ELU-FRα-1: First-in-Human Study of ELU001, a Targeted C'Dot Drug Conjugate, in Subjects with Folate Receptor α (FRα) Overexpressing Solid Tumors

FPN: 692P

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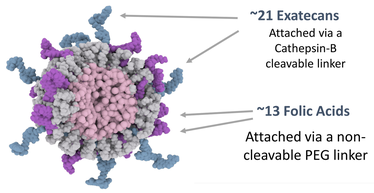
Study sponsored by Elucida Oncology, Inc.

BACKGROUND

ELU001 is Folate Receptor Alpha (FRα) targeted C'Dot Drug Conjugate (CDC). CDCs are small nanoparticle drug conjugates approximately 6 nm in diameter that can be functionalized with up to ~80 small targeting moieties and payloads. The small size and neutral charge of CDCs facilitates deep penetration into solid tumors and rapid systemic elimination by the kidneys potentially enhancing efficacy and reducing toxicities that have been commonly observed with antibody drug conjugates (ADCs).

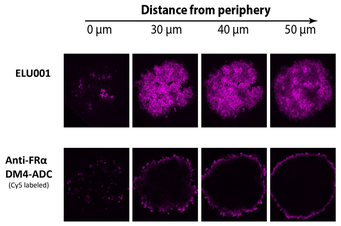
ELU001: A FRα-targeted Exatecan CDC

C'Dots have a silica core surrounded by a layer of short polyethylene glycol chains



TUMOR PENETRATION

After just four hrs. at 37°C ELU001 penetrates to the center of a tumor spheroid expressing high (3"+") FRα levels, while an ADC based upon mirvituximab soravtansine remains at the periphery.



Penetration evaluated by confocal microscopy performed after a 4 hr ex vivo incubation at 37°C with multicellular human KB tumor spheroids.

Presented at the, AACR 2021 Adams GP, et al. Annual Meeting, Abstract 305

PRECLINICAL STUDIES

ELU001 exhibited significant activity in *in vitro* cytotoxicity assays against tumor cell lines in monolayer culture and Patient Derived Xenograft (PDX) tumor spheroids. *In vivo,* ELU001 was effective in treating established human Cell line Derived (CDX) and PDX tumors expressing all levels of FRα (1 "+" to 3 "+") suggesting a potentially broader range of activity than mirvetuximab soravtansine.

Unlike ADCs, ELU001 penetrates the disrupted blood brain barrier and rapidly targets and penetrates deep into and treats lung tumors implanted in the brains of mice.

Data presented in Wu, F, et al. ACS Nano, 16(12) 20021-20033, 2022 and AACR Annual Meeting 2023, Adams GP, et al. Abstract 837.

NONCLINICAL TOXICOLOGY STUDIES

IND-enabling nonclinical toxicology studies were performed in Wistar Han Rats and Beagle Dogs prior to initiating the clinical study described here. The toxicology study also included non-GLP cohorts of rats treated with free exatecan and revealed that both free exatecan and ELU001 had the same pattern of toxicity in normal tissues - limited to the bone marrow and the GI tract. No anti-drug antibodies were induced by treatment with ELU001.

Data presented at AACR Annual Meeting 2022, Adams, GP, et al., Abstract 1077.

ELU001 First in Human Study: Manageable Safety Profile and Promising Clinical Activity

METHODS / DESIGN

Phase 1 / 2 multicenter, open label clinical trial:

- **Part 1, Dose Escalation**, basket of cancers likely to overexpress FRα (retrospective FRα analysis). Escalating doses of ELU001, administered once a week (QW) (0.58-1.94mg/m^2 for 3 weeks, 1 week rest), every other week (Q2W) (1.5-2.25mg/m^2), or every three weeks (Q3W) (2.75-3.5mg/m^2).
- **Part 2, Dose Expansion**, specific groups of cancers at 2mg/m^2 Q2W Exploratory Dose.

STUDY OBJECTIVES

Study Part	Primary	Secondary
Part 1 Dose Escalation	MTD and/or RP2D	ORR, PFS, TFST, PFS2, PK, Biomarkers, Immunogenicity
Part 2 Tumor Group Expansion	ORR	Safety, Tolerability, PFS, TFST, PFS2, OS, PK, Biomarkers, Immunogenicity

PART 2 – TUMOR GROUP EXPANSION

2mg/m^2 Q2W Exploratory Dose in adult patients with 1-4 prior therapies:

- Group 1: Ovarian High FRα (≥75%*)
- Group 2: Ovarian Low/Moderate FRα (≥ 25% & < 75%*)
- Group 3: Endometrial Positive FRα (≥ 25%*)
- Future: TNBC or NSCLC metastasized to the brain

Other groups may be added based on available data

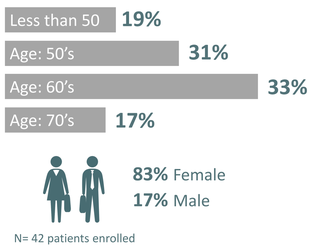
Currently Enrolling at US sites

*Based on VENTANA FOLR1 (FOLR-2.1) RxDx assay using PS2+ scoring

ELU001 STUDY DEMOGRAPHICS OVERVIEW - PART 1 DOSE ESCALATION

Prior Lines of Therapy	Range	Median
QW / N=15	3 – 11	5
Q2W / N=17	2 – 8	4
Q3W / N=10	2 – 8	4.5
Overall / N=42	2 – 11	4.5

Subject population only included those who had no other meaningful life-prolonging therapy option available.



Part 1 Dose Escalation Cancer Types	# Pts	FRα[2] H / M / L / -	FRα Unknown[3]
Ovarian Cancer	17	5 / 2 / 6 / 1	3
Endometrial Cancer	8	0 / 1 / 3 / 3	1
Colorectal Cancer	12	0 / 0 / 1 / 9	2
Non-small cell lung cancer	3	0 / 0 / 0 / 3	-
Cholangiocarcinoma	2	0 / 0 / 1 / 1	-

[3] insufficient tissue for FRα testing, or sample not received due to site error or patient request

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.

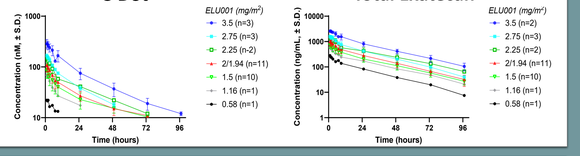
Plasma Pharmacokinetics Following ELU001 Infusion (All schedules, dose-escalation phase; cycle 1, day 1)

ELU001 Dose (mg/m^2) (n)	C'Dot $AUC_{0\text{-}inf}$ (nM*h)	C'Dot C_{max} (ng/mL)	C'Dot t_{max} (h*)	C'Dot $t_{1/2}$ (h)	C'Dot CL (mL/h)	C'Dot V_d (mL)	Total Exatecan $AUC_{0\text{-}inf}$ (nM*h)	Total Exatecan C_{max} (ng/mL)	Total Exatecan t_{max} (h*)	Total Exatecan $t_{1/2}$ (h)	Total Exatecan CL (mL/h)	Total Exatecan 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

$AUC_{0\text{-}inf}$ 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



ELU001 SAFETY

Grades ≥ 3 Treatment Emergent AEs

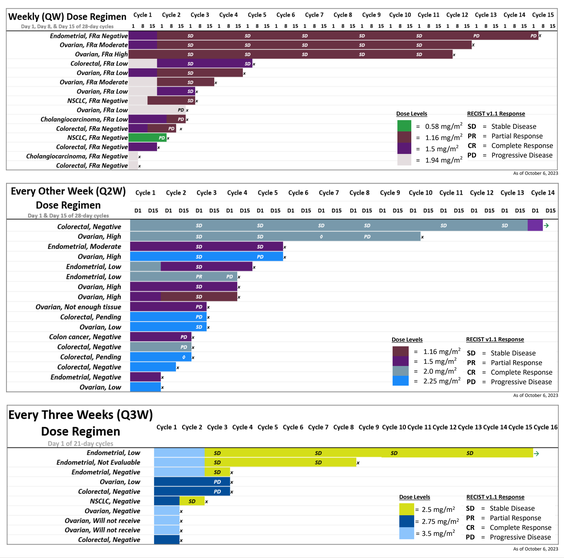
TEAEs* occurring in ≥ 2 patients irrespective of attribution

Grades ≥ 3 TEAEs**	QW Total N=15	Q2W Total N=17	Q3W Total N=10	Overall Total N=42
Anaemia	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%)
Hypokalaemia	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%)
Dyspnoea	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

** Data Cut: 11-Aug-2023

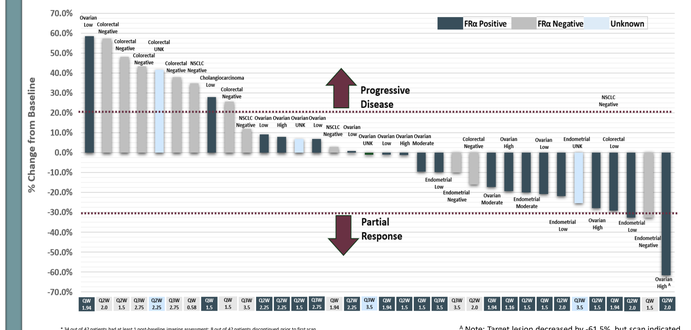
Duration on Study by Schedule and Dose



ELU001 EFFICACY

Objective Response by RECIST v1.1

ALL INDICATIONS (N=42)

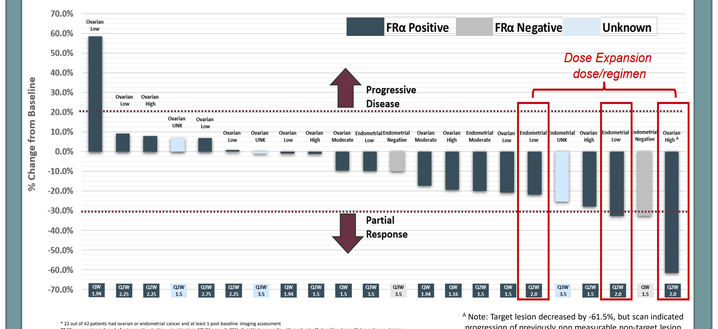


* 34 out of 42 patients had at least 1 post-baseline imaging assessment; 8 out of 42 patients discontinued prior to first scan.
** FRα expression is based of retrospective testing using Ventana FOLR1 assay (≥ 25% of viable tumor cells with moderate (2+) and/or strong (3+) membrane staining.
*** Data cut-off October 6, 2023.

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

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.

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

SUMMARY

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.*