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TECHNOLOGY TRANSFER

Syndax

Syndax Pharmaceuticals to Commercialize First-in-Class Lung Cancer Treatment Developed at the University of Colorado

--Licensing agreement allows development of a novel combination therapeutic for non-small-cell lung carcinoma, a type of lung cancer difficult to treat with conventional chemotherapy—

Aurora, Colo.-- May 9, 2013-- The University of Colorado (CU) has signed an exclusive, worldwide licensing agreement with Syndax Pharmaceuticals (Waltham, MA) a company focused on the development of novel combination strategies for cancers that have become resistant to standard treatments. The license allows Syndax to commercialize and market a treatment approach developed by a team led by Paul Bunn (a professor of medical oncology at the CU School of Medicine and a former director of the CU Cancer Center) in which two existing classes of drugs are combined to create a more effective, synergistic chemotherapy for a resistant type of non-small cell lung cancer (NSCLC). Syndax, in collaboration with Bunn and his colleagues at CU, completed a phase 2 clinical trial in NSCLC, the results of which were published in 2012, and based on those findings intends to begin key phase 3 testing across a number of solid tumor indications.

Lung cancer is the leading cause of cancer death in men and women in the U.S., and the leading worldwide cause of cancer death. Nearly 80% of lung cancers are categorized as non-small-cell lung carcinoma (NSCLC), a grouping that includes all lung cancers except the small-cell type (the type mostly closely associated with smoking). NSCLCs are much less sensitive to chemotherapy and radiation compared to small-cell lung carcinoma, so surgical removal of the affected lobe of the lung is often the preferred treatment if the disease is diagnosed early enough. Most often, by the time the disease is diagnosed it has already begun to metastasize, making surgical treatment a less effective treatment option; for advanced or metastatic NSCLC, chemotherapy and radiation can improve life expectancy and relieve some symptoms, but these treatments do not typically cure the disease. The five-year survival rate for stage IV disease (40% of newly-diagnosed patients) is just 1%.

Several oral cancer chemotherapies (such as Tarceva) target EGFR (epidermal growth factor receptor), a receptor that exists on the surface of human cells for epidermal growth factor (EGF), which helps normal cells grow, multiply and differentiate into the specific types of cells needed by the body. When genetic mutations cause cells to produce too much EGFR, cells begin to grow and multiply too rapidly, and a number of different types of cancer can result, including lung cancer. Drugs that inhibit EGFR can be effective treatments for patients whose cancers have this particular mutation, but even these cancers are likely to develop resistance to EGFR inhibitors when their cells mutate to become less dependent on EGF.

Bunn's CU research group, working in collaboration with Syndax, learned that the company's drug entinostat – a highly selective histone deacetylase (HDAC) inhibitor – prevents NSCLC cells from developing resistance to EGFR inhibitors. HDAC inhibitors have been in use for decades as mood stabilizers and anti-seizure drugs, but only recently have been investigated as potential treatments for cancer. When entinostat was combined with an EGFR inhibitor in a clinical trial taking place at CU and other locations, the results showed promising benefits to NSCLC patients whose tumors had high levels of E-cadherin, a molecular marker for cancer. CU Cancer Center researchers, who are faculty at the CU School of Medicine, were the first to identify elevated E-cadherin as a targetable NSCLC biomarker, the first to develop the biomarker tumor testing process for elevated E-cadherin in NSCLC, and the first to test the combined therapy.

"Cancer cells that remain most similar to normal lung lining (epithelial) cells are most likely to benefit from the combined therapy, and these most susceptible cells can be identified with an antibody to a protein on the cells called E-cadherin," said Paul Bunn, MD, professor of medical oncology at the CU medical school and principal investigator of the University of Colorado Cancer Center's Specialized Program of Research Excellence in Lung Cancer, funded by the National Cancer Institute. "Entinostat causes an even higher expression of E-cadherin, and this is associated with increased sensitivity to oral anti-EGFR drugs." About 40 percent of NSCLC patients have elevated E-cadherin levels, making this a significant advance towards highly personalized treatment for lung cancer patients.

The license agreement between CU and Syndax will allow the company to move forward with testing and development of this combined treatment approach, and also includes an option to license the CU-discovered biomarkers needed to identify the patients who are most likely to benefit from the treatment.

“We have had a longstanding and productive research and clinical collaboration with Dr. Bunn and his colleagues at CU, and are excited to complete this licensing agreement as a culmination of that work and to take a significant step towards the development and commercialization of entinostat in NSCLC,“ said Arlene Morris, CEO of Syndax.

“The university has held great hope for this particular line of therapy since Dr. Bunn and his team first disclosed their findings,“ said David Poticha, a senior licensing manager at the CU Technology Transfer Office. “We are extremely pleased to be partnered with a company like Syndax to develop this treatment.“

About Syndax Pharmaceuticals

Syndax is a late-stage oncology company initiating pivotal programs in solid tumors based on employing epigenetic strategies to overcome the problem of resistance in oncology care. Syndax holds worldwide rights to entinostat, an oral, highly selective histone deacetylase (HDAC) inhibitor being developed in advanced breast and lung cancer. Randomized, placebo-controlled phase 2 studies with entinostat have demonstrated promising results in combination with aromatase inhibitors in breast cancer (ENCORE 301) and with the EGFR-TKI erlotinib (ENCORE 401) in non-small cell lung cancer providing the basis for moving entinostat into pivotal, phase 3 testing across a platform of solid tumor indications. NCI and Syndax are collaborating on the development of entinostat under a Cooperative Research and Development Agreement. The company is supported by top venture capitalists and led by industry experts developing treatments for large markets including metastatic breast and lung cancer. Formed in 2005, Syndax's intellectual property is based on work from scientific founder Ronald Evans, Ph.D., recipient of the 2004 Albert Lasker Prize for Basic Medical Research, a Member of the National Academy of Sciences, a professor at the Salk Institute for Biological Studies and a Howard Hughes Medical Institute Investigator. For more information please visit www.syndax.com.

About the Technology Transfer Office and the University of Colorado:

The CU Technology Transfer Office pursues, protects, packages, and licenses to business the intellectual property generated from research at CU. The TTO provides assistance to faculty, staff, and students, as well as to businesses looking to license or invest in CU technology. For more information about technology transfer at CU, visit www.cu.edu/techtransfer.

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