A Fully Humanized Anti-TF ADC for the Treatment of Solid Tumors

Characterized by High Specificity, Minimal Toxic Side Effects, and Favorable Pharmacokinetic Properties

Overview

Drug Name	ADC0320
Description	ADC0320 is a fully humanized antibody-drug conjugate consisting of an antibody targeting human tissue factor (TF) conjugated to an MMAE payload via a linker. It is being developed for the treatment of advanced solid tumors. Preclinical efficacy data showed that ADC0320 specifically binds to TF on the surface of tumor cells and ADC0320 showed significant anti-tumor efficacy in mouse models of xenograft tumors. This ADC has received the Investigational New Drug (IND) approval from the U.S. Food and Drug Administration (FDA).
Target	Tissue factor
Drug Modality	Antibody-drug conjugate
Indication	Solid tumors (such as cervical cancer, lung cancer, and pancreatic cancer)
Product Category	Cancer Immunotherapy
Mechanism of Action	Delivering cytotoxins specifically into target tumor cells
Status	IND approval
Patent	International PCT under application

Collaboration Opportunity

Protheragen Inc. is actively seeking partnership for ADC0320. Potential collaboration can be strategic alliance, licensing, or marketing agreement.
We look forward to hearing from you.

E-mail: inquiry@protheragen.com

www.protheragen.com

101-4 Colin Dr, Holbrook, NY 11741, USA

Target

Tissue Factor

Introduction	Tissue factor (TF), also known as thromboplastin, factor III, F3, and CD142, is a transmembrane glycoprotein receptor for coagulation factors VIIa and X with a molecular weight of 47 kDa. TF is expressed in two native protein isoforms, full-length TF (flTF) and alternative spliced TF (asTF). TF can initiate coagulation upon binding to FVIIa and plays a key role in the coagulation cascade. In addition, TF plays important roles in a variety of physiological processes such as tissue repair, inflammation, angiogenesis, tumor metastasis, and embryogenesis.
Approved Name	F3
Official Symbol	Coagulation factor III, tissue factor
Gene Type	Gene with protein product
Synonyms	CD142; TF
Ensembl	ENSG00000117525
Gene ID	2152
mRNA Refseq	NM_001993.5
Protein Refseq	NP_001984.1
OMIM	134390
UniProt ID	P13726
Chromosome Location	1p21.3

Clinical Resources

Gene Function	TF has been found to be upregulated in a number of different types of cancers, including gynecological and genitourethral cancers, head and neck squamous cell carcinoma (HNSCC), lung cancer, gastrointestinal cancer, breast cancer, malignant melanoma, and pancreatic cancer. Dysregulation of TF in tumors may lead to tumor growth and spread. TF contributes to tumor growth by promoting angiogenesis, which is the process of forming new blood vessels that deliver nutrients and oxygen to the tumor. TF stimulates the expression of vascular endothelial growth factor that is the key factor in angiogenesis. TF is also involved in the metastasis of cancer cells. TF stimulates

	the release of matrix metalloproteinases, which can lyse the extracellular matrix surrounding cells. Therefore, cancer cells have the potential to invade the surrounding tissues and spread to distant parts of the tumor origin. In addition, TF can also stimulate signaling molecules, regulating immune and promoting inflammation to induce cancer.
Pathway	Activation of blood coagulation via clotting cascade; activation of plasma proteins involved in acute inflammatory response; blood coagulation
Major Conditions	*Cervical cancer, colorectal cancer, pancreatic cancer, etc.*

Drug Modality

Antibody-drug Conjugate

ADC0320 is an antibody drug conjugate (ADC) consisting of a tissue factor-specific human antibody conjugated to tubulin polymerization inhibitor monomethylauristatin E (MMAE) with an average drug to antibody ratio (DAR) of 4.0. ADC0320, which is being developed for the treatment of patients with advanced solid tumors, will be prepared as a sterile freeze-dried powder, packaged in single-use vials, and reconstituted for intravenous infusion.

Indication

Solid Tumors

According to estimates by the International Agency for Research on Cancer (IARC), there were 20 million new cancer cases and 9.7 million cancer-related deaths worldwide in 2022. With population growth and aging trends, it is projected that by 2040, there will be 29.4 million new cancer cases and 16.3 million cancer-related deaths globally. The increasing incidence of malignant tumors will place a heavy burden on patients, healthcare systems, and the overall socioeconomic landscape.

Cervical Cancer	According to Global cancer statistics 2020, GLOBOCAN estimates that cancer of the uterine cervix is the fourth most common malignancy affecting women

	worldwide, and the eighth most common overall, with more than 604,000 new cases diagnosed worldwide in 2020, giving a corresponding age-standardized incidence rate of 13.3 cases per 100,000 women-years. According to the Global Burden of Disease Study, in 2021, the age-standardized incidence rate for cervical cancer in women of childbearing age was 15.4 per 100,000 population, equivalent to 307,428 new cases. Assuming that rates remain constant, and in the absence of new interventions or changing risk factors, the global incidence of cervical cancer could reach 948,000 by 2050.
Lung Cancer	According to the International Agency for Research on Cancer (IARC), lung cancer is the malignancy of highest impact among men and women globally, both in terms of the total number of individuals it affects (2.2 million new cases in 2020) and the total number of resulting deaths (1.8 million in 2020s). Based on IARC data and assuming that incidence rates remain stable over time, by 2050 the number of new cases could reach 4.62 million per year. IARC estimated a global five-year prevalence of lung cancer of more than 2.48 million in 2022.
Pancreatic Cancer	According to the IARC, 495,773 individuals were newly diagnosed with pancreatic cancer worldwide in 2020, including 262,865 men and 232,908 women. In 2017, according to the Global Burden of Disease (GBD) study, there were 448,000 incident cases of pancreatic cancer worldwide. The age-standardized incidence rate was 6.4 and 5.0 per 100,000 person-years in men and women, respectively. The American Cancer Society estimates that in 2024, there would be approximately 66,440 new cases of pancreatic cancer.

Mechanism of Action

Delivering Cytotoxins Specifically into Target Tumor Cells

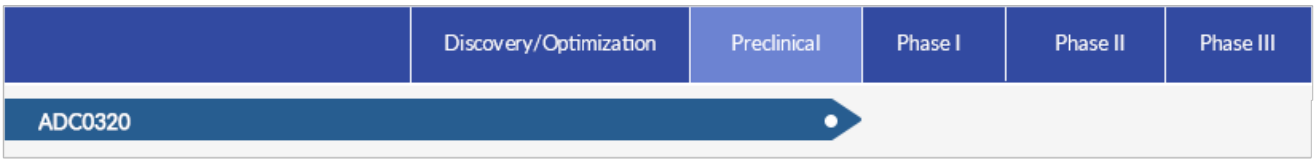
ADC0320 is a novel antibody-drug conjugate targeting human tissue factor (CD142) antigen expressed on tumor cell membranes. The therapeutic complex exerts dual antitumor effects through distinct biological pathways: antibody-dependent cellular cytotoxicity (ADCC) mediated by Fc domain engagement with immune effector cells effectively eliminates target tumor cells; following receptor-mediated endocytosis, lysosomal proteases cleave the linker to release MMAE cytotoxic payload, which induces G2/M phase arrest through microtubule disruption, leading to mitotic catastrophe and apoptosis in target tumor cells. This dual mechanism

of action ensures comprehensive tumor cell eradication through both direct cytotoxicity and immune-mediated clearance. In addition, MMAE has the advantage of being able to diffuse out of the target cell and enter adjacent tumor cells to cause bystander killing.

Status

The Status of ADC0320

The IND application for clinical investigations has been approved by the U.S. Food and Drug Administration (FDA).



Data

Preclinical Pharmacology Studies	Pharmacological studies have demonstrated that ADC0320 exhibited concentration-dependent effective binding to human and cynomolgus monkey TF proteins. ADC0320 showed batch-consistent binding activity with Fc receptors (FcRn, FcγRIIIα). Furthermore, ADC0320 demonstrated strong binding activity with high affinity and specificity towards SKOV-3, BXPC-3, and A-431 cells, while showing no binding activity towards normal cells.
Preclinical Pharmacokinetic studies	The pharmacokinetic profile of ADC0320 was determined in cynomolgus monkeys. The results demonstrated that the systemic exposure (AUC0-t) of ADC and Tab in serum increased approximately proportionally or slightly higher than dose-proportional with ascending doses. The systemic exposure (AUC0-t) of MMAE in plasma increased in a dose-proportional or slightly higher than dose-proportional manner.