IDEAYA Biosciences Announces Positive Interim Phase 2 Data for Darovasertib and Successful FDA Type C Meeting on Registrational Trial Design for Regulatory Approval in Neoadjuvant Uveal Melanoma

- Phase 2 company-sponsored and IST neoadjuvant uveal melanoma (UM) clinical data update in 49 evaluable patients, demonstrates ~49% of patients with ≥30% tumor shrinkage by product of diameters, and ~61% eye preservation rate for enucleation patients
- Targeting to initiate Phase 3 randomized registrational trial in neoadjuvant UM following finalization of the clinical protocol with FDA
- Clinical endpoints supportive of full approval based on FDA guidance: Eye preservation rate as the primary endpoint for enucleation patients. Time to vision loss as the primary endpoint for plaque brachytherapy patients. No detriment to Event-Free-Survival (EFS) in the treatment arms is a secondary endpoint
- Discussions ongoing with FDA to include ORR as a potential surrogate and composite endpoint to support earlier approval scenarios
- Based on FDA meeting, potential for consideration of broad indication label in neoadjuvant UM for subjects with low, intermediate, and high risk for metastatic disease
- Pending FDA discussions, we project registrational trial enrollment will be ~400 patients
- North America, Europe, and Australia annual incidence of primary UM is projected to be ~12k patients where there are currently no FDA-approved therapies
- Investor webcast with Company management and KOL scheduled for Mon Sept 23, at 8am ET

SOUTH SAN FRANCISCO, Calif., Sept. 23, 2024 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA), a precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced positive interim Phase 2 clinical trial data for darovasertib in neoadjuvant uveal melanoma (UM) and a successful FDA Type C meeting on registrational trial design for regulatory approval in neoadjuvant UM.

"Darovasertib has demonstrated compelling preliminary clinical efficacy and a favorable AE profile in the neoadjuvant UM setting, with approximately 49% of patients demonstrating greater than 30% tumor shrinkage and importantly approximately 61% eye preservation rate for enucleation patients. The primary clinical endpoints supported by discussions with the FDA of eye preservation and time to vision loss are clinically meaningful for neoadjuvant UM patients, and darovasertib has the potential to provide a new standard of care in this setting," said Dr. Carol L. Shields, M.D., Chief of the Ocular Oncology Service at Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University.

"The successful FDA Type C meeting provides darovasertib a potential registrational path in neoadjuvant UM, using primary clinical endpoints of eye preservation and time to vision loss, with no detriment to EFS in the treatment arms as a secondary endpoint. Based on the highly promising preliminary clinical efficacy and manageable safety profile observed with darovasertib and the high unmet medical need of neoadjuvant UM, we are excited to advance darovasertib rapidly to a registrational trial in this indication," said Dr. Darrin Beaupre, M.D., Ph.D., Chief Medical Officer, IDEAYA Biosciences.

Darovasertib is a potent and selective protein kinase C (PKC) inhibitor being developed to broadly address primary and metastatic UM. Darovasertib is currently being evaluated in four ongoing clinical trials, two of which are in collaboration with Pfizer. The darovasertib and crizotinib combination in metastatic uveal melanoma (MUM) has FDA Fast Track designation.

IDE196-009 (NCT05907954) is a company-sponsored Phase 2 trial evaluating darovasertib as neoadjuvant treatment for UM prior to primary interventional treatment of enucleation or radiation therapy, and as adjuvant therapy following the primary treatment. In addition, there is an investigator-sponsored trial (IST), NCT05187884, evaluating darovasertib as a neoadjuvant UM treatment.

Phase 2 Clinical Data Update – Darovasertib in Neoadjuvant UM

The company observed further evidence of encouraging clinical activity from an ongoing company-sponsored Phase 2 trial (NCT05907954) evaluating darovasertib in neoadjuvant uveal melanoma. The data cut-off date is August 15th, 2024, with an enrollment cut-off of May 13th, 2024, for the Phase 2 company-sponsored trial. Collectively, these clinical efficacy data from the Phase 2 company-sponsored and IST further substantiate clinical proof of concept for the use of darovasertib in the neoadjuvant uveal melanoma setting.

Clinical data update highlights include:

- 31 enucleation and 18 plaque brachytherapy evaluable UM patients treated with darovasertib neoadjuvant therapy in Phase 2 company-sponsored and IST trials
- ~59% (29 of 49) of patients with≥20% ocular tumor shrinkage by product of diameters
- ~49% (24 of 49) of patients with≥30% ocular tumor shrinkage by product of diameters
- ~61% (19 of 31) eye preservation rate observed
- Evidence of visual preservation observed by reducing the amount of radiation associated with plaque brachytherapy
- Manageable AE profile observed from Phase 2 company-sponsored trial (n=38), including 11% grade 3 or higher AEs, and 5% serious AE rate. The discontinuation rate observed was 3%. The most common AEs observed included diarrhea, nausea, vomiting and fatigue.

IDEAYA's ocular oncology advisory board recommended product of diameters for tumor measurement to determine overall response rate (ORR) criteria in ocular melanoma. In IDEAYA's ongoing Phase 2 clinical study with darovasertib, a ≥20% ocular tumor shrinkage by product of diameters correlates to clinical benefit, including eye sparing for enucleation UM patients and visual preservation for plaque brachytherapy UM patients.

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

IDEAYA is targeting to initiate a potential registration-enabling Phase 3 randomized clinical trial in neoadjuvant UM patients following finalization of the clinical protocol with the FDA. The randomized Phase 3 clinical trial design incorporates guidance and feedback from the U.S. FDA following a recent Type C meeting.

In the Phase 3 clinical trial, we currently project approximately 400 patients will be randomized for treatment with darovasertib in the treatment arm or the control arm, with potential modifications pending further FDA feedback. Based on the currently

targeted clinical trial design, there will be 2 cohorts enrolled: 1) enucleation eligible UM patients, 2) plaque brachytherapy eligible UM patients. For the enucleation cohort, the randomization will be with or without darovasertib as neoadjuvant therapy. For the plaque brachytherapy cohort, the randomization will be darovasertib followed by plaque brachytherapy versus plaque brachytherapy alone.

Key highlights of the target registrational trial design in neoadjuvant UM, based on FDA guidance and information provided in IDEAYA's FDA briefing book:

- Eye preservation rate is the primary endpoint for enucleation UM patients. Time to vision loss is the primary endpoint for plaque brachytherapy UM patients
- No detriment to Event-Free-Survival (EFS) in the treatment arms is a secondary endpoint
- Discussions ongoing with FDA to include ORR as a potential surrogate and composite endpoint to support earlier approval scenarios. The FDA briefing book notes a ≥20% ocular tumor shrinkage by product of diameters correlates to clinical benefit in the ongoing Phase 2 clinical study, including eye sparing for enucleation UM patients and visual preservation for plaque brachytherapy UM patients
- Primary endpoint of % eye preservation rate: The FDA briefing book notes objective to exceed lower bound of 10% eye preservation rate with a 95% confidence interval
- The registrational study will enroll UM patients with high risk for metastatic disease. Based on our preliminary projections, we anticipate the no detriment to EFS in the treatment arms for this high-risk population will take approximately 2-years of data maturity to initial readout
- Based on FDA meeting, potential for consideration of broad indication label in neoadjuvant UM for subjects with low, intermediate and high risk for metastatic disease
- 300mg BID darovasertib noted in FDA briefing book as the move-forward dose for registrational trial

Addressable Patient Population in neoadjuvant UM

Neoadjuvant UM represents a significant expansion opportunity for darovasertib – with a potential annual incidence of approximately 12,000 patients aggregate in North America, Europe, and Australia.

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

IDEAYA Investor Webcast and Conference Call

IDEAYA will host an investor webcast and conference call today, Monday, September 23, 2024 at 8:00 am ET, to present the darovasertib Phase 2 clinical efficacy and tolerability data, and the potential registrational clinical trial design based on guidance and feedback from the recent FDA Type C meeting.

Presenters at the investor webcast and conference call will include Dr. Carol L. Shields, M.D., Chief of the Ocular Oncology Service at Wills Eye Hospital and Professor of Ophthalmology at Thomas Jefferson University. IDEAYA management, Yujiro S. Hata, Chief Executive Officer and President of IDEAYA Biosciences, and Darrin Beaupre, M.D., Ph.D., Chief Medical Officer of IDEAYA Biosciences, will also serve as presenters.

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 today, Monday, September 23, 2024, at approximately 8:00 am ET.

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.

IDEAYA's updated corporate presentation is available on its website, at its Investor Relations page:https://ir.ideayabio.com/.

Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to (i) the timing of FDA regulatory guidance and a potential registration-enabling Phase 3 randomized clinical trial in neoadjuvant UM patients, (ii) the potential therapeutic benefits of IDEAYA therapeutics, (iii) the translation of preliminary clinical trial results into future clinical trial results, and (iv) the estimate of patient populations. 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, 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 Annual Report on Form 10-K dated February 20, 2024 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

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