# IDEAYA Announces Selection of IDE397 Phase 2 Monotherapy Expansion Dose For Global Enrollment Targeting High Priority MTAP-Deletion Solid Tumor Types

- Phase 2 monotherapy expansion dose selected for enrollment in high priority MTAP-deletion solid tumor types – NSCLC, bladder and gastroesophageal cancers
- Observed partial response by RECIST 1.1 (~40% tumor reduction) at first post-baseline scan in a pre-treated patient having a high priority MTAP-deletion solid tumor type
- Clinical strategy focused on IDE397 combinations, including with AMG 193, the Amgen MTA-cooperative PRMT5 inhibitor, for which IND-clearance was received in May 2023

SOUTH SAN FRANCISCO, Calif., June 12, 2023 /PRNewswire/ -- IDEAYA Biosciences, Inc. (NASDAQ: IDYA), a precision medicine oncology company committed to the discovery and development of targeted therapeutics, announced selection of a monotherapy expansion dose for the Phase 2 clinical trial evaluating IDE397 in patients having solid tumors with MTAP deletion.

"We have selected a IDE397 Phase 2 monotherapy expansion dose for evaluation in our high-priority solid tumor types with MTAP deletion, including NSCLC, bladder cancer and gastroesophageal cancer.  We are in the early stages of enrollment into our global Phase 2 clinical trial monotherapy expansion and have clinical objectives to further define IDE397's monotherapy efficacy in our high priority solid tumor types and to address contribution of components for clinical combinations," said Dr. Darrin M. Beaupre, M.D., Ph.D., Chief Medical 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 the global Phase 2 clinical trial.

IDEAYA is focusing monotherapy expansion cohorts in high-priority tumor types with MTAP deletion, including NSCLC, bladder cancer and gastricesophageal cancer.  MTAP deletion is estimated to occur in ~16% of non-small cell lung cancer (NSCLC), ~30% of bladder cancer and ~15% to ~25% of gastricesophageal cancer. These monotherapy indications are being prioritized based on preliminary clinical efficacy and preclinical data demonstrating *in vivo* efficacy in relevant patient- and/or cell-derived xenograft models and observed endogenous pathway suppression in MTAP deleted tumors.  These data were presented at the 2023 Annual Meeting of the American Association of Cancer Research (AACR 2023).

The company observed tumor shrinkage in multiple patients treated with IDE397 monotherapy in IDEAYA's high-priority MTAP-deletion solid tumor types, including a pre-treated patient that had an observed partial response (PR) by RECIST 1.1 (~40% tumor reduction) at the first post-baseline scan.

IDEAYA is collaborating with Amgen to clinically evaluate IDE397 in combination with AMG 193 in patients having solid tumors with MTAP deletion. AMG 193 is the Amgen investigational 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.

In May 2023, IDEAYA reported clearance of the Amgen-sponsored Investigational New Drug (IND) application and U.S. FDA authorization to proceed with the IDE397 / AMG 193 Phase 1/2 clinical trial. 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 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 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 clinical objectives for the IDE397 Phase 2 clinical trial. 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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