IDEAYA Reports Clinical Data from Phase 2 Expansion Dose of Darovasertib and Crizotinib Synthetic Lethal Combination in Heavily Pre-Treated Metastatic Uveal Melanoma

- 100% Disease Control Rate (DCR): 16 of 16 evaluable patients demonstrate tumor shrinkage
- 31% Overall Response Rate (ORR): 4 of 13 patients with > 2 post-baseline scans had a confirmed Partial Response (PR); no patients have come off-treatment prior to the 2nd scan
- 46% of patients (6 of 13) with > 2 post-baseline scans observed >30% tumor shrinkage, including an unconfirmed PR awaiting next tumor assessment
- Manageable side effect profile observed with darovasertib and crizotinib combination at the Phase 2 expansion dose, with predominantly Grade 1 or 2 drug-related adverse events
- Darovasertib and crizotinib expansion dose selected for potential registrational studies
- Investor Day webcast and conference call scheduled for this morning, December 7, 2021 at 8:30 am ET, to present darovasertib and crizotinib Phase 1/2 clinical efficacy and tolerability

SOUTH SAN FRANCISCO, Calif., Dec. 7, 2021 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA), a synthetic lethality focused precision medicine oncology company committed to the discovery and development of targeted therapeutics, provided a clinical data update for the Phase 1/2 trial evaluating darovasertib and crizotinib synthetic lethal combination in metastatic uveal melanoma (MUM) patients.

"The partial responses, percentage of patients with tumor shrinkage and disease control rate observed from the darovasertib and crizotinib synthetic lethal combination in heavily pre-treated MUM patients represents a new clinical efficacy benchmark and provides an opportunity to deliver meaningful patient impact in this high unmet medical need patient population," said Meredith McKean, M.D., Sarah Cannon Research Institute at Tennessee Oncology, Associate Director, Melanoma and Skin Cancer Research.

"These data provide clinical proof-of-concept for the PKC and cMET synthetic lethal combination, and further validate IDEAYA's synthetic lethality platform. We look forward to exploratory evaluation of this novel PKC and cMET synthetic lethal combination in other potential tumor settings, including GNAQ/11 skin melanoma and MET-amplified and MET high expression tumors," said Yujiro S. Hata, President and Chief Executive Officer of IDEAYA Biosciences.

There are currently no FDA approved therapies for metastatic uveal melanoma or GNAQ/GNA11 solid tumors, highlighting the high unmet medical need. The historical overall response rate (ORR) in metastatic uveal melanoma has generally been reported with an ORR from approximately 0 to 5%, including: pembrolizumab and tebentafusp (each ~5%); MEK inhibitor selumetinib in combination with dacarbazine (3%); and cMET inhibitor cabozantinib monotherapy (~0%).

Darovasertib (IDE196) is a small molecule, potential first-in-class PKC inhibitor. IDEAYA is evaluating the synthetic lethal combination of darovasertib and crizotinib, a small molecule cMET inhibitor, pursuant to a clinical trial collaboration and drug supply agreement with Pfizer. The companies have agreed to support a target enrollment of approximately 40 patients into the ongoing Phase 1/2 clinical combination arm in MUM.

Clinical Data Update – Darovasertib and Crizotinib Combination

At the time of the data and analyses cutoff on November 25, 2021, twenty-two (22) heavily pre-treated (91% with prior therapies, and 59% with 2 or more prior therapies) MUM patients had enrolled in the darovasertib and crizotinib combination arm at the expansion dose, with sixteen (16) evaluable patients who have received one or more tumor scans and 6 patients who are awaiting their 1st tumor scan. Thirteen (13) patients have received two or more tumor scans for evaluation of potential responses. Reported data is preliminary and based on an unlocked database. Enrollment in the darovasertib and crizotinib combination arm of the clinical trial is ongoing.

The company observed encouraging clinical activity in Phase 1/2 clinical trial evaluating darovasertib and crizotinib synthetic lethal combination in metastatic uveal melanoma (MUM) patients in the expansion dose cohort.

The preliminary interim data includes:

- 100% Disease Control Rate (DCR): 16 of 16 evaluable patients with $\geq$1 post-baseline scan showed tumor shrinkage as determined by target lesion size reduction;
- 31% Overall Response Rate (ORR): 4 of 13 patients with $\geq$ 2 post-baseline scans had a confirmed partial response (PR) as determined by RECIST 1.1 based on investigator or central review; and no patients have come off-treatment prior to the 2^{nd} scan
- 46% of patients (6 of 13) with $\geq$ 2 post-baseline scans observed >30% tumor reduction, including one patient with an unconfirmed PR as determined by RECIST 1.1 is awaiting follow-on tumor scan.

These data provide clinical proof-of-concept for the darovasertib and crizotinib synthetic lethal combination treatment. These data also validate the company's translational research discovery that Phase 1 clinical response to darovasertib monotherapy associated with low cMETactivity, as measured by gene signature score.

The darovasertib and crizotinib combination therapy has a manageable side effect profile in MUM patients (n=22), with a low rate of drug-related serious adverse events (SAE's); predominantly Grade 1 or 2 drug-related adverse events. Eighteen (18) patients experienced a drug-related AE, of which six (6) patients observed Grade 3, and no patients observed Grade 4 or Grade 5.

Upcoming Milestones

IDEAYA has selected a darovasertib and crizotinib combination expansion dose to support potential registrational studies. The company is targeting regulatory feedback for potential darovasertib and crizotinib combination registrational path in the first half of 2022.

IDEAYA is also targeting a further clinical data readout for the darovasertib and crizotinib combination, including median progression free survival (mPFS) in MUM patients, in the first half of 2022.

Darovasertib Expansion Opportunities

IDEAYA is also evaluating other indications as potential expansion opportunities, including GNAQ/11 mutant skin melanoma being evaluated in an ongoing arm of the current clinical trial, and adjuvant uveal melanoma (UM) that the company anticipates will be initiated through an investigator sponsor clinical trial (IST) in the first half of 2022. The company also has exploratory evaluation ongoing of the PKC-cMET synthetic lethal hypothesis in additional tumor settings with MET-amplification and MET high expression, such as hepatocellular carcinoma (HCC).

IDEAYA Investor Day – Webcast and Conference Call

IDEAYA will host an Investor Day webcast and conference call this morning, December 7, 2021 at 8:30 am ET, to present darovasertib and crizotinib Phase 1/2 clinical efficacy and tolerability data, as well as clinical landscape, potential registrational strategies and expansion opportunities. Presenters at the Investor Day will include Dr. Meredith McKean, M.D., Sarah Cannon Research Institute at Tennessee Oncology, Associate Director, Melanoma and Skin Cancer Research, a key opinion leader and clinical investigator. Yujiro S. Hata, President and Chief Executive Officer, and other members of the IDEAYA management team will also present.

Corporate Updates

IDEAYA's Darovasertib Investor Day 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/) following the Investor Day event at approximately 10:30am ET.

IDEAYA had cash, cash equivalents and marketable securities of approximately $386 million as of September 30, 2021, which it believes will fund its planned operations into 2025.

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. IDEAYAs 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) the future patient impact of the darovasertib and crizotinib combination, (ii) the evaluation of the darovasertib and crizotinib combination in additional tumor settings, (iii) the timing of obtaining regulatory feedback for potential darovasertib and crizotinib combination registrational path, (iv) the timing of a further clinical data readout for the darovasertib and crizotinib combination, (v) the timing of initiation of an IST to evaluate darovasertib in adjuvant uveal melanoma and (vi) the extent to which IDEAYA's existing cash, cash equivalents, and marketable securities will fund its planned operations. 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, the effects on IDEAYA's business of the worldwide COVID-19 pandemic, 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 recent Quarterly Report on Form 10-Q filed on November 15, 2021 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

SOURCE IDEAYA Biosciences, Inc.

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