IDEAYA Announces Positive Interim Phase 1 Expansion Data of IDE397 in MTAP-Deletion Urothelial and Lung Cancer as Late-Breaker Oral Presentation at EORTC-NCI-AACR 2024

- ~33% ORR by RECIST 1.1: 1 CR + 8 PRs out of 27 evaluable heavily pre-treated (median 2-3 prior lines, ranging from 1-7) MTAP-deletion UC and NSCLC patients
- 9 of 9 responses have confirmed by RECIST 1.1 (5 confirmed responses out of 18 evaluable patients reported on July 8, 2024, IDE397 webcast)
- MTAP-deletion UC: 40% (4 of 10) confirmed ORR and 3 pts on treatment >250 days
- MTAP-deletion SqNSCLC: ~38% (3 of 8) confirmed ORR and 4 pts on treatment >200 days
- Multiple PRs with genetic co-alterations, including MTAP-deletion and KRAS G12D mutation in NSCLC, and MTAP-deletion and FGFR-TACC3 fusion in UC
- Median DOT not yet reached and >6.2 months, and median TTR ~2.7 months
- ~81% (17 of 21) ctDNA MRR, and high DCR of 93% (25 of 27 with SD or better)
- AE Profile: No drug-related SAEs or discontinuations at 30 mg once-a-day expansion dose
- Targeting expansion of Phase 1/2 study of IDE397 in combination with Trodelvy® in MTAP-deletion UC in Q4 2024; patient case study of PR by RECIST 1.1 and rapid >95% ctDNA reduction of combination will be presented at ENA 2024
- IDE397 demonstrated deep and durable regressions in combination with PRMT5 inhibitors BMS-986504 and AMG 193 in preclinical models

SOUTH SAN FRANCISCO, Calif., Oct. 25, 2024 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq: IDYA), a precision medicine oncology company committed to the discovery and development of targeted therapeutics, announces Phase 1 expansion data for IDE397 in methylthioadenosine phosphorylase (MTAP)-deletion urothelial cancer (UC) and non-small cell lung cancer (NSCLC) patients as a late breaker abstract (LBA) oral presentation at the 36th edition of the EORTC-NCI-AACR Symposium (ENA 2024) in Barcelona, Spain. In addition, IDEAYA had additional poster presentations at ENA 2024 highlighting preclinical data for the MAT2A and PARG programs. IDE397 is a potent and selective potential first-in-class methionine adenosyltransferase 2 alpha (MAT2A) inhibitor in Phase 2 clinical trials for the treatment of MTAP-deletion solid tumors.

"We are excited by the clinical efficacy and safety profile observed with the potential first-in-class MAT2A inhibitor IDE397 at the 30mg once-a-day RP2D, including multiple confirmed responses observed as a monotherapy agent in non-small cell lung cancer and urothelial cancer patients with MTAP-deletion. In addition, at the 30mg once-a-day expansion dose, we observed a manageable safety profile with no drug-related serious adverse events or discontinuations. These data support potential combination development," said Dr. Benjamin Herzberg, M.D., Assistant Professor of Medicine, Columbia University.

"The clinical data update from the late breaker oral presentation at ENA 2024 provides further clinical proof-of-concept for IDE397 in the setting of MTAP-deletion urothelial cancer and non-small cell lung cancer to deliver a high disease control rate and confirmed RECIST responses, with an overall manageable adverse event profile," said Darrin M. Beaupre, M.D., Ph.D., Chief Medical Officer, IDEAYA Biosciences.

"IDE397 is rapidly advancing as a monotherapy agent in MTAP-deletion urothelial cancer and non-small cell lung cancer. Next, we are well positioned to advance our broad and potential first-in-class IDE397 rational combination strategy, including the targeted expansion in the fourth quarter with Trodelvy® in urothelial cancer, the ongoing combination with AMG 193 with targeted expansion in NSCLC, combinations with IDEAYA's internal MTAP-deletion pipeline that includes a targeted development candidate by year-end, among others," said Yujiro S. Hata,

President and Chief Executive Officer, IDEAYA Biosciences.

There are currently no FDA-approved therapies for patients with MTAP-deletion solid tumors, highlighting the unmet medical need. The priority MTAP-deletion solid tumor types for the IDE397 Phase 1/2 monotherapy program are UC and NSCLC. MTAP-deletion has been reported at over 15% in NSCLC and over 25% in UC, based on The Cancer Genome Atlas (TCGA) database. We estimate that the annual incidence of MTAP-deletion in the U.S. in UC and NSCLC is approximately 48,000 patients, based on the 2024 Surveillance, Epidemiology, and End Results (SEER) database. In addition, there are several potential expansion MTAP-deletion solid tumor types that are also being considered for monotherapy and combination development, including pancreatic, gastric, esophageal, and head and neck cancer, among others. Based on the TCGA database, MTAP-deletion in pancreatic cancer has been reported in more than 20% of patients, representing a U.S. annual incidence of approximately 14,000 patients.

ENA 2024 Clinical Data Update – IDE397 Phase 2 Expansion in Subjects with MTAP-Deletion UC and NSCLC
The company observed encouraging clinical activity at the 30 mg once-a-day (QD) Recommended Phase 2 Dose (RP2D) in its Phase 1 clinical trial evaluating its potential first-in-class MAT2A inhibitor IDE397 in heavily pre-treated MTAP-deletion UC and NSCLC patients. The patients evaluated had a median of two (2) to three (3) prior lines-of-therapy, ranging from one (1) to seven (7). The reported Phase 1 clinical expansion data are based on twenty-seven (27) evaluable MTAP-deletion patients, including ten (10) UC, nine (9) adenocarcinoma NSCLC, and eight (8) squamous (sq) NSCLC patients at the expansion dose of 30 mg QD of IDE397.

The clinical efficacy and tolerability data are preliminary and based on investigator review from an unlocked database as of the data analysis cutoff date of August 22, 2024.

The clinical data update in the twenty-seven (27) evaluable patients by RECIST 1.1 include:

- ~33% Overall Response Rate (ORR). One (1) complete response (CR) and eight (8) partial responses (PRs) by RECIST 1.1 evaluation out of twenty-seven (27) evaluable patients. Nine (9) of nine (9) responses have been confirmed by RECIST 1.1, including four (4) UC patients, of which one was a CR, three (3) squamous NSCLC patients, and two (2) adenocarcinoma NSCLC patients. Two patients confirmed after the data cutoff date. In the earlier reported July 8, 2024, IDE397 webcast program update, five (5) confirmed responses were reported out of eighteen (18) evaluable patients. There were zero (0) non-evaluable patients reported as of the data analysis.
- Confirmed ORR% by RECIST 1.1 by Solid Tumor Type: MTAP-deletion UC = 40% (4 of 10) confirmed ORR%; MTAP-deletion squamous NSCLC = ~38% (3 of 8) confirmed ORR%; MTAP-deletion adenocarcinoma NSCLC = ~22% (2 of 9) confirmed ORR%
- Multiple confirmed partial responses by RECIST 1.1 harbor genetic co-alterations, including MTAP-deletion and KRAS G12D mutation in NSCLC, and MTAP-deletion and FGFR-TACC3 fusion in UC
- ~93% Disease Control Rate (DCR). One (1) CR, eight (8) PRs, and sixteen (16) stable disease (SD) by RECIST 1.1 evaluation out of twenty-seven (27) evaluable patients
- Preliminary durability assessment: Fifteen (15) of twenty-seven (27) patients still on treatment. Seven (7) of nine (9) RECIST 1.1 responses remain on treatment. Median duration of treatment (DOT) has not been reached and is greater than 6.2 months and median time to response (TTR) is ~2.7 months. The median duration of response and median progression free survival data is still immature. Three (3) UC patients on treatment greater than 250 days, four (4) squamous NSCLC patients on treatment greater than 200 days, and three (3) adenocarcinoma NSCLC patients on treatment greater than 200 days
- ~81% ctDNA Molecular Response Rate (MRR). Seventeen (17) of twenty (21) patients with 50% or greater ctDNA reduction, and ~33% (7 of 21) with deep 90% or greater ctDNA reduction. All MRs (17 of 17) were rapid occurring at the first ctDNA sample analysis. There were several quality control failures of patient samples that led to unavailability for MR analysis

- Favorable adverse event (AE) profile. Approximately 18% grade 3 or higher drug-related AEs and no drug-related serious adverse events (SAEs) observed at the IDE397 30mg once-a-day expansion dose. No drug-related AEs leading to discontinuations were observed. We anticipate that the favorable AE profile and dosing convenience of a 30 mg once-a-day tablet has the potential to enable long-term dosing and combination development, including with MTA-cooperative PRMT5 inhibitors and topoisomerase payload antibody drug conjugates (ADCs)

ENA 2024 IDE397 and Trodelvy Clinical Combination Case Study in MTAP-deletion UC

IDEAYA reports the first preliminary clinical case study of the IDE397 and Trodelvy combination in MTAP-deletion UC, including a PR by RECIST 1.1 in a patient case report with a genetic co-alteration of MTAP-deletion and a FGFR3-TACC3 fusion, and rapid and deep first-evaluation molecular responses with ctDNA reduction of greater than 95% observed that will be presented at ENA 2024. IDEAYA is targeting to initiate the IDE397 and Trodelvy Phase 1/2 combination expansion in MTAP-deletion UC in Q4 2024.

IDEAYA has activated over 35 clinical trial sites globally in the U.S., Canada, Europe, and Asia Pacific to enable potential rapid enrollment for the IDE397 Phase 2 monotherapy expansion in MTAP-deletion lung and bladder cancer in its ongoing trial (NCT04794699). There is also an ongoing Amgen-sponsored Phase 1/2 trial of the IDE397 and AMG 193 combination in MTAP-Deletion NSCLC (NCT05975073). IDEAYA published at ENA 2024 preclinical combination efficacy data and the combination mechanistic rationale for IDE397 with clinical stage PRMT5 inhibitors, including BMS-986504 and AMG 193.

Next, IDEAYA is enrolling a Phase 1 clinical trial evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics and efficacy of IDE397 in combination with Trodelvy in MTAP-deletion UC patients (NCT04794699). Pursuant to the clinical study collaboration and supply agreement, IDEAYA and Gilead retain the commercial rights to their respective compounds, including with respect to use as a monotherapy or combination agent. IDEAYA is the study sponsor and Gilead will provide the supply of Trodelvy to IDEAYA. IDE397 monotherapy or in combination with Trodelvy has not been approved by any regulatory agency and the efficacy and safety of this combination has not been established.

36th edition of the EORTC-NCI-AACR Symposium (ENA 2024) in Barcelona, Spain

Details of the late breaker oral presentation today are as follows:
Presenter: Dr. Benjamin Herzberg, MD, Assistant Professor, Columbia University
Title: Phase 1 expansion results of IDE397, a first-in-class, oral, MAT2A inhibitor (MAT2Ai) in MTAP deleted(del) non-small cell lung cancer (NSCLC) and urothelial cancer (UC)
Abstract #: 501 LBA
Session: Plenary Session 7, Late Breaking Abstracts and Proffered Papers: Novel discoveries in drug development
Date and Time: Friday, October 25, 2024 at 3:54pm CEST

In addition, IDEAYA had additional poster presentations at ENA 2024 highlighting preclinical data for the MAT2A and PARG programs. In the ENA 2024 concomitant publication, IDE397 demonstrated deep and durable regressions in combination with clinical stage PRMT5 inhibitors BMS-986504 and AMG 193 in multiple MTAP-deletion preclinical models.

Poster presentation details are below:
Author: Garbett, D. et al.
Title: The mechanistic basis of both deep and durable antitumor activity by combinatorial inhibition of MAT2A and PRMT5 in MTAP-deleted tumors
Poster Number: PB204

Session Title: Combination Therapies
Date and Time: Thursday, October 24, 2024, 9:00am - 5:30pm CEST, Exhibition Hall

Author: Munoz, D. et al.
Title: IDE161, a potential first-in-class clinical candidate PARG inhibitor, selectively targets solid tumors with replication stress and DNA repair vulnerabilities
Poster Number: PB337
Session Title: DNA Repair Modulation (e.g. PARP, CHK, ATR, ATM)
Date and Time: Friday, October 25, 2024, 9:00am - 3:00pm CEST, Exhibition Hall

The IDE397 late breaker oral presentation at ENA 2024, as well as an updated corporate presentation, which will incorporate the IDE397 Phase 1 clinical data update from ENA 2024 at the 30mg RP2D in UC and NSCLC patients, will be available on the company's website, at its Investor Relations portal at approximately 10:15 am ET on Friday, October 25, 2024, after the presentation has concluded.

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 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) expectations regarding the clinical activity profile and potential advantages of IDEAYA's clinical programs, (ii) the timing of enrollment for the IDE397 Phase 2 monotherapy expansion in MTAP-deletion lung and bladder cancer, (iii) the timing of initiation of the IDE397 and Trodelvy Phase 1/2 combination expansion in MTAP-deletion UC and (iv) the timing and content of future presentations. 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, 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 Annual Report on Form 10-K dated February 20, 2024 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

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Deletion-Urothelial-and-Lung-Cancer-as-Late-Breaker-Oral-Presentation-at-EORTC-NCI-AACR-2024