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Cybrexa targets solid tumors with pH-tied intracellular delivery technology

By Michael Fitzhugh, Staff Writer

Cybrexa Therapeutics, a New Haven, Conn.-based company developing a solid tumor-targeting technology to work with an already-approved PARP inhibitor, said it plans to submit an investigational new drug application for its lead candidate, CBX-11, by the fourth quarter of 2019. A phase I trial evaluating the drug is expected to begin in the first quarter of 2020. If preclinical findings hold, the approach could potentially enhance the therapeutic index of the PARP inhibitor, improve overall survival and limit the toxicities associated with combining PARP inhibitors and DNA-damaging chemotherapy.

Founded in 2017, the company is advancing a tumor-targeting peptide technology that it calls Alphalex. Born at Yale University in the lab of Donald Engelman and further advanced at the University of Rhode Island, the technology combines a peptide, linker and small molecule in an agent targeted to low pH conditions thought to be common across all solid tumors.

"Unlike an [antibody-drug conjugate] that requires a specific antigen be targeted, presuming there's one to target, this is a more universal technology that can be more broadly applied," Cybrexa's co-founder, president and CEO, Per Hellsund, told *BioWorld*.

Once in contact with the acidic environment of the tumor, Cybrexa's peptide forms an alpha-helix, or corkscrew, dragging its attached cancer agent across the tumor cell membrane and depositing it inside the cell. That targeting mechanism appears to have the potential to reinvigorate the broader potential of PARP inhibitors for solid tumors, broadening their applicability beyond their current limited use today.

"We have significant, really powerful animal data showing that we can do very high doses of a combination of a PARP inhibitor and a DNA-damaging agent and pretty much spare the bone marrow," Hellsund said.

Preclinical data presented during the 30th EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium in Dublin in November evaluated the attachment of the PARP inhibitor talazoparib to Cybrexa's Alphalex peptide. The study demonstrated pH-dependent delivery of functional talazoparib into tumor cells in vitro, target engagement and penetration by talazoparib in tumor tissue and prevention of bone marrow toxicity when combined with chemotherapy.

Hellsund co-founded Cybrexa with the company's board chair, Kevin Didden, and board member Kevin Rankin, colleagues from his days at Cyvek Inc., an immunoassay-developer acquired by Bio-Techne Corp. in 2016. In a sage move many startups might smartly heed, they picked the name with no specific meaning in mind, heading off the need to rebrand should a pivot ever be called for. For good luck, the moniker also extended a growing lineage of company names starting with "C" in which the trio has had a hand.

The company relies on a team of about 20 employees and about a dozen external consultants and is based in New Haven's Science Park. Since its founding, Cybrexa has raised $7.7 million. Now, with positive feedback from the FDA on its proposed IND and phase I development plans in hand, the team is in the process of closing a $10 million series B1 round that will support CBX-11's development, Hellsund said.

With other classes of DNA repair inhibitors and DNA-damaging agents in its sights, Cybrexa is also working to advance additional candidates leveraging the fundamental biology of the tumor microenvironment, an increasingly popular area of focus for companies such as Roche Holding AG subsidiary Genentech Inc., Molecular Partners AG and Agenus Inc. ♦