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Yiviva takes botanical cancer drug deeper into the clinic

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VANCOUVER, British Columbia – Yiviva Inc. (https://www.cortellis.com/intelligence/qsearch/Yiviva), a pharmaceutical company focused on developing botanical drugs, has moved its lead candidate further into an international phase IIb trial for liver cancer and closer to an application through the FDA's little-used botanicals pathway and a similar pathway in China. The company's lead candidate, YIV-906 (https://www.cortellis.com/intelligence/report/ci/nextgendrugall/73468), is intended for use in immunotherapy, chemotherapy and radiation therapy.

With YIV-906, Yiviva is working to develop a product that can minimize the number of drugs cancer patients have to take by modulating their immune and inflammatory responses. Results from early studies, that have to date reached about 170 patients with liver, pancreatic, colorectal and rectal cancers, are promising, says Yiviva co-founder and CEO Peikwen Cheng.

"We actually developed it out of a four-herb extract, four very common herbs, licorice, peonies, dates and skullcap," Cheng told *BioWorld*. "We built upon what was known and based upon how we source and how we process, created a product that now can enhance the immune system, cytoprotect the (gastrointestinal tract) and lead to tissue regeneration."

YIV-906 is an immune system modulator that has shown an ability to strengthen antitumor activity in a broad range of cancer treatments by boosting the immune response in the tumor microenvironment. It also cytoprotects the gastrointestinal tract to reduce inflammation and side-effects and speeds up tissue regeneration by promoting the growth of progenitor and stem cells.

The researchers behind Yiviva have spent the last 20 years building platforms to develop system biology drugs with a particular focus on diseases often associated with aging.

Single chemical drugs or single antibodies are limited in what they can do by themselves, particularly in regard to complex diseases. This means that patients have to take multiple drugs at the same time and these drugs have very targeted effects.

"When we look at cancer treatment, we believe the next generation of cancer treatment will move beyond the tumor microenvironment," said Cheng. "The goal is to improve survival and quality of life for patients."

Yung-Chi Cheng (https://www.bioworld.com/articles/print/378412-new-data-help-phytoceutica-push-botanical-drug-pathway), the Henry Bronson Professor of Pharmacology at Yale University and Yiviva's co-founder and chairman, started researching botanicals back in 2000. As a professor of pharmacology, he discovered and patented small-molecule drugs, particularly for Hepatitis B, and started working on addressing heterogeneous causes of disease by hitting multiple targets at once.

Yiviva was founded in 2015 after being spun out of Yale University to build on earlier research. The company has developed three key platforms for drug discovery and production. The first is its Signal Transduction, Activity and Response Drug Discovery Platform (STAR) to design drugs with sophisticated mechanisms of action; the second is a mechanism-based quality control platform to ensure batch-to-batch consistency; and the third is a symbiotic microbiota for agriculture resource and technology platform to ensure a scalable and quality supply of raw materials.

Furthest along the clinic among the company's programs, YIV-906 is undergoing a randomized, placebo-controlled, first-line phase IIb study in combination with Nexavar (sorafenib, Bayer AG), a multi-kinase inhibitor, for the treatment of hepatocellular carcinoma. The company is targeting enrollment of 125 patients across 20 sites in four regions: the U.S., mainland China, Hong Kong and

Taiwan. The first patient was enrolled in April 2020. The primary endpoint is to evaluate progression-free survival of patients while secondary endpoints include safety, quality of life assessments and some measures of clinical efficacy.

Other Yiviva products will target similarly complex diseases. YIV-111 is an anti-inflammation, anti-oxidation and antiviral drug targeting lung fibrosis, cancer pneumonia and COVID-19 pneumonia. YIV-006 is a cytoprotector and regeneration drug for inflammatory bowel disease. YIV-201 has multiple mechanisms of action to target hepatitis C. All these drugs are in preclinical development and would generally target disease progression.

"We are thinking about a patient's journey and their life cycle and how we may be able to treat them," said Peikwen Cheng.

Yiviva's goal is to combine metabolomics, systems biology and bioinformatics to speed up drug discovery and develop products that are evaluated based on botanical drug regulatory pathways from the US FDA and the China National Medical Product Administration.

"In the past, there's always been a black box around trying to understand these botanicals medicines because, by themselves, they are complex mixtures," said Cheng. "They have been used for hundreds or thousands of years but they are a bit of a black box."

The challenge for researchers is to understand their mechanisms of action and to manufacture them consistently.

The FDA's botanicals pathway dates back to 2003. The agency wrote the first guidance in 2004 and revised it in 2016. Since that time, the regulator has received hundreds of IND applications and has received and approved just two NDAs.

The FDA regulates botanical more like biologics than small-molecule drugs, "in that they view botanicals as complex mixtures," said Cheng. "Because of that, they treat the entire mixture as the active ingredient. They say in the guidance very clearly that it is impossible to know every chemical that is in there and it is not essential to what the active compounds are."

Linking bioassays with clinical endpoints is sufficient to meet regulatory needs because the FDA says it will look at the "totality of evidence." The regulator will also take into account historical data for safety purposes, particularly for products that have been use for hundreds of years.