ELU-FRα-1: A Study to Evaluate ELU001, a C'Dot Drug Conjugate, in Patients with Solid Tumors that Overexpress Folate Receptor Alpha (FRα)

Abstract Number: CT255

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Abstract

ELU001 is a novel, first-in-class, new molecular entity described as a C'Dot Drug Conjugate (CDC) nanoparticle. ELU001 consists of ~13 folic acid targeting moieties and a payload of ~22 molecules of the topoisomerase-1 inhibitor, exatecan.

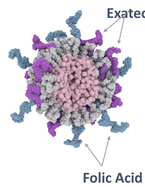
Folic acid and exatecan are covalently bound by non-cleavable and cathepsin-B cleavable linkers, respectively, to short polyethylene glycol chains which surround the C'Dot's silica core. CDCs are very small (~6 nm), allowing greater ability to penetrate more efficiently into solid tumors compared to ADCs. CDCs are rapidly eliminated by the kidneys, which is expected to lead to less toxicity than ADCs that have a longer half-life in circulation. ELU001's high avidity is designed to promote binding to FRα on the surface on FRα overexpressing cancer cells with a wide range of antigen expression including high, moderate and low expressing tumor cells. Following antigen binding, ELU001 internalizes into the tumor cell, and traffics to the lysosome where enzymatic cleavage releases the exatecan payload.

The first-in-human trial, ELU-FRα-1, is currently recruiting patients that have advanced, recurrent or refractory tumors associated with indications that are known to potentially overexpress FRα and have been shown to be topoisomerase 1 inhibitor-sensitive, and, in the opinion of the Investigator, have no satisfactory therapeutic options available.

Part 1 Dose Escalation will recruit about 25 patients per dose regimen (QW; Q2W; Q3W). The first stage of Part 2 (Dose Expansion) will recruit about 15 patients per tumor group expansion cohort. The study is actively enrolling in the US and currently recruiting in Q2W Cohort 201 and Q3W Cohort A. QW Cohorts 1-3 and Q2W Cohort 101 are complete. Clinical trial information: NCT05001282. See "Methods and Materials" in the 2nd column for more information.

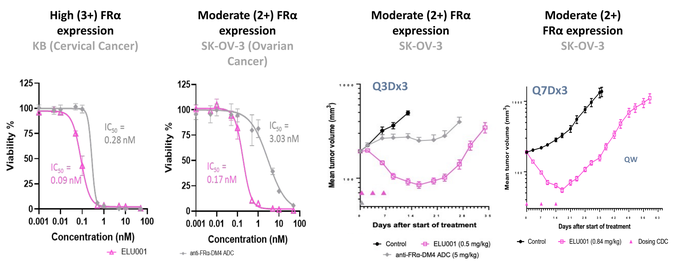
Background**

Figure 1. ELU001, a C'Dot Drug Conjugate



- High potency: ~22 exatecan payloads per C'Dot
- High avidity: ~13 folic acid targeting ligands per C'Dot
- Ultra-small size: ~6 nM, facilitates deep tumor penetration and rapid systemic elimination – avoidance of liver toxicity.
- Potential to cross disrupted blood-brain-barrier.

Figure 2. In vitro Potency of ELU001 vs ADC



Study Design

Part 1: Dose Escalation

Adult Patients

Single study drug in basket design enrolling:

Ovarian, Endometrial, Colorectal, Gastric, Gastroesophageal Junction, Triple Negative Breast, Non-small Cell Lung, and Bile duct Cancers

Weekly Dosing (QW)	Every Other Week Dosing (Q2W)	Every Three Weeks Dosing (Q3W)
Day 1, 8, 15 of a 28-day cycle	Day 1, 15 of a 28-day cycle	Day 1 of a 21-day cycle

Until radiographic or clinical disease progression or unacceptable toxicity.

Part 2: Dose Expansion

Up to 6 Cohorts of Specific Cancer Types, Dose Regimen, and FRα expression level.

Eligibility Criteria

Inclusion Criteria

Part 1:
- ✓ In the opinion of the Investigator, no other meaningful life-prolonging therapy option available
- ✓ Diagnosed with 1 of the 8 Solid Tumor cancer types (see left), with tumor tested retrospectively for FRα expression

Part 2:
- ✓ No more than 3 prior lines of anti-cancer therapy
- ✓ Prospective FRα expression testing using the Ventana FOLR1 RxDx Assay and the PS2+ scoring system
- ✓ Three Initial Cohorts:
  - ✓ Ovarian High FRα (≥75%)
  - ✓ Ovarian Low/Moderate FRα (> 25% and < 75%)
  - ✓ Endometrial Positive FRα (> 25%)

✓Measurable (Part 1 & 2) and non-measurable disease (Part 1 only), as per RECIST v1.1

✓Part 1: ECOG 0, 1, 2; Part 2: ECOG 0 or 1

✓Adequate organ function

Exclusion Criteria

× Significant active or chronic corneal disorder
× Significant cardiovascular or respiratory conditions
× Active autoimmune diseases or brain metastases
× QTcF > 470 ms

For More Information on the trial:
ClinicalTrialInfo@ElucidaOncology.com

Methods

Phase 1 / 2 multicenter, open label clinical trial with two parts: Part 1 Dose Escalation and Part 2 Tumor Group Expansion Cohort(s). In Part 1, a basket trial of patients with cancer types with a high likelihood of having FRα overexpressing tumors, are being enrolled, using 3 dose regimens. Part 2 will use Simon's Two-Stage design to evaluate 4-6 Expansion Cohorts, each consisting of patients with the most promising specific tumor types and ELU001 dose regimen.

- **Primary Objective:**
  - Part 1: MTD/RP2D; Part 2: ORR
- **Secondary Objectives:** Safety, PFS, TFST, PFS2, OS, Safety, PK, ADA, FRα expression

Interim Results and Discussion

Nonclinical toxicology studies in dogs and rats identified hematologic and gastrointestinal adverse events associated with the exatecan payload as potential risks.

Initial clinical safety results are presented for the QW and Q2W cohorts with a cutoff date of March 24, 2023, and are consistent with the nonclinical toxicology results. The Q3W cohort was opened later, and results are too early to present.

Out of 28 adult patients dosed with ELU001 to date in the QW and Q2W cohorts, the following Grade ≥ 3 treatment-emergent Adverse Events occurred in ≥ 15% of patients:

- QW Grade ≥ 3: Anemia (60%), white blood cell count decreased (46.7%), neutrophil count decreased (40%), platelet count decreased (20%) in 15 patients enrolled.
- Q2W Grade ≥ 3: Neutrophil count decreased (30.8%), white blood count decreased (15.4%) in 13 patients enrolled.

Related Serious Adverse Events (SAEs) included:

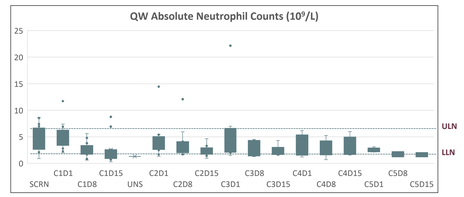
- QW: white blood count decreased
- Q2W: no related SAEs experienced

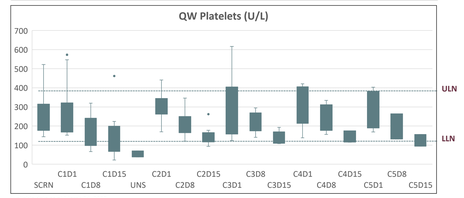
Preliminary available PK data indicated that for the 3 analytes tested in the plasma (C'DOT; total exatecan; released (free) exatecan), peak concentrations are present at the end of infusion, clearance appears dose-independent, and the half life ranges from approximately ~20-24 hours for C'DOT and total exatecan and approximately ~50 hours for released exatecan likely due to its slow metabolism.

The Q2W schedule provides more time for bone marrow recovery and to date is associated with an improved hematologic safety profile as compared to the QW cohort with clinical activity observed in both (efficacy results to be presented at a future meeting)

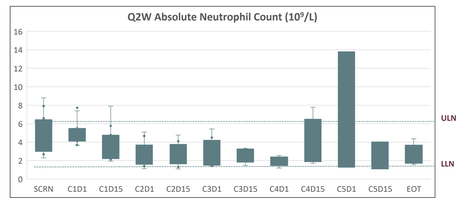
<u>No evidence</u> of ocular toxicities, interstitial lung disease, peripheral neuropathy, pneumonitis, liver toxicity, renal toxicity, cardiac toxicity have been observed to date in any patient treated with ELU001.

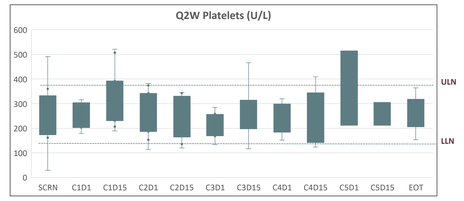
Interim Results and Discussion





Available data as of March 24, 2023





Available data as of March 24, 2023

Conclusions

The data for ELU001 administered on a QW or Q2W schedule, collected up to the March 24, 2023 cutoff date, shows that the ELU001 safety profile includes generally short-lived, manageable and reversible hematologic and gastrointestinal adverse events consistent with it's exatecan payload.

ELU001 is better tolerated when administered on a Q2W schedule than on a QW schedule - to date Q2W is associated with lower observed hematologic toxicities than QW and can be escalated to a higher dose.

There has been no evidence of ocular toxicities, interstitial lung disease, peripheral neuropathy, pneumonitis, liver toxicity, renal toxicity, cardiac toxicity have been observed to date in any patient treated with ELU001.

Efficacy data from the dose escalation phase is forthcoming. We anticipate advancing to expansion cohorts shortly.

**Disclosure: MSK[7] has institutional financial interest relative to Elucida Oncology.* ***Presented at the Amer. Assoc. for Cancer Research 2021 Annual Meeting (Poster #305)*