Preliminary safety, pharmacokinetics, pharmacodynamics and efficacy of FL-115, a novel IL-15 superagonist, from a Phase 1 study in patients with advanced solid tumors

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Background

FL115 is an engineered IL-15/IL15Rα-Fbody fusion protein, in which Fbody is a single-chain Fc designed to eliminate classical Fc effects including ADCC/CDC/ADCP while retaining FcRn engagement. It aims to enhance anti-tumor immunity via IL-15-mediated signaling on NK and CD8+ T cells while minimizing complexity from Fc. Here we present the preliminary safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy results from an ongoing phase 1 study of FL115 in patients with advanced solid tumors.

Phase I Study Design

Protocol No: FL115-102

Patient Population

Patients with histologically or cytologically confirmed incurable, unresectable, locally advanced or metastatic cancer

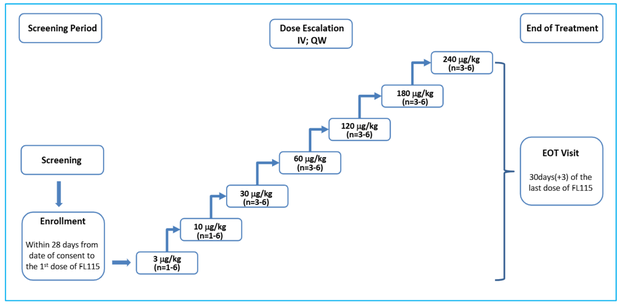
Study Primary Objectives

- To evaluate the safety and tolerability of FL115 in patients with unresectable locally advanced or metastatic solid tumors
- To determine the maximum tolerated dose (MTD) and/or recommended Phase II dose (RP2D) of FL115 administered intravenously (IV)

Study Secondary Objectives

- To assess pharmacokinetics and pharmacodynamics of FL115 administered intravenously (IV) as monotherapy
- To assess anti-tumor activity of FL115 monotherapy (IV)
- To assess anti-drug antibody (ADA) of FL115 monotherapy (IV)
- To assess cytokine release after FL115 monotherapy (IV)

Dose Escalation Phase



Results

Heavily Treated Patient Population Enrolled

		≤ 30 μg/kg (n=11)	45 μg/kg (n=3)	60 μg/kg (n=3)	90 μg/kg (n=3)	Total (n=20)
Median age, years		54	66	58	61	57.5
Sex, n	Female	6	2	3	2	13
	Male	5	1	0	1	7
ECOG PS, n	0	2	0	1	1	4
	1	9	3	2	2	16
Median number of prior therapies		3	4	3	5	4
Number of prior therapies (≥3), n		5	1	2	2	10
Previous CPI, n		8	2	2	2	14

Note: All enrolled patients had advanced solid tumors. The majority were elderly, heavily pretreated, and had experienced disease progression following prior treatment including immune checkpoint inhibitors (ICIs).

FL115 was Well Tolerated with no Grade 4/5 AEs

	≤ 30 μg/kg (n= 11)	45 μg/kg (n=3)	60 μg/kg (n= 3)	90 μg/kg (n=3)	Total (n=20)
TRAEs; n (%)	11(100.0)	3 (100.0)	3 (100.0)	3 (100.0)	20 (100.0)
Grade 1 or 2; n (%)	8(72.7)	3 (100.0)	2 (66.7)	3 (100.0)	16 (80.0)
Grade ≥3; n (%)	3(27.3)	0	1 (33.3)	0	4 (20.0)

Data Cut: Aug 20, 2025

Note: The most commonly reported TRAEs can be classified into two categories: cytokine release syndrome (CRS)-related adverse events and conditions associated with elderly patients presenting with advanced-stage tumors.

Grade 3 TRAEs (All Occurred during the 1st Treatment Cycle (28 Days))

	≤ 30 μg/kg (n= 11)	45 μg/kg (n=3)	60 μg/kg (n= 3)	90 μg/kg (n=3)	Total (n=20)
Aspartate aminotransferase increased*	2(18.2)	0	0	0	2(10.0)
Cytokine release syndrome	1(9.1)	0	0	0	1(5.0)
Atrial fibrillation	0	0	1(33.3)	0	1(5.0)

Data Cut: Aug 20, 2025

*: Not accompanied by a concurrent with increased Total-bilirubin.

Cytokine Release Syndrome (CRS)

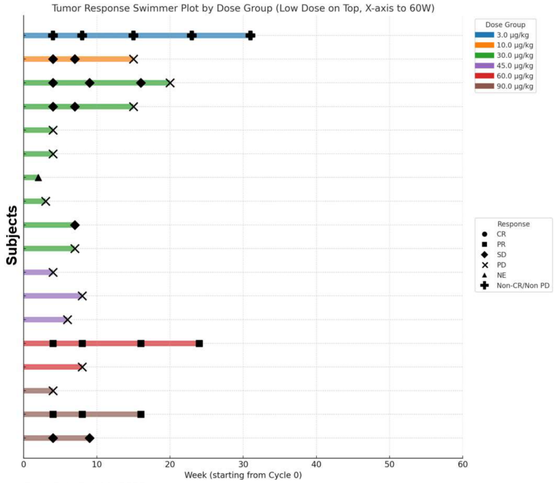
	≤ 30 μg/kg (n= 11)	45 μg/kg (n=3)	60 μg/kg (n= 3)	90 μg/kg (n=3)	Total (n=20)
Grade 1, 2	3(27.3)	1(33.3)	1(33.3)	1(33.3)	6 (30.0)
Grade 3	1(9.1)*	0	0	0	1(5.0)

Data Cut: Aug 20, 2025

*: The subject was a male patient aged 59 years with non–small cell lung cancer (NSCLC). A Grade 3 cytokine release syndrome (CRS) related to FL115 occurred on Day 1 post 1st dose of FL115 and resolved by Day 2. Although reported as Grade 3, the event resolved promptly with routine supportive care alone, without requiring vasopressor therapy, high-flow nasal cannula oxygen, or tocilizumab administration. This adverse event was also considered a dose-limiting toxicity (DLT).

FL115 Monotherapy Showed Evidence of Preliminary Efficacy

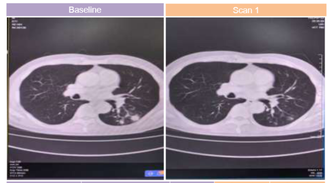
Among 18 efficacy evaluable patients, 2 (11.1%; both≥3L prior treatments) achieved confirmed partial responses, 5 (27.7%) had stable disease and 1 (5.55%) had non-CR/non-PD.



Data Cut: Oct 11, 2025

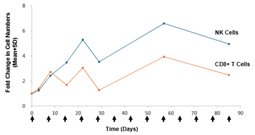
Note: Patients with post-baseline tumor assessments were included in the efficacy-evaluable population. The SD finding at Week 3 did not fulfill RECIST 1.1 confirmation requirements; hence, the BOR was designated as NE.

A 4L LELC (Lymphoepithelioma-like carcinoma) Patient Achieved Confirmed PR with Target Lesion Resolution with FL115



	Tumor assessment	Baseline	Scan 1 (Week 8)	Scan 2 (Week 16)
Target lesions measurements,mm	T1-Lung	14	0	0
Non-target lesions	NT01 – Other； NT02 - Bone； NT03 – Lung； NT04 – Lymph Node	Present	Present	Present
Sum of diameters,mm(% change from baseline)		14	0(-100)	0(-100)
Overall response (RECIST v1.1)			PR	PR

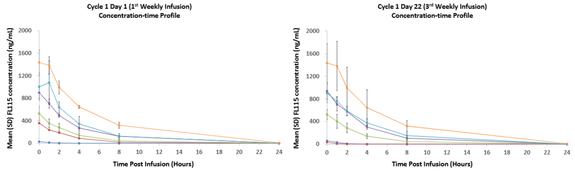
Significant Expansion of NK and CD8+ T Cells



Data Cut: Sep 22, 2025

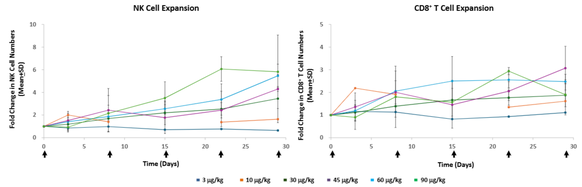
Note This LELC patient is a 61 yrs male and had undergone four prior lines of treatment, including chemotherapy, immune checkpoint inhibitors, antibody-drug conjugates (ADC), and tyrosine kinase inhibitors (TKIs).

FL115 Demonstrated Dose-proportional PK with Minimal Accumulation



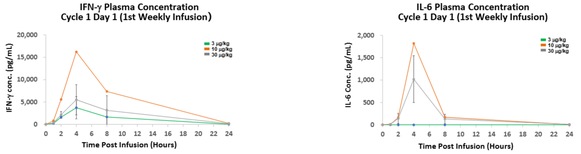
Note: Data cutoff: Sept 5, 2025; Protocol No: FL115-102; A validated method was used to measure plasma concentration of FL115

FL115 Led to Significant Expansion of NK and CD8+ T Cells



Note: Data cutoff: Sept 5, 2025; Protocol No: FL115-102; An outlier value was recorded at Day 15 pretreatment for the subject at 10 μg/kg, and was not included in this representation

FL115 Demonstrated Transient Upregulation and Fast Decline of Inflammatory Cytokines in Hours Post Dosing: Potent Inducer of Interferon-γ (IFN–γ)



Note: Data cutoff: Sept 5, 2025; Protocol No: FL115-101

Conclusions

- FL115 (IV) was well tolerated in this heavily pretreated patient population, with the common AE profile consistent with cytokine-based therapies and the underlying comorbidities of patients with advanced cancer or elderly patients.
- All Grade 3 TRAE and most CRS events occurred during the first treatment cycle, suggesting improved tolerability with prolonged administration.
- FL115 (IV) demonstrated dose-proportional Pharmacokinetics and on-target Pharmacodynamic activities including expansion of NK and CD8+ T cells as well as strong transient induction of IFN-γ.
- Preliminary clinical efficacy was observed with 2 patient achieving a confirmed PR, 5 patients experiencing SD and 1 patient with non-CR/non-PD in this heavily pre-treated and highly refractory patient population.
- Phase 1 studies of FL115 (IV infusion and subcutaneous injection) in combination with anti-PD1 antibody will be initiated shortly.