Primary and Metastatic Uveal Melanoma

## (Neo)Adjuvant Treatment Represents Substantial Expansion Opportunity for Darovasertib

### Uveal Melanoma (UM) – Darovasertib Clinical Strategy



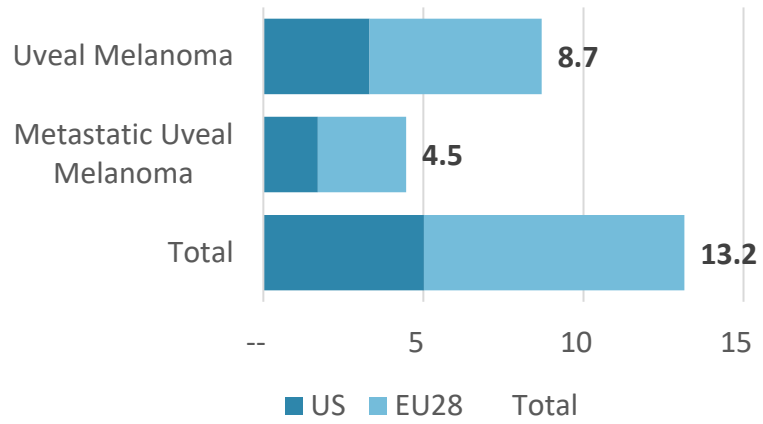

### Metastatic Uveal Melanoma – Daro/Crizo Clinical Strategy




★Darovasertib clinical plan targets ~85% of addressable UM and MUM Patient Population

### Market Landscape Overview in UM / MUM

Annual Incidence (1000's Patients)*



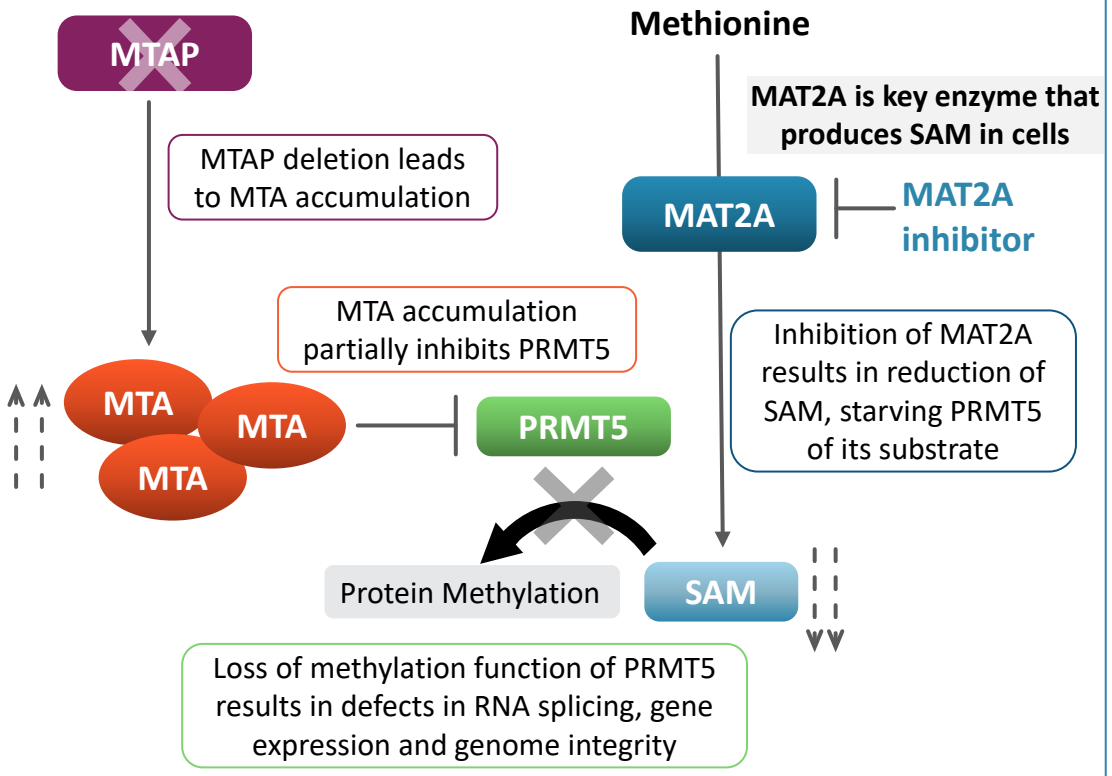

- Darovasertib does not require patient selection in UM / MUM (GNAQ/GNA11 ~95%). The "indication is the diagnostic"
- UM / MUM annual incidence >13k patients in US & EU
- ~$1 billion (~$650M to ~$1.5B) peer group analyst peak revenue projections for Choroidal Melanoma indication (subset of UM)**
- Tebentafusp launch uptake observed in MUM HLA-positive***

* IDEAYA / ClearView Analysis
** Aura Analyst Reports: BTIG, Cowen, Evercore, JPM, SVB
*** Immunocore, 2022

# MAT2A Inhibition is Synthetic Lethal with MTAP Deletion

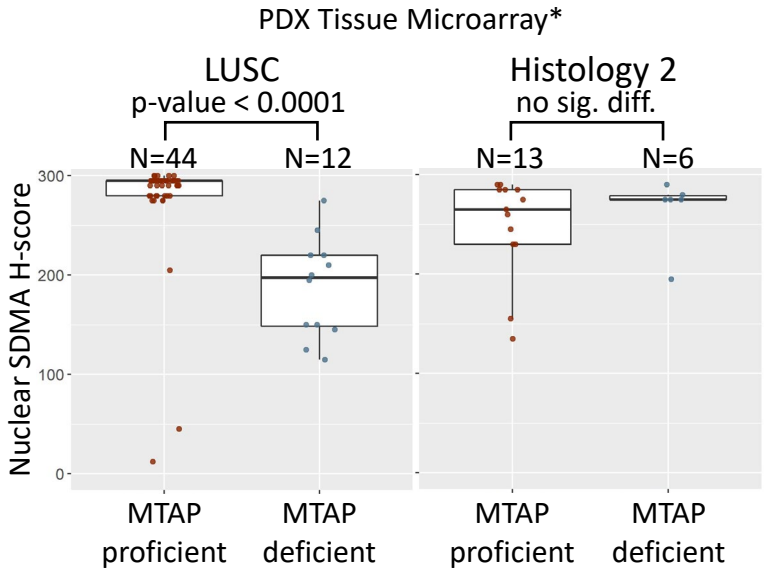
## Strategies to address MTAP$^{-/-}$ Prevalence in ~15% of all Solid Tumors

### MTAP-MAT2A Synthetic Lethality Biology




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

Robust association of MTAP$^{-/-}$ with partial Methylation Pathway Suppression in Squamous Lung (LUSC)



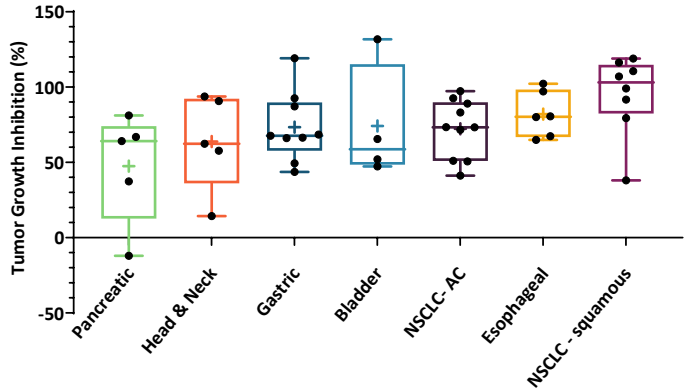

*MTAP status confirmed by both NGS and CAP/CLIA IHC
IDEAYA Data

# IDE397 demonstrates Broad Efficacy across MTAP-deficient PDX Models

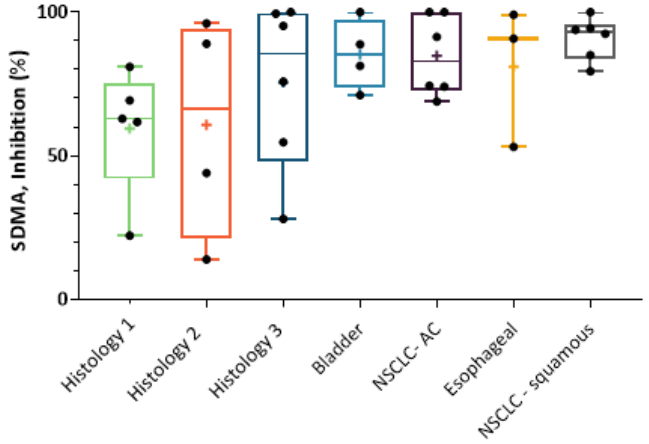
## Deep Regressions observed in NSCLC-squamous (LUSC), Esophageal and Bladder Cancers

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

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



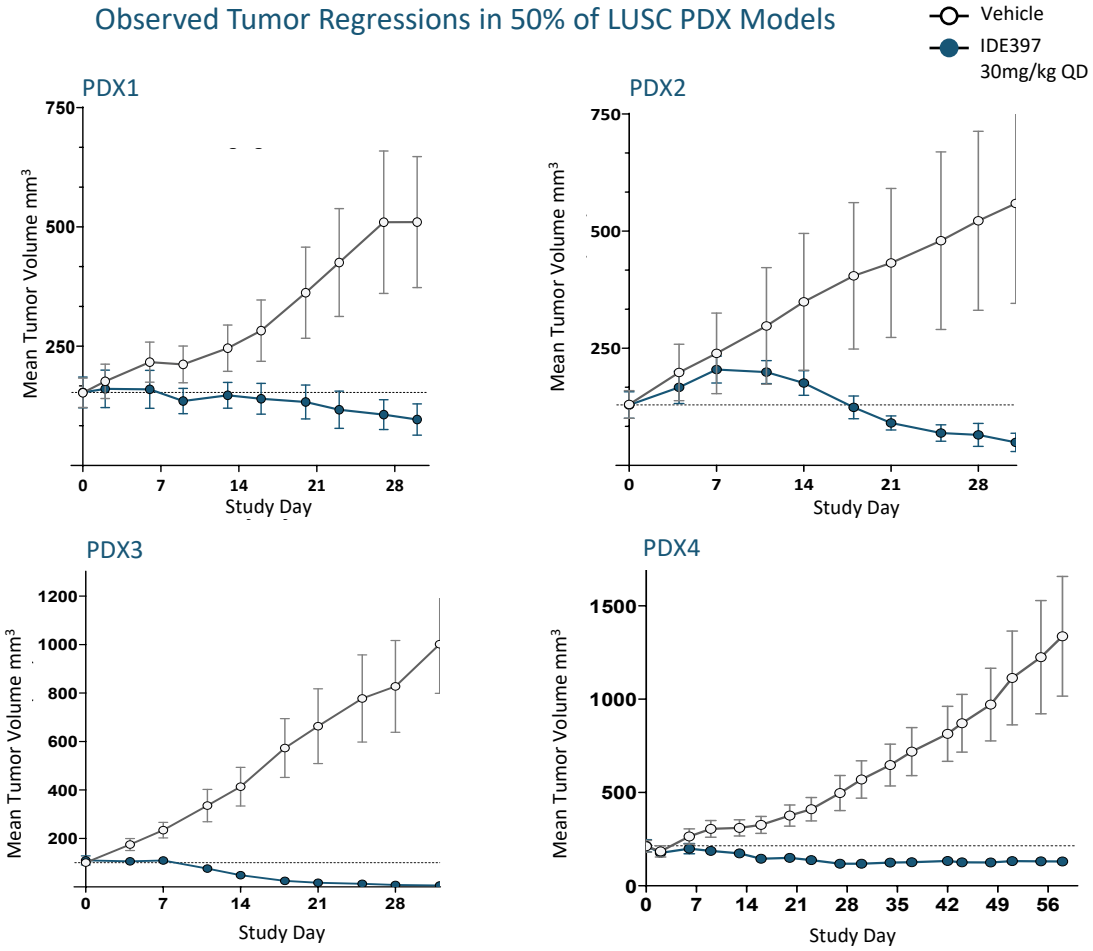

SDMA Suppression in Residual Tumors* at End of Study




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

### IDE397 In Vivo Efficacy in LUSC PDX Models

Observed Tumor Regressions in 50% of LUSC PDX Models

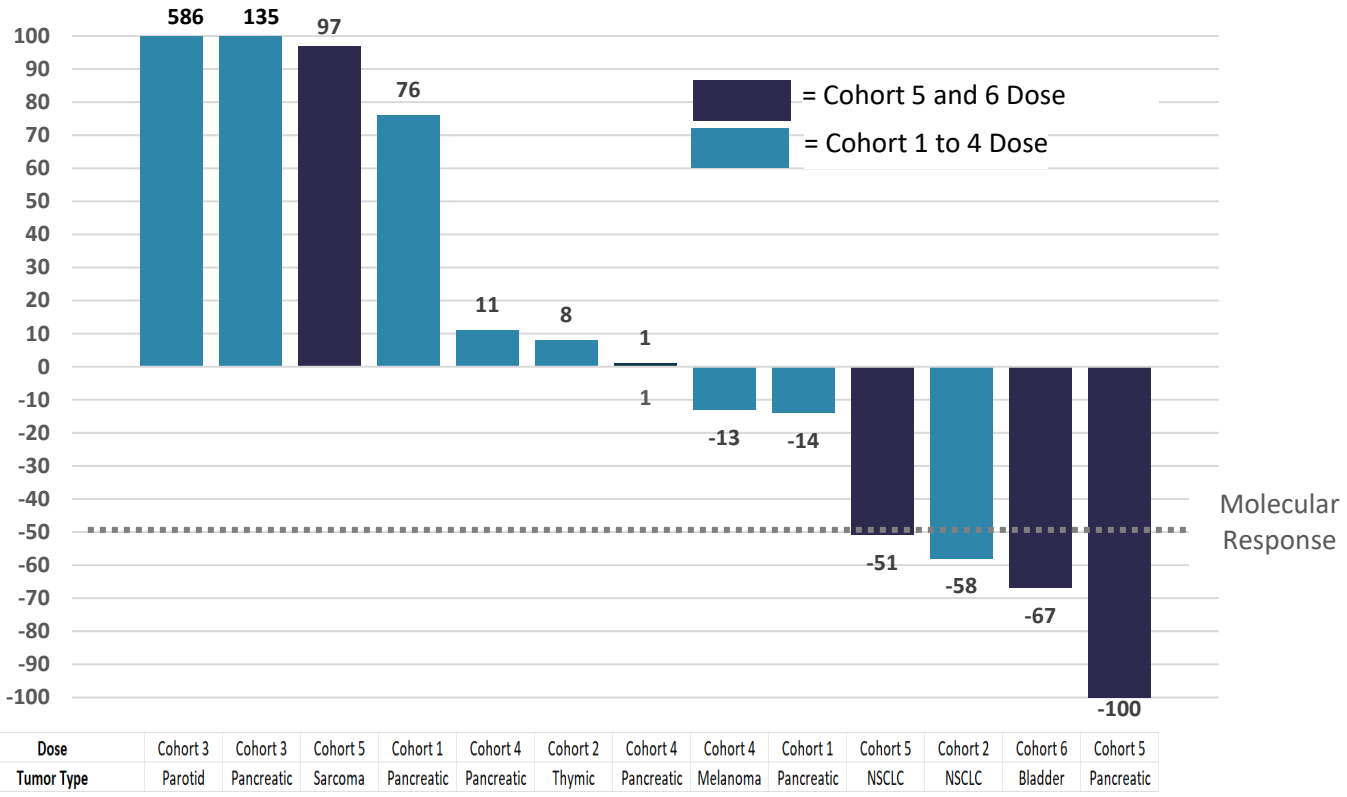



IDEAYA Data

# IDE397 Clinical Data Summary – Monotherapy Dose Escalation Cohorts

## ctDNA Molecular Response demonstrates Tumor Pharmacodynamic Modulation

### Molecular Response Waterfall (Baseline to C2D1)




| Dose | Cohort 3 | Cohort 3 | Cohort 5 | Cohort 1 | Cohort 4 | Cohort 2 | Cohort 4 | Cohort 4 | Cohort 1 | Cohort 5 | Cohort 2 | Cohort 6 | Cohort 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tumor Type | Parotid | Pancreatic | Sarcoma | Pancreatic | Pancreatic | Thymic | Pancreatic | Melanoma | Pancreatic | NSCLC | NSCLC | Bladder | Pancreatic |

IDEAYA Data: Guardant OMNI™ ctDNA Molecular Response (n=13 evaluable IDE397 Phase 1 dose escalation samples)

### ctDNA Molecular Response: IDE397 Dose-Dependent Tumor Pharmacodynamic Modulation

- 100% (2 of 2) Molecular Responders in NSCLC
- 75% (3 of 4) Molecular Responders in Cohort 5 and Cohort 6 Patients
- 31% (4 of 13) Molecular Responders across all dose-escalation Cohorts 1 to 6

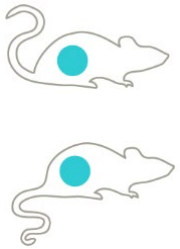
# IDE397 is a Potential Backbone for SL Combination Therapy in MTAP$^{-/-}$ Tumors

MAT2Ai induces Biological Responses in MTAP$^{-/-}$ Tumors that are Synthetic Lethal with select Chemotherapies and Targeted Therapies in Multiple Disease Indications with High Unmet Clinical Need

## Strategy for Identification of Synergistic IDE397 Combination Opportunities

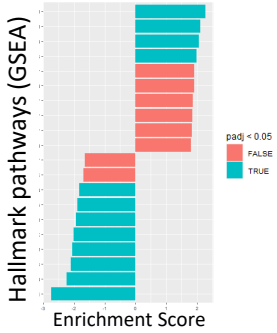
**1** Molecular profiling of drug effect on MTAP$^{-/-}$ tumors *in vivo*

Multi-lineage PDX RNAseq



IDE397 treated
vs
Vehicle treated

Consensus IDE397 GE response

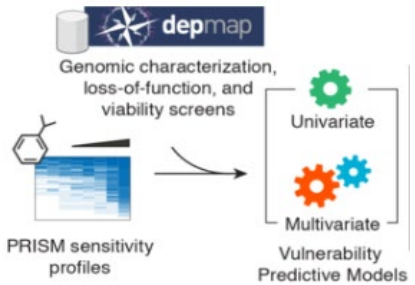



IDE397 perturbs biological processes supporting:

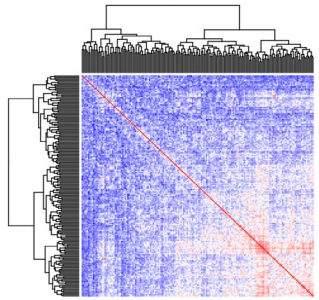
- pre-mRNA splicing
- genome integrity
- mitotic spindle assembly

**2** Chemogenomic evaluation of selective drug sensitivities in MTAP$^{-/-}$ across the CCLE

184 drug sensitivity profiles across ~1000 cancer cell lines




IDE397 correlation consensus cluster

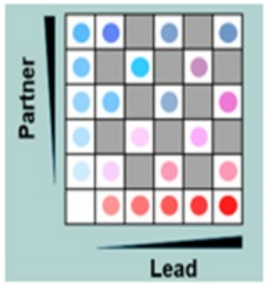


Compounds enriched in *MTAP*$^{-/-}$ cell lines perturb same biological processes as IDE397:

- pre-mRNA splicing
- genome stability
- microtubule stability

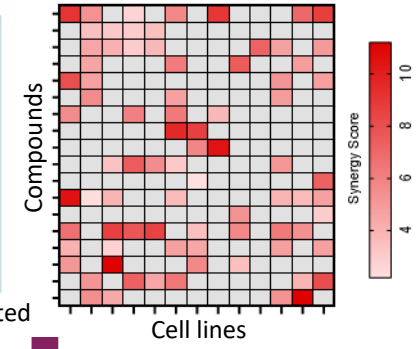
**3** High throughput in vitro drug combination screens

Dose matrix for synergy detection




>400 compounds evaluated

Hits with IDE397 synergy



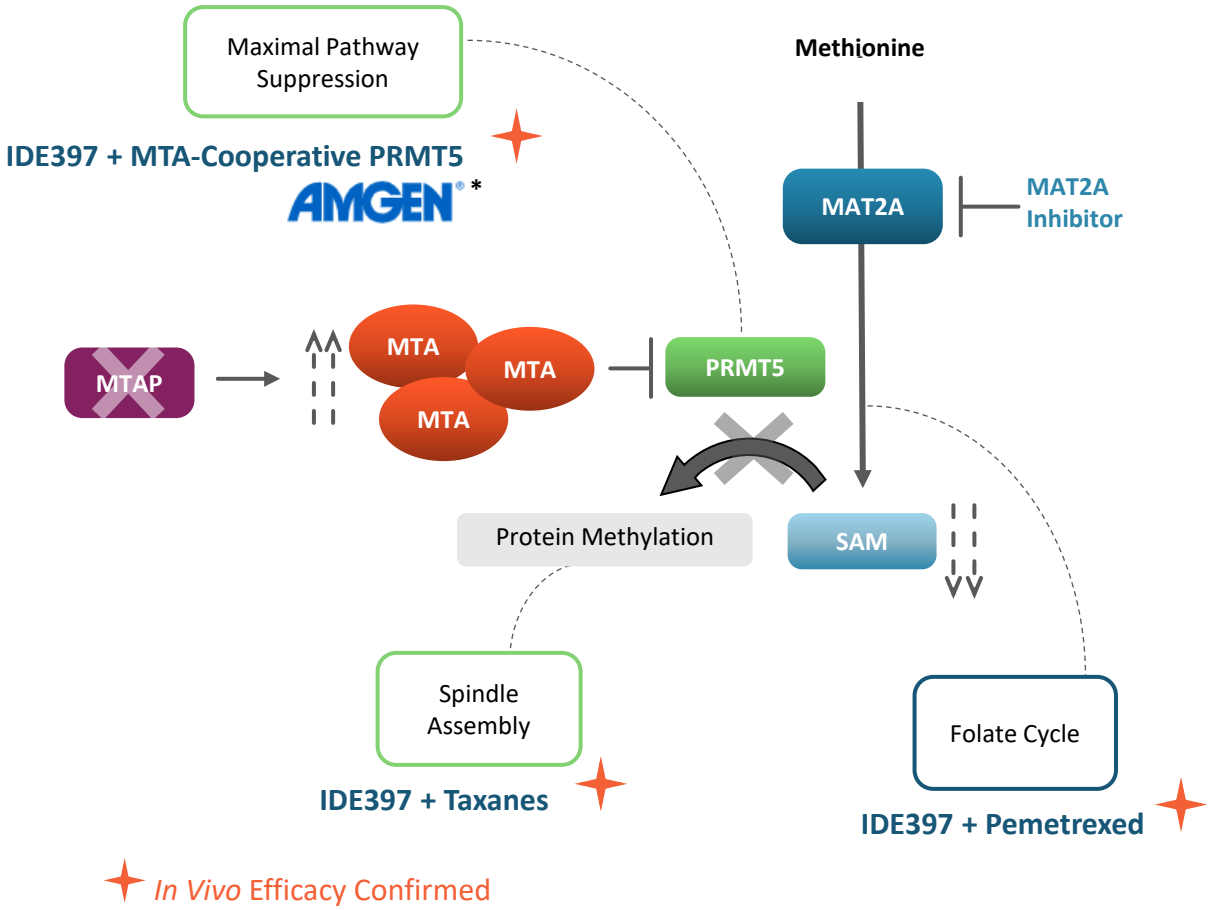

IDE397 synergy observed with taxanes, platins, targeted DDR, splicing inhibitors, anti-folates

- synergy is on-mechanism
- presents strategy for synthetic lethal combinations

Precision Medicine Strategy: Synthetic Lethal Combination Therapies

# Clinically Evaluating Multiple MAT2Ai Rational Combination Strategies

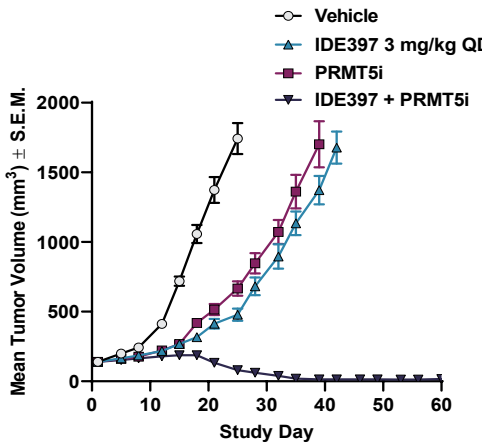
## Combination Strategies based on Mechanistic Hypothesis and Preclinical Efficacy




## IDE397 Novel Combinations

### IDE397 + MTA-Cooperative PRMT5i

(NSCLC MTAP-/- CDX Model)



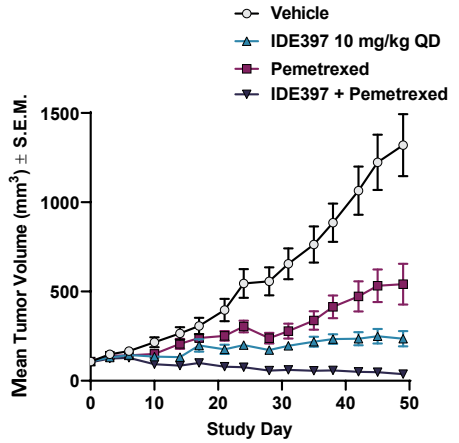

Observed Complete Response (CR) @ Study Day ~40+ durable to Study Day ~60+

IDE397 dosed at 3 mg/kg QD = 1/10th of typical preclinical dose of 30 mg/kg QD

Observed selective sensitivity in MTAP-null tumors (no observed TGI in MTAP-wt tumors)+

### IDE397 + Pemetrexed

(NSCLC MTAP-/- PDX Model)




Observed Tumor Regressions (>100% TGI) by Study Day ~30+ durable to Study Day ~50+

IDE397 dosed at 10 mg/kg QD = 1/3 of typical preclinical dose of 30 mg/kg QD

IDEAYA Data; + HCT-116 engineered +/- MTAP CDX models
PRMT5 Inhibitor = representative tool compound PRMT5i

IDEAYA / GSK Data



* Pursuant to Amgen Clinical Trial Collaboration and Supply Agreement for clinical evaluation of IDE397 and Amgen's AMG 193, an investigational MTA-cooperative PRMT5 inhibitor; Amgen will sponsor the study; IDEAYA and Amgen will jointly share external costs of the study

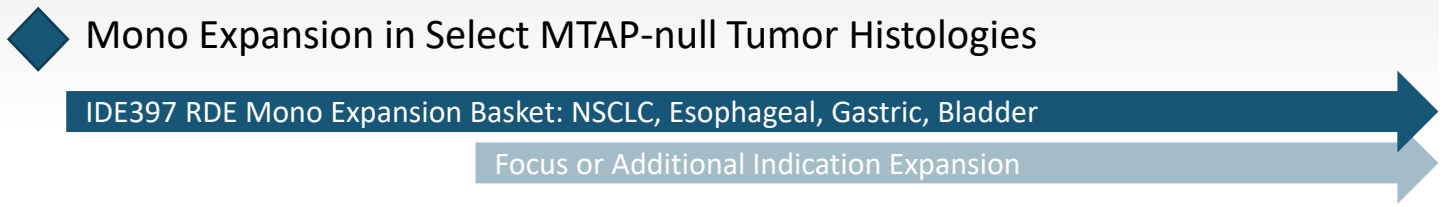
# IDE397 Phase 1/2 Clinical Development Plan

## Clinical Strategy Focused on Rational Combinations

### IDE397 Development Candidate – Clinical Profile

- Exposure-Dependent Pharmacokinetic (PK) Profile with low $C_{max}$:$C_{min}$
- Robust, Exposure-Dependent Pharmacodynamic (PD) Response
- Monotherapy Expansion at Projected Clinically Active Dose *
- Maximum Tolerated Dose Not Yet Observed ^

IDE397 is uniquely positioned to evaluate efficacy in MTAP pathway, with a favorable PK/PD profile and observed therapeutic window




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

* Monotherapy Expansion at Cohort 5 dose, projected to be a potentially efficacious dose based on clinical PK/PD and preclinical data and models
^ Continuing with concurrent dose escalation cohorts (e.g., Cohort 6)
# AMG193 = Amgen's investigational MTA-cooperative PRMT5 inhibitor

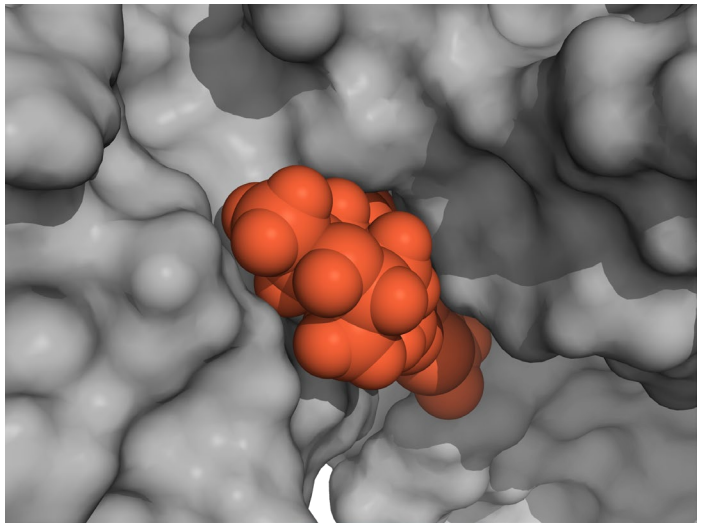
# IDEAYA's Potential First-in-Class Synthetic Lethality DDR Pipeline

Synthetic Lethality with Tumor-Promoting defects in DNA Repair Mechanisms

## IDE161

PARG Inhibitor

Development Candidate



Phase 1

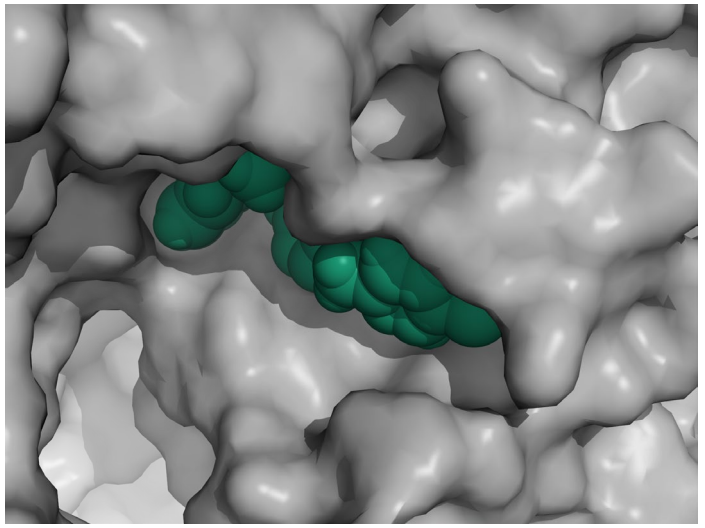
Monotherapy in HRD Breast, Ovarian

Potential to develop beyond HRD

## Pol Theta ϕ

Helicase Inhibitor

Development Candidate

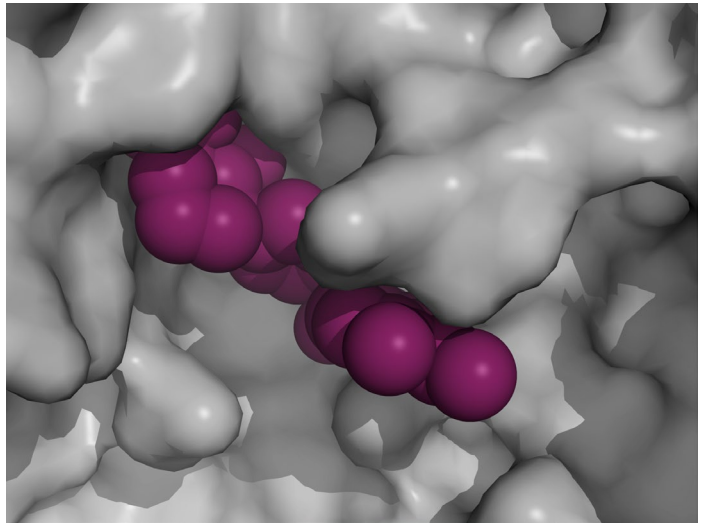


Targeting First-in-Human H1 2023

Niraparib combination in HRD

## Werner ϕ

Helicase Inhibitor



Targeting Development Candidate in 2023

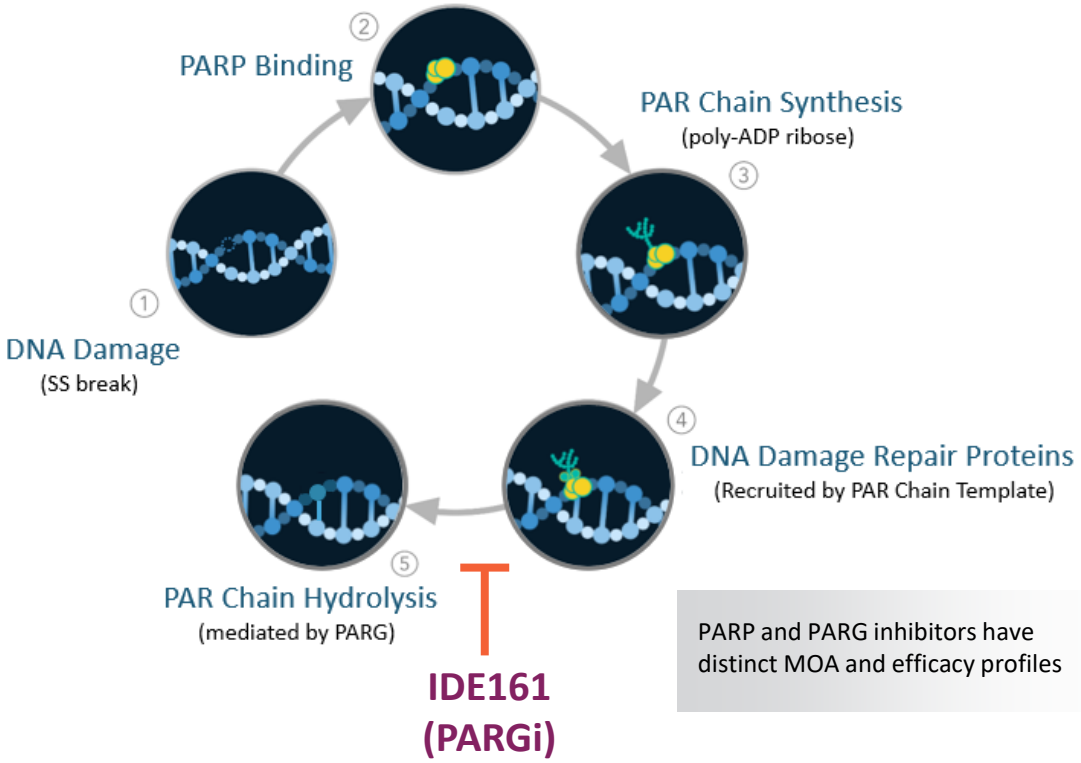
MSI-high tumor agnostic

ϕ Pursuant to GSK Collaboration, Option and License Agreement

# PARG Inhibition is Synthetic Lethal with HRD

## Novel, Mechanistically-Differentiated Target in a Clinically Validated Pathway

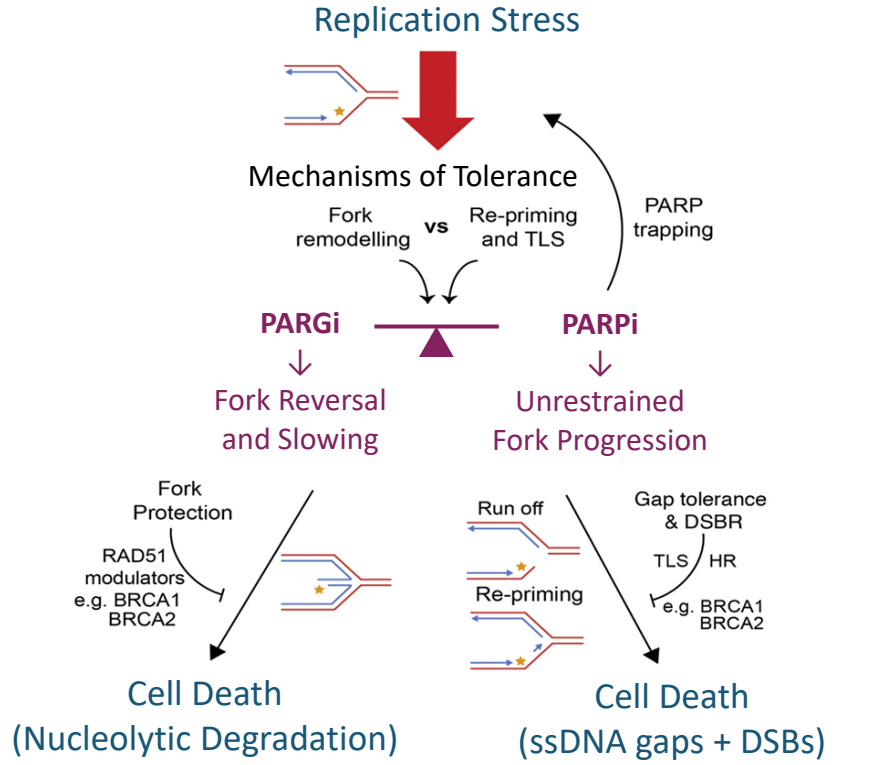
### PARG Activity is required to resolve DNA Repair




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

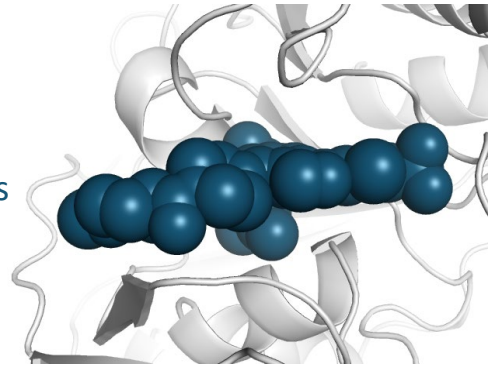



Pillay et al., Progress in Biophysics and Molecular Biology 2021; McDermott et al., Cancer Cell 2019; Zeman and Cimprich, Nature Cell Biology 2014

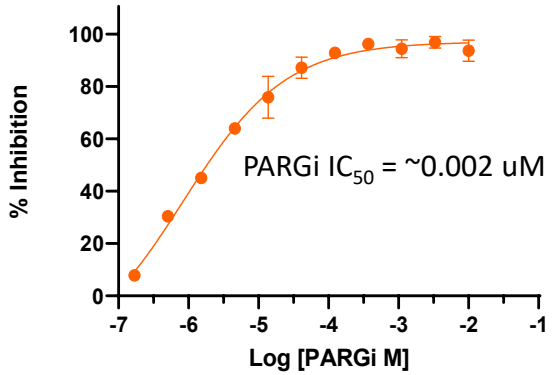
# IDE161: Potential First-in-Class Phase 1 PARG Inhibitor

## IDE161 Profile: Potent, Selective with Favorable Properties

- IDE161 is a potent, selective small molecule PARGi for tumors with HRD
- Demonstrated cellular activity and efficacy in biomarker defined settings
- Positive physical property profile
- Favorable nonclinical-safety profile



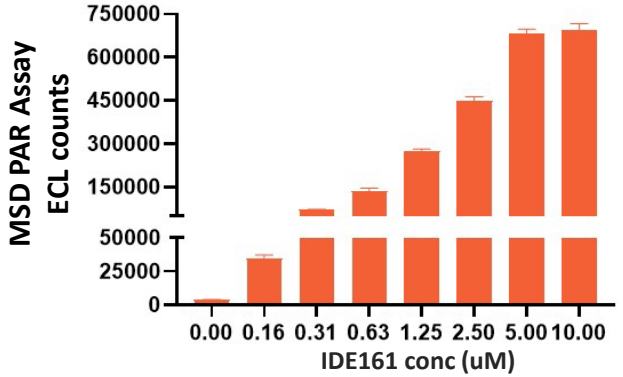
Biochemical IC50



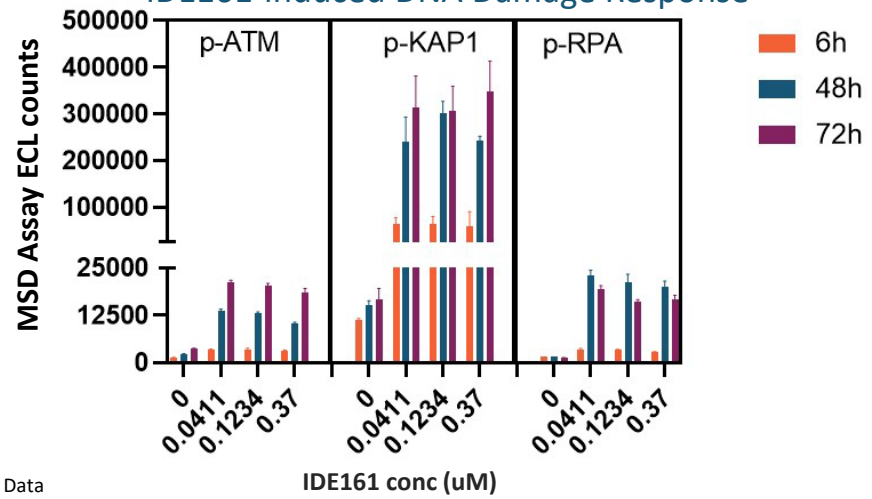

IDEAYA Data

## IDE161 induces PAR Accumulation and Selective DDR

IDE161-induced Cellular PAR Accumulation




IDE161-induced DNA Damage Response



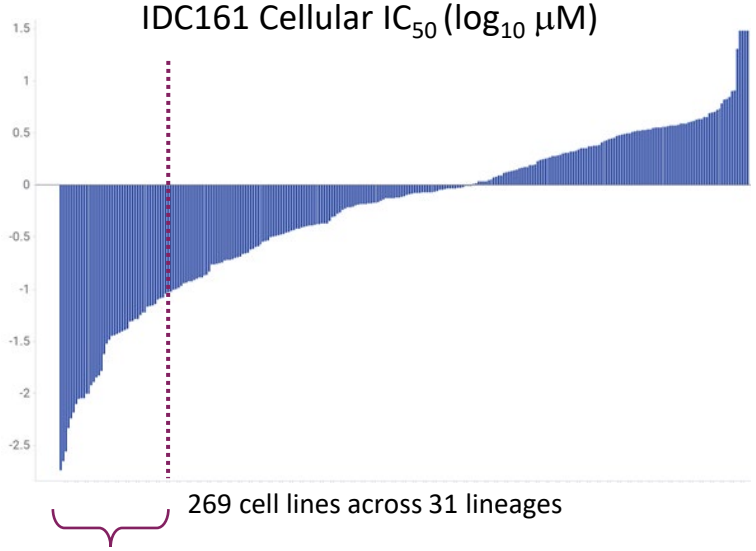

IDEAYA Data

# IDE161 shows Selective Sensitivity in HRD and Differentiation from PARPi

## IDE161 Sensitivity Profile in Cell Panel

Cellular response profiles reveal mechanistic associations with PARGi sensitivity

IDC161 Cellular $IC_{50}$ ($log_{10}$ µM)

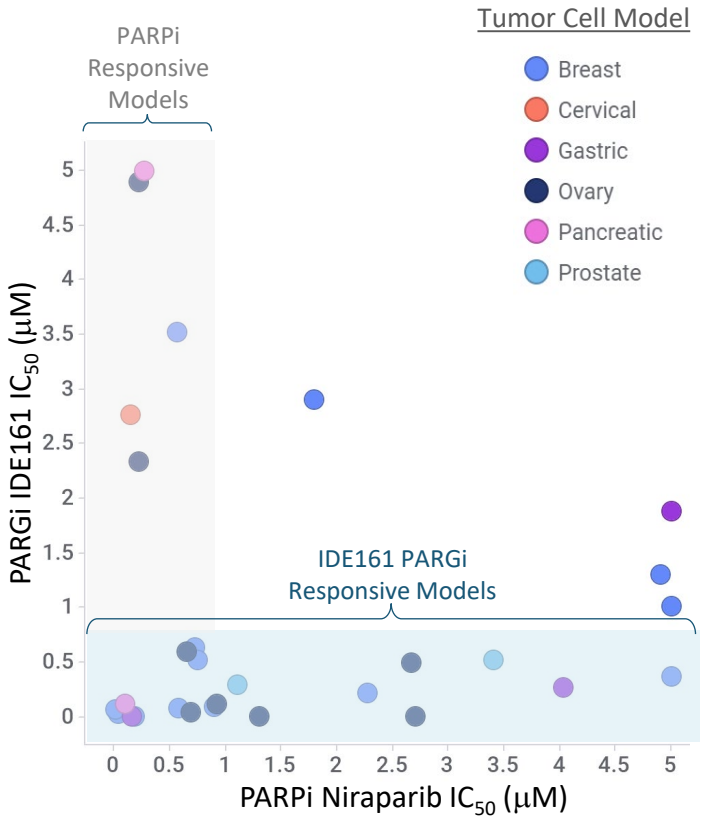



Top predictive response biomarkers* include HRD, replication stress, nucleotide excision repair and parylation cycle

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

## IDE161 Selective Sensitivity vs PARPi

HRD cell lines are selectively sensitive to IDE161 versus PARPi

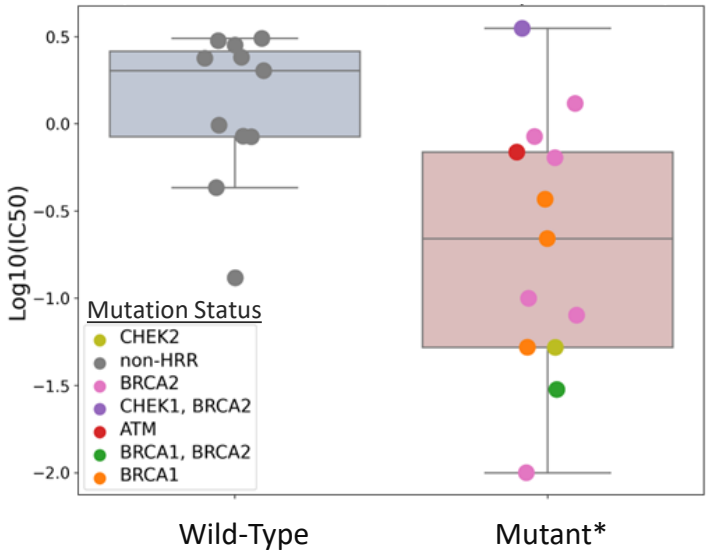



## IDE161 Sensitivity in HRD Breast Cancer

Response to IDE161 is strongly associated with HRD status in Breast Cancer Cell Lines

Cellular antiproliferative response to IDE161 stratified by HRR status

(Breast Cancer: n=24, Wilcoxon pval=0.008)



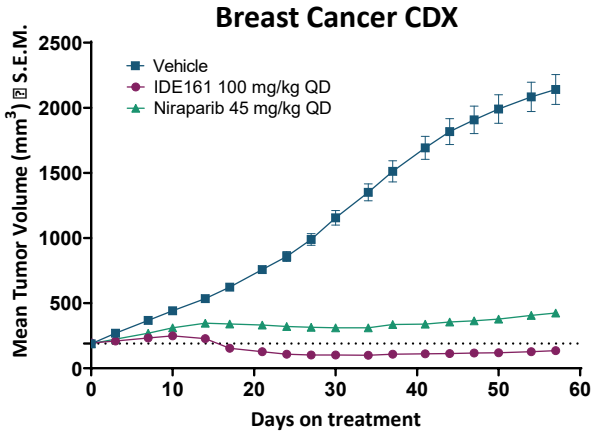

*HRR mutation status assigned according Foundation Medicine HRR gene panel: ATM, BRCA1, BRCA2, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L

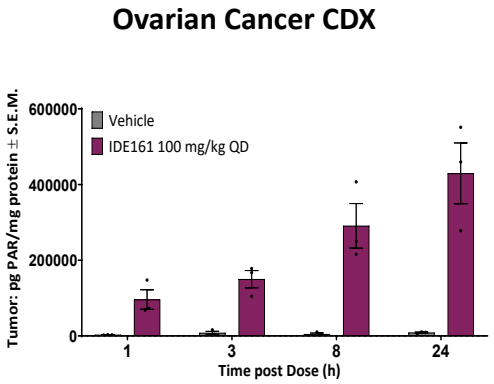
# IDE161 is Active and Well-Tolerated in HRD Tumor Models

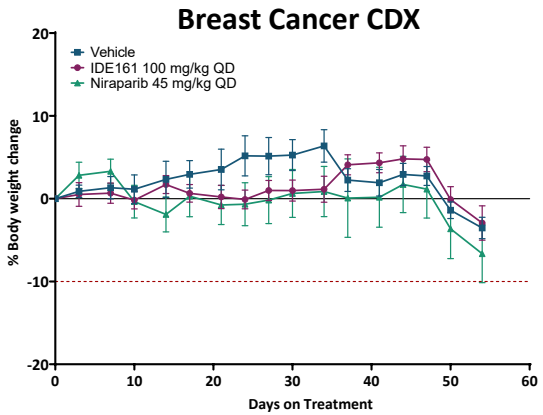
## Observed PARG inhibitor Activity is Distinct from PARP Inhibition

### Durable Disease Control with IDE161 in BRCA-altered CDX

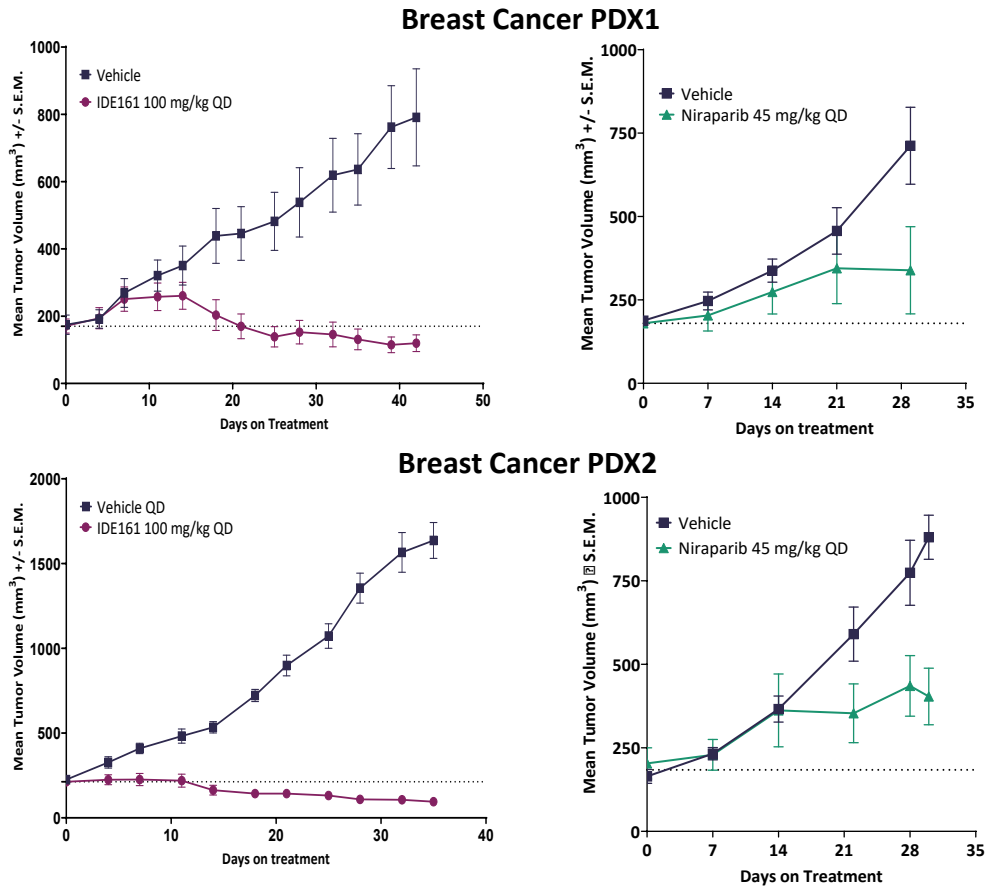
- Durable regressions (vs stasis with niraparib)
- Robust dose- and time-dependent PAR accumulation
- Well tolerated; no body weight loss >10%




### Regression in BRCA altered BC PDX with IDE161 vs. PARPi



# IDE161 Demonstrates Favorable Safety Profile in Preclinical Studies

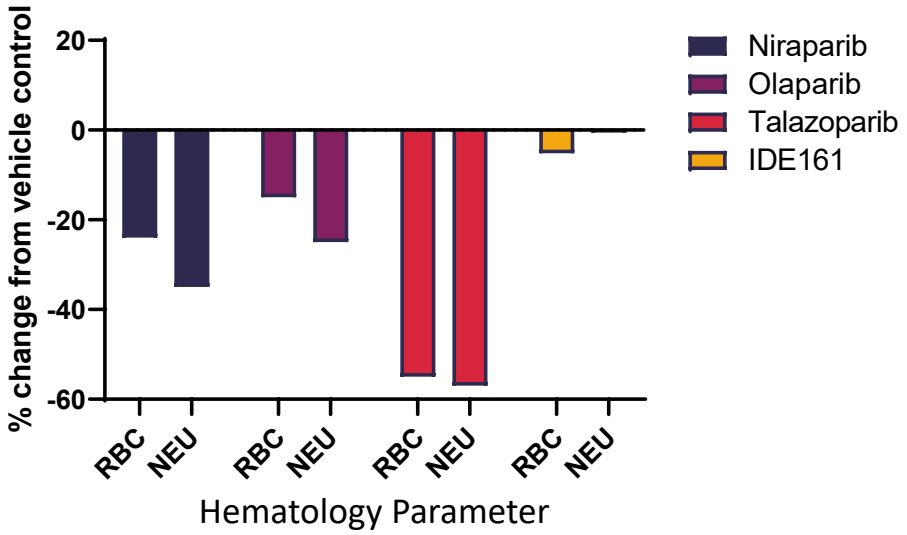
## Non-Clinical Pharmacology and Toxicology Studies Support Clinical Evaluation

### IDE161 Differentiates versus PARPi in Nonclinical Safety Studies

PARP inhibition causes myelosuppression in rat and dog at clinically relevant systemic exposures

In contrast, IDE161 does not alter hematology parameters in rodents at relevant exposures associated with the estimated therapeutic dose

IDE161 versus PARPi in Rat Studies *



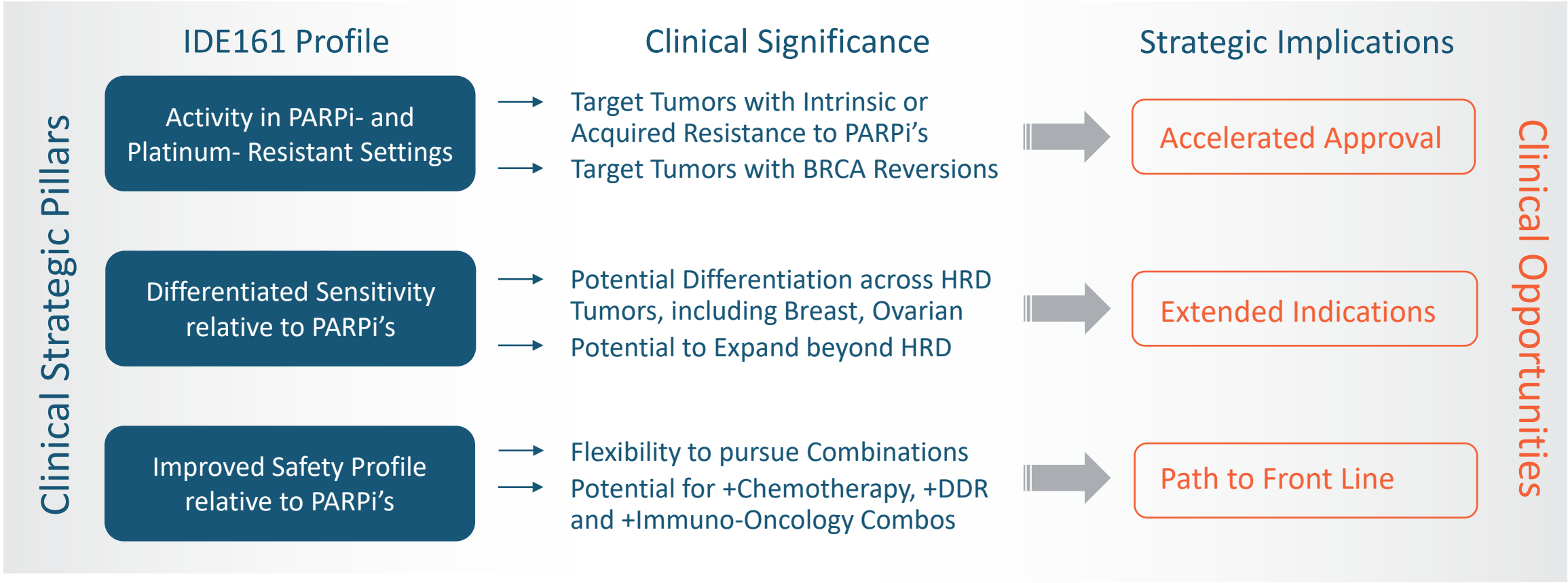

IDE161 Drug Product

* PARPi data extracted from repeat dose toxicology data presented in NDA reviews (Drugs@FDA.gov) and prescribing labels. Species chosen for data illustration (rat) was based on availability of data at a dose level that most closely approximated systemic exposure (AUC) associated with the clinically recommended dose.

- IDE161 well tolerated preclinically with tumor regressions observed at doses below mouse MTD
- Human efficacious dose projection based on maximum efficacious dose in mouse (100 mg/kg/day) which covers cellular $IC_{90}$ for ≥ 22 hours
- Data from GLP toxicology studies support a proposed safe starting dose of 0.5X the estimated therapeutic dose
- IDE161 API synthetic process and drug product tablet formulation developed

# IDE161 Clinical Development Strategy

## First-in-Class Opportunity for Patients with Breast, Ovarian & Other Tumors




Significant Market Opportunity in ER+, Her2- Breast Cancer Patients with HRD → Represents ~10% to ~14% of Breast Cancer

ER+ /Her2− subtype occurs in ~68% of breast cancer, and ~14% to ~20% of ER+/Her2− breast cancer patients may be HRD^



^ Moore et al., Breast Cancer Research and Treatment 192:649–653 (2022): ER+/Her2- subtype analysis based on SEER data; HRD analyses based on Pan-Cancer Analysis of Whole Genomes (PCAWG)

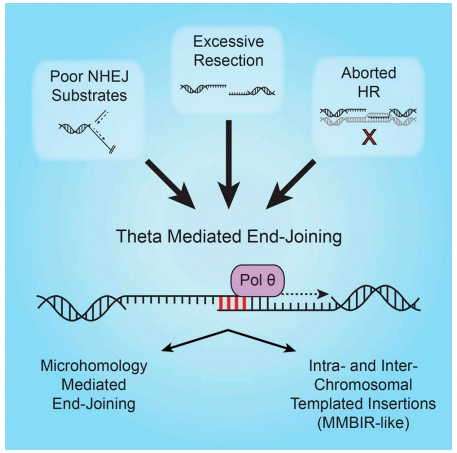
# Polymerase Theta (Pol Theta) Synthetic Lethality Program

## First-in-Class Helicase Inhibitor is Synthetic Lethal to HR and NHEJ Perturbation

### Role of Pol Theta in Tumor Biology

Pol Theta is an error-prone multi-domain protein with helicase / polymerase activities


Pol Theta DNA break end-joining is critical when canonical repair pathways fail



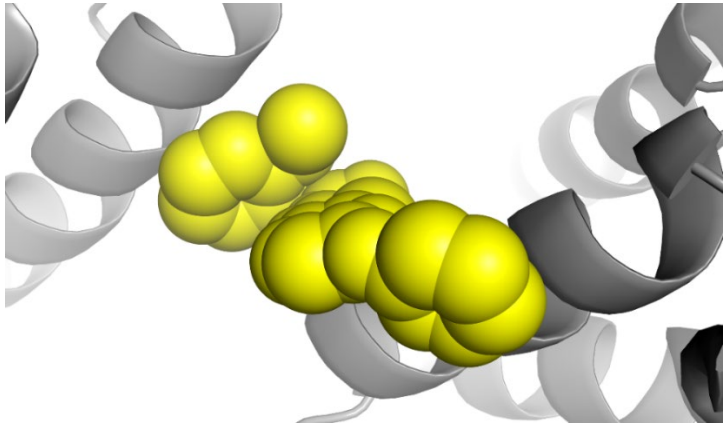

D. Wyatt et al. *Mol Cell* (2016)

### Pol Theta Inhibitor Drug Discovery

Discovered Pol Theta inhibitors with $IC_{50}$ <10 nM in biochemical assays against Polθ

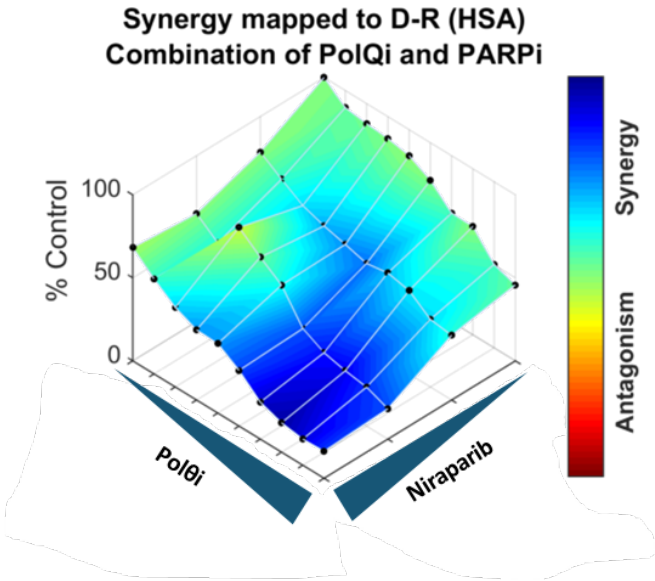
Drug-like properties of Polθ inhibitors support oral dosing in humans

Development candidate nominated in 2022



### Pol Theta Inhibitor Synergy in HRD

Pol Theta inhibition is synthetic lethal with PARP inhibition in HR-deficient cancer cells



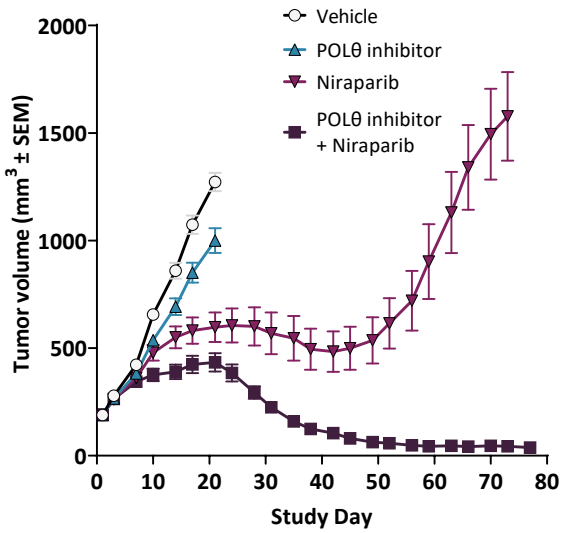

IDEAYA / GSK Data

# Pol Theta Helicase Synthetic Lethality Program

## Targeting First-in-Human Phase 1 Clinical Trial Initiation in H1 2023

### Pol Theta Helicase *In Vivo* Activity

Pol Theta Helicase Inhibitor + PARPi

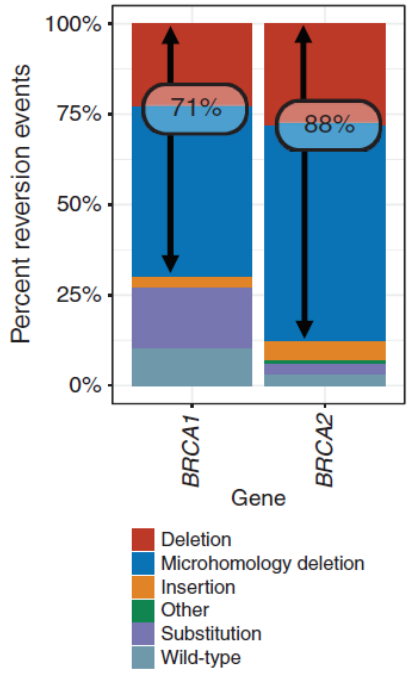



Observed Deep and Durable Responses in Multiple Xenograft Models

IDEAYA / GSK Data

### BRCA 1/2 Clinical Reversions

BRCA Reversions Mediated by MMEJ




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

### Clinical Development Strategy

Pol Theta Helicase Inhibitor + PARP Inhibitor

Pol Theta Helicase Inhibitors Disrupt MMEJ Alternative DNA Damage Repair:

- Inhibit DSB Repair by MMEJ
- Dysregulate Replication Fork Stabilization

| Potentiate PARPi Efficacy | Prevent PARPi Resistance | Overcome PARPi Resistance |
|---|---|---|

Potential Clinical Opportunities

GSK Strategic Partnership: Global Royalties with GSK covering all Costs, ~$1B Milestones, incl up to $20M Preclinical / Ph1 Clinical

Potential Combination with GSK's Zejula™, a PARP Inhibitor

# Werner Helicase is Synthetic Lethal with Microsatellite Instability

## Targeting Development Candidate in 2023

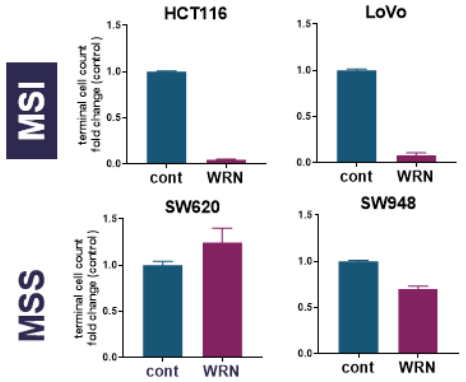
### Werner Helicase Synthetic Lethal with High-MSI

CellPress

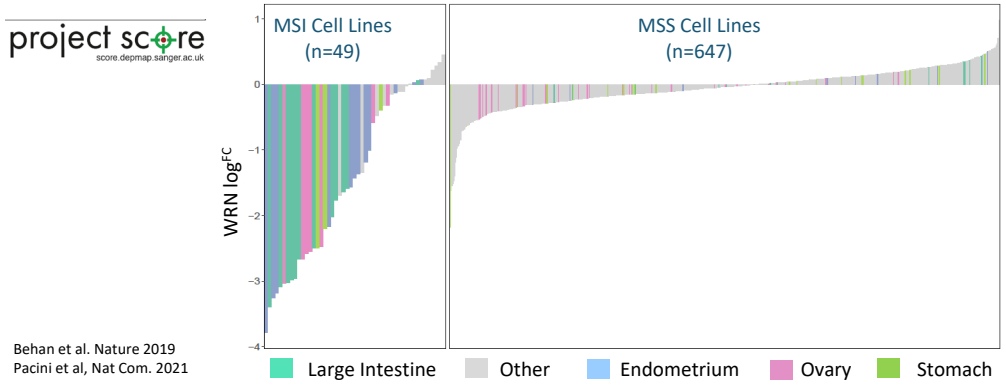
**Werner Syndrome Helicase is Required for the Survival of Cancer Cells with Microsatellite Instability**

IDEAYA Publication

Cell Press, iScience, March 2019, Hager et al




#### Werner Helicase – Dependence in Cancer Cell Models

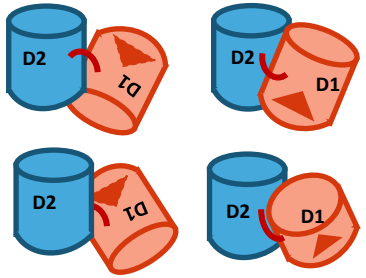



Behan et al. Nature 2019
Pacini et al, Nat Com. 2021

### Discovery of Potent and Selective WRN Inhibitors

#### Werner Helicase Inhibitor Drug Discovery

Solved >85 X-ray Co-Crystal Structures

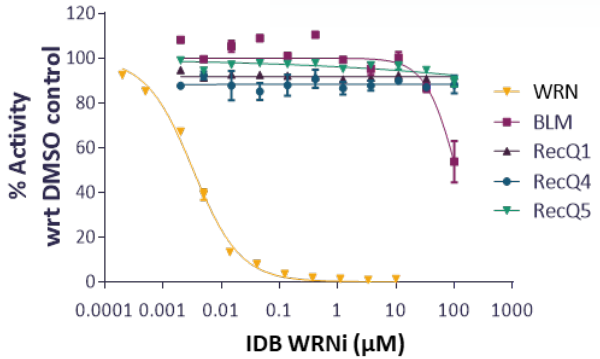



Achieved >10,000,000-fold Affinity Increase

Initial Hits
*Low Affinity*
*Poor Druglike Properties*

Improved Inhibitors
*High Affinity*
*Good Druglike Properties*

**WRN inhibitors** have nanomolar potency, biochemical and cellular activity, and selectivity over other RecQ Helicases




IDEAYA Data

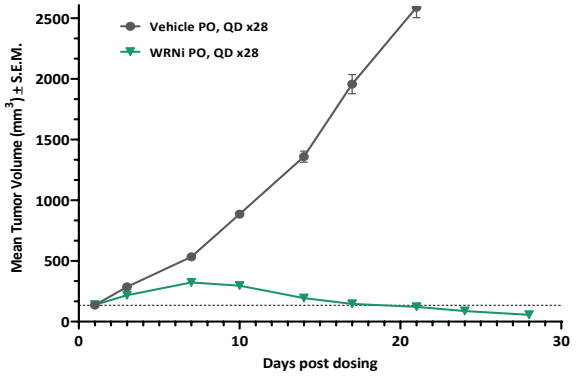
GSK Strategic Partnership: 50/50% US Profit Share and ex-US Royalties, ~$1B Milestones, incl up to $20M Preclinical / Ph1 Clinical; Cost Share 80% (GSK) / 20% (IDEAYA); Potential Combination with GSK's Jemperli™, a PD-1 IO Agent

# Werner Inhibitor *In-Vivo* Efficacy in MSI-High Models

## WRNi Shows Pharmacological Activity in Therapy-Refractory CRC MSI-High Models

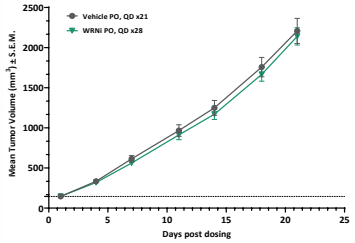
### *In-Vivo* Efficacy in Xenograft Models

MSI-High




**WRN inhibitors** show *in vivo* efficacy with ~100% TGI and tumor regression in MSI-High models with selectivity over MSS models

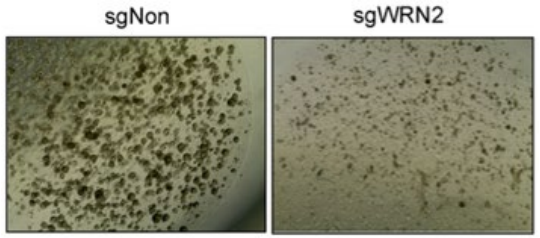
MSS



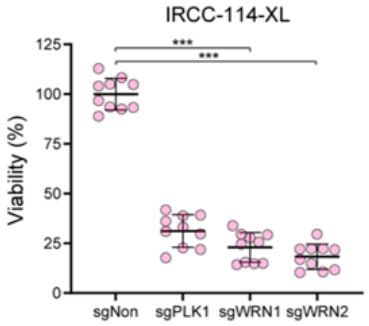

IDEAYA Data

### WRN Activity in Therapy-Refractory CRC Organoid Models

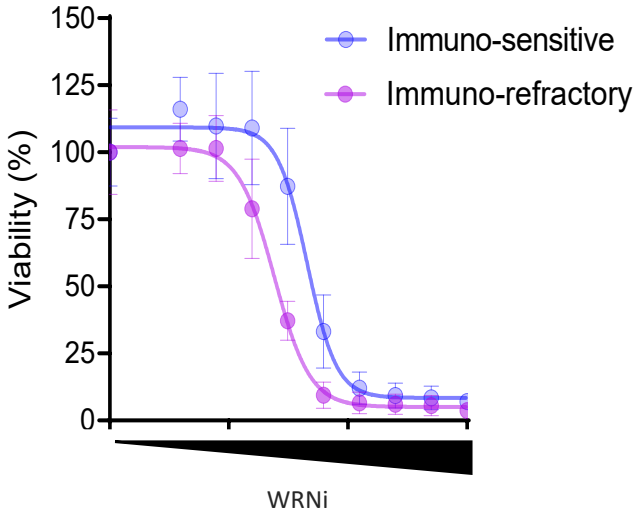
Immuno-Refractory (Genetic Sensitivity)




Chemo-Refractory (Genetic Sensitivity)




Immuno-Refractory (Pharmacological Sensitivity)




**Pharmacological** activity in therapy-refractory models supports clinical thesis

Wellcome Sanger / GSK / IDEAYA Data

# Synthetic Lethality Focused Precision Medicine Oncology Biotech

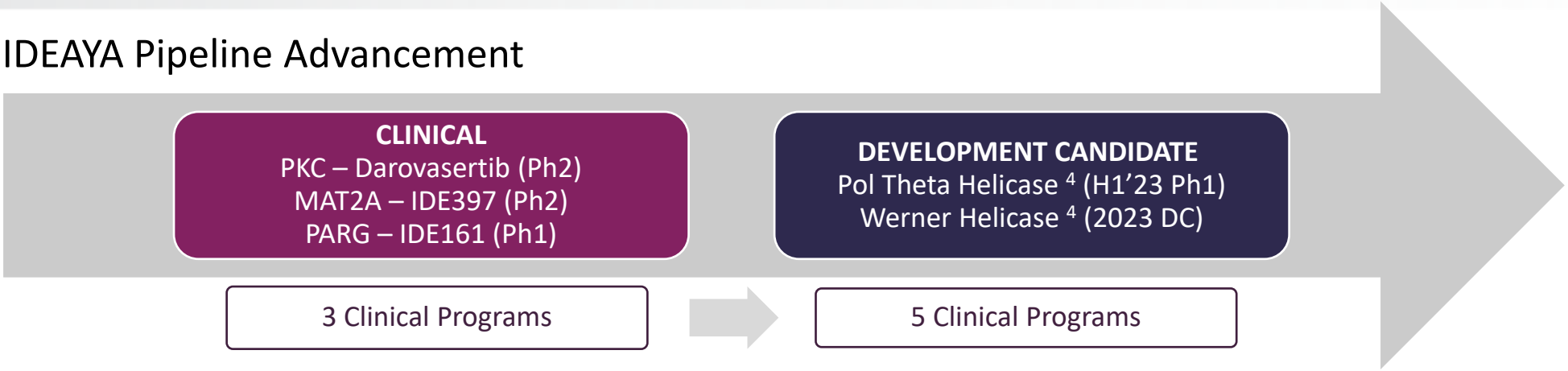
## *First-in-Class* Synthetic Lethality Pipeline and Leading SL Platform

Broad Pipeline of Potential First-in-Class Synthetic Lethality Programs with large addressable patient populations in major solid tumor types, including Phase 2 (Darovasertib, IDE397), Phase 1 (IDE161) and Late Preclinical (Pol Theta, Werner Helicase)

Validating and Value-Accretive Pharma Partnerships and Collaborations with Amgen on MAT2A-PRMT5 Combination,[3] Pfizer on Darovasertib-Crizotinib Combination,[3] GSK on Pol Theta (100% Cost Paid by GSK, ~$1B Milestones, WW Royalties) and GSK on Werner Helicase (80% Cost Paid by GSK, ~$1B Milestones, 50/50 US Profits)

Strong Balance Sheet with ~$394 M in cash anticipated to fund operations into 2026 [1, 2] and opportunity to realize GSK collaboration milestones to further extend cash runway

### IDEAYA Pipeline Advancement




(1) Includes aggregate of ~$393.9M cash, cash equivalents and marketable securities as of September 30, 2022
(2) IDEAYA Form 10-Q dated November 8, 2022, as filed with the U.S. Securities and Exchange Commission
(3) Clinical Trial Collaboration and Supply Agreements, independently with Pfizer (Darovasertib + Crizotinib) and Amgen (IDE397 + AMG193); IDEAYA retains all commercial rights
(4) Cost Share for Pol Theta and Werner Helicase Programs: 100% GSK and 80% GSK / 20% IDEAYA, respectively