IDEAYA Announces Positive Interim Phase 2 Data for Darovasertib and Crizotinib Combination and Successful FDA Type C Meeting on Registrational Trial Design for Accelerated Approval in First-Line Metastatic Uveal Melanoma

- Confirmed overall response rate (ORR) of 45%, disease control rate (DCR) of 90% and median PFS of ~7 months in 20 evaluable First-Line MUM patients
- Based on FDA meeting, initiating Phase 2/3 registrational trial in Q2 2023 in First-Line HLA-A2 negative MUM, with median PFS as primary endpoint for potential accelerated approval
- Confirmed overall response rate (ORR) of 30%, disease control rate (DCR) of 87% and median PFS of ~7 months in 63 evaluable Any-Line MUM patients
- Confirmed overall response rate (ORR) of 35%, disease control rate (DCR) of 100% and median PFS of ~11 months in 20 evaluable Hepatic-Only MUM patients
- Historical % ORR and median PFS by other therapies in MUM have been low, ranging from ~0% to 5% confirmed ORR and ~2 to 3 months median PFS
- Neoadjuvant PoC: Ocular tumor shrinkage in 9 of 9 (100%) UM / MUM patients, including a neoadjuvant UM patient with a partial response at 1 month and a second neoadjuvant UM patient who was spared enucleation with ~80% tumor shrinkage at 4 months
- Investor webcast and call with management and key opinion leaders scheduled for Monday, April 24, 2023, at 8:00 am ET

SOUTH SAN FRANCISCO, Calif., April 23, 2023 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq: IDYA), a precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced further interim results from its Phase 2 clinical trial evaluating darovasertib and crizotinib combination in metastatic uveal melanoma (MUM) patients (ClinicalTrials.gov Identifier: NCT03947385).

"The observed efficacy in first-line metastatic uveal melanoma patients – including confirmed ORR of 45% and median PFS of ~ 7 months – is clinically significant and represents a potential paradigm shift for treating MUM patients. The interim data for the darovasertib and crizotinib combination treatment in MUM suggests a compelling clinical efficacy and tolerability profile," said Dr. Meredith McKean, M.D., MPH, Director, Melanoma and Skin Cancer Research at Sarah Cannon Research Institute.

"These clinical data, considered with the FDA's guidance from our recent Type C meeting, provides IDEAYA with a registrational trial design in first-line HLA-A2 negative MUM patients which includes a path to potential accelerated approval based on median PFS as the primary endpoint," said Dr. Darrin Beaupre, M.D., Ph.D., Chief Medical Officer, IDEAYA Biosciences.

There are currently no FDA approved therapies for MUM patients with HLA-A2*02:01 (HLA-A2) negative serotype. Current therapies for MUM have relatively low confirmed overall response rates and short median progression free survival (PFS), highlighting the high unmet medical need. The historical overall response rate (ORR) in MUM clinical trials has generally been reported with a confirmed ORR ranging from approximately 0% to 5%. The historical median PFS in MUM clinical trials has been reported ranging from approximately 2 to 3 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 pursuant to a clinical trial collaboration and drug supply agreement with Pfizer.

Clinical Data Update – Darovasertib and Crizotinib Combination in MUM

The company observed encouraging clinical activity in the Phase 2 clinical trial evaluating the darovasertib and crizotinib combination in first-line and any-line MUM patients. The reported Phase 2 clinical data are based on twenty (20) evaluable first-line and sixty-three (63) evaluable 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 as of the data analyses cutoff date of March 8, 2023. Enrollment in the darovasertib and crizotinib combination expansion dose cohort of the Phase 2 clinical trial is ongoing.

In the twenty (20) evaluable first-line MUM patients in the expansion cohort, the investigator-reviewed data by RECIST 1.1 include:

- 45% confirmed Overall Response Rate (ORR) in First-Line MUM: 9 of 20 evaluable patients had a confirmed partial response (PR)
- 90% Disease Control Rate (DCR) in First-Line MUM: 18 of 20 evaluable patients showed disease control, including 9 confirmed PRs, 1 unconfirmed PR and 8 stable disease
- ~7 months median Progression Free Survival (PFS) in First-Line MUM

In the sixty-three (63) evaluable any-line MUM patients at the expansion dose, the investigator-reviewed data by RECIST 1.1 include:

- 30% confirmed Overall Response Rate (ORR) in Any-Line MUM: 19 of 63 evaluable patients had a confirmed partial response (PR); the Any-Line MUM patients were heavily pre-treated, with 63% of patients having received 1 or more prior lines of treatment and 43% of patients having received 2 or more prior lines of treatment in the metastatic setting
- 87% Disease Control Rate (DCR) in Any-Line MUM: 55 of 63 evaluable patients showed disease control, including 19 confirmed PRs, 4 unconfirmed PRs and 32 stable disease
- ~7 months median Progression Free Survival (PFS) in Any-Line MUM
- Observed median PFS increased versus median PFS of ~5 months previously reported in September 2022 with thirty-five (35) evaluable Any-Line MUM patients

There were twenty (20) evaluable hepatic-only MUM patients, including first-line and pre-treated patients with only hepatic metastases, for whom the investigator-reviewed data by RECIST 1.1 include:

- 35% confirmed Overall Response Rate (ORR) in Hepatic-Only MUM: 7 of 20 evaluable patients had a confirmed partial response (PR)
- 100% Disease Control Rate (DCR) in Hepatic-Only MUM: 20 of 20 evaluable patients showed disease control, including 7 confirmed PRs, 1 unconfirmed PR and 12 stable disease
- ~11 months median Progression Free Survival (PFS) in Hepatic-Only MUM

These data demonstrate robust clinical efficacy of the darovasertib and crizotinib combination in first-line and any-line MUM patients.

The darovasertib and crizotinib combination has a manageable adverse event profile in MUM patients (n=68), with a low rate of drug-related serious adverse events (SAEs). Patients reported predominantly Grade 1 or 2 drug-related adverse events (AEs): 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. Four (6%) patients discontinued treatment with either darovasertib or crizotinib due to a drug-related adverse event.

FDA Guidance in Type C Meeting Supports Initiation of Potential Registrational Trial

IDEAYA is targeting to initiate a potential registration-enabling Phase 2/3 clinical trial in Q2 2023 in first-line HLA-

A2 negative MUM patients. The Phase 2/3 clinical trial design incorporates guidance and feedback from the FDA following a recent Type C meeting.

The protocol includes an integrated Phase 2/3 open-label study-in-study design in first-line MUM patients with an HLA-A*02:01 negative serotype. The clinical trial design employs a Phase 2 portion with median PFS as a primary endpoint for potential accelerated approval. Patients enrolled in Phase 2 will continue on treatment within the same clinical trial and will be considered together with additional enrolled patients to evaluate OS in support of a potential Phase 3 registrational trial.

In the Phase 2 portion of the clinical trial, approximately 230 patients will be randomized on a 2:1 basis for treatment with the darovasertib and crizotinib combination in the treatment arm or investigators choice in the control arm, selected from a combination of ipilimumab (ipi) and nivolumab (nivo), PD1-targeted monotherapy or DTIC. The treatment arm of the Phase 2 portion includes a nested study to confirm the move forward combination dose for the integrated Phase 2/3 clinical trial – including cohorts at the Phase 2 expansion doses of (i) darovasertib 300 mg BID + crizotinib 200 mg BID and (ii) darovasertib 200 mg BID + crizotinib 200 mg BID. Under the nested study design, patients enrolled in the cohort at the move forward dose will be included within the Phase 2/3 registrational clinical trial. The Phase 2 portion of the clinical trial contemplates an efficacy and safety data set of approximately 200 patients randomized 2:1 with the treatment arm at the move forward dose to support a potential accelerated approval based on median PFS by blinded independent central review (BICR) as a primary endpoint.

Patients enrolled in Phase 2 at the selected dose would continue on treatment and be included in the Phase 3 study analysis, supplemented by enrollment of approximately 120 additional patients into the Phase 3 portion of the clinical trial with 2:1 randomization on the same basis as the Phase 2 portion. Efficacy data from the Phase 3 could support potential approval using median OS as a primary endpoint.

Clinical Data Update – Darovasertib in (Neo)Adjuvant Primary UM

The company observed further evidence of encouraging clinical activity for darovasertib as neoadjuvant therapy in primary uveal melanoma (UM), including responses in primary ocular tumor lesions. Data was reported from an ongoing investigator sponsored trial (IST) evaluating darovasertib in (neo)adjuvant uveal melanoma, from compassionate use protocol(s) and from the company's Phase 1/2 clinical trial evaluating darovasertib as monotherapy and in combination with crizotinib. Best ocular tumor response is reported based on maximal percentage reduction in measured apical height or longest basal diameter.

Collectively, these data further substantiate clinical proof of concept (PoC) for the use of darovasertib in the (neo)adjuvant uveal melanoma setting:

- Ocular tumor shrinkage by investigator review in 9 of 9 (100%) UM (n=6) or MUM (n=3) patients treated as monotherapy or in combination with crizotinib, including a neoadjuvant UM patient treated with darovasertib with a partial response at 1 month, and a second neoadjuvant UM patient treated with the darovasertib and crizotinib combination with ~80% ocular tumor shrinkage at 4 months who was spared enucleation, as described below.
- A UM patient who was already blind in one eye from vascular disease developed a large uveal melanoma lesion in his other eye and sought neoadjuvant treatment with a goal to avoid enucleation and potentially preserve vision in the affected eye to prevent blindness. This patient, who remains on therapy, was treated with darovasertib and crizotinib combination under a compassionate use protocol. The preliminary clinical data showed:
    - observed ~80% ocular tumor shrinkage after 4 months of treatment and remains on therapy
    - avoided enucleation of the affected eye, which we believe to be a first reported case of systemic

neoadjuvant therapy resulting in eye preservation
- prompt responsiveness to treatment, including progressive tumor shrinkage, as determined by investigator measurement of tumor apical height, over each month of treatment, including approximately 30% ocular tumor shrinkage after 1 month, with ocular lesion size reduced to approach threshold for plaque brachytherapy, and further ocular tumor shrinkage to ~50% after 2 months, ~70% after 3 months and ~80% after 4 months of treatment
- improved vision following course of treatment and treatment of a severe cataract: pretreatment vision score was 6/120, where 6/60 is legally blind; post-treatment vision score was 6/5, reflecting a greater than 20-fold improvement and resulting in better than normal vision. Vision scoring was based on AU meter measurement system: 6/6 m = 20/20 ft (normal vision).

"These additional clinical data underscore the potential for darovasertib as a (neo)adjuvant approach for the treatment of uveal melanoma patients. If clinically validated, this approach could significantly improve current primary treatment paradigms, which typically include radiotherapies and/or enucleation of the eye," said Prof. Anthony Joshua, MBBS Ph.D. FRACP, Head of the Department of Medical Oncology, Kinghorn Cancer Centre, St Vincent's Hospital/Garvan Medical Research Institute, Sydney, Australia.

IDEAYA is initiating a company-sponsored clinical trial to evaluate darovasertib as monotherapy in (neo)adjuvant uveal melanoma and is evaluating potential near-term clinical neoadjuvant endpoints such as organ preservation (avoiding enucleation) for large ocular tumors and reduction in radiation dose and/or vision preservation for small or medium ocular tumors.

IDEAYA is also supporting St. Vincent's Hospital Sydney Limited, which has initiated an ongoing IST captioned as "Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma" (NADOM) (NCT05187884), to evaluate darovasertib monotherapy in a neoadjuvant and adjuvant setting in primary UM patients.

Addressable Patient Population in MUM and UM

The potentially addressable patient population for metastatic uveal melanoma is estimated to include approximately 4,500 patients across U.S. and Europe, based on estimated annual incidence, and approximately 14,000 patients in total prevalence in the US and Europe. (Neo)Adjuvant UM represents a significant expansion opportunity for darovasertib – with a potential annual incidence of approximately 8,700 patients aggregate in U.S. and Europe, and approximately 100,000 patients in total prevalence in the U.S. and Europe.

IDEAYA owns or controls all commercial rights in darovasertib, including in MUM and in UM, subject to certain economic obligations pursuant to the Novartis exclusive, worldwide license.

IDEAYA Investor Webcast and Conference Call

IDEAYA will host an investor webcast and conference tomorrow morning, Monday, April 24, 2023 at 8:00 am Eastern Time (ET), to present the further darovasertib and crizotinib Phase 2 clinical efficacy and tolerability data in metastatic uveal melanoma, and the potential registrational clinical trial design based on guidance and feedback from the recent FDA Type C meeting. The company will also provide a clinical data update for darovasertib in neoadjuvant uveal melanoma.

Presenters at the investor webcast and conference call will include Dr. Meredith McKean, M.D., MPH, Director, Melanoma and Skin Cancer Research at Sarah Cannon Research Institute, Prof. Anthony Joshua, MBBS Ph.D. FRACP, Head of the Department of Medical Oncology, Kinghorn Cancer Centre, St Vincent's Hospital/Garvan Medical Research Institute, Sydney, Australia, and Prof. Mark Shackleton, MBBS, Ph.D., FRACP, Professor of Oncology, Monash University, Director of Oncology, Alfred Health, Chair, Melanoma and Skin Cancer Trials, Melbourne, Australia, each of whom are key opinion leaders and clinical investigators. Yujiro S. Hata, Chief

Executive Officer of IDEAYA Biosciences, and Darrin Beaupre, M.D., Ph.D., Chief Medical Officer of IDEAYA Biosciences, will also present.

IDEAYA's darovasertib investor webcast presentation, as well as an updated corporate presentation, which incorporates the updated darovasertib clinical data as well as IDE397, IDE161 and Werner Helicase program updates from AACR 2023, 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 $373 million as of December 31, 2022, which it currently projects will be sufficient to fund its planned operations into 2026.

About IDEAYA Biosciences
IDEAYA is a 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
Certain statements contained herein are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These statements relate to future events and involve known and unknown risks, uncertainties and other factors that may cause the actual results, levels of activity, performance or achievements of IDEAYA Biosciences, Inc. (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, but not limited to, statements related to (i) the timing for initiation of and trial design for the darovasertib and crizotinib combination Phase 2/3 registrational trial, (ii) the timing and content of the IDEAYA investor webcast and conference call, (iii) the potential clinical benefit of darovasertib as a (neo)adjuvant therapy, and (iv) the potentially addressable patient population for MUM and (neo)adjuvant UM. 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 the Company'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, the Company's ability to successfully establish, protect and defend its intellectual property, the effects on the Company'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. 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 contained herein 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 IDEAYA in general, see the Company's periodic filings with the Securities and Exchange Commission, including the Company's 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.

Investor and Media Contact
IDEAYA Biosciences
Paul Stone
Senior Vice President and Chief Financial Officer
investor@ideayabio.com

SOURCE IDEAYA Biosciences, Inc.

---

https://media.ideayabio.com/2023-04-23-IDEAYA-Announces-Positive-Interim-Phase-2-Data-for-Darovasertib-and-Crizotinib-Combination-and-Successful-FDA-Type-C-Meeting-on-Registrational-Trial-Design-for-Accelerated-Approval-in-First-Line-Metastatic-Uveal-Melanoma