IDEAYA Biosciences, Inc. Reports Fourth Quarter and Full-Year 2023 Financial Results and Provides Business Update

- Targeting two independent Phase 2 clinical efficacy updates for darovasertib in neoadjuvant uveal melanoma (UM) in mid-2024, including from the Phase 2 IST and Phase 2 company-sponsored study
- Targeting FDA regulatory guidance on darovasertib in neoadjuvant UM indication in 2024
- Ongoing enrollment of IDE397 and AMG 193 Phase 1 combo in MTAP solid tumors and targeting development of joint Amgen / IDEAYA publication strategy in 2024
- Established clinical study collaboration with Gilead Sciences to evaluate IDE397 and Trodelvy® combo in MTAP bladder cancer with FPI targeted for mid-year 2024
- Targeting IDE161 clinical program update(s) and enabling of clinical combination(s) in 2024
- Targeting Werner IND-filing in 2024 ($7.0 million milestone upon IND clearance) in collaboration with GSK
- Targeting multiple wholly-owned next generation development candidate nominations in 2024, including in MTAP, representing 7 or more potential first-in-class programs
- $632.6 million cash balance as of December 31, 2023, supplemented by net proceeds of $342.3 million from January 2024 ATM offerings, expected to fund operations into 2028

SOUTH SAN FRANCISCO, Calif., Feb. 20, 2024 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq: IDYA), a precision medicine oncology company committed to the discovery and development of targeted therapeutics, provided a business update and announced financial results for the quarter and full-year ended December 31, 2023.

"We believe the ongoing clinical advancement of darovasertib in neoadjuvant Uveal Melanoma, IDE397 and AMG 193 clinical combination in MTAP solid tumors, and IDE161 and GSK101 both in HRD solid tumors, represent important clinical initiatives for IDEAYA in 2024 as potential first-in-class opportunities that address high unmet medical needs. Next, we are targeting this year the Werner IND-filing and multiple development candidate nominations, including in MTAP, representing 7 or more potential first-in-class programs and further advancing our vision to build a leading precision medicine oncology company," said Yujiro S. Hata, President and Chief Executive Officer, IDEAYA Biosciences.

"We have seen compelling results from our Phase 2 darovasertib and crizotinib program in patients with MUM and are targeting two clinical efficacy updates from our Phase 2 company sponsored neoadjuvant UM study and Phase 2 IST in mid-year 2024. Our IDE397 program trials remain on track, and we established a new clinical trial collaboration with Gilead Sciences to evaluate IDE397 in combination with Trodelvy® in patients with bladder cancer, with trial initiation activities now underway. Additionally, IND-enabling studies of the Werner helicase inhibitor for microsatellite instability (MSI)-high cancers are progressing well, further expanding our pipeline of first-in-class precision medicine candidates." added Dr. Darrin Beaupre, M.D., Ph.D., Chief Medical Officer, IDEAYA Biosciences.

Recent Key Developments

- Reported top-line results of darovasertib and crizotinib combination demonstrating evidence of superior clinical efficacy in any-line and first-line MUM patients compared to standard of care as a Proffered Paper oral presentation at the 2023 European Society for Medical Oncology's Congress (ESMO).
- Expanded Phase 2 trial evaluating the darovasertib and crizotinib combination in GNAQ/11 metastatic cutaneous melanoma based on preliminary clinical efficacy observed.
- Selected Werner helicase inhibitor development candidate and progressing IND-enabling GLP studies in collaboration with GSK; received $3.0 million milestone and eligible to receive $17.0 million aggregate milestones payments through early Phase 1 clinical studies, including $7.0 million upon investigational new drug (IND) clearance. IDEAYA is also eligible to receive future aggregate development milestones of up to $465.0 million and commercial milestones of up to $475.0 million and 50% of U.S. net profits.
- Established clinical study collaboration with Gilead Sciences to evaluate IDE397 and Trodelvy® combination in

MTAP-deletion bladder cancer.
- Significantly expanded balance sheet
  - Raised gross proceeds of approximately $352.0 million in January 2024 through at-the-market offerings.
  - Raised gross proceeds of approximately $143.7 million in October 2023 through a follow-on public offering.
- Hosted an R&D Investor Day in December 2023 showcasing the synthetic lethality pipeline, including IDE397 in Phase 2, IDE161 in Phase 1, GSK101/IDE705 in Phase 1, and the Werner Helicase program, as well as its next generation initiatives for MTAP-deletion.

Clinical Programs Update and Upcoming Milestones

Darovasertib Program in Tumors with GNAQ or GNA11 Mutations

Darovasertib is a potent and selective protein kinase C (PKC) inhibitor for which the Company owns the worldwide commercial rights, subject to certain economic obligations pursuant to its exclusive, worldwide license with Novartis. IDEAYA is developing darovasertib to broadly address primary and metastatic UM.

Darovasertib is currently being evaluated in four ongoing clinical trials, three of which are in collaboration with Pfizer. The darovasertib + crizotinib combination in MUM has U.S. Food & Drug Administration (FDA) Fast Track designation.

IDE196-002: *Phase 2/3 Potential Registration-Enabling Clinical Trial of Darovasertib + Crizotinib combination in First-Line HLA-A2*02:01(-) MUM*

This study (NCT05987332) has an accelerated approval trial design and international site activation, and double-digit patient enrollment has been achieved to date. The company has several clinical sites open and is targeting to open an aggregate of over 50 clinical sites across U.S., Canada, Europe and Australia to support this registrational study. Clinical program update(s) are anticipated in 2024.

IDE196-001: Phase 1/2 Clinical Trial Evaluating Darovasertib + Crizotinib Combination in MUM

A clinical update of preliminary data from 20 evaluable first-line and 63 evaluable any-line patients from the study (NCT03947385) at the expansion dose of 300 mg twice-a-day darovasertib and 200 mg twice-a-day crizotinib was presented at ESMO 2023. Darovasertib and crizotinib combination treatment demonstrated evidence of superior clinical efficacy in any-line and first-line compared to standard of care. The detailed results can be found here.

Phase 2 Clinical Trial Evaluating Darovasertib Combination in Cutaneous Melanoma

Based on the Cancer Genome Atlas, about 5% of patients with cutaneous melanoma harbor the GNAQ/11 mutation. Therefore, the annual incidence is estimated to be 5,000 patients in the U.S. and 8,000 patients in the EU-28, and the estimated total prevalence of GNAQ/11 cutaneous melanoma is approximately 70,000 patients in the U.S. and 110,000 patients in the EU-28. There are currently no FDA approved therapies in this genetically-defined GNAQ/11 cutaneous melanoma patient population. Hence, GNAQ/11 metastatic cutaneous melanoma presents a potentially significant expansion opportunity for darovasertib, reflecting approximately double or more of the annual addressable metastatic patient population of metastatic uveal melanoma alone, especially given that GNAQ/11 is available on multiple next-generation sequencing and liquid biopsy platforms, enabling patient identification.

Along with other available data and IDEAYA's strategic priority to broaden its darovasertib program to the multiple solid tumor setting, in October 2023, the Company expanded its Phase 2 expansion of the darovasertib and crizotinib combination in metastatic cutaneous melanoma.

The expansion was based on preliminary clinical activity observed in three cohorts of patients treated with darovasertib, either as monotherapy or in combination with either binimetinib or crizotinib. The detailed results were reported in October 2023 and can be found here.

Phase 1 and 2 Trials Darovasertib as Neoadjuvant / Adjuvant Therapy in Primary UM

Darovasertib is being evaluated as monotherapy in two clinical trials as neoadjuvant / adjuvant therapy:

- IDE196-009: a company-sponsored Phase 2 trial (NCT05907954) evaluating darovasertib as neoadjuvant treatment of UM prior to primary interventional treatment of enucleation or radiation therapy, and as adjuvant therapy following the primary treatment.
- Phase 1 Neoadjuvant / Adjuvant trial of Darovasertib in Ocular Melanoma, or NADOM: an investigator-sponsored trial (IST) Phase 1 study (NCT05187884). The study is being led by Anthony Joshua, MBBS, PhD, FRACP, Head Department of Medical Oncology, Kinghorn Cancer Centre, St. Vincent's Hospital in Sydney with additional participating sites in Melbourne, Australia.

The clinical objectives of neoadjuvant therapy are to save the eye by avoiding enucleation and/or to reduce the tumor thickness in the eye, enabling treatment with less radiation to preserve vision. As an adjuvant therapy, a clinical goal is to potentially extend relapse free survival. Preliminary clinical data of darovasertib as neoadjuvant treatment showed evidence of anti-tumor activity and supported further clinical evaluation of darovasertib to determine its potential as a neoadjuvant therapy or an adjuvant therapy.

As of February 1, 2024, double digit patients have been dosed with several sites open and actively recruiting additional patients into the company-sponsored Phase 2 clinical trial. Two independent clinical efficacy updates for darovasertib in neoadjuvant UM are anticipated in mid-2024, including from the Phase 2 IST study and IDEAYA's Phase 2 company-sponsored study. A regulatory guidance update is planned in 2024.

In preliminary results from the Phase 1 NADOM trial darovasertib demonstrated eye preservation in 3 of 6 (50%) evaluable patients treated with darovasertib as neoadjuvant therapy for primary UM. The detailed results can be found here.

IDE397 Program in Solid Tumors and Bladder Cancer with MTAP Deletion

IDE397 is a potent and selective small molecule inhibitor targeting methionine adenosyltransferase 2 alpha (MAT2A) in patients having solid tumors with methylthioadenosine phosphorylase (MTAP) deletion. MTAP deletion is found in 15% of solid tumors and is estimated to have annual incidence of greater than 50,000 patients in the US, EU5 and Japan across priority solid tumor types of non-small cell lung cancer (NSCLC), bladder, gastric, and esophageal cancers.

The Company is focused on evaluating IDE397 in select monotherapy indications and in high conviction clinical combinations with AMG 193, Amgen's investigational MTA-cooperative PRMT5 inhibitor, and in combination with Gilead's Trop-2 directed antibody-drug conjugate (ADC) Trodelvy (Sacituzumab-govitecan-hziy). IDEAYA owns all rights, title, and interest in and to the IDE397 and MAT2A program, including all worldwide commercial rights thereto.

IDE397-001: Phase 2 IDE397 Monotherapy Expansion in MTAP-Deletion NSCLC and Bladder Cancer

The Company-sponsored IDE397 monotherapy Phase 2 expansion trial (NCT04794699) is continuing to enroll patients with MTAP-deletion squamous NSCLC and bladder cancers.

Preliminary clinical data demonstrated responses in multiple MTAP-deletion high-priority tumor types based on experience across several patients in the early phase of the monotherapy dose expansion:

- RECIST 1.1 compete response in a bladder cancer patient and a 33% tumor reduction in squamous NSCLC patient as measured by CT-PET.
- Multiple ctDNA molecular responses were observed in NSCLC and bladder cancer patients.
- Low rates of discontinuations and serious adverse events (SAEs) were observed.
- As of October 13, 2023: 8 patients have been dosed in the IDE397 monotherapy expansion in the priority tumor types, and 2 patients have not yet had a first tumor scan assessment.

Phase 1/2 trial of IDE397 + AMG 193 in MTAP-Deletion NSCLC

Enrollment is ongoing in the dose escalation portion of the Amgen-sponsored Phase 1/2 trial (NCT05975073) evaluating IDE397 and AMG 193 ($PRMT5^{MTA)}$) combination in patients with MTAP-deletion solid tumors. Additionally, in 2024, the Company will develop a joint publication strategy with Amgen.

Phase 1 trial of IDE397 + Trodelvy in MTAP-Deletion Bladder Cancer

The Company-sponsored Phase 1 (NCT04794699) in patients with MTAP-deletion bladder cancer will evaluate IDE397 in combination with Trodelvy, a Trop-2 directed ADC which is currently approved in the U.S. for the treatment of HR+/HER2- metastatic breast cancer, metastatic triple-negative breast cancer and metastatic urothelial cancer.

Trial initiation activities are under way and the first-patient-in is anticipated in mid-2024.

IDE161 Program in Tumors with Homologous Recombination Deficiency

IDE161 is a potential first-in-class inhibitor of poly(ADP-ribose) glycohydrolase (PARG), a novel, mechanistically distinct target in the same clinically validated biological pathway as poly(ADP-ribose) polymerase (PARP). IDEAYA owns or controls all commercial rights to IDE161 and its PARG program, subject to certain economic obligations pursuant to its exclusive, worldwide license with Cancer Research UK and University of Manchester.

IDE161 received two FDA Fast Track designations in platinum-resistant advanced or metastatic ovarian cancer patients having tumors with BRCA1/2 mutations, and pretreated advanced or metastatic HR+, Her2-, BRACA1/2 mutant breast cancer.

IDE161-001: Phase 1/2 of IDE161 Monotherapy Dose Escalation and Expansion in HRD Solid Tumors

The Phase 1 trial (NCT05787587) is evaluating the safety, tolerability, pharmacokinetic and pharmacodynamic properties and preliminary efficacy of IDE161 in patients having tumors with homologous recombination deficiency (HRD). Early clinical data from the dose escalation cohorts showed:

- Multiple partial responses (PRs) by RECIST 1.1 and tumor shrinkage observed in multiple HRD solid tumor patients, including:
    - An endometrial cancer subject with a first imaging assessment of a PR, which was subsequently confirmed by RECIST 1.1 at the second scan and an 87% reduction of the CA-125 marker.
    - A colorectal cancer subject with a second imaging assessment of a PR, which was subsequently confirmed by RECIST 1.1
    - Over 50% reduction in prostate-specific antigen (PSA) in prostate cancer patient with non-measurable disease
- No drug related discontinuations or SAEs at the IDE161 expansion dose observed.
- Phase 1 dose optimization is ongoing to confirm move forward Phase 2 expansion dose.

The Phase 1 expansion trial continues to enroll in HRD solid tumor types, including ER+ HER- breast, colorectal, endometrial, and prostate cancers. Clinical program update(s) are expected in 2024. IDEAYA is also validating IDE161 combination opportunities preclinically and is targeting identification of potential combination(s) in 2024.

GSK-Partnered Programs

GSK101 (IDE705) Program in Tumors with Homologous Recombination Mutations or HRD

GSK101 (IDE705) is a potential first-in-class small molecule inhibitor of Pol Theta Helicase being developed as a combination treatment with niraparib for advanced solid tumors with HRD. IND clearance was obtained from the U.S. FDA to enable the GSK-sponsored Phase 1/2 clinical trial to evaluate GSK101 in combination with niraparib, the GSK

small molecule inhibitor of PARP, for patients having solid tumors with BRCA or other HR mutations, or with HRD. IDEAYA earned a $7.0 million milestone payment for IND clearance and will receive an additional $10.0 million upon initiation of Phase 1 clinical dose expansion, as well as potential further aggregate later-stage development and regulatory milestones of up to $465.0 million. GSK is the sponsor of the Phase 1/2 clinical trial and will lead clinical development for the Pol Theta program pursuant to its global, exclusive license from IDEAYA. GSK is responsible for all research and development costs for the program.

Werner Helicase Inhibitor in Tumors with High Microsatellite Instability

IDEAYA, in collaboration with GSK, selected a Werner Helicase inhibitor for further development and IDEAYA earned a $3.0 million milestone from GSK in connection with IND-enabling studies. IDEAYA has the potential to earn up to an additional $17.0 million aggregate milestones through early Phase 1, including $7.0 million upon IND effectiveness. IDEAYA is entitled to receive up to $465.0 million in additional later-stage development and regulatory milestones. The companies are targeting IND submission in 2024. Subject to IND submission and clearance, GSK will lead clinical development for the Werner Helicase program pursuant to its global, exclusive license to develop and commercialize the Werner Helicase Inhibitor DC. GSK is responsible for 80% of global research and development costs and IDEAYA is responsible for 20% of such costs.

Next-Generation Precision Medicine Pipeline Programs

IDEAYA has initiated early preclinical research programs focused on pharmacological inhibition of several new targets for patients with solid tumors characterized by defined biomarkers based on genetic mutations and/or molecular signatures. These research programs have the potential for discovery and development of first-in-class or best-in-class therapeutics with multiple wholly owned development candidate nominations targeted in 2024, including to treat MTAP-deletion solid tumors.

Select Fourth Quarter and Full-Year 2023 Financial Results

As of December 31, 2023, IDEAYA had cash, cash equivalents and marketable securities of $632.6 million, compared to $373.1 million as of December 31, 2022. The increase was primarily driven by total net proceeds of $323.3 million from underwritten public follow-on offerings completed in April and October 2023 partially offset by cash used in operations.

Subsequent to the reporting period for the quarter ended December 31, 2023, the Company generated gross proceeds of approximately $352.0 million from the sale of shares of its common stock through at-the-market (ATM) offerings in January 2024.

IDEAYA believes that its cash, cash equivalents and marketable securities of $632.6 million as of December 31, 2023, supplemented by estimated net proceeds of $342.3 million, after deducting underwriting discounts and commissions and other offering expenses, from the January 2024 ATM sales of common stock, will be sufficient to fund its planned operations into 2028. These funds will support the Company's efforts through potential achievement of multiple preclinical and clinical milestones across multiple programs.

Collaboration revenue for the three months ended December 31, 2023, totaled $3.9 million compared to $4.0 million for the three months ended December 31, 2022. Collaboration revenue was recognized for the performance obligations satisfied through December 31, 2023, under the GSK Collaboration Agreement, and the Werner Helicase program's GLP toxicology study initiation milestone achievement. As of December 31, 2023, IDEAYA has fully recognized the contract liability related to the upfront payment research and development performance obligations under the GSK Collaboration Agreement.

Research and development (R&D) expenses for the three months ended December 31, 2023, totaled $38.8 million compared to $24.7 million for the three months ended December 31, 2022. The increase was primarily due to higher personal-related expenses, consulting expenses and clinical trial expenses to support the portfolio growth.

General and administrative (G&A) expenses for the three months ended December 31, 2023, totaled $7.1 million compared to $5.8 million for the three months ended December 31, 2022. The increase was primarily due to higher personnel-related expenses, higher legal and audit fees.

The net loss for the three months ended December 31, 2023, was $34.0 million compared to the net loss of $24.2 million for the three months ended December 31, 2022. Total stock compensation expense for the three months ended December 31, 2023, was $4.8 million compared to $3.0 million for the same period in 2022.

The net loss for the year ended December 31, 2023, was $113.0 million compared to $58.7 million for the same period in 2022. Total stock compensation expense for the year ended December 31, 2023, was $18.5 million compared to $11.6 million for the same period in 2022.

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.

IDEAYA's updated corporate presentation is available on its website, at its Investor Relations page: https://ir.ideayabio.com/.

Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to (i) the timing, content and venue of clinical program updates, (ii) the timing of FDA regulatory guidance, (iii) the timing for the development of a joint Amgen/IDEAYA publication strategy, (iv) the timing of a first-patient-in in the IDE397 and Trodelvy combination study, (v) additional clinical combinations, (vi) the timing of IND submission for the Werner Helicase inhibitor DC, (vii) the timing of designation of next generation development candidates, (viii) the extent to which IDEAYA's existing cash, cash equivalents, and marketable securities will fund its planned operations, (ix) the potential therapeutic benefits of IDEAYA therapeutics, (x) the translation of preliminary clinical trial results into future clinical trial results, (xi) the estimate of patient populations, and (xii) the receipt of development and regulatory milestones. 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, banking sector volatility, 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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IDEAYA Biosciences, Inc.

Condensed Statements of Operations and Comprehensive Loss

(*in thousands, except share and per share amounts*)

	Three Months Ended December 31,		Year Ended December 31,	
	2023	**2022**	**2023**	**2022**
	(Unaudited)		**(Unaudited)**	
Collaboration revenue	$ 3,923	$ 4,022	$ 23,385	$ 50,931
Operating expenses:				
Research and development	38,770	24,714	129,508	89,536
General and administrative	7,068	5,752	28,306	23,897
Total operating expenses	45,838	30,466	157,814	113,433
Loss from operations	(41,915)	(26,444)	(134,429)	(62,502)
Interest income and other income, net	7,960	2,243	21,468	3,847
Net loss	(33,955)	(24,201)	(112,961)	(58,655)
Unrealized gains (losses) on marketable securities	1,312	1,131	3,433	(2,159)
Comprehensive loss	$ (32,643)	$ (23,070)	$ (109,528)	$ (60,814)

Net loss per share attributable to common stockholders, basic and diluted	$ (0.52)	$ (0.50)	$ (1.96)	$ (1.42)
Weighted-average number of shares outstanding, basic and diluted	65,246,361	48,132,003	57,519,929	41,444,696

IDEAYA Biosciences, Inc.

Condensed Balance Sheet Data

(*in thousands*)

	December 31, 2023	December 31, 2022
	(Unaudited)	
Cash and cash equivalents and short-term and long-term marketable securities	$ 632,606	$ 373,146
Total assets	649,316	387,969
Total liabilities	28,226	38,514
Total liabilities and stockholders' equity	649,316	387,969

SOURCE IDEAYA Biosciences, Inc.

https://media.ideayabio.com/2024-02-20-IDEAYA-Biosciences,-Inc-Reports-Fourth-Quarter-and-Full-Year-2023-Financial-Results-and-Provides-Business-Update