HighField Biopharmaceuticals

HighField Biopharmaceuticals' New Vision:

ADCplex, TCEplex and tLNPplex Designed for Greater On-Target Efficacy and Efficiency in Treating Cancer and Other Complex Diseases

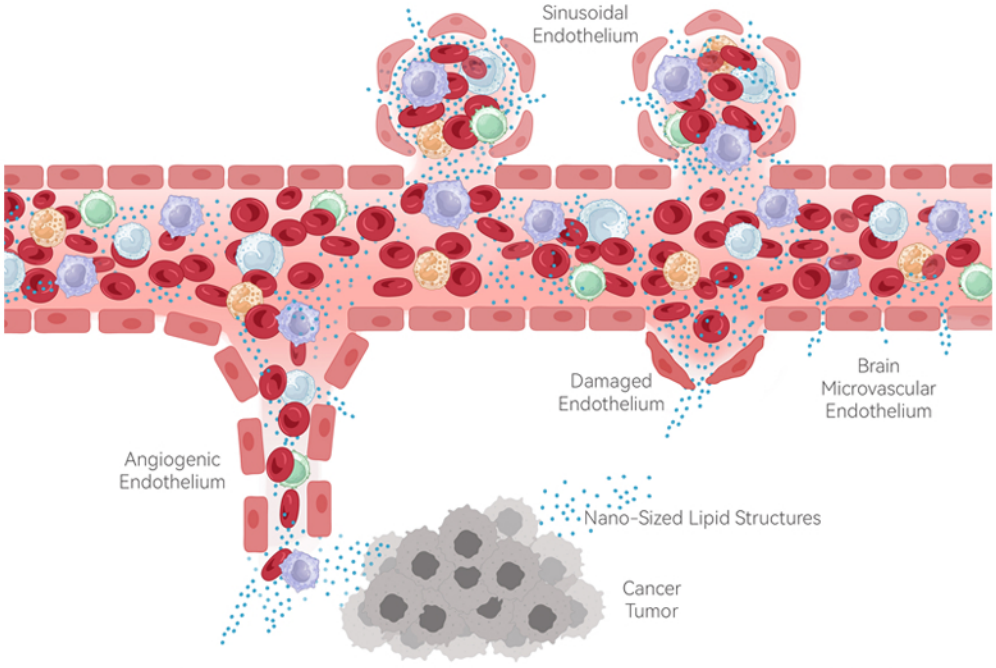
HighField Biopharmaceuticals has developed a novel and mechanistic driven strategy for targeted immunotherapy, chemotherapy and gene therapy which leverage the unique characteristics of lipid structures.

The HighField pipeline includes immunoliposome-based ADCplex™, TCEplex™ and tLNPplex™ platforms. They are designed based on lipid self-assembly mechanisms to intergrade multiple functions, including targeting, immune modulating, chemotherapy and gene modification for improved safety, efficacy and quality compared to current antibody drug conjugate (ADC) approaches and gene delivery methods.

"Lipids are the scaffold of most biological systems on earth," explained HighField CEO and Scientific Founder Yuhong Xu, Ph.D. "Cells even communicate with each other via nano-sized lipid assemblies. We design nano-sized lipid structures to approach different target cells in the complex disease biology. These little structures are biocompatible and can be used to carry multiple payloads in large quantity, making the treatment approach highly efficient."

HighField's Nano-Sized Drugs Accessing Diseased Tissues

The nano-sized lipid structures are biocompartible. They travel in circulation to find diseased tissues continuedly and persistently.



HighField Biopharmaceuticals' New Vision:

The ADCplex™ Platform

HighField's ADCplex platform delivers toxic drugs into cancer cells, much like ADCs, but it offers greater payload capacity and a different tumor tissue penetration mechanism than ADCs, allowing for greater payload uptake by cancer cells. This results in a larger therapeutic window and improved efficacy towards a variety of cancers.

"We leverage the passive tumor targeting characteristics of lipid nanoparticles in combination with active tumor cell engagement," Dr. Xu explained. "The toxic chemotherapeutic drugs are 'locked up' until they were internalized by tumor cells."

HFK1 (K1) and HFK2 (K2), both part of the ADCplex platform, target HER2 low and HER2 high cancer cells and carry chemotherapy drugs with different mechanisms of cell growth inhibition. HFK3 (K3) is a bispecific ADCplex structure targeting two different tumor associated antigens (TAAs) to possess a broader spectrum of antitumor effects.

The multiple antibody moieties on the liposome surface can bind so efficiently that very few tumor antigen receptors on the cancer cells are needed. Preclinical data show that K1 is effective in HER2 very low expressing tumor models including triple negative breast cancer (TNBC). Preclinical data also show they can achieve better efficacy than marketed ADCs.

The versatility of the ADCplex structure makes it readily applicable in other disease modalities, using different payloads. HighField's pipeline also includes HFK5 (K5) and HFK6 (K6), which target autoimmune diseases.

ADCplex™ Pipeline

Pipeline	Type	Indication	PD	CMC	PK/PD	TOX	IND	Phase 1a
K1	HER2 Doxorubicin ADCplex	Solid Tumors	K1					
K2	HER2 Irinotecan ADCplex	Solid Tumors	K2					
K3	Bispecific ADCplex	Solid Tumors	K3					
K5	Bispecific ADCplex	Autoimmune	K5					
K6	Bispecific ADCplex	Autoimmune	K6					

ADCplex™: Antibody Drug Complex

HighField Biopharmaceuticals' New Vision:

The TCEplex™ Platform

HighField's TCEplex platform also leverages the lipid self-assembly approach to combine the antibody targeting effect with immune cell engaging functions.

The lead program is HF50 containing an anti-CD3 antibody for engaging T cells and a HER2 antibody to interact with HER2 on cancer cells. In addition, an immune modulator is encapsulated inside the lipid structure to complement the immune clearance effect.

"Our studies show the liposome format can engage T cells in a controllable way, where the T cells are not over-stimulated nor exhausted." explained Dr. Xu.

HighField is initiating a Phase I trial of HF50 to treat HER2 expressing solid tumors. A second TCEplex structure, HF60, is designed for autoimmune diseases and is in the PCC (Preclinical Compound) stage.

TCEplex™ Pipeline

Pipeline	Type	Indication	PD	CMC	PK/PD	TOX	IND	Phase 1
HF50	CD3×HER2 R848 TCEplex	Solid Tumors	HF50					
HF30	CD3×CD19 Dasatinib TCEplex	Hematologic Cancer	HF30					
HF60	CD3×CD22×CD19 Rapamycin TCEplex	Autoimmune	HF60					

TCEplex™: T Cell Engager Complex

HighField Biopharmaceuticals' New Vision:

Gene Therapy for Complex Diseases

Traditionally, gene therapy involves the use of viral vectors to deliver genetic material to the patient. Given the cost and risks involved, this limited the use of gene therapy to rare and deadly genetic diseases. HighField's tLNPplex platform enables applications of gene therapy well beyond the limitations of genetic diseases.

HFG1 is a tLNPplex structure that provides sustained expression of a GLP-1R agonist for treating diabetes. HFG1 is presently in IND enabling studies. The components of HFG1's LNP complex were selected to provide prolonged expression of the GLP-1R agonist.

HFG1 requires far fewer injections than existing GLP-1 products while providing steady-state agonist activity.

The varied application of this platform expands beyond protein replacement therapy and further includes constructs like antibody conjugated LNPs for targeting and engaging immune cells. HFG2 is an innovative in vivo CAR-T approach utilizing a bispecific tLNPplex structure that directs efficient mRNA delivery to T cells, activating them to target and deplete B cells to treat autoimmune diseases.

tLNPplex™ Pipeline

Pipeline	Type	Indication	PD	CMC	PK/PD	TOX	IND
HFG1	GLP-1R mRNA-LNP	Diabetes, Obesity	HFG1				
HFG2	Bispecific tLNP In-vivo CAR-T	Autoimmune	HFG2				
HFG3	Bispecific mRNA-tLNP	Solid Tumors/ Anti-aging	HFG3				
HFG4	CD22 siRNA-tLNP	Autoimmune	HFG4				

HighField Biopharmaceuticals' New Vision:

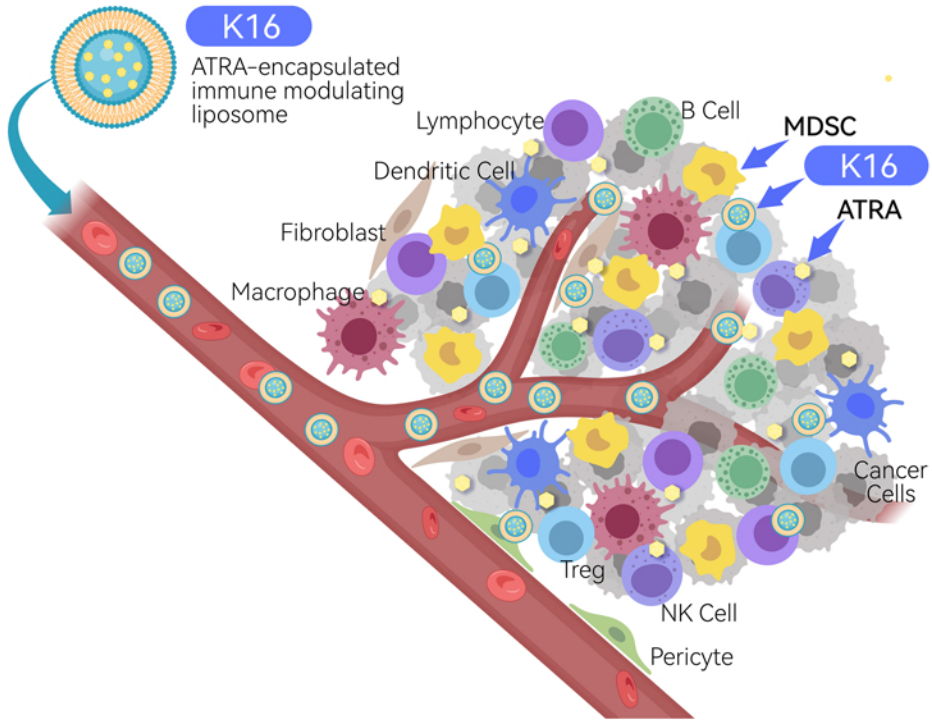
A Different Kind of Immune Modulation

HighField's other entry into oncology therapeutics is its Immune Modulation Platform. The lead candidate, HFK16 (K16), is a drug encapsulated immune modulating liposome presently Phase 2 ready. Phase 1 data to date show encouraging results in a range of solid tumors, including difficult to treat cancers, such as glioblastoma.

K16 targets myeloid-derived suppressor cells (MDSCs), which are immature myeloid cells that promote tumor growth by creating an immune-suppressive tumor microenvironment and contributing to immunotherapy resistance.

K16 infiltrates the solid tumor microenvironment and initiates the maturation and differentiation of MDSCs into functional immune cells, such as dendritic cells, which then summon T cells to attack the cancer.

"In heavily pretreated patients with recurring glioma, K16 has shown a 68.75% disease control rate as a single agent therapy," explained Dr. Xu. "We have a high expectation that patients with healthier immune systems or the use of K16 in combination with other therapies will have even better outcomes."



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