IDEAYA Biosciences
Improving Lives Through Transformative Precision Medicines
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
- **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)

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(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

Reference: Charles Boone

## IDEAYA’s Precision Medicine Oncology Pipeline

Building the Industry Leading Synthetic Lethality Focused Biotechnology Company

### Precision Medicine Pipeline

<table>
<thead>
<tr>
<th>Modality/Indication</th>
<th>Biomarker</th>
<th>Preclinical</th>
<th>IND Enabling</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>2021 Goals</th>
<th>Collaborations</th>
<th>Commercial (IDEAYA)</th>
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<tr>
<td>IDE397 MAT2A</td>
<td>MTAP</td>
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<td>Clinical Pharmacodynamic Data (PD) Tumor PD Q4 2021</td>
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<td>MTAP</td>
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<td>Preclinical Data to enable Combos (Taxanes, PRMTi, Others)</td>
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<td>Platform</td>
<td>Defined Biomarker</td>
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<td>Lead Series (DNA Damage Targets) New Target / Biomarker Validation</td>
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<td>Kinase</td>
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<td>Regulatory Guidance in MUM H2 2021 (Monotherapy) and/or H1 2022 (Combination)</td>
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<td>Clinical Data Update - Combination(s) H2 2021</td>
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(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](image)
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
- 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 Form 8-K current report filed with the U.S. Securities and Exchange Commission on June 16, 2020; GlaxoSmithKline Q2 2020 Earnings Presentation
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 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 five SL programs obtained to enable structure-based design
  - Differentiated candidate compounds discovered, including IDE397
  - Protein degraders advancing for selected targets, including Pol Theta

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

Fully-Integrated Target, Biomarker, Drug Discovery and Translational Capabilities
IDEAYA Synthetic Lethality Platform
Synthetic Lethality Target and Biomarker Discovery and Validation

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.

IDEAYA Proprietary Libraries and Datasets – Strategic Collaborations with Broad Institute and UC San Diego

>20 Novel Drug Targets Identified
Target Validation Ongoing

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
MTAP-MAT2A Synthetic Lethality Biology

**MTAP**

MTAP deletion leads to MTA accumulation.

**MTA**

MTA accumulation partially inhibits PRMT5.

**MAT2A inhibitor**

MAT2A is a key enzyme that produces SAM in cells.

**Inhibition of MAT2A**

Inhibition of MAT2A results in reduction of SAM, starving PRMT5 of its substrate.

**MTA**

MTA accumulation leads to MTA accumulation.

**SAM**

Loss of methylation function of PRMT5 results in defects in RNA splicing, gene expression and genome integrity.

**Methionine**

**MTA**

MTA accumulation partially inhibits PRMT5.

**PRMT5**

Protein Methylation

**Data from The Cancer Genome Atlas in cBioPortal**

### MTAP Deletion Prevalence

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

MTAP Deletion Prevalence ~15% of all Solid Tumors
IDE397: MAT2A Development Candidate *in vitro* Profile

IDE397 is selective for MTAP-/- Cell Lines

IDE397 is Selective for MTAP-/- Cell Lines

IDE397 is selective for MTAP-/- Cell Lines

IDE397 has Broad Activity across Tumor Types

IDE397 has Broad Activity across Tumor Types

MTAP-/- cell lines are sensitive to IDE397

MTAP WT cell lines are generally insensitive

Pharmacological inhibition correlates with MAT2A genetic knockdown

MTAP-/- cell lines are sensitive to IDE397

MTAP WT cell lines are generally insensitive

Pharmacological inhibition correlates with MAT2A genetic knockdown

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 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)¹ 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 ¹

Biochemical and in vitro Potency and Selectivity

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<tr>
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<th>IDE397</th>
<th>AG-270</th>
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<tr>
<td>MAT2A biochemical IC₅₀ (nM)</td>
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<td>12</td>
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<td>KP4 EC₅₀ cellular (nM) MAT2A dependent</td>
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<td>731</td>
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<tr>
<td>BXPC3 cellular EC₅₀ (nM) MAT2A independent</td>
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<td>1630</td>
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<tr>
<td>HuCCT1 cellular EC₅₀ (nM) MAT2A independent</td>
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Differentiating ADME/Physicochemical Properties

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<tr>
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<th>IDE397</th>
<th>AG-270</th>
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<tr>
<td>BSEP inhibition @10µM (%)</td>
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<td>25.2</td>
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<tr>
<td>UGT1A1 inhibition (%)</td>
<td>34</td>
<td>83</td>
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<tr>
<td>PXR Emax @30 µM (%)</td>
<td>9</td>
<td>35</td>
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<td>Solubility @pH 7.4 (µM)</td>
<td>&gt;100µM</td>
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(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

SDMA and SAM are Proximal PD Biomarkers of MAT2A inhibition

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

Robust dose-dependent efficacy and PD modulation observed in NSCLC CDX Model
IDE397 evaluation in Patient Derived Xenograft (PDX) models with homozygous MTAP deletions in Solid Tumors

- Tumor Regressions (> 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

TGI = Tumor Growth Inhibition, CR = Complete Response
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

Program Goal:
Targeting ≥~60% plasma SAM PD reduction, based on IDE397 preclinical in vivo efficacy data in MTAP-deletion

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*

IDEAYA Data based on preliminary analysis of unlocked database as of June 25, 2021 (Cohort 1 n=2, Cohort 2 n=3)

* Agios, AACR-EORTC-NCI (Triple Meeting), 2019
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

- IDE397 Mono Expansion in NSCLC
- IDE397 Mono Expansion in Other Tumor Indication(s)
- IDE397 + Taxane Expansion(s)
- IDE397 + NCP Expansion(s)

MTAP Deletion in Solid Tumors (e.g., NSCLC, pancreatic, thymic)

PK/PD Expansion Cohorts *

* Tumor Biopsy Cohorts: PK=Pharmacokinetic, PD=Pharmacodynamic

NCP = Novel Combination Partner

Launch Accelerated Approval Enabling Studies
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

- 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


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 \textit{in vitro} \& \textit{in vivo} Models are Sensitive to IDEAYA PARGi

Differentiated Activity to PARP inhibition in Ovarian, Gastric and Breast Cancer Models
IDEAYA PARGi shows Robust TGI in Breast PDX Models

Monotherapy Tumor Regressions observed across Multiple Breast PDX Models

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

- Tumor Regressions (> 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

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**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-/− vs. wildtype cell lines.

Advancing both small molecule inhibitors and protein degraders.

**Pol Theta ATPase inhibitor In Vivo Activity**

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

Regressions observed for all animals dosed within combination study:

- 55% TGI
- 86% TGI
- 134% TGI

[Graph showing tumor volume over study days for different treatments, including Vehicle, IDB-Polθi, Niraparib, and IDB-Polθi + Niraparib.]
Werner Helicase Synthetic Lethality Program
Candidate Biomarker: High-MSI (15% GI Cancers and 16% CRC) \(^1\)

**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

**Werner Inhibitor Cellular PD and Viability**

**PD-marker:** dose dependent increase of DNA damage marker γH2AX

**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

\(^1\) Cancer Res., November 1998
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

- 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 in similar predominantly 2L/3L+ patient population

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

Darovasertib Combination Activity in MUM

- 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 + Binimetinib
n=24 with 14 evaluable patients

- > 2 post-baseline scans
- 1 post-baseline scan

Darovasertib + Crizotinib
n=4 with 2 evaluable patients

* prior uPR confirmed at subsequent scan (-51.7%)
* prior uPR confirmed at subsequent scan (-56.5%)

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1 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)

2 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%)

<table>
<thead>
<tr>
<th>Patient Profile</th>
</tr>
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<tbody>
<tr>
<td>56 year old woman</td>
</tr>
<tr>
<td>GNAQ mutant MUM</td>
</tr>
<tr>
<td>Elevated baseline LDH</td>
</tr>
<tr>
<td>2 prior therapies:</td>
</tr>
<tr>
<td>‒ immunoembolization</td>
</tr>
<tr>
<td>‒ chemoembolization</td>
</tr>
<tr>
<td>Significant tumor burden</td>
</tr>
<tr>
<td>‒ multiple liver and lung lesions</td>
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<tr>
<td>‒ axillary adenopathy</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient Experience</th>
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</thead>
<tbody>
<tr>
<td>Tolerating treatment well</td>
</tr>
<tr>
<td>Initial response at 4 months and confirmed response at 6 months</td>
</tr>
<tr>
<td>56.5% reduction in target lesions</td>
</tr>
<tr>
<td>6 months into therapy</td>
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</tbody>
</table>

**Patient Response**

**Baseline**

**4 Months**
Darovasertib (IDE196) Phase 1/2 Clinical Program Overview
Clinical Data Supports Potential Registrational Strategies

Metastatic Uveal Melanoma ¹, ²

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

¹ 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
² Preclinical rationale and synergy demonstrated for darovasertib combinations IDE196+MEKi Combination Preclinical Data AACR 2020; IDE196+cMET Preclinical Combination Data AACR 2021

Addressable GNAQ/11 Patients (US/EU5)

No FDA Approved Therapies for MUM or Other GNAQ-Mutation Tumors
Total Addressable Patient Population = ~9K patients/ yr

Preclinical Evaluation
Clinical Phase 1/2
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