IDEAYA Announces Top-Line Phase 2 Results at ESMO 2023 of Darovasertib and Crizotinib Combo in MUM, and Clinical Efficacy Updates for Neoadjuvant UM, GNAQ/11 Cutaneous Melanoma, and Synthetic Lethality Pipeline

- 60% confirmed ORR% by RECIST 1.1 in HLA-A2(+) in 1L MUM, and 42% confirmed ORR% by RECIST 1.1 in HLA-A2(-) in 1L MUM
- Median PFS of 7.1 months in 1L MUM and 11 months in hepatic-only MUM
- On further follow-up, ~30% of any-line MUM treated >1 year and multiple PRs on treatment >2 years, with potential for further enhancement with ~20% of patients ongoing treatment
- Historical ORR% and median PFS by other therapies in MUM have ranged from 0% to 5% and 2 to 3 months, respectively
- 94% ctDNA molecular response rate observed in any-line MUM
- ~70% of MUM patients were HLA-A2(-) based on 149 patients tested for HLA-A2 status
- 2 of 4 (50%) GNAQ/11 cutaneous melanoma patients on darovasertib combo observed PRs by RECIST 1.1, with responses on treatment approximately 600 days
- 50% eye preservation rate (3 of 6 evaluable patients) in enucleation neoadjuvant IST cohort with darovasertib monotherapy until maximal benefit
- Synthetic Lethality: Updates on PRs by RECIST 1.1 for IDE397/MAT2A and IDE161/PARG
- Updated corporate presentation with clinical data updates on darovasertib, IDE397/MAT2A, and IDE161/PARG is available on IDEAYA homepage

SOUTH SAN FRANCISCO, Calif., Oct. 23, 2023 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA), a precision medicine oncology company committed to the discovery and development of targeted therapeutics, announces clinical data presented at a proffered paper session of the European Society of Medical Oncology Congress 2023 (ESMO 2023) from the company's ongoing Phase 2 clinical trial evaluating darovasertib in combination with crizotinib in patients having metastatic uveal melanoma (MUM).

"These data contribute to the growing clinical evidence that the darovasertib and crizotinib combination represents an emerging treatment advance in metastatic UM, a disease with a historically poor prognosis," said Meredith McKean, M.D., MPH, Director, Melanoma and Skin Cancer Research at Sarah Cannon Research Institute, who is an investigator on the Phase 2 trial and presented the clinical data at ESMO 2023. "The manageable safety profile and pronounced efficacy observed in first-line patients and in all-line hepatic-only patients based on available data supports the ongoing potentially registrational Phase 2/3 clinical trial in metastatic UM," concluded Dr. McKean.

ESMO 2023 Data:

The Phase 2 evaluation of the darovasertib and crizotinib combination in first-line and pretreated MUM patients

showed a manageable safety profile (n=68) and demonstrated clinical efficacy in any-line (n=63) and first-line (n=20) MUM patients that appears superior to current standards of care. The reported Phase 2 clinical data are based on evaluable first-line and any-line patients enrolled in the darovasertib and crizotinib combination study at the expansion dose of 300 mg twice-a-day darovasertib and 200 mg twice-a-day crizotinib as of September 22, 2022. Reported data are preliminary and based on investigator review from an unlocked database for 68 patients as of the data analyses cutoff date of August 22, 2023.

Circulating tumor DNA (ctDNA) molecular responses were determined based on measured changes in mean allele frequency (MAF) on-treatment as compared to MAF levels at baseline for a subset of any-line MUM patients (n=32). Patients whose ctDNA showed a reduction of greater than 50% MAF following treatment were characterized as having a ctDNA molecular response.The reported ctDNA data showed a reduction in MAF in all but one patient. Significantly, molecular responses were observed in 30 of 32 evaluable patients, reflecting a molecular response rate of 94%. The determined ctDNA molecular responses were deep and sustained, with approximately 80% of measured patients having >80% reduction in MAF. The ctDNA molecular responses correlated with observed efficacy, including confirmed partial responses (PRs) as determined by RECIST 1.1.

Clinical efficacy was observed in both human leukocyte antigen (HLA)-A2 positive (HLA-A2(+)) and HLA-A2 negative (HLA-A2(-)) patients. There were 50 all-line MUM patients with known HLA-A2 status among the 63 patients evaluable for efficacy, with 31 of these being HLA-A2(-) and 19 being HLA-A2(+). The reported efficacy data by HLA-A2 serotype was based on a preliminary analysis of an unlocked database as of August 22, 2023 by investigator review and RECIST 1.1. For HLA-A2(-) MUM patients, confirmed PRs were observed in 9 of 31 (29% overall response rate (ORR)) any-line and in 5 of 12 (42% ORR) first-line patients. For HLA-A2(+) MUM patients, confirmed PRs were also observed in 6 of 19 (32% ORR) any-line and in 3 of 5 (60% ORR) first-line patients. With approximately 5.5 months of additional follow-up from the previous data analysis cut-off date (March 8, 2023 to August 22, 2023), now approximately 30% of any-line MUM patients have been on treatment greater than one year and multiple patients with confirmed PRs by RECIST 1.1 have been on treatment greater than 24 months, with the potential for further enhancement on the duration of treatment (DOT) analysis as approximately 20% (13 out of 63 evaluable patients) of any-line MUM patients are continuing on treatment. Based on the two-year progression-free survival (PFS) Kaplan–Meier (KM) curve of the darovasertib and crizotinib combination in any-line MUM, the combination provides a promising PFS trend compared to other therapies, including tebentafusp. Intriguingly, the observed tail of the PFS curve implies durable benefit in a significant proportion of patients who remain progression free as far out as 2 years.

HLA-A*02:01 (HLA-A2) status was known in subsets of patients enrolled in clinical trials evaluating darovasertib. Prevalence of HLA-A2(+) and HLA-A2(-) in MUM patients was determined from a first data set of 149 MUM patients treated with darovasertib as monotherapy or in a combination arm of a clinical trial, and separately in a second data set of 118 MUM patients treated with the darovasertib and crizotinib combination.

Collectively, these data demonstrate that approximately 70% of MUM patients with known HLA-A2 status were HLA-A2(-). These data include 102 of 149 (68%) patients in the all-treatment subset and 81 of 118 (69%)

patients in the darovasertib + crizotinib combination treatment subset.

The darovasertib and crizotinib combination continued to demonstrate an overall manageable adverse event profile in MUM patients (n=68), with a low rate (10%) of drug-related serious adverse events (SAEs) and limited Grade 4 and Grade 5 SAEs and discontinuations. Drug-related adverse event (AE), were predominantly Grade 1 or Grade 2. 31% of patients reported at least one Grade 3 AE; no patients observed a Grade 4 AE; and one patient observed a Grade 5 AE. Five patients (7%) discontinued treatment with darovasertib and crizotinib combination due to a drug-related adverse event.

The reported data support IDEAYA's ongoing potentially registrational Phase 2/3 study (NCT05987332) for potential accelerated approval of darovasertib and crizotinib for treatment of first-line HLA-A2(-) MUM patients, where there are currently no FDA approved therapies.

GNAQ/11 Cutaneous Melanoma:

In the genetically defined GNAQ/GNA11 patient population with cutaneous melanoma, 3 cohorts of patients treated with darovasertib, either as monotherapy or in combination with either binimetinib or crizotinib, have shown preliminary clinical activity:

- Darovasertib Monotherapy Cutaneous Melanoma Cohort (n=8): 5 of 7 evaluable patients had tumor shrinkage (~71%) with one patient having a PR and remaining on treatment over 10 months after previously receiving multiple prior lines of immunotherapy
- Darovasertib plus Binimetinib Cutaneous Melanoma Cohort (n=2): 1 of 2 cutaneous melanoma patients with a PR demonstrated 50% tumor shrinkage and remained on treatment approximately 600 days after previously receiving multiple prior lines of immunotherapy
- Darovasertib plus Crizotinib Cutaneous Melanoma Cohort (n=2): 1 of 2 cutaneous melanoma patients had tumor shrinkage of 60% with one patient having a PR and remaining on treatment (approximately 600 days) after previously receiving multiple prior lines of immunotherapy

Darovasertib, as monotherapy or in combination with either binimetinib or crizotinib, has indicated a manageable adverse event profile in cutaneous melanoma patients with certain drug-related AEs being reported in certain cohorts. These preliminary clinical data support initiation of a Phase 2 expansion of the darovasertib and crizotinib combination in GNAQ/11 metastatic cutaneous melanoma to advance the darovasertib and crizotinib combination in this indication where there are currently no FDA approved therapies in this genetically-defined patient population.

The GNAQ/11 prevalence in cutaneous melanoma has been reported at approximately 5% in The Cancer Genome Atlas. The GNAQ/11 cutaneous melanoma estimated annual incidence is approximately 5,000 patients in the U.S. and 8,000 patients in the EU28, and the estimated total prevalence of GNAQ/11 cutaneous melanoma is approximately 70,000 patients in the U.S. and 110,000 patients in the EU28. It has been reported that approximately 12.5% to 15% of cutaneous melanoma patients have been reported to develop metastatic disease, whereas in uveal melanoma, a predominantly GNAQ/11 mediated cancer, the metastatic rate has been

reported at approximately 50%. In addition, 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. In addition, GNAQ/11 mutation patients are known to have low tumor mutational burden making these patients less likely to benefit from immune checkpoint inhibitor therapies.

Darovasertib Neoadjuvant Monotherapy:

In the ongoing investigator-sponsored Phase 1 clinical trial (IST) captioned as "Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma" (NADOM) being led by principal investigator Professor Anthony Joshua, MBBS, PhD, FRACP, Head Department of Medical Oncology, Kinghorn Cancer Centre, St. Vincent's Hospital in Sydney with participating sites of Alfred Health and the Royal Victorian Eye and Ear Hospital in Melbourne, the study reports a preliminary interim update with an enrollment cut-off as of July 17, 2023 of seven patients treated to maximal response in the neo-adjuvant setting (up to 6 months of darovasertib monotherapy in patients who were enrolled with planned enucleation); 2 patients have confirmed Eye Saved (i.e., converted to plaque brachytherapy) with a third patient confirmed as plaque-eligible and is ongoing with darovasertib neo-adjuvant treatment until maximal benefit; providing 50% overall eye preservation rate for the evaluable patients. Of the evaluable patients (6 of 7) treated to maximal benefit, defined as at least one ultrasound scan, approximately 83% of patients had tumor shrinkage. Two patients did not complete their treatment to maximal response; one patient had sub-retinal blood present at baseline and with lack of shrinkage and visual deterioration, the patient discontinued treatment after 6 weeks. A non-evaluable second patient had a Grade 3 drug-related AE of dermatitis and discontinued treatment before first scan. Two out of four additional patients after the enrollment cutoff date of July 17, 2023 are likely plaque eligible and are continuing darovasertib neoadjuvant therapy until maximal benefit with 1 patient being enucleated. In total, 11 patients eligible to receive 6 months of neoadjuvant therapy are enrolled to date in the neoadjuvant UM enucleation cohort IST.

IDEAYA's Phase 2 company sponsored (neo)adjuvant darovasertib monotherapy study is observing rapid enrollment to date, with 6 UM patients now enrolled, including 4 enucleation patients and 2 plaque-therapy patients.

Synthetic Lethality Pipeline:

For IDE397, a potential first-in-class MAT2A inhibitor, we have observed multiple PRs in the Phase 2 expansion evaluating priority solid tumor types of squamous NSCLC and bladder cancer. There have been 8 patients dosed in the Phase 2 expansion in the priority tumor types, of which 2 have not yet had a first tumor scan assessment. The PRs include an earlier reported -33% tumor shrinkage by CT-PET (without contrast) for a squamous NSCLC patient, and a confirmed PR (47% tumor shrinkage) by RECIST 1.1 with IDE397 in a previously undisclosed tumor type (bladder cancer). This bladder cancer patient has converted to a complete response by RECIST 1.1 at the week 18 CT-scan. In addition, of patients evaluable for ctDNA pre and post treatment, a high ctDNA molecular response rate of 83% was observed in these MTAP-deletion priority tumor types. As of the October

13, 2023 cut-off date, in the dose escalation and expansion phases, we have observed relatively low rates of drug-related discontinuations and SAEs. The IDE397 and AMG 193 clinical combination study in MTAP-deletion solid tumors is in ongoing dose escalation, with an expansion focus on NSCLC.

For IDE161, a potential first-in-class PARG inhibitor, we have observed multiple PRs by RECIST 1.1. and tumor shrinkage in priority solid tumor types early in the Phase 1 dose escalation and at the expansion dose. There have been a total of 7 patients treated at the expansion dose as of the October 13 2023 cut-off date, of which 2 patients have not yet had a first scan tumor assessment. The earlier reported IDE161 partial response at first scan in a BRCA1/2 endometrial cancer patient, is now a confirmed PR by RECIST 1.1 at the second scan. At the IDE161 expansion dose, we have observed no drug-related discontinuations or SAEs as of the October 13, 2023 cut-off date.

Updated IDEAYA Corporate Presentation:

An updated corporate presentation reflecting clinical data updates for darovasertib, and updated clinical efficacy for the IDE161 and IDE397 programs, including PRs by RECIST 1.1 and ctDNA molecular responses for IDE397 priority tumor types, will be available at approximately 6:00am ET on the IDEAYA Biosciences homepage and at its Investor Relations portal at approximately 8:30am ET (https://ir.ideayabio.com/).

About IDEAYA Biosciences

IDEAYA is a 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) expectations regarding the clinical activity profile and potential advantages of IDEAYA's clinical programs, (ii) the translation of preliminary clinical trial results into future clinical trial results, (iii) the enrollment of clinical trials and (iv) whether the Phase 2/3 clinical trial will be considered a registrational trial by the FDA. Such forward-looking statements involve substantial risks and uncertainties that could cause IDEAYA's 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, serious adverse events, undesirable side effects or unexpected characteristics of drug development programs, 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.

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 Quarterly Report on Form 10-Q filed on August 10, 2023 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

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