



Alkermes and Clovis Oncology Initiate Research Collaboration to Explore Combination Cancer Therapies

February 19, 2019

-- Combinations of ALKS 4230 with Rucaparib and Lucitanib to be Evaluated in Multiple Preclinical Tumor Models --

DUBLIN and BOULDER, Colo., Feb. 19, 2019 /PRNewswire/ -- [Alkermes plc](#) (Nasdaq: ALKS) and [Clovis Oncology, Inc.](#) (Nasdaq: CLVS) today announced that the companies have entered into a research collaboration to evaluate ALKS 4230, Alkermes' investigational engineered interleukin-2 (IL-2) variant immunotherapy, in combination with rucaparib, Clovis' marketed PARP inhibitor, and lucitanib, Clovis' investigational tyrosine kinase inhibitor. The collaboration will explore the potential anti-cancer effects of both treatment combinations in preclinical models across multiple tumor types. Results of this research may form the basis for potential future clinical studies of the novel combinations of ALKS 4230 with rucaparib and/or lucitanib.

"Our preclinical partnership with Clovis reflects our ongoing efforts to explore the numerous combination options afforded to ALKS 4230. The collaboration will allow us to examine combinations in two areas of keen interest, PARP and tyrosine kinase inhibition pathways," said Mark Namchuk, Ph.D., Senior Vice President, Research, Pharmaceutical and Non-Clinical Development at Alkermes. "Evidence of combined benefit of ALKS 4230 with rucaparib and/or lucitanib from these preclinical studies may provide a strong rationale to advance into clinical development."

"The unique profiles of rucaparib, lucitanib and ALKS 4230 may offer the potential for complementary therapies that could represent a meaningful opportunity for the development of new anti-cancer combination treatment options," said Patrick J. Mahaffy, President and CEO of Clovis Oncology. "We are committed to exploring combinations such as these with Alkermes in order to bring improved therapeutic outcomes to patients with multiple tumor types."

Under this collaboration agreement, Alkermes and Clovis will perform preclinical studies to examine the mechanism of action and efficacy of the combinations of ALKS 4230 with rucaparib and ALKS 4230 with lucitanib in multiple tumor models. Under the terms of the agreement, the companies will share costs related to the preclinical studies, and each will contribute their respective compounds to the research collaboration.

About ALKS 4230

ALKS 4230 is an investigational, novel, engineered fusion protein designed to selectively activate tumor-killing immune cells while avoiding the expansion of immunosuppressive cells by preferentially binding to the intermediate-affinity interleukin-2 (IL-2) receptor complex. The selectivity of ALKS 4230 is designed to leverage the proven anti-tumor effects of existing IL-2 therapy while mitigating certain limitations.

About Rucaparib

Rucaparib is an oral, small molecule inhibitor of the poly (ADP-ribose) polymerase (PARP) enzymes PARP-1, PARP-2, and PARP-3, which play a role in DNA repair. Rucaparib stimulates an anti-tumor immune response through the activation of the stimulator of interferon (STING) pathway and tumor cell death, resulting in the infiltration of multiple immune subsets including CD8 positive T-cells.¹

Rucaparib is being developed in multiple tumor types, including ovarian, metastatic castration-resistant prostate, and bladder cancers, as monotherapy, and in combination with other anti-cancer agents. Exploratory studies in other tumor types are also underway. Clovis holds worldwide rights for rucaparib. Rucaparib is an unlicensed medical product outside of the U.S. and Europe.

About Lucitanib

Lucitanib is an oral, potent inhibitor of the tyrosine kinase activity of vascular endothelial growth factor receptors 1 through 3 (VEGFR1-3), platelet-derived growth factor receptors alpha and beta (PDGFR α / β) and fibroblast growth factor receptors 1 through 3 (FGFR1-3).

Emerging clinical data support the combination of angiogenesis inhibitors and immunotherapy to increase effectiveness in multiple cancer indications.² Angiogenic factors, such as vascular endothelial growth factor (VEGF), are frequently up-regulated in tumors and create an immunosuppressive tumor microenvironment.³ Use of antiangiogenic drugs reverses this immunosuppression and can augment response to immunotherapy.

Lucitanib is an unlicensed medical product.

About Alkermes

Alkermes plc is a fully integrated, global biopharmaceutical company developing innovative medicines for the treatment of central nervous system (CNS) diseases. The company has a diversified commercial product portfolio and a substantial clinical pipeline of product candidates for chronic diseases that include schizophrenia, depression, addiction, multiple sclerosis and oncology. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, Ohio. For more information, please visit Alkermes' website at www.alkermes.com.

About Clovis Oncology

Clovis Oncology, Inc. is a biopharmaceutical company focused on acquiring, developing and commercializing innovative anti-cancer agents in the U.S., Europe and additional international markets. Clovis Oncology targets development programs at specific subsets of cancer populations, and simultaneously develops, with partners, diagnostic tools intended to direct a compound in development to the population that is most likely to benefit from its use. Clovis Oncology is headquartered in Boulder, Colorado; please visit www.clovisoncology.com for more information, including additional office locations in the U.S. and Europe.

Alkermes Note Regarding Forward-Looking Statements

Certain statements set forth in this press release constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the potential therapeutic and commercial value of ALKS 4230, including in combination with rucaparib and/or lucitanib; and development plans for ALKS 4230 in combination with rucaparib and/or lucitanib, including preclinical studies and potential future clinical studies of such combinations. You are cautioned that forward-looking statements are inherently uncertain. Although the company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and are subject to a variety of risks and uncertainties, many of which are beyond the company's control, which could cause actual results to differ materially from those expressed or implied in the forward-looking statements. These risks and uncertainties include, among others, whether preclinical and early clinical results for ALKS 4230, including ALKS 4230 in combination with rucaparib and/or lucitanib, will be predictive of future clinical study results; whether ALKS 4230, alone or in combination, could be shown to be unsafe or ineffective; whether future clinical trials or future stages of ongoing clinical trials for ALKS 4230, whether alone or in combination, will be initiated or completed on time or at all; changes in the cost, scope and duration of development activities for ALKS 4230; and those risks and uncertainties described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2018 and in subsequent filings made by the company with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release.

Clovis Oncology Note Regarding Forward-Looking Statements

To the extent that statements contained in this press release are not descriptions of historical facts regarding Clovis Oncology, they are forward-looking statements reflecting the current beliefs and expectations of management. Examples of forward-looking statements contained in this press release include, among others, statements regarding our expectations regarding the timing and pace of commencement of and enrollment in our clinical trials, including those being planned or conducted in collaboration with partners. Such forward-looking statements involve substantial risks and uncertainties that could cause our future results, performance or achievements to differ significantly from that expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in our clinical development programs for our drug candidates, including rucaparib and lucitanib, and those of our partners, whether preclinical results will be predictive of future clinical study results, whether safety and efficacy results from monotherapy trials are predictive of safety and efficacy in combination with other compounds, the corresponding development pathways of our companion diagnostics, the timing of availability of data from our clinical trials and the results, the initiation, enrollment and timing of our planned clinical trials, actions by the FDA, the EMA or other regulatory authorities regarding whether to accept or approve drug applications that may be filed, as well as their decisions regarding drug labeling, reimbursement and pricing, and other matters that could affect the development, availability or commercial potential of our drug candidates or companion diagnostics. Clovis Oncology does not undertake to update or revise any forward-looking statements. A further description of risks and uncertainties can be found in Clovis Oncology's filings with the Securities and Exchange Commission, including its Annual Report on Form 10-K and its reports on Form 10-Q and Form 8-K.

¹Nguyen, et al. "Rucaparib Induces IFN Type 1 Regulated Genes and Enhances Immune-Associated Tumor Suppression," presented at the 2018 American Association for Cancer Research (AACR) Annual Meeting. Abstract 1716.

²Makker et al. "Lenvatinib + Pembrolizumab in Advanced Endometrial Cancer: Updated Results." Presented at the 2018 American Society of Clinical Oncology (ASCO) Annual Meeting. Abstract 5596.

³Fukumara, et al *Nat Rev Clin Oncol*. 2018 May;15(5):325-340. *Nat. Rev. Clin. Onc.* "Enhancing cancer immunotherapy using antiangiogenics: opportunities and challenges."

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