IDEAYA Announces IDE397 Phase 1 Clinical Pharmacodynamic Data and Phase 2 Initiation of Darovasertib and Crizotinib Combination

– Observed plasma SAM reduction in each of the first two dose escalation cohorts of the IDE397 Phase 1 clinical trial, satisfying the clinical protocol threshold of approximately 60% or greater plasma S-adenosyl methionine (SAM) pharmacodynamic (PD) reduction to initiate IDE397 tumor biopsy cohort for evaluation of tumor PD markers
– The GSK MAT2A option is exercisable with a $50M option exercise fee within a review period after IDEAYA's delivery of preclinical and clinical data from the Phase 1 dose escalation, including tumor PD data to be obtained from the tumor biopsy cohort
– IDE397 has initiated the third cohort of the dose escalation portion of the Phase 1 clinical trial, and has enrolled multiple solid tumor types with MTAP-deletion, including NSCLC, pancreatic cancer and thymic cancer, with no drug-related serious adverse events reported
– Earlier reported unconfirmed partial responses (PR) have been confirmed in a patient in each of the darovasertib / crizotinib combination and the darovasertib / binimetinib combination arms, with a 56.5% and 51.7% tumor reduction, respectively

SOUTH SAN FRANCISCO, Calif., June 28, 2021 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA), a synthetic lethality focused precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced updates for its Phase 1 clinical trial evaluating IDE397 in patients having solid tumors with MTAP deletion and Phase 1/2 clinical trial evaluating darovasertib combination therapies in metastatic uveal melanoma (MUM).

"The observation of a clinical pharmacodynamic signal in the initial cohorts of the IDE397 dose escalation study is significant. Modulation of plasma SAM is evidence of target engagement and supports our preclinical observations that IDE397 is a highly potent and active MAT2A inhibitor," said Mark Lackner, Ph.D., Senior Vice President, Head of Biology and Translational Sciences of IDEAYA Biosciences.

"We continue to be encouraged by the early clinical responses observed in the daraovasertib combination treatments in heavily pretreated patients and are excited to initiate our Phase 2 clinical trial to further evaluate the darovasertib and crizotinib combination in MUM patients," said Matthew Maurer, M.D., Vice President, Head of Clinical Oncology and Medical Affairs, IDEAYA Biosciences.

IDE397 in MTAP Deletion Solid Tumors

IDEAYA is evaluating IDE397, a potent and selective small molecule inhibitor targeting methionine adenosyltransferase 2a (MAT2A), as monotherapy in the dose escalation portion of a Phase 1 clinical trial in patients having solid tumors with methylthioadenosine phosphorylase (MTAP) deletion, a patient population estimated to represent approximately 15% of solid tumors.

The company is currently enrolling patients in the third cohort of the dose escalation portion of the IDE397 clinical trial. Four clinical trial sites are currently open for enrollment with an additional five sites targeted in the second half 2021. IDEAYA has entered into a collaboration with Tempus Labs to identify additional patients for the open clinical sites. The enrolled patients have tumors with MTAP deletion in non-small cell lung cancer (NSCLC), pancreatic cancer and thymic cancer. As of June 25, 2021, IDE397 has been generally well tolerated with only grade 1 drug-related adverse events, including constipation, nausea and fatigue. There were no reported drug-related serious adverse events, and no reported myelosuppression, or changes to bilirubin or to aminotransaminase (AST) or alanine aminotransferase (ALT) enzymes.

IDEAYA has met the criteria to initiate a IDE397 tumor biopsy cohort arm in each of the first two cohorts of the dose escalation study, with observed clinical pharmacodynamic (PD) modulation of plasma S-adenosyl methionine (SAM) satisfying the clinical protocol threshold of approximately 60% or greater. The PD data showed a maximal plasma SAM reduction from baseline of 68.9% and 88.0% for the first (n=2) and second (n=3) cohorts, respectively. The clinical protocol threshold was established based on IDE397 preclinical *in vivo* efficacy data in MTAP-deletion xenograft models. The company plans to obtain pre-treatment and post-treatment tumor biopsies from patients enrolled into this tumor biopsy cohort to evaluate tumor PD response, including measurement of tumor SAM and tumor symmetric dimethyl arginine (SDMA) biomarkers.

The PD data to be obtained from the IDE397 tumor biopsy cohort is expected to support an option data package for review by GlaxoSmithKline (GSK) in consideration of whether to exercise its exclusive option to develop and commercialize IDE397. The GSK option is exercisable within a certain period after IDEAYA delivers a data package comprising preclinical data and clinical data from the IDE397 monotherapy dose escalation portion of the Phase 1 clinical trial, including safety and tolerability data, pharmacokinetic data, and pharmacodynamic modulation of SAM and tumor SDMA. IDEAYA is leading early clinical development of IDE397. If GSK exercises its option and pays an option exercise fee of fifty million dollars ($50,000,000), GSK will lead later stage global clinical development and costs will be shared with GSK responsible for 80% and IDEAYA responsible for 20%. If GSK exercises the option, IDEAYA will be eligible to receive future development and regulatory milestones of up to $465 million, 50% of U.S. net profits, tiered royalties on global ex-U.S. net sales ranging from high single digit to sub-teen double digit percentages and certain commercial milestones of up to $475 million.

Darovasertib Combinations in Metastatic Uveal Melanoma (MUM)

IDEAYA is executing on its strategy to evaluate darovasertib combinations in MUM, including combinations of darovasertib and crizotinib, and independently, darovasertib and binimetinib, in each case under a clinical trial collaboration and supply agreement with Pfizer Inc.

The company initiated Phase 2 of the clinical trial evaluating darovasertib and crizotinib combination in MUM based on observed early clinical activity of this combination. In the first cohort of the dose escalation portion of the Phase 1 clinical trial, an earlier-reported unconfirmed partial response of 54.3% tumor reduction has subsequently confirmed with a 56.5% tumor reduction in a subsequent scan, which represents the deepest response observed to date in the Phase 1/2 clinical trial evaluating darovasertib as monotherapy or in combinations.

Drug-related adverse events observed in the darovasertib and crizotinib combination arm in MUM as of June 22, 2021 based on preliminary data from an unlocked database, primarily include: serious adverse events of syncope and hypotension, each of which resolved with patients continuing dosing; and adverse events that occurred in at least two treated patients of nausea, diarrhea, vomiting, edema, decreased appetite, rash, hypotension and syncope. The observed syncope and hypotension were transient, often occurring in the first week of dosing, and are being managed / mitigated through a one week run-in dosing regimen and by limiting use of certain concurrent medications such as diuretics.

In the darovasertib and binimetinib combination arm of the Phase 1 clinical trial, an earlier-reported unconfirmed partial response of 40.5% tumor reduction has been confirmed with a 51.7% tumor reduction in a subsequent scan.

Drug-related adverse events observed in the darovasertib and binimetinib combination arm in MUM, as of June 22, 2021 data cutoff based on preliminary data and analysis from an unlocked database, primarily include: serious adverse events of liver toxicity, nausea and vomiting, syncope and fall; and adverse events that occurred in greater than 10% of patients of nausea, vomiting, diarrhea, rash, edema, fatigue, hypotension and creatine phosphokinase increase.

As of June 22, 2021, IDEAYA has enrolled 30 MUM patients in the darovasertib and binimetinib combination arm, and 15 MUM patients in the darovasertib and crizotinib combination arm. IDEAYA is targeting a further clinical data update for darovasertib combination(s) in the second half of 2021. The company is planning to obtain FDA regulatory guidance on potential registration-enabling trial design for darovasertib monotherapy and/or darovasertib combination(s) in MUM in the second half of 2021 or the first half of 2022, respectively.

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

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 timing of additional clinical trial sites in the IDE397 Phase 1 dose escalation study, (ii) the obtention of pre-treatment and post-treatment tumor biopsies from patients enrolled into the IDE397 tumor biopsy cohort to evaluate PD response, (iii) exercise of the GSK option, cost sharing, milestone payments, profit share and royalties related to IDE397, and (iv) the timing of a clinical data update for either of the darovasertib combination arms and FDA guidance for potential darovasertib registrational pathway. 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 risk that results of earlier studies and trials may not be predictive of future trial results, the risk that regulatory authorities, including the FDA may not agree with IDEAYA's interpretation of the data from clinical trials of IDEAYA's drug candidates, the risk that that IDEAYA may experience delays in the commencement, enrollment, completion or analysis of clinical testing for its drug candidates, or significant issues regarding the adequacy of IDEAYA's clinical trial designs or the execution of its clinical trials may arise, which could result in increased costs and delays, or limit IDEAYA's ability to obtain regulatory approval, unexpected adverse side effects or inadequate therapeutic efficacy of IDEAYA's drug candidates that could delay or prevent clinical results, regulatory approval or commercialization, 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 the Company's business of the worldwide COVID-19 pandemic and other matters. 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 May 10, 2021 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

SOURCE IDEAYA Biosciences, Inc.

For further information: Investor and Media Contact, IDEAYA Biosciences, Paul Stone, Senior Vice President and Chief Financial Officer, investor@ideayabio.com

---

https://media.ideayabio.com/2021-06-28-IDEAYA-Announces-IDE397-Phase-1-Clinical-Pharmacodynamic-Data-and-Phase-2-Initiation-of-Darovasertib-and-Crizotinib-Combination