

A clinical-phase cancer biotech with nanomedicine partnering opportunities

Harnessing its unique CriPec technology, Cristal Therapeutics is improving the treatment options for patients with a range of solid tumors by creating transiently stable nanomedicines.

Cristal Therapeutics has transformed itself over the past year. Having begun as a research-stage startup focused on refining a nanoparticle platform, it is now a well-established, clinical-phase business with a burgeoning pipeline of promising in-house oncology programs. The transformation has created a wealth of promising later-phase and early-stage partnering opportunities.

The transformation of Cristal Therapeutics is underpinned by years of research into its technology platform CriPec. Using tailor-made CriPec polymers, the company's expert team is able to create transiently stable nanomedicines designed to have better therapeutic profiles than those of the native drug molecules.

Cristal Therapeutics' lead application of the technology is an encapsulated version of docetaxel, a cornerstone of standard-of-care chemotherapy regimens for solid tumors that suffers from multiple shortcomings in its native form. The unique ability of CriPec to address these shortcomings and, by extension, enhance the efficacy of the drug illustrates the potential of this nanoparticle technology.

Cristal Therapeutics' technology is designed to keep drugs away from healthy tissues. The drug is covalently entrapped in a particle that stops it interacting with tissues and enables the nanomedicine to circulate safely in the body for longer than it would otherwise. Over time, the particles passively accumulate in the tumor owing to the enhanced permeability and retention effect.

The release of the drug from the particle is driven by chemical hydrolysis. This enables Cristal Therapeutics and its collaborators to control the site and rate of release, resulting in a higher proportion of the administered drug hitting the targeted tumor. In addition to boosting its efficacy, the safety profile can also be improved resulting in a substantially enhanced therapeutic index.

Validating CriPec by improving docetaxel

The docetaxel-based program, with its lead asset CPC634, stands to validate the CriPec technology and improve the treatment of patients with a range of solid tumors. Cristal Therapeutics has put CPC634 through phase 1 studies that found it is safe and well tolerated at potential therapeutic doses. The studies also showed that the asset has a better pharmacokinetic profile than that of docetaxel.

CPC634 emerged from the early-phase program with encouraging signs of efficacy prompting Cristal Therapeutics to move it into a phase 2 trial in October 2018. The clinical trial is assessing the safety and

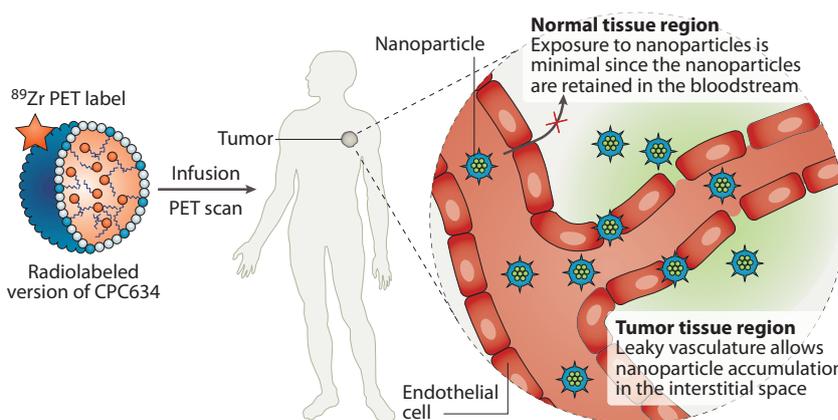


Fig. 1 | Clinical visualization of the tumor uptake. The radiolabelled CPC634 carries a ^{89}Zr PET label enabling non-invasive imaging by PET/CT scans. A clinical trial (NCT03712423) is currently ongoing to further evaluate the tumor uptake of CPC634 in patients. CT, computed tomography; PET, positron emission tomography.

efficacy of CPC634 in patients with platinum-resistant ovarian cancer, an area of high unmet medical need.

Having built up its clinical and regulatory expertise, Cristal Therapeutics is sponsoring the trial of the wholly owned asset but plans to find a partner for late-phase clinical development and registration. By forming such a partnership, they intend to extend the development of CPC634 into more solid tumor indications, including gastric, prostate and breast cancers.

Many of the indications potentially suitable for treatment with CPC634, including gastric and liver cancers, are particularly prevalent in China. As such, they are looking for a partner with a focus in Asia, a track record of winning marketing approvals in the region and a salesforce capable of turning drugs into successes once they come to market.

To support these efforts, Cristal Therapeutics is working on a radiolabeled version of CPC634 (Fig.1). This version enables visualization of CriPec-nanomedicines distribution in the body. In doing so, the radiolabeled version has the potential to serve as a companion diagnostic.

Partnering to expand CriPec use

The choice of docetaxel, a well-established drug, for the lead program has enabled Cristal Therapeutics to run a streamlined development program while controlling costs and risks, but the versatility of the CriPec technology means the biotech could have picked many other molecules.

CriPec is suitable for use with modalities including small molecules, peptides and oligonucleotides, both as monotherapies and in combination. The broad

applicability reflects Cristal Therapeutics' ability to customize the technology to fit the needs of different drugs and diseases, for example, by changing the size of the nanoparticles to anything from 30 to 100 nm. The targeting of the nanoparticles can be further enhanced by adding ligands that actively zero in on cancer cells.

To fully unlock the potential of the platform, Cristal Therapeutics is looking to expand its range of current partnerships with large pharma and biotech companies that are developing oncology and immunology drugs that may be improved by the targeting technology.

Companies that partner with Cristal Therapeutics will reap the benefits of working with an established company that has a strong intellectual property portfolio and a robust good manufacturing practice (GMP) site that is producing CPC634 for the phase 2 program. These strong foundations have enabled the company to transform into a fast-advancing development-stage organization with the ability to help its partners improve cancer care by fully realizing the potential of docetaxel and other drugs.

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