Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of DA-1726, an Oxyntomodulin Analogue: Phase 1 Higher-Dose Cohort Results

Chris Fang[2], Yuna Chae[1], Dae Young Lee[1], Eun Jin Kim[1], Robert Homolka[2], Ji Eun Lee[2], Kyunghyun Lee[1,2], Sung-Jin Kim[1,2], Mi-Kyung Kim[1], Hyung Heon Kim[2]

[1] Dong-A ST Co., Ltd. South Korea; [2] MetaVia Inc., United States

3102-LB

Background

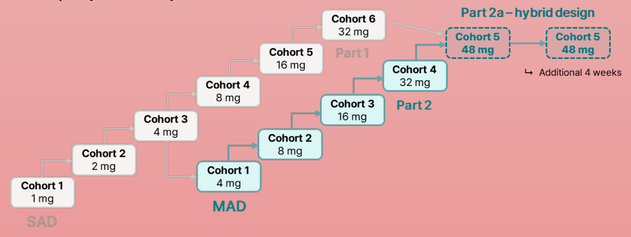
- DA-1726 is a novel oxyntomodulin analogue in Phase 1 clinical development, acting as a dual agonist of the GLP-1 and glucagon receptors (NCT06252220).
- In this first-in-human Phase 1 study, results through Part 2 (up to 32 mg) demonstrated favorable safety and tolerability, along with clinically meaningful body weight reduction.
- Based on these findings, a higher-dose cohort was subsequently investigated to characterize DA-1726 at an expanded dose range.

Objective

To evaluate the safety, tolerability, pharmacokinetics (PK), and preliminary pharmacodynamics of DA-1726 in the higher-dose cohort of adults with obesity who were otherwise healthy.

Methods and Materials

- Subjects were randomized to receive multiple ascending doses (MAD) of subcutaneous DA-1726 or placebo in a 2:1 ratio, once weekly for 4 weeks without titration.
- Of 9 subjects randomized in the 48 mg cohort, 6 entered an optional four-week extension phase at the same dose (4 DA-1726; 2 placebo).



Results

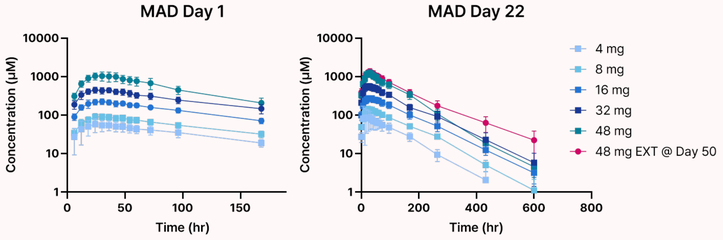
Demographics and baseline characteristics

Number of Subjects	4 mg (N=6)	8 mg (N=6)	16 mg (N=6)	32 mg (N=6)	48 mg (N=6)	48 mg Ext (N=4)	Pooled Placebo (N=15)
Age (years)							
Mean (SD)	46.8 (11.8)	45.0 (8.7)	45.8 (13.4)	46.7 (5.9)	48.0 (12.6)	46.8 (16.0)	40.6 (12.2)
Male							
n (%)	2 (33.3)	4 (66.7)	4 (66.7)	2 (33.3)	4 (66.7)	2 (50.0)	9 (60.0)
Weight (kg)							
Mean (SD)	84.4 (11.0)	89.3 (11.8)	96.0 (9.1)	90.4 (14.4)	110.4 (12.7)	108.4 (15.3)	99.1 (14.5)
Body Mass Index (kg/m²)							
Mean (SD)	32.6 (2.4)	31.2 (1.1)	35.3 (3.9)	34.0 (2.6)	38.1 (3.3)	37.9 (4.2)	36.1 (4.6)
Waist Circumference (cm)							
Mean (SD)	98.8 (8.4)	102.2 (4.5)	108.0 (7.8)	104.8 (4.0)	118.7 (10.1)	115.0 (10.5)	111.0 (12.8)

Summary of Pharmacokinetics Profiles of DA-1726 on Day 22

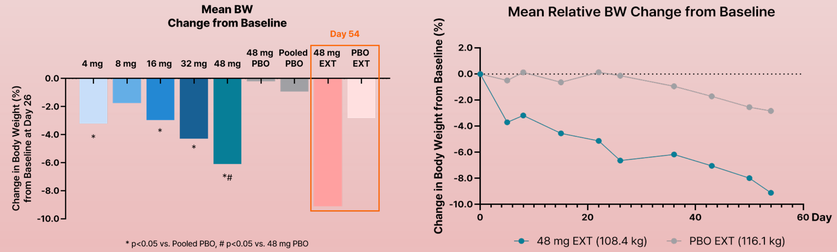
Mean (SD) Median (Range)	4 mg (N=6)	8 mg (N=6)	16 mg (N=6)	32 mg (N=6)	48 mg (N=6)	48 mg Ext Day50 (N=4)
C_{max} (nM)	102.1 (79.3)	145.6 (24.6)	279.0 (39.3)	571.3 (101.6)	1293.1 (222.1)	1397.0 (245.0)
T_{max} (hr)	24 (6-30)	30 (24-36)	24 (23.98-36)	24 (18-42)	30 (24-36)	33 (24-36)
$t_{1/2}$ (hr)	77.7 (7.6)	79.1 (9.1)	81.9 (6.6)	80.3 (13.5)	84.6 (12.7)	103.8 (20.0)
$AUC_{0\text{-tau}}$ (h*nM)	9,094 (3,666)	15,578 (1,017)	31,593 (5,149)	61,637 (9,422)	116,948 (19,096)	134,370 (13,514)
$AUC_{0\text{-inf}}$ (h*nM)	12,239 (4,413)	21,417 (494)	43,077 (7,941)	85,582 (16,386)	158,682 (34,433)	188,578 (29,554)

Note: 48 mg Ext was assessed on Day 50; all other groups were assessed on Day 22.



DA-1726 substantially reduced body weight and waist circumference

- **Body weight (48 mg):** **−6.1%** at Day 26 and **−9.1%** at Day 54, with no plateau through Week 8
- **Waist circumference (48 mg)**: **−5.8 cm** at Day 26 and **−9.8 cm** at Day 54
- **Body mass index (48 mg)**: **−2.3 kg/m²** at Day 26 and **−3.4 kg/m²** at Day 54



Conclusion

- DA-1726 was generally well tolerated through 48 mg, with no new safety signals identified
- Most GI AEs were mild-to-moderate and transient, even without dose titration
- PK was linear and dose proportional, supporting once-weekly dosing
- Substantial weight reduction was observed in the 48 mg cohort, with no apparent plateau
- Ongoing Phase 1 Part 3a/3b dose-titration studies are evaluating longer-term outcomes

Contact information : Hyung Heon Kim, HHKim@metaviatx.com; Mi-Kyung Kim, kmk@donga.co.kr