Darovasertib Investor Day
December 7, 2021
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.

Welcome and Introduction

Yujiro Hata – President and Chief Executive Officer
IDEAYA Biosciences

Welcome to our Participants and Guest Speaker

Darovasertib Investor Day – December 7, 2021

Meredith McKean, M.D.
Sarah Cannon Research Institute at
Tennessee Oncology, Associate Director,
Melanoma and Skin Cancer Research

IDEAYA's Precision Medicine Oncology Pipeline

Building the Industry Leading Synthetic Lethality Focused Biotechnology Company

Precision Medicine Pipeline

	Modality/Indication	Biomarker	Preclinical	IND Enabling	Phase 1	Phase 2	Program Goals	Collaborations	Commercial (IDEAYA)
IDE397 *MAT2A*	Monotherapy Solid Tumors	MTAP					Cohort Expansion H1 2022 Option Package & Clin Data Update H1 2022	gsk (1)	US 50/50 Profit Share Ex-US Royalties
	Combinations Solid Tumors	MTAP					Preclinical Data to enable Combos (Taxanes, PRMTi, Others)		
PARG	Ovarian, Gastric, Breast Cancers	HRD					Development Candidate Lead Selected	CANCER RESEARCH UK (2)	WW Commercial Rights
Pol Theta	Small Molecule Protein Degraders	HRD					Select Small Molecule Helicase Inhibitor Development Candidate December 2021	gsk (1)	Global Royalties
WRN	GI Cancers	High-MSI					Chemistry Lead Optimization	gsk (1)	US 50/50 Profit Share Ex-US Royalties
MTAP-SL	Solid Tumors	MTAP					Lead Series		WW Commercial Rights
SL Platform	Solid Tumors	Defined Biomarker					Lead Series New Target / Biomarker Validation		WW Commercial Rights
Darovasertib *PKC*	Monotherapy MUM, UM Adjuvant	GNAQ/11					Expand to UM Adjuvant - IST H1 2022		WW Commercial Rights
	+MEK, +cMET Combos MUM	GNAQ/11					Clinical Data – IDE196 + Crizotinib Q4 2021 Regulatory Guidance H1 2022	Pfizer (3)	
	GNAQ/11 Basket Skin, Mucosal	GNAQ/11					Enhance enrollment of GNAQ/11 Basket		

(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

= Target Program Milestone

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, SWS = Sturge Weber Syndrome, PWS = Port Wine Stain, WW = worldwide

Agenda

Welcome and Introduction

Yujiro Hata, President and Chief Executive Officer

Metastatic Uveal Melanoma (MUM): Clinical Landscape & Efficacy Benchmarks

Matt Maurer, M.D., VP, Clinical Oncology and Medical Affairs

Darovasertib (PKC) / Crizotinib (cMET) Synthetic Lethal: Mechanistic Rationale, Preclinical & Translational Data

Mike White, Ph.D., SVP, Chief Scientific Officer

Darovasertib (PKC) / Crizotinib (cMET) Phase 1/2 Combination: Clinical Efficacy and Adverse Event Profile

Meredith McKean, M.D., Sara Cannon Research Institute

Darovasertib Potential Registrational Strategies and Evaluation of Expansion Opportunities

Matt Maurer, M.D., VP, Clinical Oncology and Medical Affairs

Darovasertib Population Analysis: GNAQ/11 Melanomas & Additional MET-Amplified / High Expression Tumors

Paul Stone, SVP, Chief Financial Officer

Closing and Analyst Q&A

Yujiro Hata, President and Chief Executive Officer

Metastatic Uveal Melanoma (MUM): Clinical Landscape & Efficacy Benchmarks

Matt Maurer, M.D., Vice President, Clinical Oncology and Medical Affairs
IDEAYA Biosciences

Clinical Landscape

Early Development Phase 1/2

- Targeted: FAKi + MEKi; FHD-286 (BRM / BRG1)
- IO: Nivo + Rela (Lag3); Alrizomadlin (MDM2-P53) + Pembro; LNS8801 (GPER agonist) +/- Pembro

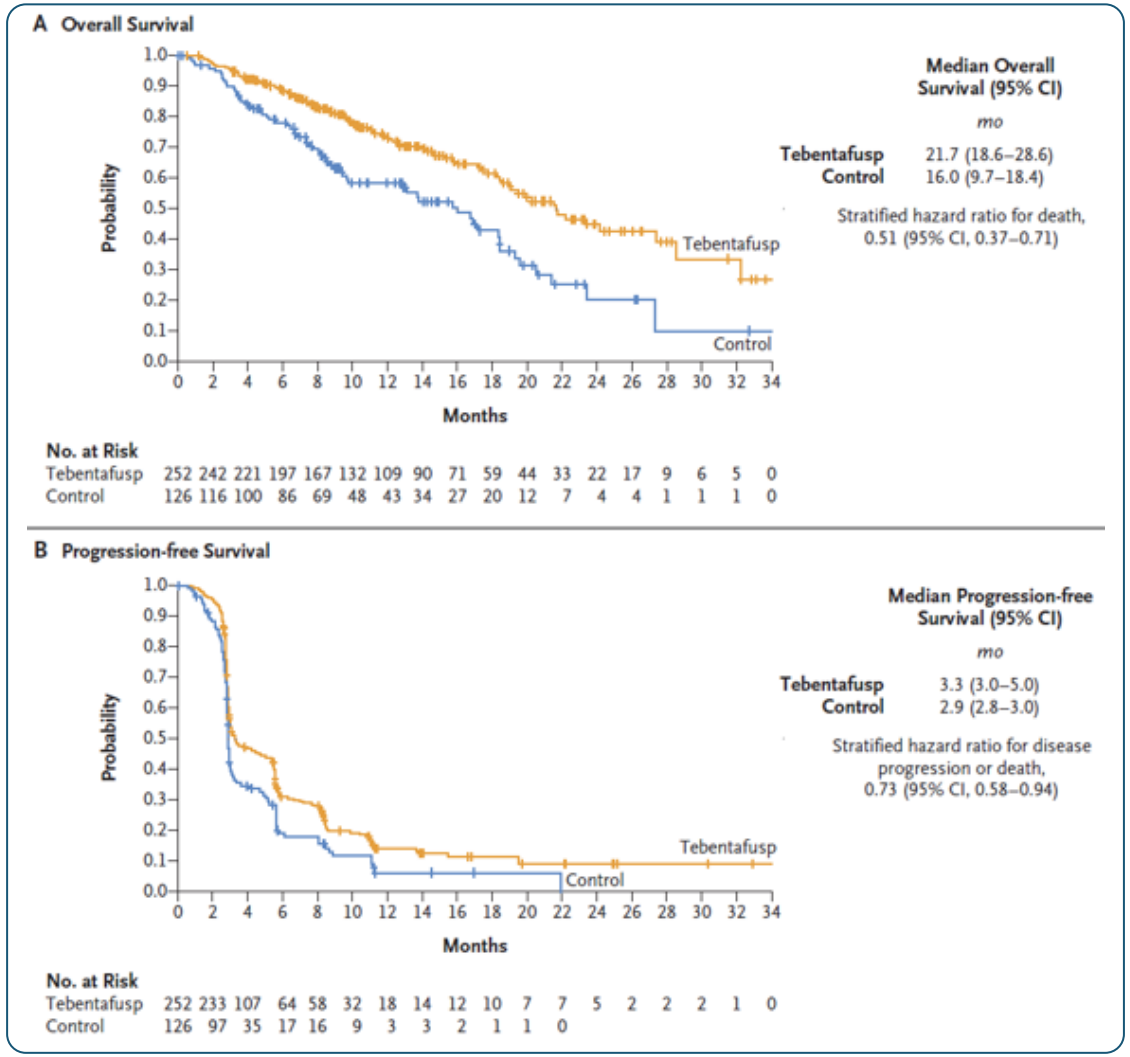
BLA – Pending FDA Review

- Tebentafusp (IMCgp100) 1st Line; LDH > ULN 36%
  - Bispecific antibody: HLA-A2-0201

	IMCgp100 1st Line Ph III	IMCgp100 2nd line Ph II	Inv Choice (82% Pembro) 1st Line Ph III
Disease Control Rate (DCR)	46% (~39% with reduction in target lesions*)	23% (≥ 24weeks)	27%
ORR	4.7%		5%
DOR (months)	9.9	8.7	9.7
mPFS (months)	3.3	2.8	2.9

Sources: Immunocore Corporate Presentation, November 2021; CT.gov: NCT02570308 results
* N Engl J Med 2021;385:1196-206, Derived from waterfall plot

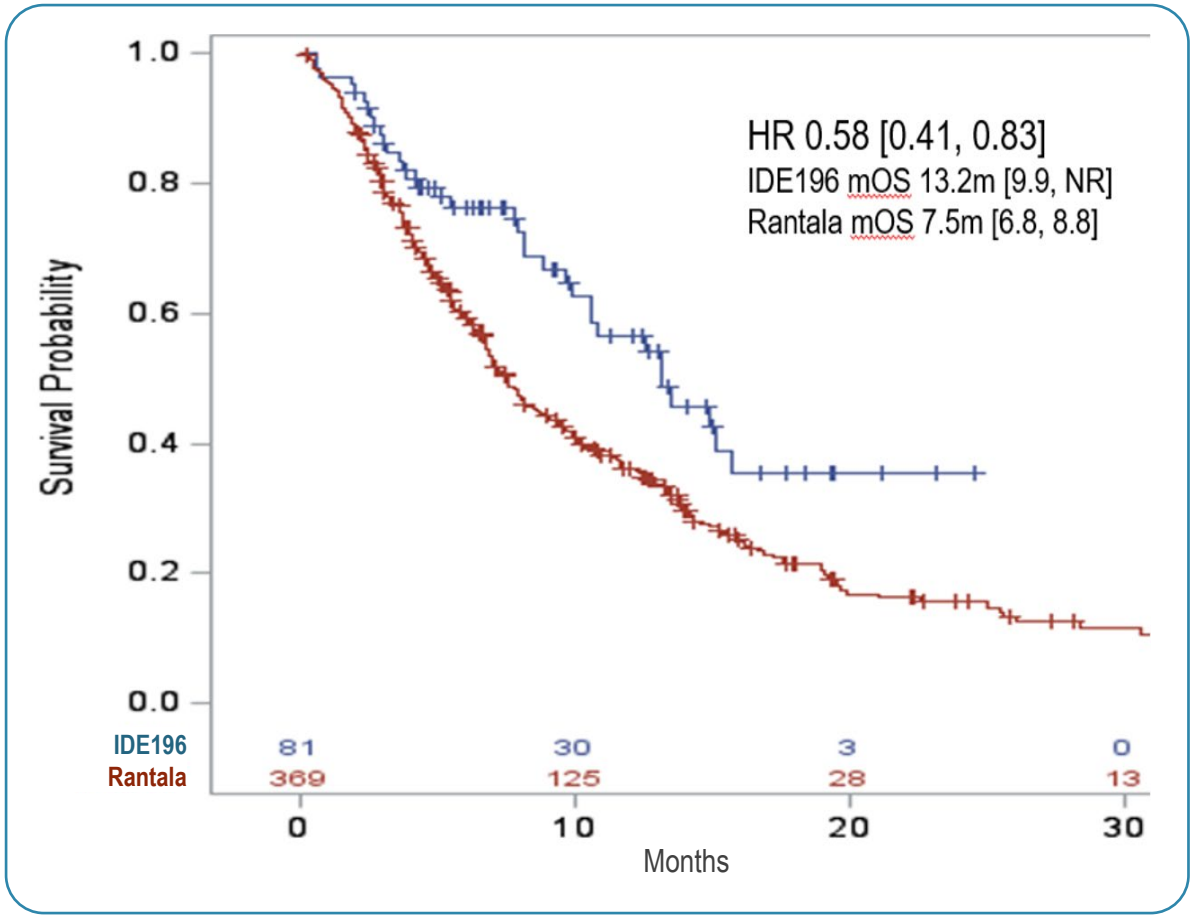
1st Line MUM Study: HLA-A2 Positive (~40-50% of MUM population)



Darovasertib Monotherapy Overall Survival in Heavily Pre-Treated MUM

Overall Survival favorable compared to Historical Pretreated Synthetic Control Arm [1,2]

Baseline Characteristics		N=81 (%)
Age	< 65	57 (70.4)
	>=65	24 (29.6)
Sex	F	41 (50.6)
	M	40 (49.4)
ECOG PS	0	61 (75.3)
	1	20 (24.7)
Baseline LDH	Normal	26 (32.1)
	>ULN	54 (66.7)
	Missing	1 (1.2)
Number of Prior Regimens	0	12 (14.8)
	1	30 (37.0)
	>=2	39 (48.1)
Tumor Burden (mm) (Sum of Target Lesions)	Median	82
	Min, Max	11, 301



[1] IDEAYA Data (based on preliminary analysis of unlocked database, including: pooled IDEAYA and Novartis BID monotherapy clinical data as of Apr 13, 2021)
[2] Synthetic Control Arm based on 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)

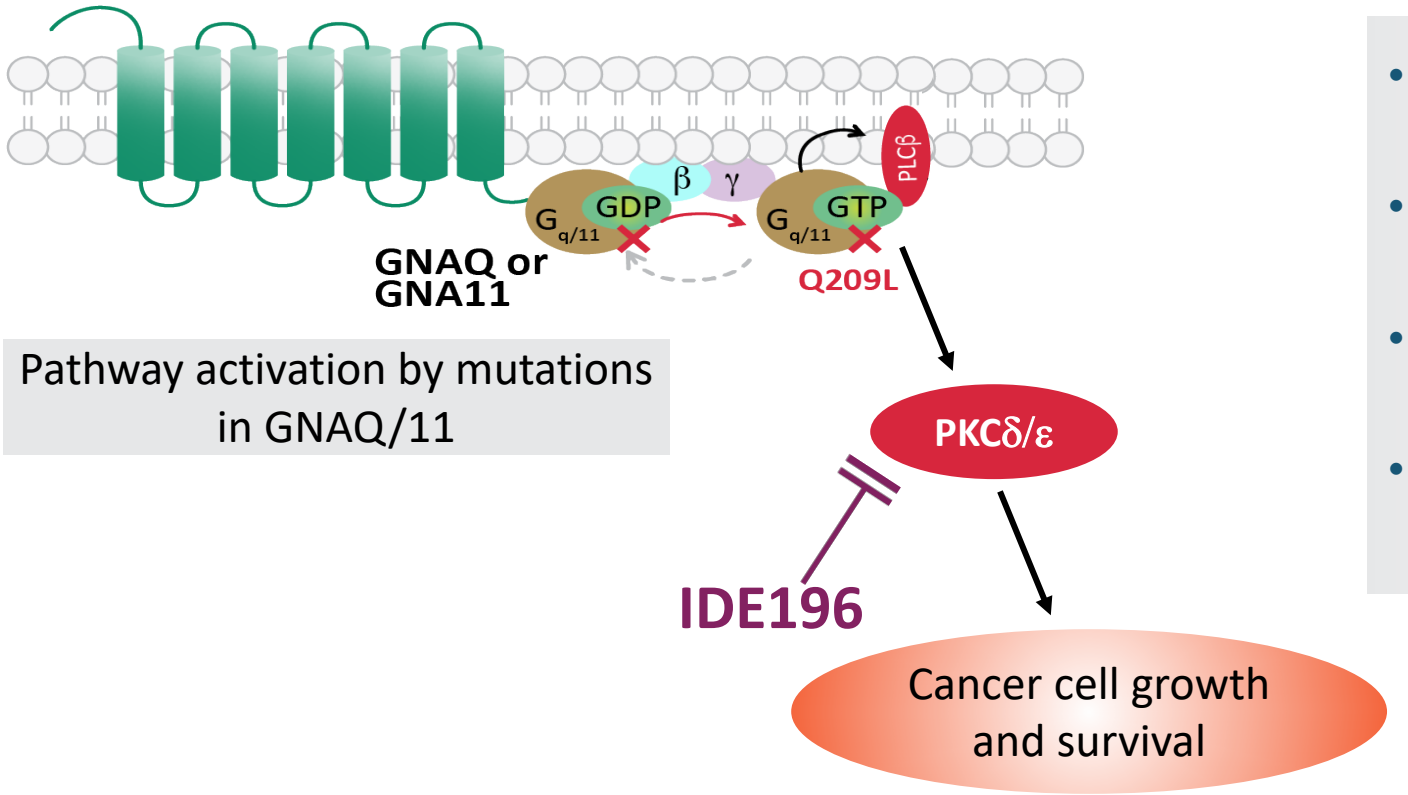
Darovasertib (PKC) / Crizotinib (cMET) Synthetic Lethal: Mechanistic Rationale, Preclinical and Translational Data

Mike White, Ph.D., Senior Vice President and Chief Scientific Officer
IDEAYA Biosciences

Darovasertib (IDE196) PKCδ/ε Inhibitor in Uveal Melanoma

GNAQ/11 mutations (>90% UM) highjack PKC signaling for tumorigenic transformation

Uveal Melanoma



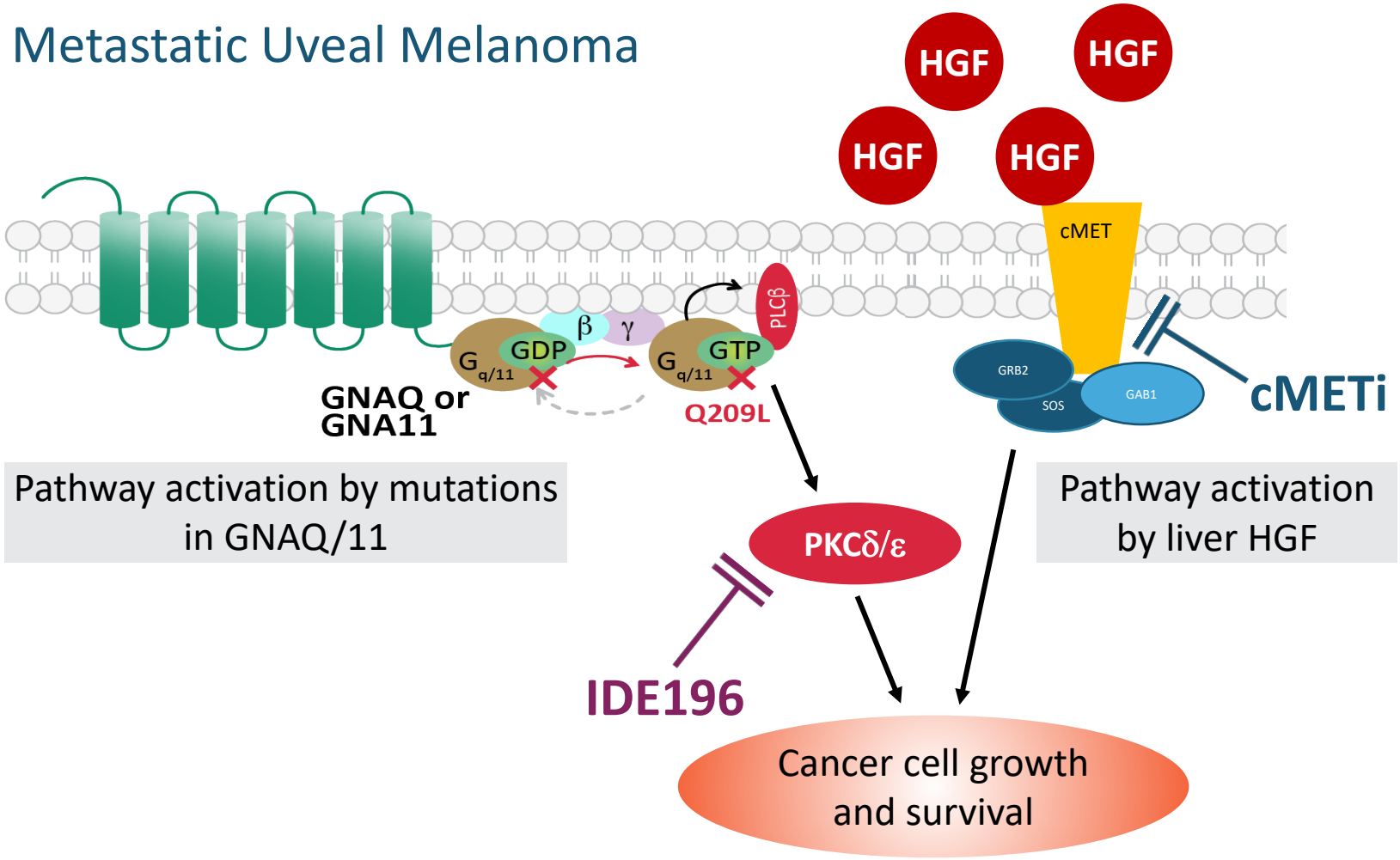
Pathway activation by mutations in GNAQ/11

- Primary Uveal Melanoma is typically treated with radiation and/or enucleation
- Metastatic Uveal Melanoma (MUM) occurs in approximately 50% of patients
- MUM presents predominantly as liver metastasis in ~90% of patients
- Historical treatment approaches have been ineffective with no approved therapies

Synthetic Lethal Combination: Darovasertib (PKC) + Crizotinib (cMET)

In metastatic disease, cMET activation by liver-derived HGF may substitute for PKC signaling

Metastatic Uveal Melanoma



Pathway activation by mutations in GNAQ/11

Pathway activation by liver HGF

- High cMET expression is associated with metastatic progression
- HGF promotes cancer cell growth and survival
- Translational Research hypothesis: HGF-induced cMET signaling in the liver microenvironment activates an alternative pathway for MUM tumor progression

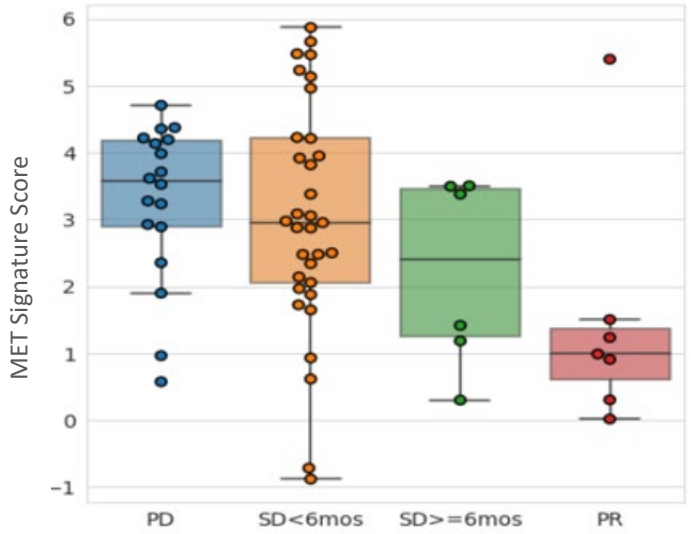
Synthetic Lethal Combination: Darovasertib (PKC) + Crizotinib (cMET)

Translational Research supports Darovovasertib + Crizotinib Combination

Clinical Phase 1 Data Association

Clinical response to Darovasertib monotherapy associated with low cMET activity

Darovasertib Monotherapy Ph 1

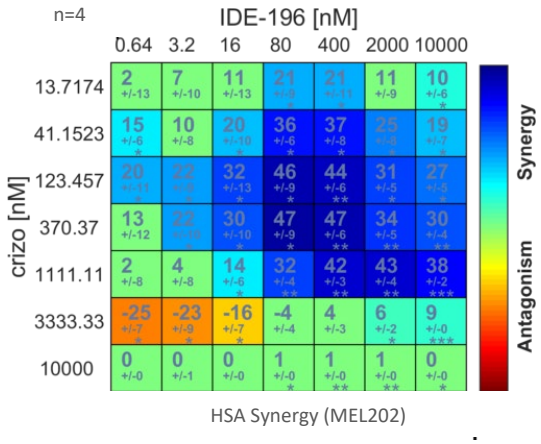


Ph 1 Clinical Outcomes
PD=Progressive Disease, SD=Stable Disease, PR=Partial Response

IDEAYA Data

Preclinical Synergy

Darovasertib + Crizotinib synergy observed in Mel202 (MUM) cell line



HSA Synergy (MEL202)

IDEAYA Data AACR 2021

- Ph1 Translational data shows that clinical responses inversely associate with MET signature and cMET expression
- Preclinical Synergy observed for darovasertib + crizotinib in MUM cell lines
- Clinical Hypothesis to evaluate darovasertib in combination with cMETi

Darovasertib (PKC) / Crizotinib (cMET) Phase 1/2 Combination: Clinical Efficacy and Adverse Event Profile

Meredith McKean, M.D., Sarah Cannon Research Institute at Tennessee Oncology, Associate Director, Melanoma and Skin Cancer Research

Darovasertib + Crizotinib Combination Safety Summary

Manageable Side Effect Profile (n=22 at Phase 1/2 Combination Expansion Dose)

Low Rates of Drug Related SAEs

Safety Summary	n=22 (%)
All Cause	
AEs	21 (96%)
Grade 3/4 AEs	8 (36%) / 0 (0%)
SAEs	5 (23%)
AEs leading to interruption	10 (46%)
Drug-Related	
AEs	18 (82%)
Grade 3/4 AEs	6 (27%) / 0 (0%)
SAEs	1 (5%)
AEs leading to interruption	8 (36%)

No drug related grade 4 or 5 AE's

Frequency of Drug-Related AEs (>10% Total)

Adverse Event	Grade 1	Grade 2	Grade 3	Total
Diarrhea	36%	36%	5%	77%
Nausea	32%	32%		64%
Edema peripheral	23%	23%		46%
Hypoalbuminemia	18%	18%		36%
Vomiting	32%	5%		36%
Hypotension	23%	9%		32%
Fatigue	5%	14%	9%	27%
Decreased appetite	18%	5%		23%
Dizziness	18%	5%		23%
Weight increased	18%	5%		23%
Dermatitis acneiform	14%	5%		18%
Rash maculo-papular	14%	5%		18%
Anemia	14%			14%
AST increased		9%	5%	14%
Dysgeusia	14%			14%

Low rates of drug-related high-grade AE's

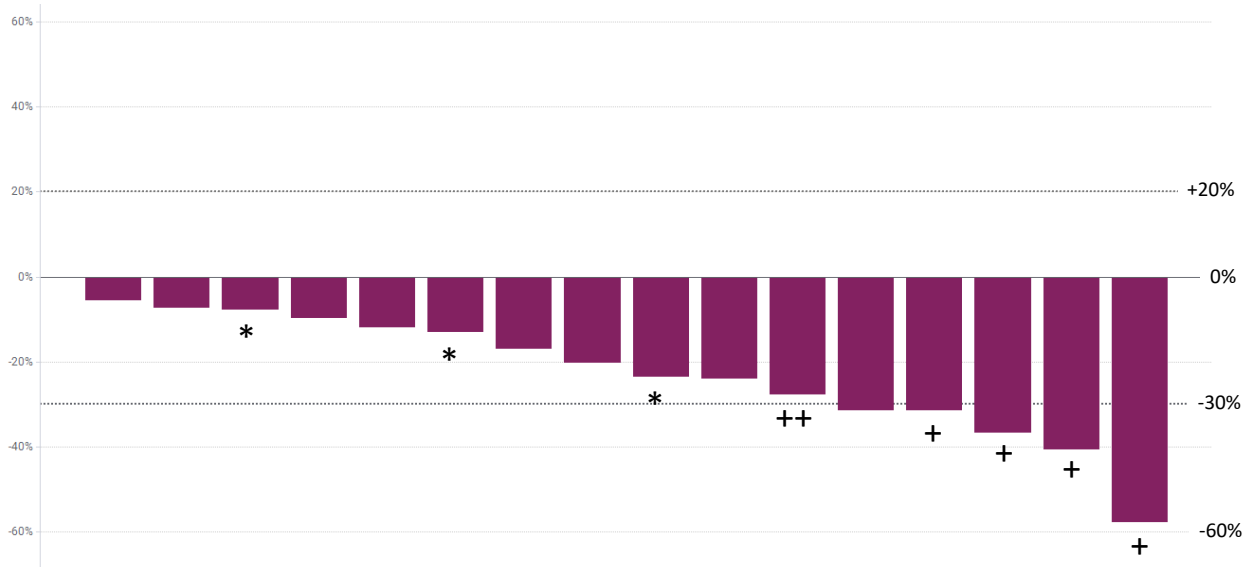
IDEAYA Data as of 11/25/2021 (based on preliminary analysis of unlocked database)

Preliminary Darovasertib + Crizotinib Phase 2 Expansion Dose Efficacy

Encouraging Clinical Activity in heavily pretreated Metastatic Uveal Melanoma

Daro + Crizo Expansion Dose Cohort, n=16 with ≥1 post-BL scan

100% of patients observed tumor shrinkage (100% DCR)
31% ORR in patients with ≥2 post baseline scans



+ Confirmed partial response by investigator or central review
++ Unconfirmed partial response by central review awaiting follow-up scans
* Has had only 1 post baseline scan
3 of 4 responders were pretreated with immunotherapy

Early Clinical PoC of PKC + cMET Synthetic Lethal

- 100% of patients show tumor reduction in target lesions (n=16 evaluable patients with ≥ 1 scan)
  - 100% Disease Control Rate
- Encouraging ORR% in heavily pre-treated MUM patients with ≥2 post-baseline scans (n=13)*
  - 4 patients with confirmed PRs (31% ORR)
  - 6 patients (46%) demonstrate >30% tumor reduction, including 1 uPR awaiting follow-up scan(s)
  - IMC-GP100/IMCR: 4.7% ORR; Pembro: 5% ORR**
- Baseline Characteristics of n=22 total patients, including 6 patients awaiting 1st scan
  - LDH > ULN in 65% of patients
  - 91% with prior therapies
  - 59% with 2 or more prior therapies
- Program Goal: ORR >20%

* No patients off-treatment prior to 2nd scan

IDEAYA Data: preliminary analysis of unlocked database as of 11/25/2021

* CT scan read by investigator or central review
** Immunocore Corporate Presentation, November 2021

Darovasertib + Crizotinib Combination Preliminary Efficacy

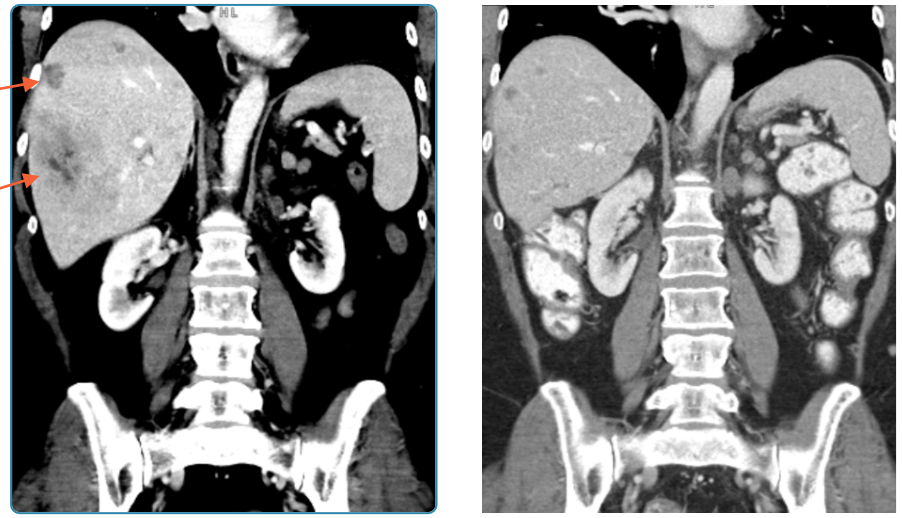
Examples of Responses with significant Anti-Tumor Activity

Patient Example 1

- 70+ year old patient with ongoing response at 6 months
- Priors: Ipi+Nivo, Chemoembolization, Radioembolization
- Diffuse disease in liver, lung, LN, subcut and elevated LDH

Baseline

5 months

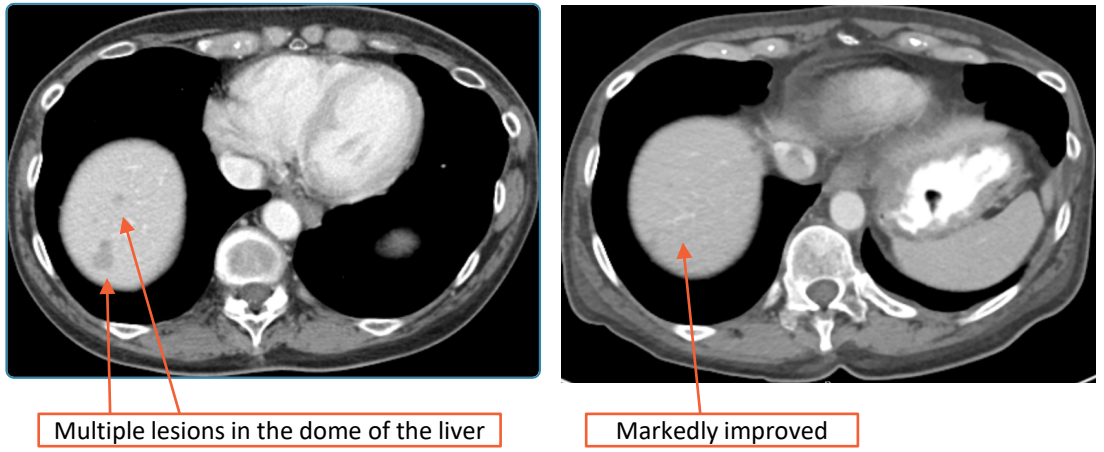


Patient Example 2

- 60+ year old patient with ongoing response at 4 months
- Priors: Ipi+Nivo
- Numerous liver lesions, normal LDH

Baseline

4 months



Darovasertib Potential Registrational Strategies and Evaluation of Expansion Opportunities

Matt Maurer, M.D., Vice President, Clinical Oncology and Medical Affairs
IDEAYA Biosciences

Darovasertib + Crizotinib SL Combination Therapy

Differentiated Novel Treatment Mechanism in MUM

	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	2L/3L+ MUM (n=16 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 (~40-50% of MUM)
Drug Form	Oral Tablets (BID)	Oral Capsules (QD)	Oral Capsules (BID) plus chemo	IV Infusion (Weekly)
Tolerability (Grade ≥3 Drug-Related AE)	27%	51.6%	63% ^^^ (All Cause)	46.5%
% of Pts with Tumor Shrinkage	100%*	23% ^^	35%^^	44%#
Overall Response Rate (ORR)	31%*	0%	3% ^^^	4.7%#
Progression Free Survival (PFS)	[TBD]	2 m	2.8 m ^^^	2.8 m#
Overall Survival (OS)	[TBD]	6.4 m	Not reported	16.8 m#

* IDEAYA Ph 1/2 (ongoing): based on preliminary analysis of unlocked database as of 11/25/2021 by investigator or central 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

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Darovasertib Clinical Preferred Plan

Potential Scenarios – Pending Regulatory Guidance H1 2022

Single-Arm Phase 2

Expansion of Current Single-Arm Trial in pretreated patients with further enrollment to registration-enabling combination arm

ORR target ≥ 20%

Confirmatory Study

Ph 3 Darovasertib + Crizotinib vs Inv Choice

1° EP PFS, 2° EP OS

Line of Therapy TBD

n=75-125 (~50-100 additional patients), excluding confirmatory study

Randomized Phase 2

New Randomized Phase 2 Trial in pretreated patients

ORR target ≥ 20%

Confirmatory Study

Ph 3 Darovasertib + Crizotinib vs Inv Choice

1° EP PFS, 2° EP OS

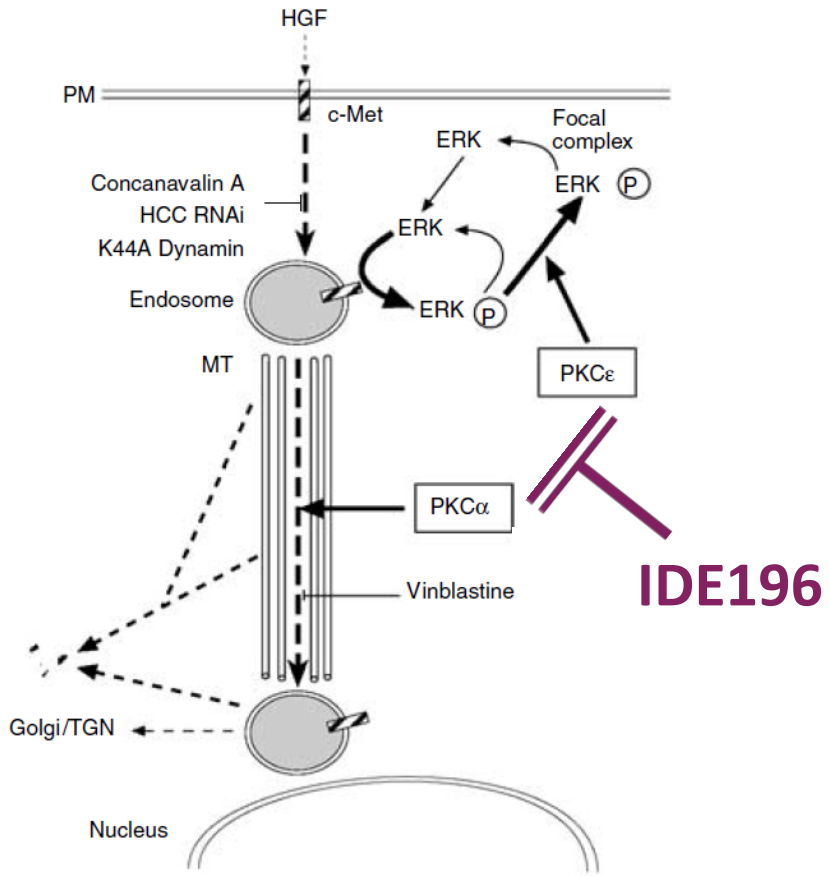
Line of Therapy TBD

n=125-175, excluding confirmatory study

PKC-cMET SL: Evaluation of Potential Indication Expansion Ongoing

Additional MET-Amplified / MET High Expression Tumors

PKC-epsilon and MET Amplified Tumors



EMBO 2004, Parker et al, modified by IDEAYA

- PKC-epsilon has been reported in literature to control HGF-dependent cMET traffic, signaling and cell migration
- Evaluating potential opportunities to expand clinical PoC of Darovasertib (PKC) + cMET combo to additional MET-amplified / high expression tumors, such as Hepatocellular Carcinoma
- Darovasertib demonstrates activity vs PKC-epsilon isoform with strong cell potency (<100nM EC50)

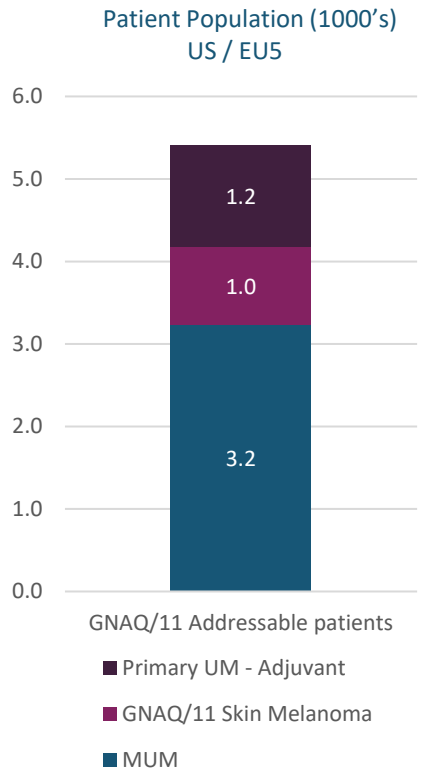
Darovasertib Population Analysis: GNAQ/11 Melanomas and Additional MET-Amplified / High Expression Tumors

Paul Stone, Senior Vice President and Chief Financial Officer
IDEAYA Biosciences

Darovasertib Patient Population Analysis

GNAQ/GNA11 Melanoma & Additional MET-Amplified / High Expression Tumors

Addressable GNAQ/11 Patients



IDEAYA Analysis

MUM, Adjuvant UM and GNAQ/11 Skin Melanoma

- No FDA Approved Therapies for MUM or GNAQ/11-Tumors
- Evaluating opportunities in Adjuvant Uveal Melanoma (Ph 1 IST) and GNAQ/11 Skin Melanoma (Ph1)
- Total Addressable Patient Population = ~5.4K pts/year

Evaluating Additional MET-Amplified / High Expression Tumors

- Patient selection based on CLIA-validated assays for MET-amplification (e.g., NGS, FISH) or high MET expression (e.g., IHC)
- HCC focus on refractory / resistant patients based on hypothesis of constitutively active cMET/HGF axis

	MET-amplification	High MET Expression
NSCLC	~1-5% [1,2]	~3-4% [2]
CRC	-	~3-9% [2]
Gastric Cancer	-	~9-20% [2]
HCC	~9% [3]	~27% [3]

1 Drilon et al., Journal of Thoracic Oncology Jan 2017, 12 (1) 15-26
2 Sierra et al., Therapeutic Advancers in Medical Oncology Nov 2011, 3 (S1) S21-S35
3 Lee et al., Anticancer Research November 2013, 33 (11) 5179-5186

Closing Remarks and Analyst Q&A

Yujiro Hata – President and Chief Executive Officer
IDEAYA Biosciences

Closing Remarks – Darovasertib Investor Day

Darovasertib (PKC) and Crizotinib (cMET) Synthetic Lethal (SL) Combination

- Novel PKC plus cMET SL mechanism discovered in IDEAYA labs; Darovasertib is a potential 1st-in-class PKC inhibitor
- Established early Ph 1/2 clinical proof-of-concept of PKC-cMET SL, validating IDEAYA platform / capabilities

Preliminary Combination Efficacy Target of ≥20% ORR & Tolerability Profile Trending Favorably

- Historical MUM ORR in 0-5% range and <50% DCR, including IMC-GP100/IMCR at 4.7% ORR and Pembro 5% ORR
- 16 of 16 patients observe tumor shrinkage, demonstrating 100% Disease Control Rate
- 31% ORR (4 cPRs) in 13 evaluable patients with ≥2 post baseline scans
- 6 patients (46%) demonstrate >30% tumor shrinkage, including 1 uPR awaiting follow-up scan(s)
- Darovasertib and Crizotinib combination generally well tolerated at target expansion dose

Potential Registration-enabling Strategies being evaluated for Darovasertib

- Darovasertib + Crizotinib combination expansion dose selected to support registrational studies
- Multiple potential options available, including response rate and PFS type clinical endpoints

Darovasertib Clinical and Commercial Market Opportunity

- High unmet need in MUM, Adjuvant UM (initiating Ph1 IST), and GNAQ/11 Skin Melanoma (enrollment ongoing)
- Evaluating potential expansion opportunities, including additional MET-amplified / high expression tumors

Next Target Program Milestones

- Target FDA feedback for potential registration-enabling trial design in H1 2022
- Next data read-out milestone in H1 2022: Median PFS of Darovasertib + Crizotinib in MUM

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