IDEAYA Biosciences, Inc. Reports 2021 Financial Results and Provides Business Update

- Strong balance sheet of ~$368 million cash, cash equivalents and marketable securities as of December 31, 2021 is anticipated to fund planned operations into 2025

- Enrolling into IDE397 Cohort 6 with no observed drug-related serious adverse events and without observing maximum tolerated dose through Cohort 5

- Observed robust dose-proportional pharmacokinetic exposures and exposure-dependent pharmacodynamic modulation of S-adenosyl methionine (SAM) in plasma and of symmetric dimethyl arginine (SDMA) in tumor biopsy samples from Phase 1 dose escalation cohorts

- Targeting IDE397 monotherapy cohort expansion and initiation of combination cohorts mid-year 2022, the timing of which may be influenced by observing the MTD

- Darovasertib and crizotinib clinical combination data presented in December 2021 showed robust clinical activity with manageable side effect profile, including 100% DCR (n=16)

- Targeting additional darovasertib and crizotinib clinical combination data mid-year 2022, the timing of which may be influenced by data maturity, including observation of median duration of response (DOR) and/or median progression free survival (mPFS)

- Expanded relationship with Pfizer under a clinical collaboration and supply agreement to support clinical evaluation of darovasertib and crizotinib combination therapy in a potential registration-enabling clinical trial in MUM, subject to FDA guidance on trial design, and in additional cMET-driven tumors such as NSCLC and/or HCC, subject to preclinical validation

SOUTH SAN FRANCISCO, Calif., March 15, 2022 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA), a synthetic lethality focused precision medicine oncology company committed to the discovery and development of targeted therapeutics, provided a business update and announced financial results for the year ended December 31, 2021.

"We are encouraged by the early clinical activity and the tolerability profile in our clinical-stage programs, including our Phase 1 MAT2A inhibitor, IDE397, in MTAP-deletion patients, and our Phase 2 PKC inhibitor, darovasertib, in MUM and other GNAQ/11 patients. As these data mature, we are evaluating multiple expansion opportunities for these clinical programs, including various combination therapies. We are also aggressively advancing our preclinical programs toward the clinic – including our potential first-in-class PARG inhibitor, IDE161, for which are targeting an IND in Q4 2022, and our potential first-in-class Pol Theta helicase inhibitor, for which we are collaborating with GSK with IND-enabling studies in H1 2022," said Yujiro S. Hata, Chief Executive Officer and President of IDEAYA Biosciences.

Program Updates

Key highlights for IDEAYA's pipeline programs include:

IDE397 (MAT2A)

IDEAYA is evaluating IDE397, a potent and selective small molecule inhibitor targeting methionine adenosyltransferase 2a (MAT2A), in patients having solid tumors with methylthioadenosine phosphorylase (MTAP) deletion, a patient population estimated to represent approximately 15% of solid tumors. IDEAYA is leading early clinical development of IDE397. Subject to exercise of its option, GlaxoSmithKline (GSK) will lead later stage global clinical development. Highlights:

- Actively enrolling patients into Cohort 6 of the Phase 1 clinical trial IDE397-001 (NCT04794699)
- Patients are being identified by next generation sequencing (NGS) or by MTAP immunohistochemistry (IHC) assay with confirmatory NGS
- Evaluating IDE397 in patients with MTAP deletion across multiple solid tumor types, including non-small cell lung cancer, pancreatic cancer, thymic cancer, adenoid cystic carcinoma, esophagogastric cancer and bladder cancer
- IDE397 has been generally well tolerated, with no observed drug-related serious adverse events, no observed dose limiting toxicities and without observing the maximum tolerated dose through Cohort 5
- Observed dose-proportional pharmacokinetic exposures across dose ranges of Cohort 1 through Cohort 5 of the Phase 1 dose escalation; achieved active exposure targets established from preclinical models at doses of Cohort 4 and Cohort 5
- Observed exposure-dependent pharmacodynamic modulation of S-adenosyl methionine (SAM) in evaluable plasma samples across dose ranges of Cohort 1 through Cohort 5
- Observed exposure-dependent pharmacodynamic modulation of symmetric dimethyl arginine (SDMA) in evaluable tumor biopsies from Cohort 4 and Cohort 5
- Observed preliminary signals of clinical activity in MTAP-deletion patients in early dose escalation cohorts, including pharmacodynamic modulation and tumor shrinkage
- Submitted a clinical protocol amendment to the FDA to support monotherapy cohort expansion in NSCLC, esophagogastric cancer, as well as one or more basket cohorts, and to support potential combinations, including taxane and other combination agents
- Targeting IDE397 monotherapy cohort expansion and initiation of combination cohorts mid-year 2022, with an aggregate of 150 or more patients across expansion cohorts; the timing of the monotherapy expansion cohorts and combination cohorts may be influenced by the timing of when a MTD is observed
- Targeting delivery of IDE397 option data package to GSK mid-year 2022, subject to initiation of expansion cohorts or establishing the MTD; the option data package will trigger an evaluation period for GSK to make an opt-in decision; subject to GSK election to opt-in and HSR clearance, the company is entitled to receive a $50 million opt-in payment from GSK, ongoing development costs will be shared as 80% GSK / 20% IDEAYA, and IDEAYA is entitled to potential development and regulatory milestones aggregate up to $465 million; upon commercialization, IDEAYA is entitled to 50% of U.S. net profits and tiered royalties on global non-U.S. net sales ranging from high single digit to sub-teen double digit percentages, as well as certain commercial milestones of up to $475 million
- Demonstrated robust preclinical PK / PD in*in vivo* models, with sustained target inhibition and biological impact, as evidenced for example, by modulation of alterations to pre-mRNA splicing profile
- Observed preclinical *in vivo* efficacy of IDE397 in combination with standard of care agents, including with taxanes showing enhanced TGI in pancreatic cancer PDX models, and with novel combination agents; evaluating additional

IDE397 combination strategies

PARG

IDEAYA is advancing preclinical research for an inhibitor of poly (ADP-ribose) glycohydrolase (PARG) in patients having tumors with a defined biomarker based on genetic mutations and/or molecular signature. PARG is a novel target in the same clinically validated biological pathway as poly (ADP-ribose) polymerase (PARP). IDEAYA owns or controls all commercial rights in its PARG program. Highlights:

- Ongoing IND-enabling studies for IDE161, a potential first-in-class PARG inhibitor development candidate for patients having tumors with homologous recombination deficiencies (HRD), including BRCA1 and BRCA2, and potentially other genetic alterations
- Targeting IND for IDE161 in the fourth quarter of 2022
- Exercised option for an exclusive worldwide license from Cancer Research Technology Ltd., also known as Cancer Research UK (CRUK), and University of Manchester; following the option exercise, IDEAYA holds an exclusive worldwide license to patent rights covering a broad class of PARG inhibitors
- Demonstrated preclinical in vivo efficacy as monotherapy, including dose-dependent efficacy with tumor regression or stasis in ovarian, gastric and breast cancer CDX models, and tumor regressions in multiple breast cancer PDX models with defined genetic and subtyping profiles
- Observed *in vivo* efficacy with enhanced TGI or tumor regressions relative to niraparib, a PARPi, in multiple CDX models, including in a niraparib-resistant CDX model, as well as in niraparib resistant breast cancer PDX models
- Showed pharmacological inhibition of PARG in a panel of homologous recombination deficient cell lines and in CDX and PDX models; study data reported at AACR 2021

Pol Theta

IDEAYA's DNA Polymerase Theta, (Pol Theta) program targets tumors with BRCA or other homologous recombination deficiency, or HRD, mutations. IDEAYA and GSK are collaborating on ongoing preclinical research, including small molecules and protein degraders, and GSK will lead clinical development for the Pol Theta program. Highlights:

- Demonstrated *in vivo* efficacy with tumor regression in BRCA2 -/- xenograft model with IDEAYA Pol Theta Helicase inhibitor in combination with niraparib, a GSK PARP inhibitor
- Targeting IND-enabling studies for a Pol Theta helicase inhibitor in the first half of 2022 in collaboration with GSK
- Potential for up to $20 million in aggregate milestone payments from GSK for advancing a Pol Theta Helicase inhibitor from preclinical to early Phase 1 clinical

Werner Helicase

IDEAYA is advancing preclinical research for an inhibitor targeting Werner Helicase for tumors with high microsatellite instability (MSI). IDEAYA and GSK are collaborating on ongoing preclinical research, and GSK will lead clinical development for the Werner Helicase program. Highlights:

- Observed dose-dependent cellular viability effect and dose-dependent cellular PD response in multiple endogenous MSI high cell lines

- Demonstrated efficacy and PD response in relevant MSI high *in vivo* models
- Targeting selection of a Werner Helicase development candidate in 2023
- Potential for up to $20 million in aggregate milestone payments from GlaxoSmithKline for advancing a Werner Helicase inhibitor from preclinical to early Phase 1 clinical

Other Synthetic Lethality Pipeline Programs

IDEAYA is advancing additional preclinical research programs to identify small molecule inhibitors for an MTAP-synthetic lethality target, as well as for multiple potential first-in-class synthetic lethality programs for patients with solid tumors characterized by proprietary biomarkers or gene signatures.

Darovasertib (IDE196)

IDEAYA continues to execute on its clinical trial strategy to evaluate darovasertib (IDE196), a potent and selective PKC inhibitor.

IDEAYA is evaluating darovasertib in combination with crizotinib, a cMET inhibitor, in metastatic uveal melanoma (MUM). The company is also clinically evaluating darovasertib as a combination with crizotinib in GNAQ/11 mutant skin melanoma in an ongoing arm of the current clinical trial, and in adjuvant primary uveal melanoma (UM) as monotherapy through an investigator sponsor clinical trial (IST). IDEAYA is also evaluating other potential darovasertib expansion opportunities, including in cMET driven tumors and in KRAS-mutation tumors.

Darovasertib / Crizotinib Combination Therapy

IDEAYA is continuing patient enrollment into the darovasertib / crizotinib combination arm of the Phase 1/2 clinical trial under clinical trial collaboration and supply agreements with Pfizer. Highlights:

- As of March 1, 2022, the company has enrolled 53 MUM patients into the darovasertib/crizotinib combination arm, and is continuing patient enrollment in the dose expansion cohort of this combination arm
- IDEAYA presented darovasertib and crizotinib clinical combination data in December 2021. As of data and analyses cutoff on November 25, 2021, twenty-two heavily pre-treated MUM patients (91% with prior therapies, and 59% with 2 or more prior therapies) had enrolled in the darovasertib and crizotinib combination arm at the expansion dose, with sixteen evaluable patients who had received one or more tumor scans and six patients who were awaiting their 1st tumor scan. Thirteen patients had received two or more tumor scans for evaluation of potential response. The reported preliminary data, based on an unlocked database, showed robust clinical activity with manageable side effect profile:
    - 100% Disease Control Rate (DCR): 16 of 16 evaluable patients with$\geq$1 post-baseline scan showed tumor shrinkage as determined by target lesion size reduction
    - 31% Overall Response Rate (ORR): 4 of 13 patients with$\geq$ 2 post-baseline scans had a confirmed partial response (PR) as determined by RECIST 1.1 based on investigator or central review; and no patients have come off-treatment prior to the 2nd scan
    - 46% of patients (6 of 13) with$\geq$ 2 post-baseline scans observed >30% tumor reduction, including one patient with an unconfirmed PR as determined by RECIST 1.1 is awaiting follow-on tumor scan
    - Observed side effect profile in MUM patients (n=22) showed a low rate of drug-related serious adverse events

(SAE's) and predominantly Grade 1 or 2 drug-related adverse events; eighteen patients experienced a drug-related AE, of which six patients observed Grade 3, and no patients observed Grade 4 or Grade 5

- These data provide clinical proof-of-concept for the darovasertib and crizotinib synthetic lethal combination treatment, and are consistent with the company's translational research discovery that Phase 1 clinical response to darovasertib monotherapy associated with low cMET activity, as measured by gene signature score
- The company is targeting a clinical data update for darovasertib and crizotinib combination in mid-2022, including tolerability and clinical efficacy. IDEAYA is also planning to seek FDA regulatory guidance for potential registration-enabling trial design to evaluate darovasertib and crizotinib combination in MUM in mid-2022. The timing of the clinical data and FDA regulatory guidance may be influenced by data maturity, including observation of median duration of response (DOR) or median progression free survival (mPFS).
- Expanded relationship with Pfizer under a clinical collaboration and supply agreement to support clinical evaluation of darovasertib and crizotinib combination in a potential registration-enabling clinical trial in MUM, subject to FDA feedback and guidance
- Associated cMET expression and activation to observed clinical response based on a retrospective analysis of human clinical biopsies from the Novartis darovasertib Phase 1 clinical trial, supporting cMET expression / activation as potential combination agent
- Observed preclinical synergies between darovasertib and crizotinib in relevant cellular models under conditions simulating a tumor microenvironment in the liver, the site of approximately 90% of uveal melanoma metastases; study data reported at AACR 2021

Darovasertib Monotherapy

IDEAYA has completed enrollment into its ongoing Phase 1/2 clinical trial evaluating darovasertib as monotherapy in MUM patients.

IDEAYA is planning to initiate an Investigator Sponsored Trial, with St. Vincent's Hospital Sydney Limited to evaluate IDE196 as monotherapy in a neo-adjuvant / adjuvant setting in (non-metastatic) uveal melanoma (UM) patients. Data from this clinical trial may offer proof of concept on its hypothesis that earlier treatment of UM patients with IDE196, prior to tumor metastasis, may lead to improved patient outcomes.

Darovasertib – Other Potential Indications

IDEAYA is evaluating the potential for darovasertib in other oncology indications, including in cMET-driven tumors and in KRAS-mutation tumors. The company is also evaluating darovasertib for potential treatment of GNAQ mutation-mediated rare diseases, including Sturge-Weber Syndrome (SWS) and Port Wine Stains (PWS), neurocutaneous disorders characterized by capillary malformations and associated with mutations in GNAQ. Highlights:

- Expanded its relationship with Pfizer under a clinical collaboration and supply agreement for clinical evaluation of darovasertib and crizotinib combination therapy in cMET-driven tumors, such as NSCLC or HCC, subject to preclinical validation studies
- Evaluating darovasertib in combination with a KRAS inhibitor in preclinical studies in KRAS-driven solid tumors

General

IDEAYA continues to monitor Covid-19 and its potential impact on clinical trials and timing of clinical data results. Initiation of clinical trial sites, patient enrollment and ongoing monitoring of enrolled patients, including obtaining patient computed tomography (CT) scans, may be impacted for IDEAYA clinical trials evaluating IDE397 and darovasertib; the specific impacts are currently uncertain.

Corporate Updates

IDEAYA's net losses were $49.8 million and $34.5 million for the years ended December 31, 2021 and December 31, 2020, respectively. As of December 31, 2021, the company had an accumulated deficit of $176.7 million.

As of December 31, 2021, IDEAYA had cash, cash equivalents and marketable securities of $368.1 million. IDEAYA believes that its cash, cash equivalents and marketable securities will be sufficient to fund its planned operations into 2025. These funds will support the company's efforts through potential achievement of multiple preclinical and clinical milestones across multiple programs.

Our updated corporate presentation is available on our website, at our Investor Relations page: https://ir.ideayabio.com/.

Financial Results

As of December 31, 2021, IDEAYA had cash, cash equivalents and short-term and long-term marketable securities totaling $368.1 million. This compared to cash, cash equivalents and short-term and long-term marketable securities of $283.6 million at December 31, 2020. The increase was primarily due to $86.0 million in net proceeds received from issuance of common stock in an underwritten public offering on July 12, 2021 and $57.3 million in net proceeds under the ATM Program received through December 31, 2021, offset by cash used in operations and purchases of property and equipment.

Collaboration revenue for the three months ended December 31, 2021 totaled $3.0 million compared to $10.6 million for the same period in 2020. Collaboration revenue was recognized for the performance obligations satisfied through December 31, 2021 under the GSK Collaboration Agreement.

Research and development (R&D) expenses for the three months ended December 31, 2021 totaled $16.1 million compared to $12.1 million for the same period in 2020. The increase was primarily due to higher personnel-related expenses, laboratory supplies expenses and consulting fees.

General and administrative (G&A) expenses for the three months ended December 31, 2021 totaled $5.2 million compared to $3.8 million for the same period in 2020. The increase was primarily due to higher personnel-related expenses, software expenses and consulting fees.

The net loss for the three months ended December 31, 2021 was $18.2 million compared to $5.1 million for the same period in 2020. Total stock compensation expense for the three months ended December 31, 2021 was $2.1 million compared to $1.0 million for the same period in 2020.

The net loss for the year ended December 31, 2021 was $49.8 million compared to $34.5 million for the same period in 2020.

Total stock compensation expense for the year ended December 31, 2021 was $8.2 million compared to $3.6 million for the same period in 2020.

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. IDEAYAs 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) the extent to which IDEAYA's existing cash, cash equivalents, and marketable securities will fund its planned operations, (ii) the timing of monotherapy cohort expansion and combination cohort initiation in the IDE397 Phase 1 clinical trial, (iii) the timing and content of an additional clinical data update for the darovasertib and crizotinib combination, (iv) the timing of submitting an IND for PARG inhibitor, IDE161, (v) the timing of initiating IND-enabling studies for a Pol Theta inhibitor, (vi) the timing of the delivery of the GSK option data package, (vii) the potential receipt of GSK milestone payments, (viii) the timing of identification of a development candidate for a Werner Helicase inhibitor, (ix) the timing of obtaining FDA guidance for potential registration-enabling trial design to evaluate the darovasertib and crizotinib combination, (x) the initiation of an IST to evaluate ID196 in a neo-adjuvant / adjuvant setting, al pathway, (xi) the initiation of a Phase 1 clinical trial to evaluate darovasertib in SWS and PWS, and (xii) the impact of COVID-19. 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, 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 Quarterly Report on Form 10Q filed on November 15, 2021 and any current and periodic reports filed with the U.S. Securities and Exchange Commission.

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,	
	2021	2020	2021	2020
	(Unaudited)		(Unaudited)	
Collaboration revenue	$ 2,963	$ 10,571	$ 27,941	$ 19,538
Operating expenses				
Research and development	16,109	12,051	58,158	39,698
General and administrative	5,223	3,800	20,051	15,184
Total operating expenses	21,332	15,851	78,209	54,882
Loss from operations	(18,369)	(5,280)	(50,268)	(35,344)
Interest income and other income, net	157	145	506	849
Net loss	$ (18,212)	$ (5,135)	$ (49,762)	$ (34,495)
Unrealized losses on marketable securities	(662)	(28)	(719)	(58)
Comprehensive loss	$ (18,874)	$ (5,163)	$ (50,481)	$ (34,553)
Net loss per share attributable to common stockholders, basic and diluted	$ (0.47)	$ (0.18)	$ (1.41)	$ (1.40)
Weighted average number of shares outstanding, basic and diluted	38,501,335	29,149,106	35,252,443	24,721,775

IDEAYA Biosciences, Inc.

Condensed Balance Sheet Data

(*in thousands*)

	December 31, 2021	December 31, 2020
	(Unaudited)	
Cash and cash equivalents and short-term and long-term marketable securities	$ 368,063	$ 283,585
Total assets	381,347	298,269
Total liabilities	79,833	99,995
Total liabilities and stockholders' equity	381,347	298,269

SOURCE IDEAYA Biosciences, Inc.

For further information: IDEAYA Biosciences, Paul Stone, Senior Vice President and Chief Financial Officer, investor@ideayabio.com

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https://media.ideayabio.com/2022-03-15-IDEAYA-Biosciences,-Inc-Reports-2021-Financial-Results-and-Provides-Business-Update