

**Eftozanermin alfa (ABBV-621) monotherapy in patients with previously treated solid tumors:
findings of a phase 1, first-in-human study**

Patricia LoRusso¹, Mark J. Ratain², Toshihiko Doi³, Drew W. Rasco⁴, Maja J.A. de Jonge⁵, Victor Moreno⁶, Benedito A. Carneiro⁷, Lot A. Devriese⁸, Adam Petrich^{9,*}, Dimple Modi⁹, Susan Morgan-Lappe⁹, Silpa Nuthalapati^{9,*}, Monica Motwani⁹, Martin Dunbar⁹, Jaimee Glasgow⁹, Bruno C. Medeiros⁹, Emiliano Calvo¹⁰

¹Yale Cancer Center, New Haven, CT, USA; ²University of Chicago, Chicago, IL, USA; ³National Cancer Center Hospital East, Kashiwa, Japan; ⁴START, San Antonio, TX, USA; ⁵Erasmus MC Cancer Institute, Rotterdam, The Netherlands; ⁶START Madrid-FJD, Hospital Fundación Jiménez Díaz, Madrid, Spain; ⁷Cancer Center at Brown University, Lifespan Cancer Institute, Providence, RI, USA; ⁸Department of Medical Oncology, University Medical Center Utrecht, Utrecht, The Netherlands; ⁹AbbVie Inc., North Chicago, IL, USA; ¹⁰START Madrid-CIOCC, Centro Integral Oncológico Clara Campal, Madrid, Spain

*Former employee of AbbVie.

Corresponding author:

Emiliano Calvo, MD, PhD

START Madrid-CIOCC

Centro Integral Oncológico Clara Campal

Hospital Madrid Norte Sanchinarro

Calle Oña, 10. 28050 Madrid, Spain

Email: emiliano.calvo@startmadrid.com

Target journal: Investigational New Drugs

Online Resource 2 – Table S1 Dose-limiting toxicities

DLTs	Dose escalation					Dose optimization	
	2.5 mg/kg	3.75 mg/kg	5 mg/kg	6.5 mg/kg	15 mg/kg	1.25 mg/kg	3.75 mg/kg
	D1/D8	D1/D8	D1/D8	D1/D8	D1/D8	QW	QW
Patients with DLT, n (%)	1/16 (6)	3/12 (25)	1/6 (17)	1/6 (17)	1/4 (25)	3/16 (19)	1/16 (6)
DLT, n							
Increased ALT	1	1	-	1 ^a	1	1 ^a	1 ^a
Increased AST	-	-	-	1 ^a	-	1 ^a	1 ^a
Increased bilirubin	-	1	-	1 ^a	-	-	-
Fatigue	-	1 ^a	-	-	-	-	-
Nausea	-	1 ^a	-	-	-	-	-
Noncardiac chest pain	-	-	-	-	-	1 ^b	-
Pleuritic pain	-	-	-	-	-	1 ^b	-
Respiratory failure	-	-	1	-	-	-	-
Toxic hepatitis	-	-	-	-	-	1	-

^{a,b}DLTs reported in the same patient in each dose cohort.

ALT, alanine aminotransferase; AST, aspartate aminotransferase; D, day; DLT, dose-limiting toxicity; QW, once-weekly.

Online Resource 2 – Table S2 Summary of treatment-emergent and treatment-related adverse events occurring in patients with CRC and PaCA enrolled in the dose-optimization cohort

Group	N	Treatment-emergent events, n (%)			Treatment-related events, n (%)			Treatment-related deaths
		TEAEs	Grade ≥3 TEAEs	SAEs	TRAEs	Grade ≥3 TRAEs	TRSAEs	
Patients with ≥1 event	48	48 (100)	31 (65)	27 (56)	44 (92)	10 (21)	7 (15)	1 (2)
By dose, mg/kg								
1.25 QW	16	16 (100)	11 (69)	10 (63)	13 (81)	3 (19)	3 (19)	0
3.75 QW	16	16 (100)	11 (69)	9 (56)	15 (94)	2 (13)	1 (6)	0
7.5 QW	16	16 (100)	9 (56)	8 (50)	16 (100)	5 (31)	3 (19)	1 (6)
By indication								
CRC	24	24 (100)	13 (54)	11 (46)	22 (92)	4 (17)	1 (4)	0
PaCA	24	24 (100)	18 (75)	16 (67)	22 (92)	6 (25)	6 (25)	1 (4)

CRC, colorectal cancer; PaCA, pancreatic cancer; QW, once-weekly; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event; TRSAE, treatment-related serious adverse event.

AUC₀₋₁₆₈, area under the serum concentration-time curve from time zero to 168 h after dosing; AUC_{0-inf}, area under the serum concentration-time curve from time zero to infinite time; CL, clearance; C_{max}, maximum observed serum concentration; CV, coefficient of variation; D, day; N, total sample size; NA, not applicable; QW, once-weekly; Q3W, every 3 weeks; t_{1/2}, terminal phase elimination half-life; T_{max}, time to maximum observed serum concentration, peak time.

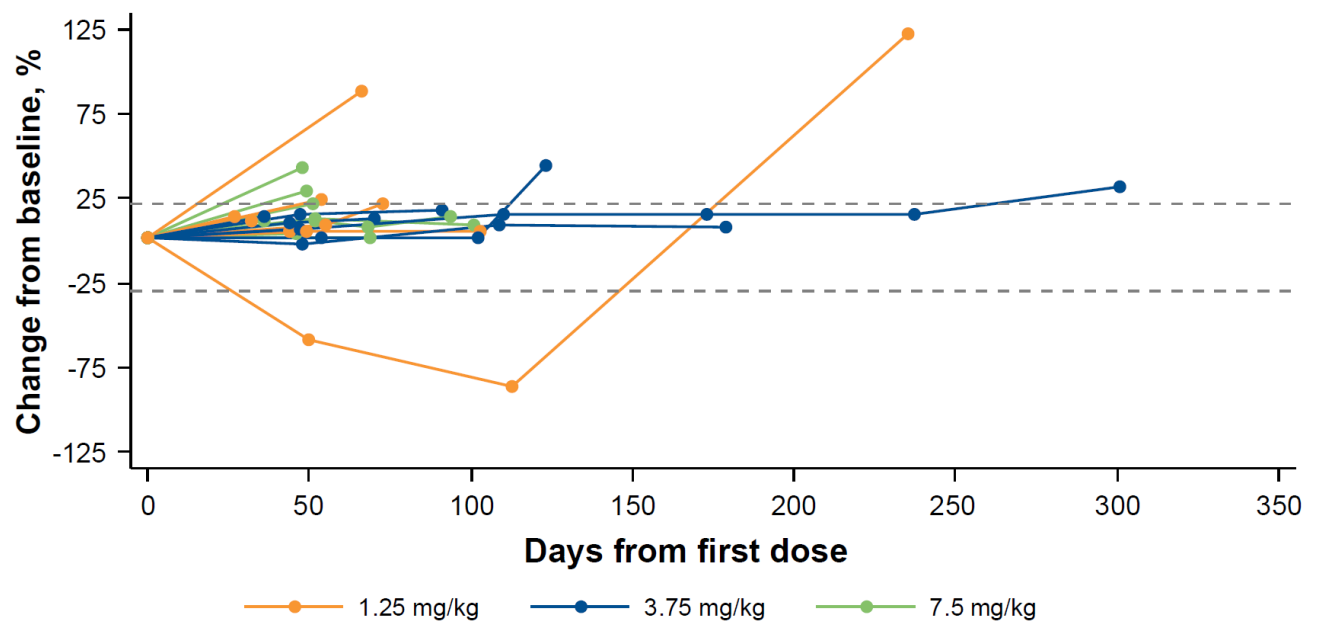
Online Resource 2 – Fig. S1 Disposition of patients enrolled in the dose-optimization cohort

according to dosing or disease group, and overall disposition. CRC, colorectal cancer; PaCA, pancreatic cancer

Dose or disease cohort Number of patients	1.25 mg/kg n=16	3.75 mg/kg n=16	7.5 mg/kg n=16	CRC total n=24	PaCA total n=24	All patients N = 48
Median (range) time on treatment, days	37 (1–232)	43 (1–290)	36 (15–254)	40 (1–290)	36 (1–288)	36 (1–290)
Median no. of cycles (range)*	2 (1–12)	3 (1–14)	2 (1–13)	3 (1–14)	2 (1–14)	2 (1–14)
Eftozanermin alfa discontinuation, n (%)						
Adverse event	1 (6)	2 (13)	2 (13)	3 (13)	2 (8)	5 (10)
Progressive disease	13 (81)	12 (75)	13 (81)	19 (79)	19 (79)	38 (79)
Consent withdrawal	0	0	0	0	0	0
Physician decision	2 (13)	1 (6)	1 (6)	2 (8)	2 (8)	4 (8)
Death	0	0	0	0	0	0
Other	0	1 (6)	0	0	1 (4)	1 (2)
Disposition according to dosing cohort			Disposition according to disease cohort			Disposition overall

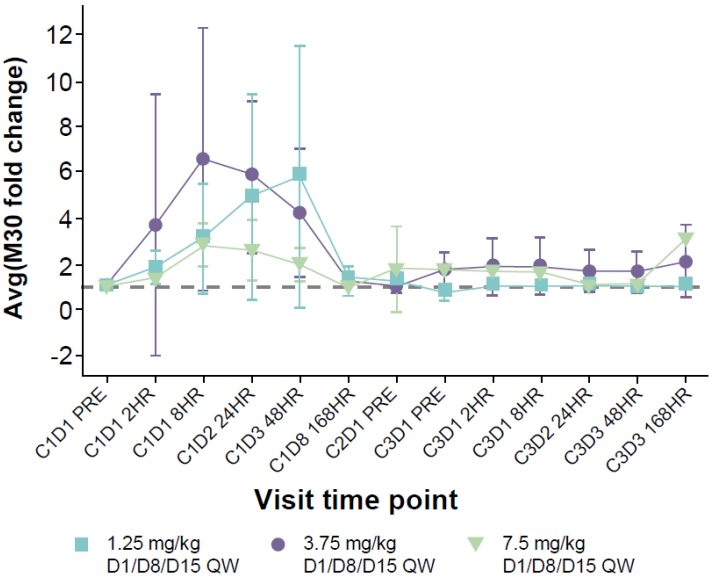
*All patients received ≥1 cycle. CRC, colorectal cancer; PaCA, pancreatic cancer.

Online Resource 2 – Fig. S2 Spider plot of percentage change in size of tumor lesions over time in patients with pancreatic cancer with one or more post-baseline tumor assessment (dose-optimization cohort). Baseline tumor assessments were performed at D1 (baseline), within 28 days of C1D1, within 7 days before dosing on C3D1 (post-baseline), and Q9W thereafter. C, cycle; D, day; Q9W, every 9 weeks



Online Resource 2 – Fig. S3 Mean fold change ($\pm$ SD) in serum M30 (a) and M65 (b) levels in patients with pancreatic cancer treated with eftozanermin alfa in the dose-optimization cohort. C, cycle; D, day; HR, hour; PRE, pre-dose; QW, once-weekly; SD, standard deviation

a



b

