Study of ELU001, a C'Dot drug conjugate (CDC) targeting folate receptor α (FRα) overexpressing solid tumors

Elucida Oncology — Target or Clear

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ELU001 *(pasifolate exatecan)*

An ultra-small (~6 nm) nanoparticle drug conjugate, known as a CDC, designed to target and penetrate solid tumors. ELU001 is composed of a silica core surrounded by short polyethylene glycol (PEG) chains covalently conjugated to folic acid (FRα targeting moieties) and exatecan topoisomerase-1 inhibitor payloads.

BACKGROUND

Part 1: Dose Escalation (completed)

Dose escalation study in basket design enrolling:
Ovarian, Endometrial, Colorectal, Gastric, Gastroesophageal Junction, Triple Negative Breast, Non-small Cell Lung, and Bile duct Cancers

Weekly Dosing	Every Other Week Dosing	Every Three Weeks Dosing
Day 1, 8, and 15 of a 28-day cycle	Day 1 and 15 of a 28-day cycle	Day 1 of a 21-day cycle

Until radiographic or clinical disease progression or unacceptable toxicity.

ELU001 SAFETY

Grades ≥ 3 Treatment Emergent AEs

TEAEs* occurring in ≥ 2 patients

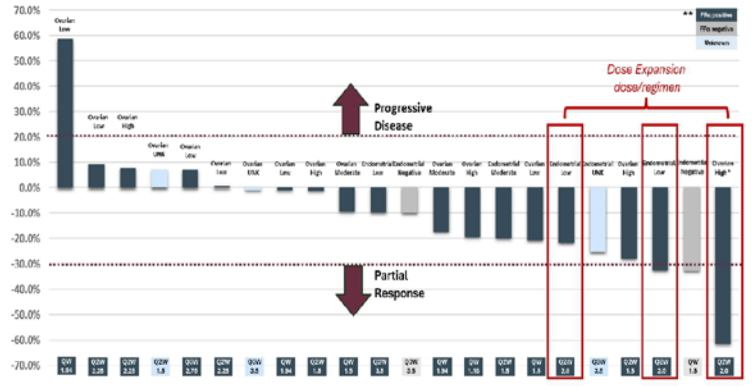
Grades ≥ 3 TEAEs**	QW Total N=15	Q2W Total N=17	Q3W Total N=10	Overall Total N=42
Anemia	9 (60.0%)	7 (41.2%)	4 (40.0%)	20 (47.6%)
Neutrophil count decreased	7 (46.7%)	5 (29.4%)	6 (60.0%)	18 (42.9%)
White blood cell count decreased	7 (46.7%)	3 (17.6%)	2 (20.0%)	12 (28.6%)
Platelet count decreased	4 (26.7%)	3 (17.6%)	5 (50.0%)	12 (28.6%)
Lymphocyte count decreased	3 (20.0%)	1 (5.9%)	1 (10.0%)	5 (11.9%)
Hypokalemia	2 (13.3%)	1 (5.9%)	1 (10.0%)	4 (9.5%)
Febrile neutropenia	-	-	3 (30.0%)	3 (7.1%)
Diarrhoea	2 (13.3%)	-	1 (10.0%)	3 (7.1%)
Vomiting	1 (6.7%)	-	2 (20.0%)	3 (7.1%)
Dyspnea	1 (6.7%)	1 (5.9%)	1 (10.0%)	3 (7.1%)
Hypertension	1 (6.7%)	1 (5.9%)	1 (10.0%)	3 (7.1%)
Ascites	1 (6.7%)	-	1 (10.0%)	2 (4.8%)
Nausea	1 (6.7%)	-	1 (10.0%)	2 (4.8%)

*AEs occurring from start of treatment irrespective of attribution
Source: ESMO Congress 2023 (Ann. Oncol. (2023) 34 (suppl_2): S458-S497)
**Data Cut: 11-Aug-2023

ELU001 EFFICACY

Objective Response by RECIST v1.1

OVARIAN CANCER & ENDOMETRIAL CANCER (N=22*)



*22 out of 42 patients had ovarian or endometrial cancer and at least 1 post-baseline imaging assessment.
** FRα expression is based of retrospective testing using Ventana FOLR1 assay (≥ 25% of viable tumor cells with moderate (2+) and/or strong (3+) membrane staining).
Data cut-off October 6, 2023. Source: ESMO Congress 2023 (Ann. Oncol. (2023) 34 (suppl_2): S458-S497)

^Note: Target lesion decreased by -61.5%, but scan indicated progression of previously non measurable non-target lesion.

INITIAL PK & ADA DATA

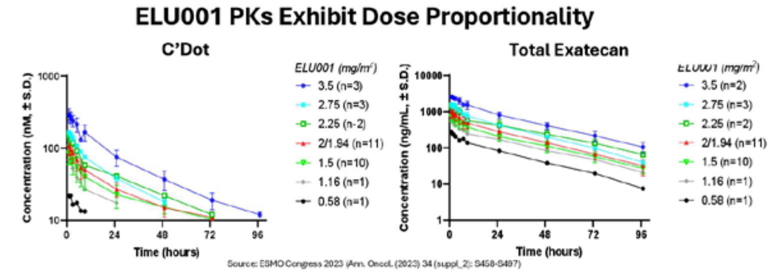
Concentrations of ELU001 C'Dot, Total Exatecan and Released Exatecan were assessed in patient plasma (currently ongoing). Preliminary data for the first 31 patients reveals dose proportionality for the C'Dot portion of ELU001 and the Total Exatecan payload and that ELU001's volume of distribution is primarily limited to the circulatory system. Released payload was ~ 5% of total payload. No anti-drug antibodies have been detected to date.

Plasma Pharmacokinetics Following ELU001 Infusion (All schedules, dose-escalation phase; cycle 1, day 1)

	C'Dot						Total Exatecan					
ELU001 Dose (mg/m²) (n)	AUC_{0-inf} (nM*h)	C_{max} (ng/mL)	t_{max} (h*)	$t_{1/2}$ (h)	CL (mL/h)	V_d (mL)	AUC_{0-inf} (nM*h)	C_{max} (ng/mL)	t_{max} (h*)	$t_{1/2}$ (h)	CL (mL/h)	V_d (mL)
0.58 (1)	-	22.1	1.0	-	-	-	6118	281	1.0	21.3	161	4948
1.16 (1)	1192	68.7	1.0	21.0	188	5697	12730	603	1.0	25.0	146	5267
1.5 (10)	1815 (693)	92 (26)	1.5	23.2 (3.4)	243 (111)	7410 (3062)	16778 (4319)	742 (162)	1.3	24.1 (2.6)	190 (68)	6455 (1876)
1.94/2 (11)	2296 (569)	112 (26)	1.0	23.1 (5.0)	2296 (569)	7361 (2705)	22566 (7383)	1127 (512)	1.0	23.8 (4.2)	194 (92)	6436 (2575)
2.25 (2)	3443 (327)	152 (0)	1.0	27.3 (0.8)	3443 (327)	5786 (154)	36136 (11251)	1440 (212)	1.0	26.5 (4.7)	114 (31)	4462 (1960)
2.75 (3)	3082 (132)	170 (8)	1.0	19.7 (1.3)	3082 (132)	6079 (596)	33246 (3899)	1593 (176)	1.0	20.8 (1.7)	156 (30)	4723 (1256)
3.5 (3)	6542 (1649)	296 (57)	1.5	24.6 (2.1)	6542 (1649)	5206 (1553)	56004	2580	1.0	22	131	4159

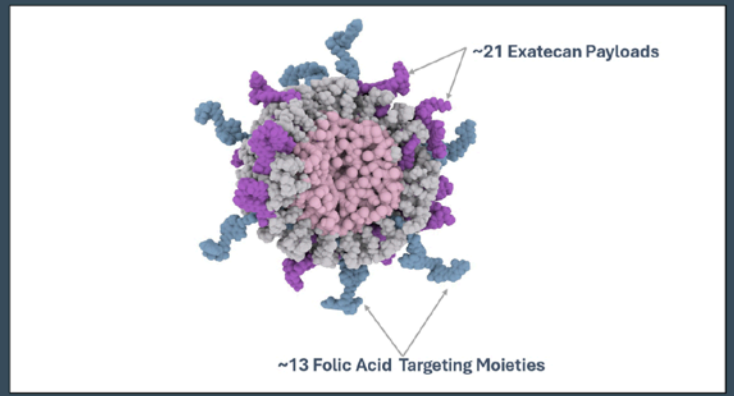
*Median
AUC_{0-inf} area under the concentration-time curve from zero time extrapolated to infinite time, C_{max} maximum observed concentration, CL total clearance, t_{max} time at which the highest drug concentration occurs, $t_{1/2}$ terminal elimination phase half-life, V_d volume of distribution

ELU001 PKs Exhibit Dose Proportionality



Source: ESMO Congress 2023 (Ann. Oncol. (2023) 34 (suppl_2): S458-S497)

ELU001
A Novel Targeted Drug Conjugate designed for efficient delivery to cancers with less toxicity



Key Points

- Novel, ultra small nanoparticle (~6 nm) based C'Dot Drug Conjugate (CDC) delivery system potentially provides advantages over Antibody Drug Conjugates (ADCs)
- Uses folic acid to target FRα overexpressing tumor cells
- Delivers multiple molecules of exatecan, a potent topoisomerase 1 inhibitor payload
- Supported by strong pre-clinical data [1, 2]
  - Significant anti-tumor activity
  - Deep penetration into the tumor
  - Effective across 1+ to 3+ levels of FRα expression
- Supported by Part 1 Clinical Data [3]
  - ELU001 can be safely administered
  - ELU001 demonstrates activity against tumors across a range of FRα expression levels.
  - During dose escalation, 2 PRs and 19 SDs achieved out of 22 patients with ovarian or endometrial cancer with ≥ 1 post-baseline scans, per RECIST v1.1

References
1. *Amer. Assoc. for Cancer Research 2021 Annual Meeting (Abstract ID: 305)*
2. *Amer. Assoc. for Cancer Research 2022 Annual Meeting (Abstract ID: 1077)*
3. *ESMO Congress 2023 (Ann. Oncol. (2023) 34 (suppl_2): S458-S497)*

Disclosures
- *[7] MSKCC has institutional financial interest relative to Elucida Oncology.*
- Clinical Trials.gov listing may be accessed through the Quick Response (QR) Code.

Want more info? Email ClinicalTrialInfo@ElucidaOncology.com or visit www.ElucidaOncology.com

STUDY DESIGN

Part 2: Tumor Group Expansion Cohorts

Group 1: Ovarian High FRα (≥75%)
Group 2: Ovarian Low/Moderate FRα (≥ 25% and < 75%)
Group 3: Endometrial Cancer any FRα expression

Other groups may be added based on available data.

Study Objectives

Study Part	Primary	Secondary
Part 2 Tumor Group Expansion	ORR	Safety, Tolerability, DOR, PFS, TFST, PFS2, OS, PK, Biomarkers, Immunogenicity

Key Eligibility Criteria

Inclusion Criteria for Part 2

- ✓ Ovarian Cancer, with histology of high-grade serous carcinoma, with 1-5 prior systemic lines of anti-cancer therapy
- ✓ Endometrial Cancer, with any histology (except carcinosarcoma [malignant mixed Müllerian tumor], or uterine sarcomas), with 1-4 cytotoxic chemotherapy-containing lines of anti-cancer therapy
- ✓ FRα expression level that meets entry threshold, based on VENTANA FOLR1 RxDx Assay
- ✓ Measurable disease, as per RECIST v1.1
- ✓ Performance Status (ECOG) of 0 or 1
- ✓ Adequate Organ Function

Exclusion Criteria for Part 2

- × Anti-cancer treatment ≤4 weeks prior to first dose
- × Significant active or chronic corneal disorder
- × Require use of folate-containing supplements
- × Symptomatic brain or leptomeningeal metastases
- × QTcF > 470 ms ≤4 weeks prior to first dose

Current Study Status

- Part 1: Dose Escalation – completed July 2023
- Part 2: Dose Expansion – currently ongoing

PART 1 SUMMARY [3]

ELU001 has a generally manageable safety profile associated with promising clinical activity across all levels of FRα expression

- ✓ **Safety profile impacting hematologic and gastrointestinal systems is predictable based on known toxicity of the payload, exatecan, and is manageable with no evidence of many of the other off target organ system toxicities seen with ADCs**
- ✓ **No Febrile Neutropenia at Exploratory Dose**
- ✓ **Activity across several tumor types – Best responses in Endometrial & Ovarian Cancers**
- ✓ **Activity across All Levels of FRα expression**
- ✓ **Significant Durability of Activity**
- ✓ **Dose Proportionality of PKs and limited distribution beyond the blood pool**
- × **No Ocular Keratopathies, impact on Visual Acuity, Interstitial Lung Disease, Peripheral Neuropathy, Liver toxicity, Renal toxicity or Cardiac toxicity.**

The authors wish to acknowledge the ELU-FRα-1 patients, investigators and site staff without whose input, this study would not have been possible.

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