STATEMENT OF WORK (SOW)

1.0 TITLE

Stability Testing Services And Drug Master File Maintenance For Antibody Drug Conjugate ADCT-701

2.0 BACKGROUND

The National Cancer Institute's (NCI's) Center for Cancer Research (CCR), National Institutes of Health (NIH), aims to improve the lives of all cancer patients by solving important, challenging, and neglected problems in cancer research and patient care. The Developmental Therapeutics Branch (DTB) advances novel therapeutic strategies and conducts clinical trials based on cancer-specific genomic, epigenetic and metabolic alterations, drug design, molecular mechanisms of drug action to achieve precision medicine.

Neuroendocrine neoplasms (NENs) are rare cancers in the gastrointestinal tract, pancreas, lungs, adrenal glands, and other areas of the body. Many of these cancers have a high risk of relapse and a low chance of survival. Pre-clinical studies have shown that Delta-like non-canonical notch ligand 1 (DLK1) is expressed in multiple neuroendocrine neoplasms. ADCT-701, a humanized antibody directed against DLK1, effectively suppresses tumor growth and improves survival in multiple cancer models which express DLK1. Antibody drug conjugates (ADCs) are an evolving class of anti-cancer therapies designed to selectively target and kill tumor cells with the intention of reducing toxicity on healthy cells, designed to selectively target and deliver cytotoxic agents to tumor cells, with the goal of offering both specificity and potency. Preliminary studies have demonstrated encouraging preclinical efficacy in several cancer types, including adrenocortical carcinoma (ACC), neuroblastoma (NB), and small cell lung cancer (SCLC). DTB launched clinical trial NCT06041516 to determine the maximum tolerated dose of antibody drug conjugate ADCT-701 in participants with neuroendocrine neoplasms or malignant adrenocortical carcinoma. This is a first in human phase I dose escalation study of ADCT-701-single agent in participants with NENs. This agent, produced by ADC Therapeutics Inc. (ADCT), has four Drug Master Files (DMFs) for an Investigational New Drug (IND) application with the Food and Drug Administration (FDA) on file.

2.1 OBJECTIVE

The objectives of this purchase order are (i) to obtain stability testing services for the drug ADCT-701 (one batch; production completion date: March 22, 2022; stability study initiation date: April 17, 2022) to stay in compliance with FDA regulations, and (ii) to maintain the related DMFs for the IND application.

3.0 SCOPE / TASKS

Product testing must be in accordance with the DMFs submitted to the FDA, including approved batch records, specifications, standard operating procedures, and all applicable laws, regulations, and cGMP standards.

Furthermore, product testing must be conducted in accordance with ADCT's SOPs, requirements set by the International Counsil for Harmonization of Technical Requirements for Pharmaceuticals (ICH; e.g. equipment qualified, maintained, calibrated), and approved stability protocols.

Independently, and not as an agent of the Government, the Contractor shall furnish all necessary labor, materials, supplies, equipment, and services not otherwise provided by the Government.

The Contractor shall perform the following tasks:

3.1 TASK 1 – STABILITY TESTING SERVICES

1. The Contractor shall store the ADCT-701 drug product at -70°C.
2. The Contractor shall conduct stability studies for the ADCT-701 drug product in accordance with the International Conference on Harmonization (ICH) guidelines. The conditions shall be as follows:

    a. "Schedule B" testing shall include:
        i. Appearance: physical state
        ii. Appearance: visible particles
        iii. Degree of coloration (visual)
        iv. Clarity and degree of opalescence (turbidity)
        v. pH determination
        vi. Protein concentration with "SoloVPE" method (by CTech Inc.)
        vii. Charge profile and identification by imaged capillary isoelectric focusing (icIEF)
        viii. Purity by size-exclusion chromatography - high-performance liquid chromatography (SEC-HPLC)
        ix. Purity by reduced capillary electrophoresis sodium dodecyl sulfate (CE-SDS)
        x. Drug-to-Antibody (DAR) and unconjugated antibody by ultra-performance liquid chromatography (UPLC)
        xi. Free drug by HPLC
        xii. Potency by enzyme-linked immunoassay (ELISA)
        xiii. Cytotoxicity by cell-based assay

    b. "Schedule C" testing shall include:
        i. All Schedule B tests
        ii. Subvisible particulate matter (USP <787>)
        iii. Light obscuration
        iv. Container closure integrity by high voltage leak detection

    c. The Contractor shall follow the following testing timeline:

Month after stability study initiation	Sample Pull Date	Schedule B Tests	Schedule C Tests
M36	4/17/2025		X
M42	10/17/2025	X	
M48	4/17/2026		X
M60	4/17/2027		X

3. The Contractor shall notify the Technical Point of Contact (TPOC) and TPOC Alternate within two (2) business days of any confirmed stability test failure(s).

4. The Contractor shall assign the expiration date for the ADCT-701 drug product batch per stability data after each stability test and provide the updated lot expiry documentation to the Government within two weeks after each stability test completion.

3.2 TASK 2 – DRUG MASTER FILE MAINTENANCE

The Contractor shall perform annual maintenance services of the following drug master files submitted to the FDA:

1. 037170, HUBA-1-3D-GAINACN3 monoclonal antibody
2. 037171, PL1601 drug linker
3. 037172, ADCT-701 drug substance
4. 037225, ADCT-701 drug product

4.0 TYPE OF ORDER

This shall be a firm fixed price purchase order for non-severable services.

5.0 PERIOD OF PERFORMANCE

The period of performance shall be as follows: 04/17/2025 through 07/17/2027.

6.0 PLACE OF PERFORMANCE

All work shall be conducted at the Contractor's facilities.

7.0 REPORT(S)/DELIVERABLES AND DELIVERY SCHEDULE

Pursuant to FAR clause 52.212-4, all work to be delivered under this purchase order is subject to final inspection and acceptance by an authorized representative of the Government. The authorized representative of the Government is the Program Technical Point of Contact (TPOC) at DTB who is responsible for inspection and acceptance of all services, materials, or supplies to be provided by the Contractor.

The NIH shall have 30 days in which to review and accept the deliverables provided by the Contractor. If no comments or request for revisions are provided within 30 days, the deliverables shall be considered acceptable.

7.1 DELIVERY SCHEDULE

#	Deliverable Description / Format Requirements	Due Date
1	Certified Analysis Report for the stability testing of ADCT-701 drug product, 36 months after manufacture (sample pull date: 4/17/2025); to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after sample pull date
2	Updated drug expiry extension date based on M36 stability test result; to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after completion of analysis

3	Certified Analysis Report for the stability testing of ADCT-701 drug product, 42 months after manufacture (sample pull date: 10/17/2025); to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after sample pull date
4	Updated drug expiry extension date based on M42 stability test result; to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after completion of analysis
5	Certified Analysis Report for the stability testing of ADCT-701 drug product, 48 months after manufacture (sample pull date: 4/17/2026); to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after sample pull date
6	Updated drug expiry extension date based on M48 stability test result; to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after completion of analysis
7	Certified Analysis Report for the stability testing of ADCT-701 drug product, 60 months after manufacture (sample pull date: 4/17/2027); to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after sample pull date
8	Updated drug expiry extension date based on M60 stability test result; to be delivered by email in PDF format or another format agreed upon to the TPOC and TPOC Alternate	Within 2 weeks after completion of analysis
9	Email notification to the TPOC and the TPOC Alternate upon any confirmed stability test failures	Within two (2) business days upon confirmation of stability test failure
10	Email notification to the TPOC and the TPOC ALTERNATE upon DMF amendment/maintenance	Within three (3) business days after DMF amendment/maintenance

8.0 PAYMENT

Payment shall be made as indicated in the Payment Schedule. Payment shall be made within 30 days of Customer's receipt of an invoice.

10.0 CONTRACT TERMS AND CONDITIONS

FAR 52.214-4 Contract Terms and Conditions—Commercial Products and Commercial Services (Nov 2023)