Curis® and DarwinHealth Announce Scientific Collaboration to Characterize Biomarkers and Tumor Subtype Alignments for Fimepinostat in DLBCL and Solid Malignancies

LEXINGTON, Mass. and NEW YORK, Jan. 13, 2020 /PRNewswire/ -- Curis, Inc (**NASDAQ:** CRIS) and DarwinHealth, Inc. today announced a multi-year scientific research collaboration to use quantitative, systems biology-based algorithms, CLIA-approved technologies, and novel, validated approaches focused on Master Regulator (MR) proteins and tumor checkpoints to: (a) better understand and articulate the role of MYC in fimepinostat's mechanism of action; and (b) explore additional potential novel biomarkers that may help patient selection in hematologic and solid tumors clinical studies.

The collaboration will deploy DarwinHealth's proprietary compound-checkpoint-tumor subtype matching platform, its VIPER algorithm to characterize protein activity signatures that are the hallmark of regulatory network dysfunction in cancer cells, and its high-throughput drug perturbation and Plate-Seq discovery platform to analyze the potential therapeutic efficacy of fimepinostat (a synthetic, orally-available, small molecule that inhibits the activity of histone deacetylase, or HDAC, and phosphatidyl-inositol 3 kinase, or PI3 kinase enzymes) across a number of tumor subtypes.

"The aim of this exciting collaboration," explained Professor Andrea Califano, Clyde and Helen Wu Professor and Chair, Department of Systems Biology, Columbia University and co-founder of DarwinHealth, "is to assess and characterize the role of MYC as a critical effector of fimepinostat activity in DLBCL, as well as its overall, tumor-specific Mechanism of Action (MoA), considering that both HDAC and PI3K inhibitors have been independently characterized among the strongest regulators of tumorigenic MYC activity. Additionally, the collaboration will mechanistically characterize additional therapeutic opportunities for fimepinostat across multiple hematopoietic and solid tumor subtypes, as selected by Curis for this scientific collaboration. The study will leverage the VIPER algorithm to characterize fimepinostat's activity against key Master Regulator (MR) protein modules (tumor checkpoints) necessary for subtype-specific tumor viability."

As part of this initiative, DarwinHealth will provide a comprehensive readout of fimepinostat's potential clinical value across a number of cancer tissue-specific contexts, including its genome-wide mechanism of action, its tumor-specific biomarkers of sensitivity and resistance, and its ability to synergize with venetoclax for combination therapy applications in DLBCL and solid tumors. Through quantitative modeling, mechanism-driven and biomarker-driven developmental trajectories for fimepinostat will be predicted to help Curis design *in vivo* validation studies and focused clinical studies to leverage key opportunities for this dual HDAC/PI3 kinase inhibitor that would not be apparent using conventional technologies.

"In light of promising clinical data already reported for fimepinostat, and its unique MOA, our Compound-2-Clinic (C2C) collaboration with Curis promises to be one of our most productive scientific collaborations," noted Dr. Gideon Bosker, CEO and co-founder of DarwinHealth. "Our C2C technologies are ideally suited to identify mechanistic alignment between compounds and cancer patients, based on their ability to inactivate the patient-specific master regulator proteins that are necessary for tumor state maintenance. Compounds and compound combinations prioritized by this technology can be efficiently validated, first in PDX models and subsequently in the clinic, using our NYS State, CLIA-certified DarwinOncoTreat/Target tests. In addition to achieving a more mechanistic characterization of MYC as a critical effector of fimepinostat activity in DLBCL, our goal is to delineate the range of additional tumor subtypes—many of which may be entirely unanticipated—where fimepinostat may consistently and predictably collapse tumor checkpoint activity, thus abrogating tumor growth. These discoveries can be quickly matured to precision, biomarker-driven, clinical human testing and commercial development."

"This scientific collaboration aligns with our development path for fimepinostat by deepening our understanding of the MYC mechanism of action and potentially identifying additional, novel trajectories, indications, mechanisms, and precision-focused drug-tumor alignments that can produce a more inclusive developmental roadmap for our lead compound," said James Dentzer, President and Chief Executive Officer of Curis. "The DarwinHealth team led by Drs. Andrea Califano and Mariano Alvarez, who co-developed VIPER technology in the Califano Lab at Columbia University, bring world-class expertise that will be invaluable for identifying the full commercialization pathway for fimepinostat."

"DarwinHealth's approach to tumor checkpoint elucidation, linked to MR proteins, will help support fimepinostat's MYC-driven mechanism of action," said Dr. Robert Martell, Head of R&D at Curis. "This approach is also ideally suited for identifying additional biomarkers in our DLBCL program and illuminating additional tumor subtypes in which fimepinostat, alone or in combination with venetoclax, may have therapeutic potential. These mechanistically relevant insights will help us to focus on, test, and prioritize with a higher likelihood of success, the comprehensive translational roadmap for fimepinostat in targeted clinical contexts."

As part of this collaboration, DarwinHealth will be eligible for milestone payments and royalties for applications that directly result from their analyses.

About DarwinHealth, Inc.

DarwinHealth: Precision Therapeutics for Cancer Medicine is a "frontiers of cancer," technology-focused company, co-founded by CEO Gideon Bosker, MD, and Professor Andrea Califano, Clyde and Helen Wu Professor of Chemical Systems Biology and Chair, Department of Systems Biology at Columbia University. The company's technology was developed by the Califano lab over the past 14 years and is exclusively licensed from Columbia University. DarwinHealth technology has been developed to identify actionable, and frequently unanticipated, mechanistic and biomarker-directed alignments at the proteomic level between small molecules and specific tumor subtypes/patient cohorts; and, therefore, it is positioned to accelerate the development of oncology pipelines, both for small molecule and immuno-oncology-based developmental pathways.

DarwinHealth utilizes proprietary, systems biology algorithms to match virtually every cancer patient with the drugs and drug combinations that are most likely to produce a successful treatment outcome. "Conversely, these same algorithms also can prioritize investigational drugs and compound combinations of unknown potential against a full spectrum of human malignancies, as well as novel cancer targets," explained Dr. Bosker, "which make them invaluable for pharmaceutical companies seeking to both optimize their compound pipelines and discover mechanistically actionable, novel cancer targets and compound-tumor alignments."

DarwinHealth's mission statement is to deploy novel technologies rooted in systems biology to improve clinical outcomes of cancer treatment. Its core technology, the VIPER algorithm, can identify tightly knit modules of master regulator proteins that represent a new class of actionable therapeutic targets in cancer. The methodology is applied along two complementary axes: first, DarwinHealth's technologies support the systematic identification and validation of druggable targets at a more foundational, deep state of the cancer cell's regulatory logic, so we and our scientific partners can exploit next generation actionability based on fundamental and more universal tumor dependencies and mechanisms; second, from a drug development and discovery perspective, the same technologies capable of identifying potentially druggable novel targets based on master regulators, and upstream modulators of those targets. This is where the DarwinHealth oncotectural approach, with its emphasis on elucidating and targeting tumor checkpoints, provides its most important solutions and repositioning roadmaps for advancing precision-focused cancer drug discovery and therapeutics.

The proprietary, precision medicine-based methods employed by DarwinHealth are supported by a deep body of scientific literature authored by its scientific leadership, including DarwinHealth CSO, Mariano Alvarez, PhD, who co-developed the company's critical computational infrastructure. These proprietary strategies leverage the ability to reverse-engineer and analyze the genome-wide regulatory and signaling logic of the cancer cell, by integrating data from in silico, in vitro, and in vivo assays. This provides a fully integrated drug characterization and discovery platform designed to elucidate, accelerate, and validate precise developmental trajectories for pharmaceutical assets, so their full clinical and commercial potential can be realized. For more information, please visit: www.DarwinHealth.com.

About Curis, Inc.

Curis is a biotechnology company focused on the development of innovative therapeutics for the treatment of cancer, including fimepinostat, which is being investigated in combination with venetoclax in a Phase 1 clinical study in patients with DLBCL. Curis is also engaged in a collaboration with Aurigene in the areas of immuno-oncology and precision oncology. As part of this collaboration, Curis has exclusive licenses to oral small molecule antagonists of immune checkpoints including, the VISTA/PDL1 antagonist CA-170, and the TIM3/PDL1 antagonist CA-327, as well as the IRAK4 kinase inhibitor, CA-4948. CA-4948 is currently undergoing testing in a Phase 1 trial in patients with non-Hodgkin lymphoma. In November 2019, Curis announced that no further patients will be enrolled in its Phase 1 study of CA-170, an orally available, dual inhibitor of VISTA and PDL1, in malignant plural mesothelioma patients (high VISTA expressors), based on initial efficacy data. CA-170 was generally safe and well-tolerated in the study. The Company continues to evaluate the translational science and clinical pharmacodynamics of CA-170, in addition to patient data from the study, to assess opportunities for further evaluation of CA-170. In addition, Curis is engaged in a collaboration with ImmuNext for development of CI-8993, a monoclonal anti-VISTA antibody. Curis is also party to a collaboration with Genentech, a member of the Roche Group, under which Genentech and Roche are commercializing Erivedge® for the treatment of advanced basal cell carcinoma. For more information, visit Curis' website at www.curis.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the U.S. Private Securities Litigation Reform Act of 1995, including, without limitation, statements regarding any expectations of the potential for the Company's proprietary drug candidate fimepinostat, including with respect to the

characterization of the role of MYC in the mechanism of action of fimepinostat, the identification of a novel biomarker in DLBCL and/or the identification of pairings of novel biomarkers and other tumor subtypes for fimepinostat, the potential advantages and benefits of small molecule checkpoint antagonists, and the Company's plans to advance its development programs, including the Company's plans for the characterization of biomarkers and tumor subtype alignment for fimepinostat. Forward-looking statements may contain the words "believes," "expects," "anticipates," "plans," "intends," "seeks," "estimates," "assumes," "will," "may," "could" or similar expressions. These forward-looking statements are not guarantees of future performance and involve risks, uncertainties, assumptions and other important factors that may cause actual results to be materially different from those indicated by such forward-looking statements. For example, Curis may experience adverse results, delays and/or failures in its drug development programs and may not be able to successfully advance the development of its drug candidates in the time frames it projects, if at all. Curis's drug candidates may cause unexpected toxicities, fail to demonstrate sufficient safety and efficacy in clinical studies and/or may never achieve the requisite regulatory approvals needed for commercialization. Favorable results seen in preclinical studies and early clinical trials of Curis's drug candidates, including without limitation fimepinostat, may not be replicated in later trials. There can be no guarantee that the research collaboration agreement with DarwinHealth will continue for its full term, that Curis or DarwinHealth will each maintain the financial and other resources necessary to continue financing its portion of the C2C initiative or biomarker discovery program under the collaboration. Curis will require substantial additional capital to fund its business and such capital may not be available on reasonable terms, or at all. Without sufficient additional funding, Curis will not be able to continue as a going concern and may be forced to delay, reduce in scope or eliminate some of its research and development programs, which could adversely affect its business prospects and its ability to continue operations. Substantial doubt about Curis's ability to continue as a going concern may adversely affect Curis's ability to access the substantial additional capital needed to continue operations. Curis faces substantial competition. Curis also faces risks relating to potential adverse decisions made by the FDA and other regulatory authorities, investigational review boards, and publication review bodies. Curis may not obtain or maintain necessary patent protection and could become involved in expensive and time-consuming patent litigation and interference proceedings. Unstable market and economic conditions and unplanned expenses may adversely affect Curis's financial conditions and its ability to access the substantial additional capital needed to fund the growth of its business. Important factors that may cause or contribute to such differences include the factors set forth under the caption "Risk Factors" in our most recent Form 10-K and Form 10-Q and the factors that are discussed in other filings that we periodically make with the Securities and Exchange Commission. In addition, any forward-looking statements represent the views of Curis only as of today and should not be relied upon as representing Curis's views as of any subsequent date. Curis disclaims any intention or obligation to update any of the forward-looking statements after the date of this press release whether as a result of new information, future events or otherwise, except as may be required by law.

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Additional assets available online: Photos (1)

https://investors.curis.com/2020-01-13-Curis-R-and-DarwinHealth-Announce-Scientific-Collaboration-to-Characterize-Biomarkers-and-Tumor-Subtype-Alignments-for-Fimepinostat-in-DLBCL-and-Solid-Malignancies