SAT-677. EB618, FIRST-IN-CLASS ORAL TABLET OF DUAL GLP-1/GLUCAGON RECEPTOR AGONIST FOR PATIENTS WITH OBESITY AND METABOLIC DISORDERS: RESULTS FROM PK-PD STUDY IN NON-HUMAN PRIMATES

Gregory Burshtein[1], Constantin Itin[1], Daniel Pery[1], Eli Reichman[1], Hillel Galitzer[1], Michal Kushnir[1], Ahuva Bar-Ilan[2], Moran Golan[2], Laura Moschcovich[2], Miri Zakar[2], Amit Rivkin[2], Moran Levy[2], Miranda Toledano[1], Jane Hsiao[3]

[1] Entera Bio Ltd., Jerusalem, Israel, [2] OPKO Biologics Ltd. Kiryat Gat, Israel, [3] OPKO Health Inc. Miami, FL, USA

BACKGROUND

Oxyntomodulin (OXM) is a naturally occurring dual GLP-1/Glucagon receptor agonist hormone that plays a key role in regulating appetite and glucose metabolism, promoting weight loss, and has demonstrated additional cardioprotective and anti-fibrotic properties. Due to its short plasma half-life, the therapeutic potential of the native hormone is limited.

OPK-88006 is a proprietary (OPKO Health Inc.) long-acting OXM analog that has shown promising activity following subcutaneous administration in rodent models of metabolic disorders. Entera (Entera Bio Ltd.) is developing EB618 (oral OPK-88006) as the first dual GLP-1/Glucagon receptor agonist once-daily tablet for patients with obesity and related metabolic disorders using its N-Tab® oral peptide platform.

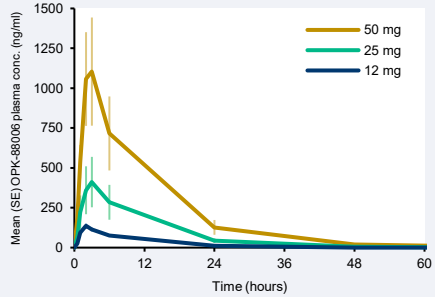
EB618 has demonstrated robust pharmacokinetic exposure and pharmacodynamic effects of lowering blood glucose levels in rat and minipig models [Burshtein G, et al. J. Endocr. Soc. 2025;9(Supp 1)].

METHODS

- In this study, EB618 was evaluated in non-human primates (NHP; Cynomolgus Macaque). Tablets of three different strengths were administered via oral gavage to 18 (n=6 per arm) males of 3-5 years old / 3-6 kg body weight following an overnight fast of at least 8 hours.
- At 2 hours post-dose a meal of fixed caloric content was provided.
- PK blood samples were withdrawn at predetermined timepoints and concentrations of the OPK-88006 peptide in plasma were analyzed by the LC-MS/MS method.
- Glucose levels in blood were monitored for 6 hours following EB618 administration.
- The animals' health and vital signs were monitored twice daily.

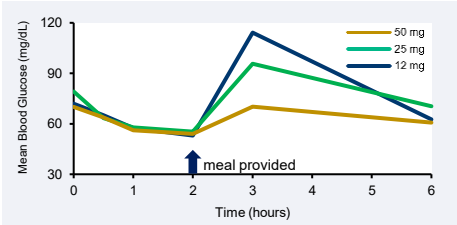
RESULTS

EB618 exhibited robust bioavailability characterized by dose-proportional systemic exposure and low variability.



Dose (mg)	Cmax (ng/ml) Mean (±SE)	AUClast (hr*ng/ml) Mean (±SE)	Tmax (hr) Median (Range)
50	1145 (±325)	14458 (±4752)	3 (2-3)
25	419 (±156)	5290 (±2035)	2 (2-3)
12	137 (±15)	1341 (±147)	2 (2)

A dose-proportional pharmacologic effect on postprandial blood glucose levels was shown.



The tested drug was well tolerated, and no safety concerns were identified, at doses exceeding the anticipated clinical dose range by more than tenfold (mg/kg body weight).

CONCLUSIONS

EB618, exhibited consistent, dose-proportional PK exposure and a robust PD effect. Together, these data support clinical development of EB618 as the first oral once-daily GLP-1/Glucagon receptor agonist for the treatment of obesity and related metabolic disorders.

CONTACT

Michal Kushnir, Director of Program Management
Michalk@enterabio.com
Entera Bio Ltd. www.enterabio.com