IDEAYA Announces IND Clearance Enabling Phase 1/2 Clinical Trial for Combination of IDE397 and AMG 193 in MTAP-Deletion Solid Tumors

- IDE397 (MAT2A) and AMG 193 (PRMT5) combination being evaluated in an Amgen-sponsored Phase 1/2 clinical trial in MTAP-deletion solid tumors
- Potential first-in-class synthetic lethality combination targets mechanistically complementary nodes of the MTAP methylation pathway – MAT2A and PRMT5
- Compelling preclinical anti-tumor efficacy presented at AACR 2023 with durable CRs for IDE397 / AMG 193 combination, each at doses below maximally efficacious dose

SOUTH SAN FRANCISCO, Calif., May 22, 2023 /PRNewswire/ -- IDEAYA Biosciences, Inc. (NASDAQ: IDYA), a precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced that the U.S. Food and Drug Administration (FDA) has completed its review of the Amgen-sponsored Investigational New Drug (IND) application and concluded that the proposed clinical study may proceed to evaluate IDE397 in combination with AMG 193 in solid tumors having MTAP deletion.

"We are pleased to collaborate with Amgen to clinically evaluate the IDE397 and AMG 193 combination as a potential first-in-class treatment for patients having solid tumors with MTAP deletion. We believe that evaluation of this combination represents an exciting and highly rational clinical study for patients with MTAP-deletion tumors, based on the observed preclinical efficacy, tolerability and selectivity," said Dr. Darrin M. Beaupre, M.D., Ph.D., Chief Medical Officer, IDEAYA Biosciences.

"We have a deep understanding of the underlying biological rationale for this combination of a MAT2A inhibitor and an MTA-cooperative PRMT5 inhibitor. As presented at AACR 2023, gene expression analysis of hallmark pathways, alternative splicing analysis and retained intron analysis collectively demonstrate that combined pharmacological inhibition of MAT2A and PRMT5 deepens the biological response through maximal pathway suppression. The enhanced combination effect was observed selectively in MTAP-null models," said Dr. Michael White, Ph.D., Chief Scientific Officer, IDEAYA Biosciences.

IDE397 is a potent and selective small molecule inhibitor targeting methionine adenosyltransferase 2a (MAT2A). IDEAYA is clinically evaluating IDE397 as monotherapy in a Phase 1/2 clinical trial in patients having solid tumors with methylthioadenosine phosphorylase (MTAP) deletion, with ongoing enrollment into Phase 2 monotherapy expansion cohorts in selected indications, including squamous cell NSCLC, esophagogastric cancer, and bladder cancer. AMG 193 is the Amgen investigational methylthioadenosine- (MTA-) cooperative protein arginine methyltransferase 5 (PRMT5) inhibitor. The clinical evaluation of IDE397 with AMG 193 represents a novel and potential first-in-class synthetic lethality combination. Targeting two mechanistically distinct nodes of the MTAP methylation pathway – MAT2A and PRMT5 provides a synergistic approach for targeting MTAP-null tumors.

IDEAYA is collaborating with Amgen to clinically evaluate the IDE397 and AMG 193 combination in patients having tumors with MTAP deletion in an Amgen-sponsored clinical trial pursuant to a Clinical Trial Collaboration and Supply Agreement, or CTCSA. The Phase 1/2 clinical trial will evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of IDE397 in combination with AMG 193.

IDEAYA and Amgen co-presented preclinical data at the 2023 Annual Meeting of the American Association for Cancer Research, or AACR 2023, demonstrating deep and durable anti-tumor efficacy for the IDE397 and AMG 193 combination in a NSCLC MTAP-null CDX model. These data showed complete responses following approximately 30 days of combination treatment at doses below the maximally efficacious preclinical dose for each compound, which were durable from approximately study-day 40 to study-day 100. The IDE397 and AMG 193 combination was well tolerated, with no observed body weight loss through the approximate 30 days of

combination treatment in these models. Additionally, the results of gene expression analysis of hallmark pathways, alternative splicing analysis and retained intron analysis collectively demonstrated that combined pharmacological inhibition of MAT2A and PRMT5 deepens the biological response through maximal pathway suppression. The enhanced combination effect was observed selectively in MTAP-deleted relative to MTAP wild-type models.

Pursuant to the mutually non-exclusive CTCSA, Amgen is the sponsor of the IDE397 and AMG 193 combination clinical trial and each of IDEAYA and Amgen will supply their respective compounds, IDE397 and AMG 193. Each party will pay fifty percent (50%) of the external third-party costs for conducting the clinical trial and be wholly responsible for their respective own internal costs and expenses in support of the clinical trial. The companies will jointly own clinical data and all intellectual property, if any, relating to the combined use of IDE397 and AMG 193 from the clinical trial. Each party retains commercial rights to its respective compounds, including with respect to use as a monotherapy or combination agent. The companies have formed a joint oversight committee responsible for coordinating all regulatory and other activities in support of the clinical trial.

About IDEAYA Biosciences

IDEAYA is a 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 precision medicine targets, including 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 the clinical benefit to patients of the combination of IDE397 and AMG 193. 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 Quarterly Report on Form 10-Q filed on May 9, 2023 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

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