



Syndax Pharma Seeks to Reprogram Tumor Cells to Treat Breast Cancer

Ryan McBride 6/8/10

Women lose a valuable weapon against their breast tumors when the potency of hormone therapy fades. But what if there was a way to “reprogram” breast tumor cells to be receptive to hormone therapy? Waltham, MA-based Syndax Pharmaceuticals might have such a way.

Syndax has shown in a 26-patient clinical trial that its drug, entinostat, could improve the ability of hormone therapies to kill breast cancer. The biotech startup—which was co-founded by scientists from the Salk Institute for Biological Studies in La Jolla, CA in 2005—has embarked on a new human study that will give it a clearer picture than previous studies provided of how well its drug improves breast cancer treatment. Its research has been displayed in recent days at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago.

The company’s new Phase II clinical trial for entinostat for breast cancer patients is a big test of the firm’s technology. The firm has raised \$49 million from venture capital firms such as the San Diego venture firms Domain Associates, Avalon Ventures, and Forward Ventures as well as MPM Capital, of Boston and South San Francisco, and Pappas Ventures in Durham, NC. (Eckard Weber, a well-known partner at Domain in San Diego, co-founded and served as an early CEO of Syndax.) Joanna Horobin, the firm’s CEO, said that the startup raised its latest \$9 million in venture financing this year to complete its new mid-stage clinical trial, which she hopes will yield evidence of its lead drug’s utility by early next year.

For several years Syndax has been one of the biotechs to watch in the hot field of epigenetics, which involves the study chemical changes in cells that impact how genes are expressed or suppressed without changing the underlying DNA code. Epigenetics grabbed the cover of Time magazine in January. For instance, breast tumor cells can undergo epigenetic changes that make them immune to hormone therapies, which are intended to stymie the production of estrogen needed to sustain tumor survival. Syndax’s drug aims to reprogram breast tumor cells in which those detrimental epigenetic switches occur.

“The idea is that you turn off the growth driver [in breast cancer],” Horobin said, “which then allows the normal tumor suppressor activity [in cells] to work again.”

Syndax reported results over the weekend at ASCO from a Phase II, 26-patient study, in which all the women with breast cancer were given the firm’s drug entinostat in combination with an approved drug

that blocks estrogen production. One patient's breast tumor shrunk during the study and, in nine other patients, the tumors stopped growing for at least four months, according to the company.

A bigger test of the drug will be the biotech's ongoing Phase II trial of 114 patients with breast cancer. One group in the study will take the firm's drug in combination with a hormone therapy, Pfizer's (NYSE:PFE) exemestane (Aromasin). Another group will take that hormone therapy and placebo, and the trial will compare how much of a difference the company's drug makes in treating patient's breast tumors. With results early next year, Horobin said, the firm hopes to find a drug company to partner with in order to pay for further development of the drug.

While Syndax has its headquarters in the Boston area, Horobin said, the firm's director of scientific affairs, Peter Ordentlich, coordinates its largely virtual R&D organization from his office in San Diego. Ordentlich, a former scientist at the Salk Institute, is one of the founders of the startup. The firm was initially formed to commercialize the research of Salk biology professor Ron Evans, who has made seminal discoveries about how epigenetics plays a role in various types of cancer. Evans, who is a consultant to Syndax, is also an advisor to the Cambridge, MA-based epigenetics startup Epizyme.

Syndax's main drug, entinostat, doesn't actually come from Salk, but rather was licensed from Germany's Bayer Schering Pharma in 2007. The drug is from a class of well-known drugs called histone deacetylase (HDAC) inhibitors, which take aim at the HDAC enzymes that play a role in expression of certain genes in cells. Due to their function, HDACs are called epigenetic enzymes.

The company believes that its lead drug could be used to treat other types of cancer in which the epigenetic enzymes are a factor, and the treatment has been tested so far in patients with Hodgkin's lymphoma, a cancer of the white blood cells, a type of lung cancer, and a precursor to leukemia known as myelodysplastic syndrome.

But breast tumors, and specifically those driven by estrogen, are Syndax's prime focus for the drug. Horobin said that a challenge in this market is to identify which patients have breast tumors that have stopped responding to hormone therapy, since that information would let her company know which patients would be most likely to benefit from the new treatment.

Keep an eye out for how Syndax's drug performs in its latest breast cancer study. The trial could provide evidence that patients might gain a new weapon against breast tumors while helping otherwise ineffective hormone therapies to do their jobs.

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