EMERGING COMPANY PROFILE

SHOT IN THE DYRK

BY EMILY CUKIER-MEISNER, SENIOR WRITER

Felicitex Therapeutics Inc. is discovering and developing small molecule cancer agents that target cell quiescence, a mechanism cancer cells can use to resist treatment.

Cell quiescence is a reversible phenomenon where cells stop dividing and enter a dormant state with greatly reduced nutrient and energy requirements. Though normal cells may become quiescent for various reasons, cancer cells can become quiescent for an indefinite amount of time to protect themselves from chemotherapies that target dividing cells or deprive them of nutrients or growth factors.

Felicitex is developing therapies that force cancer cells out of quiescence so they are again vulnerable to treatment.

"Cancer cells can go into chemical quiescence when they encounter a chemotherapeutic or cytotoxic agent, then hide from the treatment in the resting stage. And all current treatments are targeted towards actively proliferating cells," said CEO and Scientific Director Maria Vilenchik.

She also noted cancer cells can learn from and adapt to treatments they are exposed to while quiescent, which helps them resist therapies once they reactivate.

Vilenchik and her Felicitex co-founders studied cancer cell quiescence at Roche's Nutley, N.J., oncology discovery site before it closed in 2012. She said they discovered Felicitex's initial quiescence target while at Roche — dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 1B (DYRK1B; MIRK) — but hadn't found a series of inhibitors that would make good clinical candidates.

DYRK comprises a family of tyrosine, serine and threonine kinases that play multiple roles in the cell, including regulation of cell cycle progression and differentiation.

In May, Felicitex in-licensed rights to small molecule DYRK inhibitors for use in oncology from Diaxonhit.

Selvita S.A. is helping Felicitex optimize the lead series as part of a deal to discover and develop selective inhibitors of kinases involved in cancer quiescence.

Vilenchik said inhibiting DYRK1B makes cells leave the quiescent (G0) phase and progress through the cell cycle, but that doing so is not "waking up the beast."

"We're tricking cancer cells — they think they get the chance to proliferate actively, but then they get exhausted and are unable to do so, and eventually die," she said.

In 2011, Vilenchik, Roche colleagues and SUNY Upstate Medical University researchers reported in *Molecular Cancer Therapeutics* that a small molecule inhibitor of DYRK1B made pancreatic cancer cells up to fivefold more sensitive to gemcitabine or cisplatin.

According to Vilenchik, SUNY did only basic research and did not develop its own molecule series, and Roche never came up with suitable drug candidates. As a result, Felicitex did not in-license any IP from Roche or SUNY, and has no legal obligations to the pharma.

Vilenchik said Felicitex has unpublished data showing its compounds can induce tumor regression in combination with gemcitabine in a mouse model of pancreatic cancer.

She said the molecules may have a wide therapeutic window because they inhibit a kinase that is responsible for keeping cancer cells quiescent but is not expressed in normal cells.

While inhibiting the target can be cytotoxic on its own, Felicitex expects to develop its molecules as combination therapies that sensitize cancer cells to cytotoxic agents like gemcitabine.

Adding Felicitex's compounds to chemotherapy might allow physicians to lower the dose of the cytotoxic agent, reducing overall toxicity.

"One way doctors deal with quiescent cancer cells is by giving high doses of the cancer therapy to patients, hoping that by the time the cells leave quiescence, the agent will still be there. But it leads to a lot of side effects," said Vilenchik.

She said Felicitex hopes to nominate a clinical lead candidate this year. It is studying the molecules to treat pancreatic, colon, lung, ovarian and breast cancers.

Board member and investor Marc Duey said Felicitex is funded up to IND-enabling studies and is seeking $5-$10 million in funding to complete them.

Felicitex expects to submit an IND by YE16, then seek a partner.

Vilenchik said the company plans to develop a companion diagnostic to detect DYRK expression to identify quiescent cancer cells.

At least one other company is developing DYRK inhibitors, but not in oncology. Pharmasum Therapeutics A/S is studying DYRK1A inhibitors for Alzheimer's disease.

Vilenchik said in addition to its work on DYRK, Felicitex is assembling a platform to study cancer cell quiescence including a 23,000-compound library to help screen for quiescence targets and molecules. bc

FELICITEX THERAPEUTICS INC.
Cambridge, Mass.

Technology: Small molecules that inhibit targets related to quiescent cancer cells

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2012 by Maria Vilenchik, Michael Frid, Yuriy Gankin and Valeria Povolotsky

University collaborators: Memorial Sloan Kettering Cancer Center, Massachusetts General Hospital, Netherlands Cancer Institute

Corporate partners: Selvita S.A., Diaxonhit and Cureline Inc.

Number of employees: 4

Funds raised: $2 million

Investors: Yuriy Gankin and Marc Duey

CEO: Maria Vilenchik

Patents: 2 issued covering diagnostics and molecules targeting quiescent cancer cells

COMPANIES AND INSTITUTIONS MENTIONED

Diaxonhit (Euronext:ALEHT), Paris, France
Felicitex Therapeutics Inc., Cambridge, Mass.
Pharmasum Therapeutics A/S, Tromso, Norway
Selvita S.A. (Warsaw:SLV), Krakow, Poland
SUNY Upstate Medical University, Syracuse, N.Y.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland

REFERENCES

Ewton, P., et al. "Inactivation of Mirk/Dyrk1b kinase targets quiescent pancreatic cancer cells." *Molecular Cancer Therapeutics* (2011)