BAKX Therapeutics — unlocking the full therapeutic power of the biological pathways that control cell life and death

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Mysterious events impel cancerous cells to grow abnormally, invade nearby blood and tissues, and spread throughout the body. While researchers are still working to understand all of them, one hallmark of cancer is dysregulation of apoptosis, the ordered and natural process that ends a cell's lifecycle as it ages or becomes unhealthy so that it can be replaced by fresher cells.

Apoptosis is a complex process governed by the functions of many proteins. The best understood of these is the BCL-2 family, which includes two types of proteins – those that prevent apoptosis and those that trigger it. Cells that don't die as planned can become cancerous, metastasize and even develop resistance to anticancer drugs.

Cancer cell death can be induced using innovative medicines – either indirectly by addressing the multiple proteins in the process that keep a cancer cell from dying, or directly by addressing a step in the process that tells the cancer cell to die.

Drug researchers have innovated new ways of killing cancer cells by manipulating the functions of key proteins involved in apoptosis. To date, they've only been successful in devising new drugs that address those proteins along the BCL-2 pathway that are involved in preventing apoptosis from ever happening. There are many of these proteins, however, so solving for just one or even some of them isn't always effective, and over time

cancers can become resistant to treatments that target them.

BAKX Therapeutics' CoDynX™ discovery platform

BAKX Therapeutics is working on a new approach to treating cancer by unlocking the full therapeutic potential of the apoptosis pathway, including those proteins involved in triggering – not just preventing – programmed cell death.

But it's a major challenge. These proteins are known for being conformationally dynamic – in other words they rapidly change shape – and for having featureless surfaces. It's difficult to identify where or how an anti-cancer drug might bind to them and to design new drugs with the ideal shape for binding to them.

BAKX developed its CoDynX™ discovery platform specifically to crack conformationally dynamic proteins (also known as CDPs) and to design drugs that can therapeutically regulate them. The platform integrates computational techniques originally pioneered by Dr. Yibing Shan (a founding member of DE Shaw Research), and proprietary AI & ML models developed in-house at BAKX, with strong experimental drug discovery methods and deep knowledge of key biologic pathways like those involved in apoptosis led by the company's scientific co-founders, the world-renowned cancer researchers Loren D. Walensky, MD, PhD, and Evripidis Gavathiotis, PhD.

The platform enables the smart screening of small molecules at a massive scale, validating site-specific binding – both through simulation and experimental methods – and supports iterative medicinal chemistry efforts to help optimize drug candidates.

With CoDynX, BAKX is pursuing an ambitious pipeline of drugs with the potential to save or extend life

BAKX is pursuing three novel drug programs, all of which are in the preclinical and discovery phases: BT-001 is an oral small molecule activator program targeting the BCL-2 associated protein-X (BAX). It is active in leukemias and lymphomas with high unmet clinical need. In vitro and in vivo studies combining BT-001 with drugs that target the other BCL-2 family inhibitors have shown synergistic effect, providing an approach for treating resistant tumors.

BT-002 is a discovery program focused on the BCL-XL protein in solid tumors. The company's BCL-XL inhibitor is being designed using CoDynX to overcome historical challenges associated with inhibiting BCL-XL, such as toxicity to blood cells.

BT-003 is a discovery program focused on inhibiting the BAX protein. Inhibition of the BAX protein is implicated in neurodegenerative and age-related diseases. It was recently clinically validated in ALS, a genetic degenerative disease. BAKX's knowledge of the BAX protein and suite of computational tools are enabling the company to build selective next generation BAX inhibitors to tackle various diseases correlated with aging.

BAKX's plans for growth and the future

BAKX has doubled the size of its team over the past year, and now employs 16 people along with a network of 50 contractors.

The company recently raised a $25 million series A fundraising led by AB Magnitude Ventures Group with Ipsen Pharma SA and Sherpa Healthcare Partners. It also entered a significant development partnership comprising up to $852 million in upfront and potential milestone payments with Ipsen, a global biopharmaceutical company, to research, develop, manufacture and commercialize the company's lead candidate, BT-001.

BAKX will continue to raise capital and pursue development partnerships as it advances its three programs. It will also apply CoDynX to discover new potential drug candidates in additional areas where it has deep pathway knowledge. If successful, the company's programs could introduce a new treatment paradigm for cancer patients, and rival or even surpass the success of FDA approved and marketed products that target other proteins along the BCL-2 pathway, some of which have reached nearly $2 billion in annual sales. The company's approaches could also be the key to unlocking the therapeutic value of the conformationally dynamic proteins that researchers have traditionally believed were too challenging to drug. *www.BAKXTx.com*