IDEAYA Biosciences

Improving Lives Through Transformative Precision Medicines

November 2023

NASDAQ: IDYA
Safe Harbor Statement

Certain statements in this presentation and the accompanying oral commentary are forward-looking statements. These statements relate to future events or the future financial performance of IDEAYA Biosciences, Inc. (the “Company”) and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of the Company or its industry to be materially different from those expressed or implied by any forward-looking statements. In some cases, forward-looking statements can be identified by terminology such as “may,” “will,” “could,” “would,” “should,” “expect,” “plan,” “anticipate,” “intend,” “believe,” “estimate,” “predict,” “potential” or other comparable terminology. All statements other than statements of historical fact could be deemed forward-looking, including the potentially addressable patient population for the Company’s programs, any expectations regarding the Company’s target discovery platform or new target validation efforts as creating opportunities for research and development initiatives; any projections of financial information, market opportunities, cash runway or profitability; any statements about historical results that may suggest trends for the Company’s business; any statements of the plans, strategies, and objectives of management for development programs or future operations; any statements about the timing of preclinical research, clinical development, regulatory filings, manufacturing or release of data; any statements of expectation or belief regarding future events, potential markets or market size, technology developments, or receipt of cash milestones, option exercise fees or royalties; and any statements of assumptions underlying any of the items mentioned.

The Company has based these forward-looking statements on its current expectations, assumptions, estimates and projections. While the Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company’s control. Such risks and uncertainties include, among others, the uncertainties inherent in the drug development process, including IDEAYA’s programs’ early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, IDEAYA’s ability to successfully establish, protect and defend its intellectual property, and other matters that could affect the sufficiency of existing cash to fund operations. These and other important factors may cause actual results, performance or achievements to differ materially from those expressed or implied by these forward-looking statements. The Company believes these expectations, assumptions, estimates and projections are reasonable, such forward-looking statements are only predictions and involve known and unknown risks and uncertainties, many of which are beyond the Company’s control. Such risks and uncertainties include, among others, the uncertainties inherent in the drug development process, including IDEAYA’s programs’ early stage of development, the process of designing and conducting preclinical and clinical trials, the regulatory approval processes, the timing of regulatory filings, the challenges associated with manufacturing drug products, IDEAYA’s ability to successfully establish, protect and defend its intellectual property, and other matters that could affect the sufficiency of existing cash to fund operations. These and other important factors may cause actual results, performance or achievements to differ materially from those expressed or implied by these forward-looking statements. The forward-looking statements in this presentation are made only as of the date hereof. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of the Company in general, see the Company’s periodic filings with the Securities and Exchange Commission (the “SEC”), including its Annual Report on Form 10-K for the year ended December 31, 2022, and any current and periodic reports filed thereafter. Except as required by law, the Company assumes no obligation and does not intend to update these forward-looking statements or to conform these statements to actual results or to changes in the Company’s expectations.

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

Leading Precision Medicine Oncology focused biotechnology company advancing transformative First-in-Class targeted and Synthetic Lethality (SL) therapies for cancer patients

- **Broad Pipeline of Key Emerging Targets**
  - Ph 2/3 Registrational: Darovasertib (PKC) MUM
  - Ph 2: Darovasertib (Neo)Adjuvant Primary UM
  - Ph 2: Darovasertib Metastatic Cutaneous Melanoma
  - Ph 2: IDE397 (MAT2A)
  - Ph 1: IDE397 + AMG 193 (PRMT5MTA)
  - Ph 1: IDE161 (PARG)
  - Ph 1: GSK101 (IDE705) (Pol Theta Helicase)
  - Development Candidate: Werner Helicase
- **Pharma Collaborations** with Pfizer (CTCSA), Amgen (CTCSA), GSK (with ~$2B in potential milestones)
- **Balance Sheet** of ~$656M
- **NASDAQ**: IDYA

**2023 Target Milestones**
- Darovasertib (PKC) / Crizotinib – Registrational in MUM
  - Phase 2/3 Registrational Trial
- Darovasertib (PKC) – Phase 2 in Primary UM
  - Phase 2 Clinical Trial as Neoadjuvant Adjuvant Therapy in UM
- Darovasertib (PKC) / Crizotinib – Metastatic Cutaneous Melanoma
  - Phase 2 Expansion
- IDE397 (MAT2A) – Phase 1/2
  - Phase 2 Monotherapy in Priority MTAP Solid Tumors
  - Phase 1 Amgen-Sponsored IDE397 + AMG 193
- IDE161 (PARG) – Phase 1/2
  - Phase 1 Monotherapy Expansion in Priority HRD Solid Tumors
  - Clinical Program Updates – H2 2023
- GSK101 (IDE705) (Pol Theta Helicase) – Phase 1/2
  - Phase 1 GSK-Sponsored GSK101 + Niraparib – Q4 2023
- Werner Helicase
  - Development Candidate in IND Enabling Studies (Ongoing)

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(1) Includes aggregate of $511.1M cash, cash equivalents and marketable securities as of September 30, 2023, $134.7M estimated net proceeds from closing of underwritten public offering on October 27, 2023, and $10.0M receivable from GSK milestones
(2) IDEAYA Form 10-Q dated November 7, 2023 as filed with the U.S. Securities and Exchange Commission
IND = Investigational New Drug
Functional genomics combines human genetics with advances in AI and machine learning to develop effective precision medicines.

Synthetic lethality occurs when the simultaneous perturbation of two genes results in cell death.

Large-scale screening for novel synthetic lethal targets has progressed through advances in molecular biology (e.g., RNA interference, CRISPR-Cas9 editing) and bioinformatics.

Reference: Charles Boone

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.
Chief Executive Officer, Director

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Michael White, Ph.D.
Chief Scientific Officer

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Chief Legal Officer

Paul Stone, J.D.
Chief Financial Officer

Paul Barsanti, Ph.D.
Chief Technology Officer

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VP, Preclinical Sciences

IDEAYA Scientific Advisory Board

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

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

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

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

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

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
IDEAYA Precision Medicine Oncology Platform
Fully-Integrated Target, Biomarker, Drug Discovery and Translational Capabilities

Target & Biomarker Discovery and Validation
- Bioinformatics, including AI Algorithms
- Dual CRISPR, CRISPR, Chemogenomics
- Genetically Engineered Models
  - Key emerging novel targets identified, such as Werner Helicase, Pol Theta Helicase 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
  - Machine Learning and Multi-Omics platform

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 GSK101 / IDE705 (Pol Theta Helicase)

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 Precision Medicine Oncology Platform
Fully-Integrated Target, Biomarker, Drug Discovery and Translational Capabilities
IDEAYA Functional Genomics and Synthetic Lethality Platform

Novel Target and Biomarker Discovery and Validation

IDEAYA Functional Genomics Platform integrates 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.

Data-to-Knowledge Enterprise fueled by multi-omic patient and molecular data across public, partnership and proprietary data sets via IDEAYA Bioinformatics Platform.

**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

IDEAYA Proprietary Libraries and Datasets – Strategic Collaborations with Broad Institute(1) and UC San Diego(2)

IDEAYA Proprietary Libraries and Datasets – Strategic Collaborations with Broad Institute(1) and UC San Diego(2)
IDEAYA Precision Medicine Oncology 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

**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

**HARMONY™ Proprietary Machine-Learning**

Internal Machine-Learning engine empowers discovery platform through effective prioritization leading to efficient SAR cycles
# IDEAYA’s Potential First-in-Class Precision Medicine Oncology Pipeline

Building an Industry Leading and Fully-Integrated Biotechnology Company

## Precision Medicine Pipeline

<table>
<thead>
<tr>
<th>Modality/Indication</th>
<th>Biomarker</th>
<th>Pre-clinical</th>
<th>IND Enabling</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Potential Registrational</th>
<th>Program Goals / Achievements</th>
<th>Collaborations</th>
<th>Commercial (IDEAYA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darovasertib PKC +cMET1 Combination 1L HLA-A2(-) MUM</td>
<td>GNAQ/11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 2 (AA) / Phase 3 Registrational Trial * Initiated</td>
<td>WW Commercial Rights</td>
<td></td>
</tr>
<tr>
<td></td>
<td>cMET1 Combination HLA-A2(+) MUM ^</td>
<td>GNAQ/11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>HLA-A2(+) Clinical Trial ^</td>
<td>Worldwide Royalties</td>
<td></td>
</tr>
<tr>
<td>(Neo)Adjuvant UM</td>
<td>GNAQ/11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 2 Clinical Trial Initiated</td>
<td>Worldwide Royalties</td>
<td></td>
</tr>
<tr>
<td>cMET1 Combination Cutaneous Melanoma</td>
<td>GNAQ/11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 2 Expansion in Metastatic Cutaneous Melanoma</td>
<td>Worldwide Royalties</td>
<td></td>
</tr>
<tr>
<td>IDE397 MAT2A Monotherapy Solid Tumors</td>
<td>MTAP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 1 IDE397 + AMG 193 (PRMT5/MTA) Amgen-Sponsored Combination Study Initiated</td>
<td>Worldwide Royalties</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Combinations Solid Tumors</td>
<td>MTAP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 1 Dose Expansion in Ovarian, Breast, Endometrial, CRC and Other Solid Tumors</td>
<td>Worldwide Royalties</td>
<td></td>
</tr>
<tr>
<td>IDE161 PARG Breast, Ovarian Cancers</td>
<td>HRD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 1 Dose Expansion in Ovarian, Breast, Endometrial, CRC and Other Solid Tumors</td>
<td>Worldwide Royalties</td>
<td></td>
</tr>
<tr>
<td>GSK101 Pol Theta Helicase +Niraparib Combo# Solid Tumors</td>
<td>HR Mutations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase 1 GSK101 (IDE705) + Niraparib Earned $7M Milestone IND Clearance</td>
<td>GSK (4) Global Royalties</td>
<td></td>
</tr>
<tr>
<td>WRN Werner Helicase GI Cancers</td>
<td>High-MSI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Selected WRNI Development Candidate Targeting IND Submission in 2024</td>
<td>GSK (4) US 50/50 Profit Share Ex-US Royalties</td>
<td></td>
</tr>
<tr>
<td>Platform Solid Tumors</td>
<td>Defined Biomarkers</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Targeting Multiple 2024 DC Nominations, including in MTAP-deletion</td>
<td>WW Commercial Rights</td>
<td></td>
</tr>
</tbody>
</table>

### Notes:
- *Targeting enrollment of additional HLA-A2(-) patients in a separate clinical trial (e.g., ongoing IDE196-001 Phase 2 clinical trial)
- (1) Pursuant to Pfizer Clinical Trial Collaboration and Supply Agreement for Darovasertib/Crizotinib Combination, IDEAYA retains all Darovasertib Commercial Rights
- (2) Pursuant to Amgen Clinical Trial Collaboration and Supply Agreement for IDE397 + AMG 193, an investigational MTA-competitive 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; Pfizer Global Royalties; WRN: 50/50US/50% Ex-US Royalties

**MTA=methionine adenosyltransferase 2a, MTAP=methylthioadenosine phosphorylase, MTA=methylthioadenosine, PRMT5=protein arginine methyltransferase 5 (PRMT5), PARG=poly (ADP-ribose) glycohydrolase, WRN = Werner Helicase, Polθ = DNA Polymerase Theta, HRD = homologous recombination deficiency, MSI = microsatellite instability, PKC = protein kinase C, MUM = metastatic uveal melanoma, UM = uveal melanoma, Crizo = crizotinib, NSCLC = non-small cell lung cancer, WW = worldwide, HLA-A2(±)=HLA-A2*02:01 Negative, HLA-A2(++)=HLA-A2*02:01 Positive, DC = development candidate**
Darovasertib – Potential to Broadly Impact Uveal Melanoma
Potential First-in-Class and Best-in-Class in (Neo)adjuvant 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.

**Darovasertib Mono Rationale in Primary UM**

Single Agent Daro Induces Tumor Regression
Uveal Melanoma Xenograft (92.1 mutant GNAQ)


**Darovasertib + Crizo Combo Rationale for Use in Metastatic Uveal Melanoma (MUM)**

Activation of PKC and cMET Pathways with Observed cMET Overexpression in MUM Liver Metastases

IDEAYA Data, ACR 2021

IDEAYA owns or controls all commercial rights in darovasertib, including in Primary UM and MUM.
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>IDE196-001 Phase 2* Darovasertib + Crizotinib</th>
<th>Tebentasfusp First-Line Phase 3#</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any-Line n=63 (%)</td>
<td>First-Line n=20 (%)</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 65</td>
<td>35 (56)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>≥65</td>
<td>28 (44)</td>
<td>10 (50)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>32 (51)</td>
<td>9 (45)</td>
</tr>
<tr>
<td>M</td>
<td>31 (49)</td>
<td>11 (55)</td>
</tr>
<tr>
<td><strong>ECOG PS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>43 (68)</td>
<td>14 (70)</td>
</tr>
<tr>
<td>1</td>
<td>20 (32)</td>
<td>6 (30)</td>
</tr>
<tr>
<td><strong>Baseline LDH</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>25 (40)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>&gt;ULN</td>
<td>38 (60)</td>
<td>10 (50)</td>
</tr>
<tr>
<td><strong>Largest metastatic lesion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3.0 cm</td>
<td>22 (35)</td>
<td>8 (40)</td>
</tr>
<tr>
<td>3.1 to 8.0 cm</td>
<td>35 (56)</td>
<td>9 (45)</td>
</tr>
<tr>
<td>≥ 8.1 cm</td>
<td>6 (10)</td>
<td>3 (15)</td>
</tr>
<tr>
<td><strong>Location of metastases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic Only</td>
<td>19 (30)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>Extrahepatic Only</td>
<td>3 (5)</td>
<td>0</td>
</tr>
<tr>
<td>Hepatic and Extrahepatic</td>
<td>41 (65)</td>
<td>10 (50)</td>
</tr>
</tbody>
</table>

*Cross-trial comparisons are not based on head-to-head studies and are presented for informational purposes; no direct comparisons are being made

* IDEAYA Data as of August 22, 2023 (based on preliminary analysis of unlocked database by investigator review)

# N Engl J Med 2021; 385:1196-1206; ECOG data missing in Tebentafusp and Control arm of 4% and 7% respectively

^ Investigator Choice distribution in the control group: 103 (82%) received pembrolizumab, 16 (13%) received ipilimumab, and 7 (6%) received dacarbazine
Darovasertib + Crizotinib Combination Safety Summary
Overall Manageable AE Profile with Limited Grade 4/5 AEs and Discontinuations

Drug-Related AE Summary

<table>
<thead>
<tr>
<th>Safety Summary</th>
<th>n=68 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug-Related Adverse Events (AE)</td>
<td></td>
</tr>
<tr>
<td>AEs</td>
<td>67 (99%)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>21 (31%)</td>
</tr>
<tr>
<td>Grade 4/5 AEs</td>
<td>0 (0%) / 1 (2%)*</td>
</tr>
<tr>
<td>SAEs*</td>
<td>7 (10.3%)</td>
</tr>
<tr>
<td>AEs leading to Discontinuation^</td>
<td>5 (7.4%)</td>
</tr>
</tbody>
</table>

Drug-Related AEs with >20% Total Prevalence

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4/5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>50%</td>
<td>37%</td>
<td>4%</td>
<td>0%</td>
<td>91%</td>
</tr>
<tr>
<td>Nausea</td>
<td>40%</td>
<td>38%</td>
<td>2%</td>
<td>0%</td>
<td>79%</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>28%</td>
<td>27%</td>
<td>3%</td>
<td>0%</td>
<td>57%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>38%</td>
<td>13%</td>
<td>1%</td>
<td>0%</td>
<td>53%</td>
</tr>
<tr>
<td>Dermatitis acneiform</td>
<td>34%</td>
<td>10%</td>
<td>0%</td>
<td>0%</td>
<td>44%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9%</td>
<td>24%</td>
<td>4%</td>
<td>0%</td>
<td>37%</td>
</tr>
<tr>
<td>Hypotension</td>
<td>15%</td>
<td>13%</td>
<td>6%</td>
<td>0%</td>
<td>34%</td>
</tr>
<tr>
<td>Hypoalbuminaemia</td>
<td>9%</td>
<td>24%</td>
<td>0%</td>
<td>0%</td>
<td>32%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>18%</td>
<td>9%</td>
<td>2%</td>
<td>0%</td>
<td>28%</td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>16%</td>
<td>4%</td>
<td>0%</td>
<td>0%</td>
<td>21%</td>
</tr>
</tbody>
</table>

* One patient observed a Grade 5 SAE which the treating investigator assessed as most likely related to disease progression, and possibly related to the study therapies; principal investigators on the study reviewed the event and concluded this SAE was most likely due to disease progression, and Sponsor concluded it was most likely due to disease progression and not likely related to study therapies
+ The seven patients experienced SAE’s that included diarrhea, vomiting, sepsis, respiratory failure, syncopy, hypotension and toxic epidermal necrolysis
^ AEs leading to discontinuation include reference to either darovasertib or crizotinib
First-Line MUM Clinical Efficacy
Observed Compelling Confirmed Overall Response Rate and Disease Control Rate

Darovasertib + Crizotinib Phase 2
First-Line MUM (n= 20)

Confirmed 45% ORR and 90% DCR

<table>
<thead>
<tr>
<th>Response by RECIST 1.1</th>
<th>Evaluable First-Line MUM (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed ORR (9/20)</td>
<td>45%</td>
</tr>
<tr>
<td>Tumor Shrinkage (19/20)</td>
<td>95%</td>
</tr>
<tr>
<td>&gt;30% Tumor Shrinkage (12/20)</td>
<td>60%</td>
</tr>
<tr>
<td>Best Overall Response</td>
<td></td>
</tr>
<tr>
<td>cPR (9/20)</td>
<td>45%</td>
</tr>
<tr>
<td>SD (9/20)</td>
<td>45%</td>
</tr>
<tr>
<td>DCR (18/20)</td>
<td>90%</td>
</tr>
</tbody>
</table>

Clinical Efficacy supports Registrational Strategy in First-Line MUM to Enhance Patient Benefit

IDEAYA Data: preliminary analysis of unlocked database as of 08/22/2023 by investigator review; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) as of 9/22/2022, based on 20 evaluable First-Line MUM patients
ORR = Overall Response Rate; DCR = Disease Control Rate; cPR = Confirmed Partial Response; uPR = Unconfirmed Partial Response; SD = Stable Disease
Any-Line MUM and Hepatic-Only MUM Clinical Efficacy
Clinical Efficacy irrespective of HLA-A2 Status and in Hepatic & Extra-Hepatic Metastases

Darovasertib + Crizotinib Phase 2
Any-Line MUM (n=63)

- Confirmed ORR: 30%
- Tumor Shrinkage: 92%
- >30% Tumor Shrinkage: 43%
- Best Overall Response:
  - cPR: 30%
  - SD: 59%
  - DCR: 89%

Darovasertib + Crizotinib Phase 2
Hepatic-Only MUM (n=19)

- Confirmed ORR: 37%
- Tumor Shrinkage: 100%
- >30% Tumor Shrinkage: 53%
- Best Overall Response:
  - cPR: 37%
  - SD: 63%
  - DCR: 100%

IDEAYA Data: preliminary analysis of unlocked database as of 8/22/2023 by investigator review, C1D1 cutoff as of 9/22/2022, based on 63 evaluable Any-Line and 19 evaluable Hepatic-Only (includes 1L and 2L+/pre-treated) MUM patients

ORR = Overall Response Rate; DCR = Disease Control Rate; cPR = Confirmed Partial Response; uPR = Unconfirmed Partial Response; SD = Stable Disease
~70% of MUM Patients were HLA-A*02:01 Negative

All MUM Treated* vs. Daro + Crizo Combination

<table>
<thead>
<tr>
<th>HLA-A*02− negative</th>
<th>HLA-A*02− positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>All MUM Treated* (n=149†)</td>
<td>102</td>
</tr>
<tr>
<td>All MUM Treated with Daro + Crizo (n=118†)</td>
<td>81</td>
</tr>
</tbody>
</table>

†Includes all patients with known HLA status
*Includes MUM patients treated with darovasertib in the clinical trial, including monotherapy and combination arms

IDEAYA Data: preliminary analysis of unlocked database as of 08/22/2023 by investigator review; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) as of 9/22/2022
Darovasertib + Crizotinib Effective Regardless of HLA-A2 Status

HLA-A2 Negative vs. HLA-A2 Positive

**HLA-A2 Negative (n=31)**
- **First-Line:** 42% ORR; 100% DCR
- **Any-Line:** 29% ORR; 94% DCR

**HLA-A2 Positive (n=19)**
- **First-Line:** 60% ORR; 100% DCR
- **Any-Line:** 32% ORR; 84% DCR

IDEAYA Data: preliminary analysis of unlocked database as of 08/22/2023 by investigator review; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) as of 9/22/2022.
Observed 94% ctDNA Molecular Response Rate with Deep & Sustained MRs*  
Any-Line MUM Patients Treated with the Darovasertib + Crizotinib Combination

Molecular Response Regardless of BAP1 Mutation

Molecular Response Correlates with RECIST Response ^

High ctDNA Molecular Response Rate of 94% in Any-Line MUM  
Deep and Sustained MRs with approximately 80% of patients showing >80% reduction in MAF  
ctDNA MRs correlate with Clinical Efficacy (PR, SD, PD) by RECIST

IDEAYA Data: preliminary analysis of unlocked database as of 08/22/2023 by investigator review; data cutoff based on treatment Day 1 of Cycle 1 (C1D1) as of 9/22/2022

* Molecular response (MR) defined as at least 50% reduction in percentage of Mean Allele Frequency (MAF) at any timepoint
^ Best Overall Response
Median PFS in First-Line, Any-Line and Hepatic-Only MUM

Observed Compelling Median Progression Free Survival with Encouraging Trend

Any-Line MUM Swimlane Plot

Darovasertib + Crizotinib Phase 2

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

Treatment Duration – Observations
- ~50% of patients treated > 6 months
- ~30% of patients treated > 1 year

IDEAYA Data: preliminary analysis of unlocked database as of 08/22/2023 by investigator review, C1D1 cutoff as of 9/22/2022, based on 63 evaluable Any-Line MUM patients
2-Year PFS Kaplan Meier (KM) Curve: Daro + Crizo in Any-Line MUM*

Daro + Crizo Combo Observes a Promising 2-Year PFS KM Curve and a “Long Tail” Effect

2-Year PFS Kaplan Meier Curves in MUM

- **Daro + Crizo Any-Line MUM**: N=63
- **Tebentafusp 1L MUM (registrational trial)**: N=252
- **Tebentafusp Control Arm 1L MUM (registrational trial)**: N=126

**Long Tail**: >20% (13/63) of Any-Line MUM patients remain progression free at 2 years
Darovasertib + Crizotinib First-Line MUM Combo Efficacy

Examples of cPRs with Significant Tumor Shrinkage in First-Line MUM Patients

<table>
<thead>
<tr>
<th>First-Line MUM Patient</th>
<th>First-Line MUM Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 40+ year old HLA-A2 positive patient with Class 1A diagnosis metastasized after ~6 years</td>
<td>• 40+ year old HLA-A2 negative patient with Class 1A diagnosis metastasized in ~1 year</td>
</tr>
<tr>
<td>• Diffuse disease in liver and pelvis with elevated LDH of 800 U/L normalized within one month of treatment</td>
<td>• Many liver lesions with maximal target lesion reduction of 65%</td>
</tr>
<tr>
<td>• Large tumors (SLD = 210 mm) reduced by 49%</td>
<td>• Ongoing response</td>
</tr>
<tr>
<td>• On treatment for over 15 months</td>
<td>• Remains on treatment at 10 months</td>
</tr>
</tbody>
</table>

Baseline | 12 months
---|---
![Many lesions distorting and replacing the liver](image1) | ![Marked improvement across all lesions](image2)

Baseline | 8 months
---|---
![Many liver lesions & target lesion](image3) | ![Marked improvement across all lesions](image4)

IDEAYA Data as of 03/08/2023 (based on preliminary analysis of unlocked database); tumor lesion reductions by investigator review
## Darovasertib + Crizotinib Combination Clinical Summary in MUM

### Highly Differentiated Clinical Efficacy & AE Profile Observed+; ++

<table>
<thead>
<tr>
<th>Darovasertib + Crizotinib</th>
<th>Cabozantinib Mono / Crizotinib Mono</th>
<th>Selumetinib + DTIC</th>
<th>Ipi + Nivo</th>
<th>Tebentafusp</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target / Mechanism</strong></td>
<td>PKC + cMET</td>
<td>cMET</td>
<td>MEK + Chemo</td>
<td>CTLA4 + PD1</td>
</tr>
<tr>
<td><strong>Study Name(s)</strong></td>
<td>NCT03947385^ / NCT05063058 ^^^^ / NCT01974752^^^ / NCT02626962## IMCgp100-102^</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>1L/2L/3L+ MUM (n=63)</td>
<td>1L+ MUM (n=31) / 1L (n=6) 2L (n=1) MUM</td>
<td>1L+ MUM (n=97)</td>
<td>1L MUM (n=52)</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>NA / MET Overexpression</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Drug Form</strong></td>
<td>Oral Tablets</td>
<td>Oral Capsules</td>
<td>Oral Capsules + chemo</td>
<td>IV infusion</td>
</tr>
<tr>
<td><strong>Tolerability (Grade ≥3 Drug-Related AE)</strong></td>
<td>31%</td>
<td>51.6% / NA</td>
<td>63% (All Cause)</td>
<td>58%</td>
</tr>
<tr>
<td><strong>% of Patients with Tumor Shrinkage</strong></td>
<td>First-Line = 95% / Any-Line = 92% / Hepatic Only = 100%*</td>
<td>23% ^^ / NA</td>
<td>35% ^^</td>
<td>27% ^^</td>
</tr>
<tr>
<td><strong>Confirmed ORR% (by RECIST 1.1)</strong></td>
<td>First-Line = 45% / Any-Line = 30% / Hepatic Only = 37%*</td>
<td>0% / 0%</td>
<td>3%</td>
<td>11.5% (not confirmed ORR)</td>
</tr>
<tr>
<td><strong>Median PFS</strong></td>
<td>First-Line: 7.8 months / Any-Line: 6.0 months / Hepatic-Only: 11.0 months*</td>
<td>2 months / NA</td>
<td>2.8 months</td>
<td>3 months</td>
</tr>
</tbody>
</table>

+ 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: IPI + Nivo Combo in HLA-A2-0201 MUM reports ~6% ORR (2 PRs out of 33 patients)
* IDEAYA Data: preliminary analysis of unlocked database as of 08/22/2023 by investigator review, and C1D1 cutoff as of 9/22/2022
** Based on Immunocore reported 2L+ study data (to reflect comparative patient population) and by independent review and ORR% was with confirmed PRs; ** ASCO 2021, J. Piulats, et. Al, Ipi = ipilimumab, nivo = nivolumab, ORR% did not require PR/CR confirmation
^ 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
^^ Estimated from Waterfall plot
^^^ Journal of Clinical Oncology, Carjaval, et. al, 2018; 1232-1239; ^^^^ European Journal of Cancer, Leyraz, et. al, 2022; 146-155
Accelerated Approval Trial Design in First-Line HLA-A2 Negative MUM

FDA Guided Design: Open Label Ph2/3 Evaluation of Daro + Crizo vs. Investigator's Choice

FDA Project FrontRunner: Target First-Line approval strategy to enhance patient benefit in MUM

FDA Accelerated Approval: Address unmet need in MUM, which has limited effective treatment options

Integrated Phase 2/3 Study within Study Enables Potential Accelerated Approval & Full Approval

Targeting FPI
Q3 2023

Median PFS
Daro + Crizo
Investigator’s Choice
2:1 Randomization
~230 Ph 2/3 Patients
Accelerated Approval
2:1 Randomization
~120 Ph 3 Patients

Median OS

2:1 Randomization
Daro + Crizo vs Investigator’s Choice
(IC = Ipi + Nivo, PD1, or DTIC)

Primary Endpoints (BICR)
Accelerated Approval: mPFS
Full Approval: mOS

FDA Fast Track Designation for Daro + Crizo in MUM

Δ Nested study to confirm move forward dose: (i) Daro 300 mg BID + Crizo 200 mg BID or (ii) Daro 200 mg BID + Crizo 200 mg BID

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

Daro = Darovasertib, Crizo = Crizotinib, MUM=Metastatic Uveal Melanoma, HLA-A2 = HLA-A2*02:01 Serotype, IC = Investigator’s Choice, Ipi = ipilimumab, nivo = nivolumab; DTIC = dacarbazine

^ Clinicaltrials.gov: NCT05987332
Darovasertib Monotherapy in (Neo)adjuvant Primary Uveal Melanoma

3 of 6 evaluable (50%) UM Patients Observed Eye Preservation in Enucleation Cohort

IDEAYA Phase 2 and IST ongoing to evaluate Darovasertib

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 / Adjuvant Systemic Therapy goals:
- Avoid Enucleation → Save the Eye
- Reduce Tumors and Radiation Dose → Protect Vision
- Reduce Occurrence of Metastasis → Save Lives

Paradigm Shifting Opportunity to Broadly Impact UM, with annual incidence of ~8,000 – 10,000 patients in US, EU

Evaluable UM Patients Treated to Maximal Benefit

<table>
<thead>
<tr>
<th>Mths of Daro Rx</th>
<th>1</th>
<th>5</th>
<th>6</th>
<th>3</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>(%) Change from Baseline</td>
<td>5%</td>
<td>11%</td>
<td>14%</td>
<td>24%</td>
<td>33%</td>
<td>57%</td>
</tr>
</tbody>
</table>

- Data by investigator assessment with enrollment cut-off of July 17, 2023, from NADOM IST courtesy of Professor Anthony Joshua, MBBS, PhD, FRACP, St. Vincent’s Hospital
- Maximal % reduction in measured apical height or longest basal diameter
- Patient had sub-retinal blood present at baseline and with lack of shrinkage and visual deterioration discontinued after 6 weeks. One additional patient had Grade 3 drug related dermatitis and discontinued treatment before 1st scan.
- Patient is now plaque-eligible and is ongoing with darovasertib neo-adjuvant treatment till maximal benefit

2 out of 4 additional patients after the enrollment cutoff date are likely plaque eligible (20% tumor reduction in 2 months, 22% tumor reduction in 1 month) and continuing on darovasertib until maximal benefit
Case Studies of Saved Eyes: Neoadjuvant Treatment of UM Patients

**Initial Cases of Systemic Neoadjuvant Therapy resulting in Prevention of Enucleation**

**Case 1: Eye Saved by Neoadjuvant Treatment +^**

UM patient was blind in one eye, developed a large ocular tumor in other eye causing vision loss, and diagnosed with UM Large Ocular Lesion – 16.5 mm Apical Height x 18 mm LBD

Tumor Shrinkage observed at each month of treatment with Darovasertib + Crizotinib (~30% at 1 mo and ~80% at 4 mo)

Avoided Enucleation and prevented complete blindness

Restored > Normal Vision with neoadjuvant treatment and intraocular lens replacement for treatment of cataracts

Residual Tumor treated with Plaque Brachytherapy

Patient remains on Daro + Crizo Combination Therapy

**Baseline Scan: 16.5mm Apical Height**

**4 Month Scan: 3.5 mm Apical Height**

**Case 2: Eye Saved by Neoadjuvant Treatment +**

UM patient with large tumor enrolled in NADOM IST study

Reduction in Tumor Size of ~24% observed following 4 mo neoadjuvant treatment with darovasertib

Tumor Proximity to Optic Disc and Macula – observed increased separation from tumor following treatment for 3 mo

Avoided Enucleation and Preserved Vision

Residual Tumor treated with Plaque Brachytherapy

Patient remains on Darovasertib as Adjuvant Therapy

**Baseline Scan**

**3 Month Scan**
(Neo)Adjuvant Darovasertib in Primary Uveal Melanoma (UM)
Paradigm Shifting Opportunity to Save the Eye, Protect Vision and Save Lives

Phase 2 Study of Darovasertib Monotherapy as Neoadjuvant Therapy followed by Adjuvant Therapy ^

Targeting FPI
Q3 2023

Neoadjuvant

Primary
Local
Therapy

Enucleation Cohort (n~40)
Adjuvant Therapy + Follow-Up

Treatment to Maximum Benefit up to 6 Months

Neoadjuvant
Proof of Concept

Brachytherapy Cohort (n~40)
Adjuvant Therapy + Follow-Up

Treatment up to 6 Months

Adjuvant
Proof of Concept

Primary Endpoints
• Safety
• Cohort 1: Eye Preservation
• Cohort 2: Decrease in Radiation Dose

Secondary Endpoints
• Useful Vision (1 yr)
• Relapse Free Survival (RFS)
  • Local (1 yr)
  • Distal (3 yr)

Three Independent Approaches for demonstrating Clinical Benefit and defining potential Approval Pathways

Enucleation Cohort → Save the Eye
Brachytherapy Cohort → Protect Vision
Adjuvant Therapy → Save Lives

^ Clinicaltrials.gov: NCT05907954
GNAQ/11 Cutaneous Melanoma Patients Treated With Darovasertib

2 of 4 (50%) Observed Durable Partial Responses by RECIST 1.1 with Daro Combination
GNAQ Cutaneous Melanoma Patient on Daro + Crizo Combo ~600 Days

Patient had a PR by RECIST 1.1 at Cycle 5 and Remains in Response at Cycle 22 with ~60% Reduction

30+ year old HLA-A*02:01 negative woman with GNAQ cutaneous melanoma progressed on prior pembro and ipi / nivo therapies.

Significant burden of metastatic disease: lung, liver, SQ, breast, intramuscular, intraperitoneal.

Continuing treatment with Darovasertib + Crizo with ongoing response at 22 months with ~60% tumor shrinkage and tolerating treatment well.

cDNA %MAF reduced to 0% at 1st scan and remains undetectable at Cycle 8 (cycles are 4 weeks)
# Darovasertib Clinical & Commercial Strategy

**High Unmet Need and Multiple First-Line Opportunities**

+95% of UM and ~5% of Cutaneous Melanoma (CM) patients harbor GNAQ/GNA11 or upstream activating mutation of PKC-signaling, enabling Broad Applicability of Darovasertib

## Uveal Melanoma Patient Journey

<table>
<thead>
<tr>
<th>HLA-A2-Negative (<strong>~70% of UM / MUM</strong>)</th>
<th>Neoadjuvant UM</th>
<th>Adjuvant UM</th>
<th>MUM</th>
<th>Metastatic CM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Daro Phase 2 Enucleation Define Accelerated Approval Path</td>
<td>Daro Phase 2 Radiation Define Accelerated Approval Path</td>
<td>Daro + Crizo Registralional Trial Accelerated Approval</td>
<td>Daro + Crizo Phase 2 Define Accelerated Approval Path</td>
</tr>
<tr>
<td>HLA-A2-Positive (<strong>~30% of UM / MUM</strong>)</td>
<td>&gt;6 months</td>
<td>&gt;6 months</td>
<td>mPFS + ~3 months</td>
<td>mPFS + ~3 months</td>
</tr>
</tbody>
</table>

**Target Clinical Endpoints**
- Eye & Vision Preservation
- Relapse Free Survival
- ORR, mPFS, mOS
- ORR, mPFS, mOS

**Annual Incidence US/EU**
- ~8-10k
- ~8-10k
- ~4-5k
- >5K [1]

**Total Prevalence US/EU**
- ~100k
- ~100k
- ~14k
- ~180K [2]

*No FDA approved systemic therapies in multiple UM and MUM indications across the patient journey

**IDEAYA data: HLA-A2-positive and HLA-A2-negative prevalence in MUM based on IDEAYA clinical trial data; US/EU MUM annual incidence and total prevalence based on market research analysis

+ Orphan Drugs benefit from certain tax credits and may be excluded from certain mandatory price negotiation provisions of the 2022 Inflation Reduction Act

[1] GNAQ/11 cutaneous melanoma estimated annual incidence is approximately 5,000 patients in the US and 8,000 patients in the EU28. Based on several metastatic cancer patient databases, including Memorial Sloan Kettering Cancer Center (MSKCC) Impact, we project GNAQ/11 metastatic cutaneous melanoma has the potential to double or more the annual addressable metastatic patient population of metastatic uveal melanoma alone

[2] The estimated total prevalence of primary GNAQ/11 cutaneous melanoma is approximately 70,000 patients in the US and 110,000 patients in the EU28

**FDA Orphan Drug Designation in Uveal Melanoma**

*No FDA approved therapies*
MAT2A Inhibition is Synthetic Lethal with MTAP Deletion

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

**MTAP-MAT2A Synthetic Lethality Biology**

- **MTAP** deletion leads to MTA accumulation
- MTA accumulation partially inhibits PRMT5
- MAT2A is key enzyme that produces SAM in cells
- Inhibition of MAT2A results in reduction of SAM, starving PRMT5 of its substrate
- Loss of methylation function of PRMT5 results in defects in RNA splicing, gene expression and genome integrity

**Endogenous Suppression in MTAP⁻/⁻ PDX Models**

IDEAYA Data: AACR 2023 (M. Fischer et al.) – Volcano plot comparing nuclear SDMA H-Score by IHC in MTAP⁻/⁻ relative to MTAP wt across tissue microarray (TMA) of treatment-naïve PDX models; LUSC shows most significance effect across tumor histologies
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

IDE397 In Vivo Efficacy in LUSC PDX Models

Observed Tumor Regressions in 50% of LUSC PDX Models

IDEAYA Data; *2 of 8 LUSC unevaluable due to insufficient residual tumor burden
IDE397 Clinical Efficacy Observed in MTAP-Deletion NSCLC and Bladder Cancer

~83% ctDNA Molecular Response Rate in Monotherapy Priority Tumor Types

Monotherapy IDE397 has a high ctDNA Molecular Response Rate in Priority Tumor Types of NSCLC and Bladder Cancer

MTAP-Deletion Prevalence*
- Squamous NSCLC: 19%
- Adeno NSCLC: 11%
- Bladder: 26%

IDE397 clinical program priority to generate contribution-of-components data for multi-pronged combination strategy

* MTAP-deletion report, Guggenheim, 2023
60+ year old male with high grade urothelial carcinoma of the renal pelvis
Onc Hx: Neo-adjuvant Gem/Cis, Left Nephro-ureterectomy, Adjuvant Nivolumab
Recurrent disease after definitive treatment that included immunotherapy, started IDE397 monotherapy
Unconfirmed partial response (uPR) per RECIST, v1.1 at week 6 with 40% reduction, confirmed Partial Response at week 12 with 47% reduction and converted to Complete Response (CR) at week 18 with decrease of lymph node to < 10 mm

IDE397 Clinical Efficacy Observed in MTAP-Deletion Bladder Cancer
Confirmed PR Converted to a Complete Response by RECIST 1.1 in Target Lesion at Week 18

Bladder Cancer MTAP-Deletion Patient: Complete Response at 18-week CT Scan

Baseline

Week 18

Enlarged Retrocaval Lymph Node, 1.5 cm short axis

Complete Response (CR) at 3rd scan, shrinkage of retrocaval lymph node to < 10mm in short axis

IDEAYA Data (based on preliminary analysis of investigator provided images); tumor lesion reductions by investigator review
IDE397 Clinical Efficacy Observed in MTAP-Deletion Squamous NSCLC

33% Tumor Shrinkage by CT-Scan in Target Lesion at Week 12

75+ year old male with squamous NSCLC- mediastinal nodal mass causing dyspnea and hoarseness

Onc Hx: Received combination chemoradiotherapy followed by durvalumab (IO) maintenance

Recurrent disease treated with combination chemotherapy again with progression within 4 months, started IDE397 monotherapy

Baseline PET/CT: hypermetabolic mediastinal nodal mass

1st scan at 8 weeks: 9% reduction in target lesion by CT Scan*

2nd scan at 12 weeks: 33% reduction in target lesion by CT Scan*

IDEAYA Data (based on preliminary analysis of investigator provided PET/CT images); tumor lesion reductions by central review

*Patient was unable to receive "contrast" as part of CT-scan measurement due to drug-unrelated health reasons
IDE397 Clinical Efficacy Observed in MTAP-Deletion Squamous NSCLC
33% Tumor Shrinkage by CT-Scan Accompanied by Shrinking Area of FDG Uptake by PET Scan

Smaller Portion of Nodal Tumor Mass is Hypermetabolic on Sequential PET Scans
MAT2Ai Combination Strategy

Clinical Combination focus on IDE397 + PRMT5MTA based on Compelling Preclinical Efficacy

IDE397 + MTA-Cooperative PRMT5 Inhibitor enables Maximal Pathway Suppression*

Enhanced Combination Efficacy Observed in multiple Tumor Indications and Across Representative PRMT5MTA Inhibitors *

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

Deep and Durable Anti-Tumor and PD Response with Combination+

PRMT5MTA-1
NSCLC MTAP (-/-) CDX

Vehicle
IDE397 3 mg/kg
PRMT5MTA-1 25 mg/kg
IDE397 3 mg/kg + PRMT5MTA-1 25 mg/kg
IDE397 30 mg/kg
PRMT5MTA-1 100 mg/kg
IDE397 3 mg/kg + PRMT5MTA-1 100 mg/kg

PRMT5MTA-2
NSCLC MTAP (-/-) CDX

Vehicle
IDE397 3 mg/kg
PRMT5MTA-2 30 mg/kg
IDE397 3 mg/kg + PRMT5MTA-2 30 mg/kg

PRMT5MTA-1
Pancreatic MTAP (-/-) CDX

Vehicle
IDE397 3 mg/kg
PRMT5MTA-1 125 mg/kg
IDE397 3 mg/kg + PRMT5MTA-1 125 mg/kg

MTAP-deleted Tumor SDMA IHC Scores

SDMA IHC nuclear staining intensity distribution, pathologist scored, as percent of total tumor cells evaluated per sample; tumor samples from HCT116 MTAP (-/-) CDX models collected 2 hrs post-dose on Treatment Day 2

100%
75%
50%
25%
20%
10%
0

Vehicle
IDE397 3 mg/kg
PRMT5MTA
IDE397 + PRMT5MTA
Combination Effect of MAT2A Inhibitor and PRMT5^{MTA} Inhibitor
Combined Inhibition Deepens Biological Response through Maximal Pathway Suppression

**Gene Expression Analysis**
Combination Deepens Observed Monotherapy Activity

**Alternative Splicing Analysis**
Combination Increases Alternative Splicing Events

**Retained Intron Analysis**
Combination shows Selective Response by Retained Introns Analysis^
**MAT2Ai Combination Strategy**

**IDE397 (MAT2A) + AMG 193 (PRMT5MTA) Preclinical Efficacy**

**IDE397 (MAT2Ai) + AMG 193 (PRMT5MTAi)**

Observed Complete Responses (CR) @ Study Day ~40+ durable through Study Day ~100

Doses were below maximally efficacious preclinical dose for each of IDE397 and AMG 193, with IDE397 dosed at 3 mg/kg QD (1/10th of typical preclinical dose) ➔ Therapeutic Window

Well tolerated in vivo with No Observed Body Weight Loss

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

---

*Pursuant to Amgen Clinical Trial Collaboration and Supply Agreement for clinical evaluation of IDE397 and AMG 193, an Amgen 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 Focus on Select Monotherapy and High Conviction Combinations

IDE397 Development Candidate – Clinical Profile
- Exposure-Dependent Pharmacokinetic (PK) Profile with low $C_{\text{max}}:C_{\text{min}}$
- Robust Pharmacodynamic (PD) Response observed

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

Mono Expansion in Select MTAP-null Tumor Histologies

IDE397 RDE Mono Expansion Basket: NSCLC, Bladder

Focus or Additional Indication Expansion

Combination Cohorts – Clinical Proof of Concept in MTAP-null Tumors

AMGEN
IDE397 + AMG 193 MTA-Cooperative PRMT5 inhibitor[^1]: Solid Tumors

IDE397 + AMG 193: enrollment is ongoing

Other Potential Indications or Combinations

Addressable Patient Population of ~50,000 estimated in US, EUS and JP across priority tumors – NSCLC, bladder, gastric, and esophageal cancers

[^1]: Amgen reported initial clinical data at the 2023 AACR-NCI-EORTC that showed 5/18 (ORR=28%) for AMG 193 monotherapy expansion at dose > 800 mg QD in esophageal, pancreatic, renal cell, gallbladder, and Sertoli-Leydig cell cancers

Clinicaltrials.gov: NCT05975073


# AMG193 = Amgen’s investigational MTA-cooperative PRMT5 inhibitor

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

Focus or Additional Indication Expansion

Combination Cohorts – Clinical Proof of Concept in MTAP-null Tumors

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IDE397 + AMG 193 MTA-Cooperative PRMT5 inhibitor[^1]: Solid Tumors

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Clinicaltrials.gov: NCT05975073


# AMG193 = Amgen’s investigational MTA-cooperative PRMT5 inhibitor

Amgen reported initial clinical data at the 2023 AACR-NCI-EORTC that showed 5/18 (ORR=28%) for AMG 193 monotherapy expansion at dose > 800 mg QD in esophageal, pancreatic, renal cell, gallbladder, and Sertoli-Leydig cell cancers

Clinicaltrials.gov: NCT05975073
IDEAYA’s Potential First-in-Class Synthetic Lethality DDR Pipeline
Synthetic Lethality with Tumor-Promoting defects in DNA Repair Mechanisms

**IDE161**
- **PARG Inhibitor**
- Clinical Candidate

**GSK101**
- Pol Theta Helicase Inhibitor
- Clinical Candidate

**Werner**
- Helicase Inhibitor
- Development Candidate

- **Phase 1 First-in-Human**
  - Monotherapy in HRD Breast, Ovarian
  - Potential to develop beyond HRD

- **Phase 1 First-in-Human Q4 2023**
  - Niraparib Combination in Tumors with HR Mutations and HRD

- **Targeting IND Submission in 2024**
  - MSI-High Tumor Agnostic

*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

1. DNA Damage (SS break)
2. PARP Binding
3. PAR Chain Synthesis (poly-ADP ribose)
4. DNA Damage Repair Proteins (Recruited by PAR Chain Template)
5. PAR Chain Hydrolysis (mediated by PARG)

IDE161 (PARGi)

PARP and PARG inhibitors have distinct MOA and efficacy profiles

PARG Inhibition is Mechanistically Distinct from PARPi

Replication Stress
Mechanisms of Tolerance
Fork remodelling vs Re-priming and TLS
PARPi trapping

PARGi
Fork Reversal and Slowing
Unrestrained Fork Progression

Cell Death (Nucleolytic Degradation)
Cell Death (ssDNA gaps + DSBs)

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-induced Cellular PAR Accumulation

IDE161 is Synthetic Lethal with BER Gene Disruption

IDE161-induced DNA Damage Response

IDE161 is Synthetic Lethal with BER Gene Disruption

IDE161 Sensitivity Profile in Cell Panel

Cellular response profiles reveal mechanistic associations with PARGi sensitivity

IDC161 Cellular IC\textsubscript{50} (log\textsubscript{10} \mu M)

314 cell lines across 31 lineages

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 is Active and Well-Tolerated in HRD ER+ Her2- Breast Cancer Models

Observed PARG inhibitor Activity is Distinct from PARP Inhibition

IDE161 Selective Sensitivity vs PARPi

HRD cell lines are selectively sensitive to IDE161 versus PARPi

Regression in BRCA-altered Breast Cancer PDX Models

ER+ / Her2- Breast Cancer PDX1

ER+ / Her2- Breast Cancer PDX2

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HRD cell lines are selectively sensitive to IDE161 versus PARPi

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IDE161 PARGi Responsive Models

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Regression in BRCA-altered Breast Cancer PDX Models

ER+ / Her2- Breast Cancer PDX1

ER+ / Her2- Breast Cancer PDX2

IDE161 PARGi Responsive Models
IDE161 Observed Multiple Partial Responses by RECIST 1.1 in Priority Solid Tumor Types Early in the Phase 1 Escalation and at the Expansion Dose

BRCA1/BRCA2 Endometrial Cancer: Confirmed Partial Response by RECIST 1.1 at Second Scan

Baseline Scan: Target & Non-Target Lesions

Target Lesion: Cervical Lymph Node

Non-Target Mediastinal Lesions*

Prior Therapy
- CarboTaxol + Bev
- Taxol Maintenance
- Atezolizumab

Post Baseline Cervical Node Reduced by 31% Inv Response

Target Lesion: Partial Response by RECIST 1.1 at First Scan (31% tumor shrinkage)

Non-Target Lesions: Complete response

CA-125 Tumor Marker:
- BL: 2,762 U/ml
- C2D1: 2,638 U/ml
- C3D1: 518 U/ml
- C4D1: 360 U/ml (~87% reduction)

*Soft Tissue window view
IDE161 Clinical Development Strategy
First-in-Class Opportunity for Patients with Breast, Ovarian & Other Solid Tumors with HRD

IDE161 Phase 1/2 – Mono Clinical Development Plan and Combination Options

IDE161 Monotherapy Dose Escalation and Expansion in HRD Tumors [1]
- Dose Escalation
- Expansion Cohort: ER+, Her2-, HRD Breast Cancer
- Expansion Cohort: HD Ovarian Cancer
- Expansion Cohort: HRD Tumors (Basket)
- Expansion Opportunities beyond HRD Tumors

IDE161 Combinations – Preclinical Safety Profile Supports Multiple Opportunities
- Dose Escalation
- IDE161+ Rationale Combination Assets

Activity in PARPi- and Platinum-Resistant Settings
Differentiated Sensitivity relative to PARPi’s
Improved Safety Profile relative to PARPi’s

FDA Fast Track Designation for IDE161 in BRCA1/2 Ovarian and Breast Cancers*

* Fast Track Designations include (i) Pretreated, Platinum-Resistant Advanced or Metastatic BRCA1/2 mutant Ovarian Cancer, and (ii) Pretreated, Advanced or Metastatic HR+, Her2-, BRCA1/2 mutant Breast Cancer
PARG = poly (ADP-ribose) glycohyrdolase; PAR = poly (ADP-ribose; PBMC = peripheral blood mononuclear cells

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GSK101 (IDE705): Potential First-in-Class Pol Theta Helicase Inhibitor
Phase 1: Targeting First-in-Human in Q4 2023 in Combination with Niraparib (PARPi)

**Pol Theta Helicase In Vivo Activity**

GSK101 + PARPi

- Vehicle
- POLθ inhibitor
- Niraparib
- POLθ inhibitor + Niraparib

Observed Deep and Durable Responses in Multiple Xenograft Models

**BRCA 1/2 Clinical Reversions**

BRCA Reversions Mediated by MMEJ

- 71% Deletion
- 88% Microhomology deletion

**Clinical Development Strategy**

Pol Theta Helicase Inhibitors Disrupt MMEJ Alternative DNA Damage Repair:
- Inhibit DSB Repair by MMEJ
- Dysregulate Replication Fork Stabilization

**Potential Clinical Opportunities**

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

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

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

IDEAYA / GSK Data
Werner Helicase is Synthetic Lethal with Microsatellite Instability
Development Candidate in IND Enabling Studies

Werner Helicase Inhibitors Phenocopy Genetic SL in MSI-High Cancers
Nanomolar Potency, Biochemical and Cellular Activity, and Selectivity over other RecQ Helicases

Werner Helicase Synthetic Lethality in MSI-High Cancer Cells
WRN resolves TA Repeat 2° Structures to prevent Catastrophic DNA Fragmentation in MMR-deficient Cells

Werner Helicase Synthetic Lethal with High-MSI

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

IDEAYA / GSK Data: AACR 2023
Building a Fully-Integrated Biotech in Precision Medicine Oncology

Foundational First-in-Class Pipeline Enables a Leading Precision Medicine Oncology Franchise

Darovasertib Registration-Enabling Trial with Potential Accelerated Approval in HLA-A2(-) MUM is tractable for commercial execution and provides path to potential product revenue to reinvest in broad first-in-class pipeline

Emerging Pipeline of Potential First-in-Class Precision Medicine Oncology Programs with large addressable solid tumor patient populations, including Daro (Ph 2 Neoadjuvant / Adjuvant UM), Daro + Crizo (Ph 2 Metastatic Cutaneous Melanoma), IDE397 (Ph 2), IDE161 (Ph 1), GSK101 (Ph 1) and Werner Helicase (Targeting IND Submission in 2024)

Strong Balance Sheet with ~$656M1, 2 and opportunity for milestones

Validating Pharma Partnerships and Collaborations include clinical collaborations for combination therapies with Pfizer and Amgen and strategic collaboration with GSK with ~$1 billion milestones / program

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**CLINICAL PROGRAMS**
- Ph 2/3 – Darovasertib
- Ph 2 – IDE397 (MAT2A)
- Ph 1 – IDE161 (PARG)
- Ph 1 – GSK101 (Pol Theta Helicase)

**DEVELOPMENT CANDIDATES**
- Werner DC – Target IND (2024)

**PRECLINICAL**
- Targeting Multiple DC Nominations in 2024, including in MTAP deletion

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(1) Includes aggregate of $511.1M cash, cash equivalents and marketable securities as of September 30, 2023, $134.7M estimated net proceeds from closing of underwritten public offering on October 27, 2023, and $10.0 receivable from GSK milestones
(2) IDEAYA Form 10-Q dated November 7, 2023 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) GSK101 Pol Theta Program Cost Share = 100% GSK with ~$1B Milestones and WW Royalties; Werner Helicase Program Cost Share = 80% GSK / 20% IDEAYA with ~$1B Milestones, 50/50 US Profit Share and Ex-US Royalties