IDEAYA Announces Darovasertib Phase 2 Initiation in Neoadjuvant and Adjuvant Uveal Melanoma and Guidance for Clinical Data Update in Metastatic Uveal Melanoma

- Initiated Phase 2 clinical trial evaluating Darovasertib as neoadjuvant treatment of uveal melanoma prior to primary interventional treatment of enucleation or radiation therapy

- Clinical protocol includes neoadjuvant treatment with Darovasertib to maximum benefit up to 6 months, primary treatment, then up to 6 months of follow-up adjuvant therapy

- Neoadjuvant endpoints include eye preservation, reducing radiation and vision preservation; adjuvant endpoints include relapse free survival and useful vision

- UM represents an unmet medical need and potential clinical expansion opportunity with annual incidence of approximately 8,700 patients in the US and EU

- Targeting clinical data update for Darovasertib / Crizotinib Combination in MUM in 2023, including overall survival (OS) data

SOUTH SAN FRANCISCO, Calif., Jan. 23, 2023 /PRNewswire/ -- IDEAYA Biosciences, Inc. (NASDAQ: IDYA), a synthetic lethality focused precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced that it has initiated enrollment into a company-sponsored Phase 2 clinical trial to evaluate darovasertib as monotherapy in neo-adjuvant and adjuvant settings in primary, non-metastatic uveal melanoma (UM) patients. The company also provided guidance for an update on its Phase 2 clinical trial evaluating darovasertib in combination with crizotinib in metastatic uveal melanoma (MUM) patients in 2023.

"We are excited to clinically evaluate darovasertib as a neoadjuvant and an adjuvant treatment in uveal melanoma patients. This is a paradigm-shifting opportunity, as there are no approved systemic therapies in these settings. The preliminary clinical data shows clear evidence of anti-tumor activity and supports further clinical evaluation of darovasertib to determine its potential to either save the eye by avoiding enucleation, or to reduce the tumor thickness in the eye, enabling treatment with less radiation to preserve vision," said Dr. Carol Shields, M.D., Chief, Ocular Oncology Service at Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University.

"The primary tumor shrinkage we are observing from just a single month of therapy in our investigator-sponsored NADOM study is very promising. We are looking forward to seeing even greater benefits in the IDEAYA-sponsored Phase 2 study where the protocol provides for neoadjuvant treatment to maximum response," said Professor Anthony Joshua, MBBS, PhD, FRACP, Head Department of Medical Oncology, Kinghorn Cancer Centre, St. Vincent's Hospital Sydney.

"We are taking a comprehensive approach to treatment of ocular tumors. We plan to treat primary UM with darovasertib monotherapy as neoadjuvant therapy prior to enucleation or radiation treatments, and then as follow-up adjuvant therapy after the primary interventional treatment. We are also preparing to initiate a registrational clinical trial to treat patients who develop metastatic uveal melanoma, which predominantly presents as liver metastasis, with darovasertib in combination with crizotinib," said Dr. Darrin M. Beaupre, M.D., Ph.D., Senior Vice President and Chief Medical Officer, IDEAYA Biosciences.

Darovasertib is a potent, selective small molecule inhibitor of protein kinase C (PKC). Mutations in GNAQ or GNA11 (GNAQ/11) or related proteins occur in approximately 95% of patients with uveal melanoma (UM) and

activate the PKC signaling pathway, driving tumor progression. The FDA has designated darovasertib as an Orphan Drug in Uveal Melanoma. As presented at IDEAYA's Investor R&D Day in December 2022, Darovasertib has demonstrated tumor shrinkage and clinical benefit in 5 of 5 patients with an ocular tumor, including 3 UM patients from the IST as measured by ultrasound, and 2 MUM patients with an ocular lesion from IDEAYA's ongoing IDE196-001 clinical trial, including 1 MUM patient as measured by PET scan, and 1 MUM patient as measured by MRI.

Uveal melanoma is a rare, lethal form of melanoma that arises from melanocytes of the iris, the ciliary body, or most commonly the choroid, with an annual potential incidence of approximately 8,700 patients aggregate in US and Europe. Current approaches for treatment of primary UM depend on tumor size and location – enucleation of the eye for large tumors and radiation therapy (e.g., plaque brachytherapy) for small or medium tumors, which consequential vision impairment.

IDEAYA has initiated a company-sponsored Phase 2 clinical trial evaluating darovasertib as monotherapy in neoadjuvant and adjuvant UM. Pursuant to the protocol, in one cohort UM patients with large tumors will be treated with darovasertib until maximum benefit or six months, at which time they will undergo a primary interventional treatment. The endpoint for this large-tumor cohort is eye preservation – e.g., a patient who would otherwise have undergone enucleation is instead eligible for radiation treatment. In another cohort, UM patients with small or medium tumors will be treated with darovasertib until maximum benefit or six months, at which time they will undergo radiation therapy. Endpoints for this small- or medium-tumor cohort include (i) reducing the radiation dose that the patient received, relative to the radiation dose they would have otherwise received without the neoadjuvant treatment, and (ii) functional vision preservation. Each of the two cohorts will include up to six months of follow-up adjuvant therapy after the primary interventional treatment to evaluate relapse-free survival and useful vision.

In addition to IDEAYA's Phase 2 clinical trial, the company is also continuing to support the ongoing investigator sponsored trial (IST), captioned as "Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma" (NADOM), led by St. Vincent's Hospital in Sydney with participation of Alfred Health and the Royal Victorian Eye and Ear Hospital in Melbourne.

IDEAYA owns or controls all commercial rights in darovasertib, subject to certain economic obligations under its exclusive, worldwide license with Novartis.

IDEAYA is also evaluating darovasertib in combination with crizotinib in MUM patients in a Phase 2 clinical trial. The company is targeting a clinical data update on the darovasertib and crizotinib combination in MUM in 2023, including overall survival (OS) data.

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 early 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) the benefits of darovasertib as a neoadjuvant and an adjuvant treatment in uveal melanoma patients and (ii)the initiation of a registrational clinical trial and timing of a clinical data update for darovasertib in combination with crizotinib in patients with metastatic uveal melanoma. 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 November 8, 2022 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

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