IDEAYA Announces IDE397 Clinical Program Update and ctDNA Molecular Responses Demonstrating Tumor Pharmacodynamic Modulation

- Initiated monotherapy expansion cohorts with enrollment open for NSCLC and esophagogastric tumors with MTAP deletion
- Initiated combination dose escalation cohorts with enrollment open for combinations with taxanes and separately, with potential first-in-class combinations, including pemetrexed
- Entered into Clinical Trial Collaboration and Supply Agreement with Amgen to clinically evaluate IDE397 in combination with AMG 193, Amgen's investigational MTA-Cooperative PRMT5 inhibitor
- ctDNA Molecular Responses observed in 3 of 4 (75%) patients in Cohorts 5 and 6, demonstrating target engagement and tumor pharmacodynamic modulation
- Delivered Option Data Package to GSK, including preclinical data and clinical data from the IDE397 monotherapy dose escalation study of the Phase 1 clinical trial

SOUTH SAN FRANCISCO, Calif., July 27, 2022 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA), a synthetic lethality focused precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced clinical program updates for IDE397, an investigational, potential best-in-class, small molecule MAT2A inhibitor being evaluated in an ongoing Phase 1/2 clinical trial (NCT04794699).

"We are excited to advance our clinical development of IDE397 and to progress our strategic collaborations with GSK and Amgen on this program. Delivery of the IDE397 Option Data Package to GSK represents an important milestone in our collaboration with GSK. The clinical collaboration with Amgen enables clinical evaluation of a potential first-in-class combination to inhibit two synthetic lethal nodes within the MTAP pathway – MAT2A and PRMT5, providing a complementary approach for targeting MTAP-null tumors," said Yujiro S. Hata, President and Chief Executive Officer, IDEAYA Biosciences.

"The ctDNA molecular response clinical pharmacodynamic data reflects evidence of dose-dependent tumor pharmacodynamic modulation and target engagement at clinically achievable doses in patients having MTAP-deleted tumors," said Dr. Michael White, Senior Vice President and Chief Scientific Officer, IDEAYA Biosciences.

IDE397 is a potent and selective small molecule inhibitor targeting methionine adenosyltransferase 2a (MAT2A), in patients having solid tumors with methylthioadenosine phosphorylase (MTAP) deletion. The MTAP deletion patient population is estimated to represent approximately 15% of solid tumors, including approximately 15% of NSCLC, 28% of esophageal, 26% of bladder, and 10% of esophagogastric cancers.

IDEAYA is leading early clinical development of IDE397, in collaboration with GSK, in an ongoing Phase 1/2 clinical trial. The company has initiated and is actively enrolling patients into monotherapy expansion cohorts, including in NSCLC and esophagogastric cancer. The company selected Cohort 5 dose as its Phase 2 expansion dose, while it continues to dose escalate into Cohort 6; it has not yet determined a maximum tolerated dose.

IDEAYA has also initiated and is actively enrolling patients into combination cohorts to evaluate IDE397 in combination with docetaxel in NSCLC, with paclitaxel in esophagogastric cancer and with pemetrexed in NSCLC. IDEAYA also plans to clinically evaluate IDE397 in combination with AMG 193, Amgen's investigational MTA-Cooperative PRMT5 inhibitor, pursuant to a Clinical Trial Collaboration and Supply Agreement with Amgen. In preclinical studies, IDEAYA observed a complete response from evaluation of IDE397 and a representative MTA-cooperative PRMT5 inhibitor combination therapy in *in vivo* xenograft models.

IDEAYA reported additional clinical pharmacodynamic (PD) data from translational analysis of patient liquid

biopsy samples based on circulating tumor DNA, or ctDNA, molecular responses. These data were obtained using the GuardantOMNI™, a diagnostic panel for genomic analysis of ctDNA. Molecular responses were evaluated based on changes in mean variant allele frequency, or VAF, on-treatment as compared to VAF levels at baseline. Patients whose ctDNA showed a reduction of greater than 50% mean VAF following treatment with IDE397 were characterized as having a molecular response (ctDNA MR) as reported in Zhang et al (Cancer Discovery, August 2020).

The IDE397 ctDNA molecular response data demonstrates target engagement and a dose-dependent tumor pharmacodynamic modulation. Molecular responses based on ctDNA were evaluable for thirteen patients with liquid biopsy samples available at baseline and after first treatment cycle. Across dose escalation Cohort 1 thru Cohort 6, a ctDNA molecular response was observed in four (4) of thirteen (13) evaluable patients (31%). Significantly, ctDNA molecular responses were observed in three (3) of four (4) evaluable patients (75%) treated with IDE397 at higher doses in Cohorts 5 and 6, as well as in two (2) of two (2) NSCLC evaluable patients (100%). This is indicative of a preliminary signal of clinical activity and is consistent with preclinical in vivo observations in patient-derived xenograft models.

IDEAYA has delivered an IDE397 option data package to GSK. The GSK option data package comprises preclinical data and clinical data from the IDE397 monotherapy dose escalation study of the Phase 1 clinical trial.

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 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 clinical evaluation of IDE397 in combination with AMG 193. 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, the ongoing military conflict between Russia and Ukraine, 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 May 10, 2022 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/2022-07-27-IDEAYA-Announces-IDE397-Clinical-Program-Update-and-ctDNA-Molecular-Responses-Demonstrating-Tumor-Pharmacodynamic-Modulation