IDEAYA Biosciences Announces Positive Phase 2 Data for Darovasertib in the Neoadjuvant Setting of Primary Uveal Melanoma in a Proffered Paper Oral Presentation at ESMO 2025

- 83% (78/94) of patients demonstrated ocular tumor shrinkage, with 54% (51/94) achieving ≥20% tumor shrinkage
- 57% (24/42) eye preservation rate in enucleation (EN) recommended patients, which increased to 95% (19/20) in patients achieving ≥20% ocular tumor shrinkage
- 70% (26/37) of plaque brachytherapy (PB) eligible patients achieved a reduction in predicted radiation dose to the eye from baseline, resulting in 65% (24/37) of patients having lower predicted risk of vision loss 3-years post-PB treatment
- ~55% (29/53) of EN eligible and ~61% (23/38) of PB eligible patients demonstrated an improvement in baseline visual acuity scores (VAS) during neoadjuvant darovasertib treatment, with a mean gain of 17 and 10 letters, respectively
- Darovasertib has received U.S. FDA Breakthrough Therapy Designation in the neoadjuvant setting of primary uveal melanoma for EN eligible patients

SOUTH SAN FRANCISCO, Calif., Oct. 20, 2025 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq: IDYA), a leading precision medicine oncology company, today presented positive clinical data from their ongoing Phase 2 OptimUM-09 trial of neoadjuvant darovasertib in patients with primary uveal melanoma (UM). The data were presented in a Proffered Paper oral presentation by Dr. Marcus Butler, M.D., Associate Professor, Princess Margaret Cancer Center at the University of Toronto, at the 2025 European Society of Medical Oncology (ESMO) in Berlin, Germany. There are currently no approved systemic therapies for patients with primary UM, and there is a critical unmet need for new treatment options that reduce the risk of eye removal and vision loss and have the potential to delay or prevent progression to metastatic disease.

Data presented at ESMO were from a total of 95 primary UM patients, including 56 patients recommended for EN (Cohort 1) and 39 patients eligible for PB (Cohort 2) as of a data cut-off date of June 13, 2025. Patients were enrolled into Cohort 1 or Cohort 2 based on investigator recommended primary local therapy at baseline, as determined by tumor size and proximity to critical eye structures. Patients received neoadjuvant darovasertib for up to 12 cycles (or maximum benefit) prior to definitive primary local therapy. As of the cut-off date, only 94 patients were evaluable for efficacy, which reflects one patient in Cohort 2 that was excluded per protocol based on not yet receiving at least one dose of study drug and at least one post-baseline tumor assessment. Patients who derive benefit from darovasertib in the neoadjuvant setting are then eligible to receive up to six additional cycles of darovasertib as adjuvant therapy and will be monitored for disease recurrence and changes in visual acuity.

"We are highly encouraged by the data from OptimUM-09 demonstrating meaningful tumor shrinkage, eye preservation and reduced predicted risk of severe vision loss, and believe these results strongly support the potential for darovasertib as the first systemic therapy for the neoadjuvant treatment of primary uveal melanoma," said Darrin Beaupre, M.D., Ph.D., Chief Medical Officer of IDEAYA Biosciences.

"These data highlight the potential of neoadjuvant darovasertib to significantly improve the treatment paradigm for patients requiring enucleation or plaque brachytherapy in primary uveal melanoma, helping them preserve their

eye and preserve their vision with a single therapy," said Marcus O. Butler, M.D., Associate Professor, Princess Margaret Cancer Center, and lead investigator on the study.

Key Findings from OptimUM-09

- Tumor shrinkage and eye preservation
    - Patients recommended for EN (Cohort 1) demonstrated robust ocular tumor shrinkage following treatment with darovasertib, with approximately 84% (47/56) experiencing any reduction in tumor size by product of diameters, and 50% (28/56) and 37.5% (21/56) achieving a ≥20% and ≥30% reduction, respectively.
    - Similarly, among patients eligible for PB (Cohort 2) approximately 82% (31/38) achieved any reduction in ocular tumor size by product of diameters, with 60.5% (23/38) and 44.7% (17/38) achieving a ≥20% and ≥30% reduction, respectively.
    - Among 42 patients in Cohort 1 who had completed primary local therapy at the time of the data cut, a 57.1% (24/42) eye preservation rate was observed. Of these patients, 75% (18/24) received PB and 25% (6/24) received external beam radiation instead of the EN procedure.
    - Among patients in Cohort 1 with ≥20% tumor shrinkage prior to primary local therapy, the eye preservation rate jumped to 95% (19/20). Based in part on these data, and after discussions with the FDA, the company has proposed ≥20% tumor shrinkage as the definition of response in primary UM for their ongoing Phase 3 trial (OptimUM-10) of darovasertib in the neoadjuvant setting.
- Predicted radiation reduction and visual preservation
    - Among 37 evaluable patients with paired dosimetry in Cohort 2, approximately 70% (26/37) observed any reduction in the predicted dose of radiation to critical eye structures (fovea, disc, lens) compared to baseline following treatment with darovasertib in the neoadjuvant setting, with approximately 35-40% experiencing a ≥20% reduction. This magnitude of reduction is relevant since a similar decrease in radiation to the tumor apex is associated with improved visual outcomes (Perez et al, Int J Radiat Oncol Biol Phys. 2014; Kheir et al, Adv Radiat Oncol. 2022; Saconn et al, Int J Radiat Oncol Biol Phys. 2010; Puusaari et al, Invest Ophthalmol Vis Sci. 2004).
    - 64.9% (24/37) of the evaluable patients in Cohort 2 had a reduced predicted risk of vision loss at 3-years post-PB based on a vision prognostic tool developed at the Cleveland Clinic (Aziz et al; JAMA Ophthalmol. 2016) that is used to predict the risk of developing 20/200 vision (legal blindness) or worse following radiation administered during PB.
- Improved visual acuity during neoadjuvant treatment
    - 54.7% (29/53) of patients in Cohort 1 and 60.5% (23/38) of patients in Cohort 2 demonstrated an improvement in visual acuity scores (VAS) during neoadjuvant darovasertib therapy, compared to baseline.
    - Patients in Cohort 1 with improved VAS scores from baseline had a mean gain of 17 letters while on treatment, with ~72% (21/29) gaining ≥5 letters at 2 consecutive visits.
    - Similarly, patients in Cohort 2 with improved VAS scores from baseline had a mean gain of 10 letters while on treatment, with ~52% (12/23) gaining ≥5 letters at 2 consecutive visits.
- Safety and Tolerability:
    - Darovasertib was generally well tolerated with manageable adverse events, which included low-grade diarrhea, nausea, vomiting, and fatigue.
    - Grade 3 or higher treatment related adverse events (TRAEs) occurred in 16.8% (16/95) of patients.

Rates of treatment-related serious adverse events (5.3%) and treatment discontinuation due to adverse events (6.3%) were low.

IDEAYA is conducting a Phase 3 trial (OptimUM-10) of darovasertib as a single-agent in the neoadjuvant setting of primary UM. The company is also targeting to report topline median progression free survival data from its registration-enabling Phase 2/3 trial (OptimUM-02) evaluating darovasertib in combination with crizotinib in first-line, HLA*A2:01-negative metastatic UM by the end of 2025 to Q1'26 to enable a potential accelerated approval filing in the United States.

About IDEAYA Biosciences

IDEAYA is a precision medicine oncology company committed to the discovery, development, and commercialization of transformative therapies for cancer. Our approach integrates expertise in small-molecule drug discovery, structural biology and bioinformatics with robust internal capabilities in identifying and validating translational biomarkers to develop tailored, potentially first-in-class targeted therapies aligned to the genetic drivers of disease. We have built a deep pipeline of product candidates focused on synthetic lethality and antibody-drug conjugates, or ADCs, for molecularly defined solid tumor indications. Our mission is to bring forth the next wave of precision oncology therapies that are more selective, more effective, and deeply personalized with the goal of altering the course of disease and improving clinical outcomes for patients with cancer.

Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to (i) the potential therapeutic benefits of IDEAYA therapeutics, including combination therapies; (ii) the safety and efficacy profile of darovasertib; (iii) the ongoing Phase 3 registrational trial (OptimUM-10) of darovasertib; (iv) the reporting of topline PFS data from the Phase2/3 (OptimUM-02) trial of darovasertib in combination with crizotinib by the end of 2025 to Q1'26; and (v) the potential U.S. accelerated approval filing for the darovasertib and crizotinib combination in first-line HLA*A2 negative metastatic UM. 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, including those related to success in early clinical trials, especially if based on a small patient sample, does not ensure that later clinical trials will be successful, and early results, including interim results, from a clinical trial do not necessarily predict final results or results of future trials. 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. Neither Breakthrough Therapy, Orphan Drug Designation, nor an accelerated approval filing necessarily translates into approval of a drug. 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 18, 2025 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

Investor and Media Contact

IDEAYA Biosciences
Joshua Bleharski, Ph.D.
Chief Financial Officer
investor@ideayabio.com

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