IDEAYA Announces Phase 2 MAT2A Inhibitor, IDE397, Achieves First-Patient-In for Multiple Combination Cohorts in MTAP-Deletion Tumors

- First patient dosed in IDE397 combination with pemetrexed, representing a novel and potential first-in-class combination in MTAP-deletion tumors
- First patient dosed in IDE397 combination with taxane in MTAP-deletion tumors
- Clinical strategy for IDE397 also includes combination with AMG 193, Amgen's Phase 1 investigational MTA-cooperative PRMT5 inhibitor in MTAP-deletion tumors

SOUTH SAN FRANCISCO, Calif., Oct. 18, 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 clinical development of IDE397 in multiple combination therapies. The combination of IDE397 with standard-of-care agents such as pemetrexed and taxanes is supported by mechanistic rationale and compelling preclinical data," said Dr. Anthony W. Tolcher, M.D., FRCPC, Texas Oncology – San Antonio Medical Center and a Principal Investigator on IDEAYA's Phase 1/2 clinical trial.

"The initiation of clinical combinations is the next step of our clinical development plan to evaluate IDE397 in patients having tumors with MTAP deletion. Clinical data from the Phase 1 monotherapy dose escalation reflects robust tumor target engagement and an observed therapeutic window, positioning IDE397 to evaluate clinical efficacy – in Phase 2 monotherapy expansion and Phase 1 combination cohorts," said Dr. Matt Maurer, M.D., Vice President, Head of Clinical Oncology and Medical Affairs, 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.

The company has initiated and is actively enrolling patients into monotherapy expansion cohorts, with a focus on squamous cell NSCLC and esophagogastric cancer, consistent with preclinical efficacy and translational data.

IDEAYA is also evaluating IDE397 in multiple combination cohorts. The combinations include pemetrexed and taxanes, which are standard-of-care agents utilized as early-line therapies in NSCLC, mesothelioma and other solid tumor indications. The combination of IDE397 with pemetrexed is a novel and potential first-in-class combination of a MAT2A inhibitor with an antifolate agent.

The combination of IDE397 with AMG 193 is a novel and potential first-in-class synthetic lethality combination which targets two distinct and mechanistically complementary nodes of the MTAP methylation pathway – MAT2A and PRMT5, providing a complementary approach for targeting MTAP-deletion tumors. IDEAYA and Amgen plan to clinically evaluate IDE397 in combination with AMG 193, an investigational MTA-Cooperative PRMT5 inhibitor, in patients having MTAP-deletion tumors, pursuant to a Clinical Trial Collaboration and Supply Agreement.

IDEAYA's clinical development plan includes an emphasis on combination strategies based on observed *in vivo* efficacy in preclinical studies evaluating IDE397 combinations in relevant MTAP-null xenograft models. The preclinical *in vivo* efficacy data showed tumor regressions for IDE397 in combination with pemetrexed, durable complete responses for IDE397 in combination with MTA-cooperative PRMT5 inhibitors, and enhanced tumor-growth inhibition for IDE397 in combination with taxanes. Based on these preclinical studies, IDEAYA believes

that IDE397 combination therapies could potentially enhance clinical efficacy in patients having tumors with MTAP deletion.

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, the timing for enrollment and dosing of a first patient in the IDE397 with AMG 193 combination clinical trial. 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 August 15, 2022 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

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