IDEAYA Reports Positive Interim Phase 2 Clinical Results for Darovasertib and Crizotinib Synthetic Lethal Combination in Metastatic Uveal Melanoma

- Confirmed partial responses by RECIST observed in 4 of 8 (50% ORR) evaluable First-Line MUM patients and in 11 of 35 (31% ORR) evaluable Any-Line MUM patients
- Tumor shrinkage observed in 31 of 35 (89%) Any-Line MUM patients
- Median PFS not yet reached and >5 months in evaluable First-Line MUM patients; observed median PFS of ~5 months in evaluable Any-Line MUM patients
- Historical % ORR and median PFS by other therapies in MUM have been low, ranging from ~0% to 5% ORR and ~2 to 3 months median PFS
- Proof-of-concept for use in (neo)adjuvant UM with tumor shrinkage in 5 of 5 ocular lesions, including reductions of ~-74% and -67%, each with improved visual symptoms
- Total UM and MUM annual incidence in US/EU28 projected at over 13,000 patients, and total UM and MUM prevalence in US/EU28 projected at over 110,000 patients
- Targeting to initiate potential registrational trial for Daro + Crizo in First-Line MUM in Q1 2023 and company-sponsored trial for Daro monotherapy in (neo)adjuvant UM in Q4 2022
- Investor webcast and call scheduled for Monday, September 12, 2022, at 8:00am ET

SOUTH SAN FRANCISCO, Calif., Sept. 11, 2022 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA), a synthetic lethality focused precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced interim results from its Phase 2 clinical trial evaluating darovasertib and crizotinib synthetic lethal combination in metastatic uveal melanoma (MUM) patients (ClinicalTrials.gov Identifier: NCT03947385).

"The confirmed partial responses and high percentage of patients with tumor shrinkage shown in these interim Phase 2 data are extremely encouraging for patients with metastatic uveal melanoma. The 50% overall response rate and greater than 5 months median progression free survival observed in first-line MUM patients reflects the potential for a compelling clinical efficacy profile irrespective of haplotype (HLA-A*02:01) status. The partial responses shown in first-line and any-line MUM patients are clinically significant and build on previously-reported results for any-line MUM patients, now with a larger patient data set," said Dr. Marlana Orloff, M.D., Associate Professor, Sidney Kimmel Cancer Center, Jefferson Health.

"The clinical efficacy observed in first-line patients in these interim Phase 2 data presents an opportunity to pursue a front-line strategy and provides a rationale for a potential registration-enabling clinical trial in MUM," said Dr. Matt Maurer, M.D., Vice President, Head of Clinical Oncology and Medical Affairs, IDEAYA Biosciences.

There are currently no FDA approved therapies for GNAQ and GNA11 solid tumors, and current therapies for MUM have relatively low objective response rates and short median progression free survival (PFS), highlighting the high unmet medical need. Approximately 90% of MUM has either a GNAQ or GNA11 mutation that activates the protein kinase C (PKC) signaling pathway. The historical overall response rate (ORR) in MUM clinical trials has generally been reported with an ORR ranging from approximately 0 to 5%, including: pembrolizumab and tebentafusp (each ~5%); MEK inhibitor selumetinib in combination with dacarbazine (~3%); and cMET inhibitor cabozantinib monotherapy (~0%). In addition, the historical median PFS in MUM clinical trials has been reported ranging from approximately 2.0 to 2.8 months, including: tebentafusp (~2.8 months, IMCgp100-102 study); MEK inhibitor selumetinib in combination with dacarbazine (~2.8 months); and cMET inhibitor cabozantinib monotherapy (~2.0 months).

Darovasertib (IDE196) is a small molecule, potential first-in-class protein kinase C (PKC) inhibitor. IDEAYA is

evaluating the synthetic lethal combination of darovasertib and crizotinib, a small molecule cMET inhibitor, in MUM and other GNAQ/11 tumors pursuant to a clinical trial collaboration and drug supply agreement with Pfizer.

Clinical Data Update – Darovasertib and Crizotinib Combination in MUM
The interim Phase 2 clinical data update is based on an initial thirty-seven (37) patients enrolled in the darovasertib and crizotinib combination study at the expansion dose of 300mg twice-a-day darovasertib and 200mg twice-a-day crizotinib, as of the data analysis cutoff date of June 26, 2022. Out of the thirty-seven (37) patients enrolled, there were thirty-five (35) evaluable patients and two (2) non-evaluable patients. The two (2) non-evaluable patients were both pretreated and withdrew from the trial prior to the first scan. Neither of the two non-evaluable patients progressed due to disease: one (1) patient withdrew consent and one (1) patient discontinued early due to fatigue. Reported data are preliminary and based on an unlocked database as of the data analyses cutoff date, except one confirmatory scan after the data cutoff date or as otherwise noted. Enrollment in the darovasertib and crizotinib combination expansion dose cohort of the clinical trial is ongoing.

The company observed encouraging clinical activity in Phase 2 clinical trial evaluating darovasertib and crizotinib synthetic lethal combination in metastatic uveal melanoma (MUM) patients in the expansion dose cohort. These investigator-reviewed data by RECIST 1.1 include:

- 89% of Patients show Tumor Shrinkage in Any-Line MUM: 31 of 35 evaluable patients showed tumor shrinkage as determined by target lesion size reduction
- 83% Disease Control Rate (DCR) in Any-Line MUM: 29 of 35 evaluable patients showed stable disease or better as determined by target lesion size reduction
- 50% Overall Response Rate (ORR) in First-Line MUM: 4 of 8 evaluable patients had a confirmed partial response (PR)
- 31% Overall Response Rate (ORR) in Any-Line MUM: 11 of 35 evaluable patients had a confirmed partial response (PR)
- 43% of Patients with >30% Tumor Reduction in Any-Line MUM: 15 of 35 evaluable patients observed partial responses with >30% tumor reduction, including 11 confirmed and 4 unconfirmed partial responses
- Median Study Follow-Up of 6.5 months for First-Line MUM patients and 7.8 months for Any-Line MUM patients
- Median Duration of Response (DOR) in evaluable First-Line MUM patients has not yet been reached and 4 of 4 patients with confirmed PR's in First-Line MUM remain in response; median DOR in evaluable Any-Line MUM patients has not yet been reached and 7 of 11 patients with confirmed PR's in Any-Line MUM remain in response
- Median Progression Free Survival (PFS) in First-Line MUM patients has not yet been reached and is >5 months in evaluable First-Line MUM patients; median PFS for evaluable Any-Line MUM patients is ~ 5 months

These data provide robust clinical proof-of-concept for the efficacy of the darovasertib and crizotinib synthetic lethal combination treatment.

The darovasertib and crizotinib combination therapy has a manageable adverse event profile in MUM patients (n=37), with a low rate of drug-related serious adverse events (SAE's). Patients reported predominantly Grade 1 or 2 drug-related adverse events: all patients experienced a drug-related AE, of which 76% were reported as Grade 1 or 2 and 24% were reported as Grade 3. No patients observed Grade 4 or Grade 5 AE's. One patient discontinued treatment due to a drug-related adverse event.

The potentially addressable patient population for metastatic uveal melanoma is estimated to include over 4,000 patients across US and Europe, based on estimated annual incidence. As an orally-administered small molecule precision medicine therapeutic, with demonstrated anti-tumor activity and manageable adverse event profile, the

company considers the darovasertib and crizotinib combination therapy to have the potential to be broadly impactful to the MUM patient population.

IDEAYA is currently targeting to initiate a potential registration-enabling trial in Q1 2023. The company is evaluating first-line MUM as a potential registrational regulatory strategy. As of August 31, 2022, IDEAYA has enrolled 21 first-line MUM patients at the expansion dose of the darovasertib and crizotinib combination study.

Darovasertib – (Neo)Adjuvant Uveal Melanoma and Other Potential Expansion Opportunities
IDEAYA is also evaluating the potential for darovasertib in other oncology indications, including as (neo)adjuvant therapy in primary uveal melanoma (UM), in cMET-driven tumors and in KRAS-mutation tumors.

(Neo)Adjuvant UM represents a significant expansion opportunity for darovasertib – with a potential annual incidence of approximately 8,700 patients aggregate in US and Europe.

The company has observed preliminary proof of concept for potential darovasertib use in the (neo)adjuvant uveal melanoma setting, including responses of the primary orbital tumor. Clinical data reflects an observed tumor shrinkage by investigator review of primary ocular lesions in 5 of 5 (100%) UM or MUM patients treated as monotherapy or in combination with Crizotinib, including preliminary observation of tumor reductions in uvea lesion of two patients after the data cut-off date of August 19, 2022:

- a darovasertib monotherapy patient with metastatic disease and an intact primary lesion in the eye observed a reduction of approximately 74% in the eye lesion by PET Standard Uptake Value (SUV) at an initial scan after approximately 2 weeks on therapy, with observed improvement in visual symptoms in the affected eye; this patient remained on therapy for approximately 7 months;
- a darovasertib and crizotinib combination patient with metastatic disease and an intact primary lesion in the eye observed tumor shrinkage of approximately 67% by RECIST 1.1 as a contribution to an overall confirmed PR, with improvement in visual symptoms in the affected eye; this patient is continuing on therapy as of approximately 5 months; a second darovasertib and crizotinib combination MUM patient with an intact primary lesion observed a reduction of the ocular lesion based on preliminary scan after the data cut-off date; and
- a darovasertib monotherapy neoadjuvant uveal melanoma patient with a primary ocular lesion observed a reduction of approximately 20% by RECIST 1.1 at the first scan after 27 days on therapy, with an observed decrease in ocular vasculature; a second darovasertib monotherapy neoadjuvant UM patient observed a reduction in the primary ocular lesion based on preliminary scan after the data cut-off date; these two patients are enrolled in the NADOM IST and are continuing on therapy as of approximately 1 month.

"I am excited to explore the potential for darovasertib as a (neo)adjuvant approach for the treatment of uveal melanoma patients. The observed clinical experience provides a basis for clinical investigation to evaluate whether darovasertib, can improve current primary treatment paradigms, which typically include radiotherapies and/or enucleation of the eye," said Dr. Marcus Butler, Medical Oncologist, Tumor Immunotherapy Program, Melanoma/Skin Oncology Site Lead at Princess Margaret Cancer Centre in Toronto, Canada, and Ocular Melanoma Physician Task Force of Canada Co-Lead.

IDEAYA is supporting St. Vincent's Hospital Sydney Limited, which has initiated an Investigator Sponsored Trial, or IST, captioned as the "Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma" (NADOM) study, to evaluate darovasertib monotherapy in a neo-adjuvant and adjuvant setting in primary UM patients. IDEAYA is targeting initiation of a company-sponsored clinical trial in Q4 2022 to further evaluate darovasertib monotherapy in (neo)adjuvant uveal melanoma, and is evaluating potential near-term clinical endpoints such as vision and organ preservation.

IDEAYA Investor Webcast and Conference Call

IDEAYA will host an investor webcast and conference tomorrow morning, September 12, 2022 at 8:00 am ET, to present darovasertib and crizotinib Phase 2 interim clinical efficacy and tolerability data, as well as clinical landscape, potential registrational strategies and expansion opportunities.

Presenters at the investor webcast and conference call will include Dr. Marlana Orloff, M.D., Associate Professor, Sidney Kimmel Cancer Center, Jefferson Health, and Dr. Marcus Butler, Medical Oncologist, Tumor Immunotherapy Program, Melanoma/Skin Oncology Site Lead at Princess Margaret Cancer Centre in Toronto, Canada, and Ocular Melanoma Physician Task Force of Canada Co-Lead, each of whom are key opinion leaders and clinical investigators. Yujiro S. Hata, President and Chief Executive Officer, and other members of the IDEAYA management team will also present.

IDEAYA's darovasertib investor webcast presentation, as well as an updated corporate presentation, will be available on the company's website, at its Investor Relations portal (https://ir.ideayabio.com/) in advance of the investor webcast presentation at approximately 6:00 am ET.

Corporate Updates
IDEAYA had cash, cash equivalents and marketable securities of approximately $324 million as of June 30, 2022, which it currently projects will be sufficient to fund its planned operations into 2025.

About IDEAYA Biosciences
IDEAYA is a synthetic lethality focused precision medicine oncology company committed to the discovery and development of targeted therapeutics for patient populations selected using molecular diagnostics. IDEAYA's approach integrates capabilities in identifying and validating translational biomarkers with drug discovery to select patient populations most likely to benefit from its targeted therapies. IDEAYA is applying its research and drug discovery capabilities to synthetic lethality – which represents an emerging class of precision medicine targets.

Forward-Looking Statements
This press release contains forward-looking statements, including, but not limited to, statements related to (i) timing for initiating potential registration-enabling trial in MUM, (ii) potential clinical efficacy profile, and (iii) timing of initiation of a company-sponsored clinical trial for in Q4 2022 to further evaluate to evaluate darovasertib in a neo-adjuvant and adjuvant setting in primary UM patients. Such forward-looking statements involve substantial risks and uncertainties that could cause IDEAYA's preclinical and clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. 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, the effects on IDEAYA's business of the worldwide COVID-19 pandemic, the ongoing military conflict between Russia and Ukraine, and other matters that could affect the sufficiency of existing cash to fund operations. IDEAYA undertakes no obligation to update or revise any forward-looking statements. 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 IDEAYA in general, see IDEAYA's recent Quarterly Report on Form 10-Q filed on August 15, 2022 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

SOURCE IDEAYA Biosciences, Inc.

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https://media.ideayabio.com/2022-09-11-IDEAYA-Reports-Positive-Interim-Phase-2-Clinical-Results-for-Darovasertib-and-Crizotinib-Synthetic-Lethal-Combination-in-Metastatic-Uveal-Melanoma