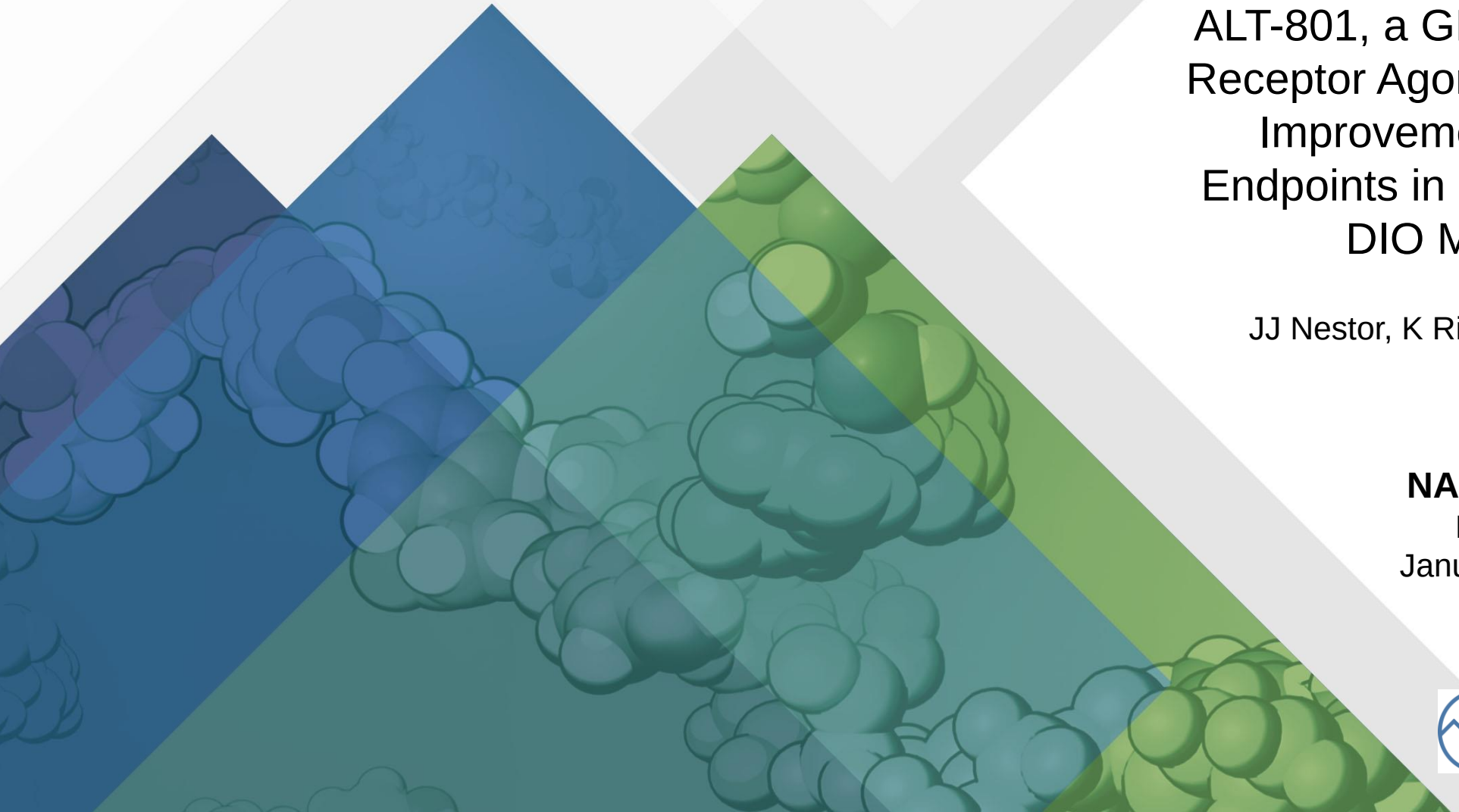

ALT-801, a GLP-1/Glucagon Dual Receptor Agonist, Shows Superior Improvement in Key NASH Endpoints in a Biopsy-Confirmed DIO Mouse Model

JJ Nestor, K Rigbolt, M Feigh, D Parkes, MS Harris

NASH-TAG 2020
Park City UT
January 10-11, 2020

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Disclosures

- John J Nestor, Jr. is a consultant to Altimmune and holds stock in the company
- David Parkes is a consultant to Altimmune
- Kristoffer Rigbolt and Michael Feigh are employees of Gubra, which conducted the animal studies in this presentation
- M. Scott Harris is an employee of Altimmune

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NASH and NAFLD

HEPATIC MANIFESTATIONS OF OBESITY AND METABOLIC SYNDROME

- NAFLD is present in up to **90% of obese patients**
- **Up to 40% of NASH patients develop NAFLD** recurrence one year after liver transplant—the underlying metabolic disease is still present
- The **treatment of obesity** is the cornerstone of treating not only NASH but the principal morbidities of NASH (cardiovascular, malignancy)
- Drugs in development should target the **weight loss range achieved by bariatric surgery**

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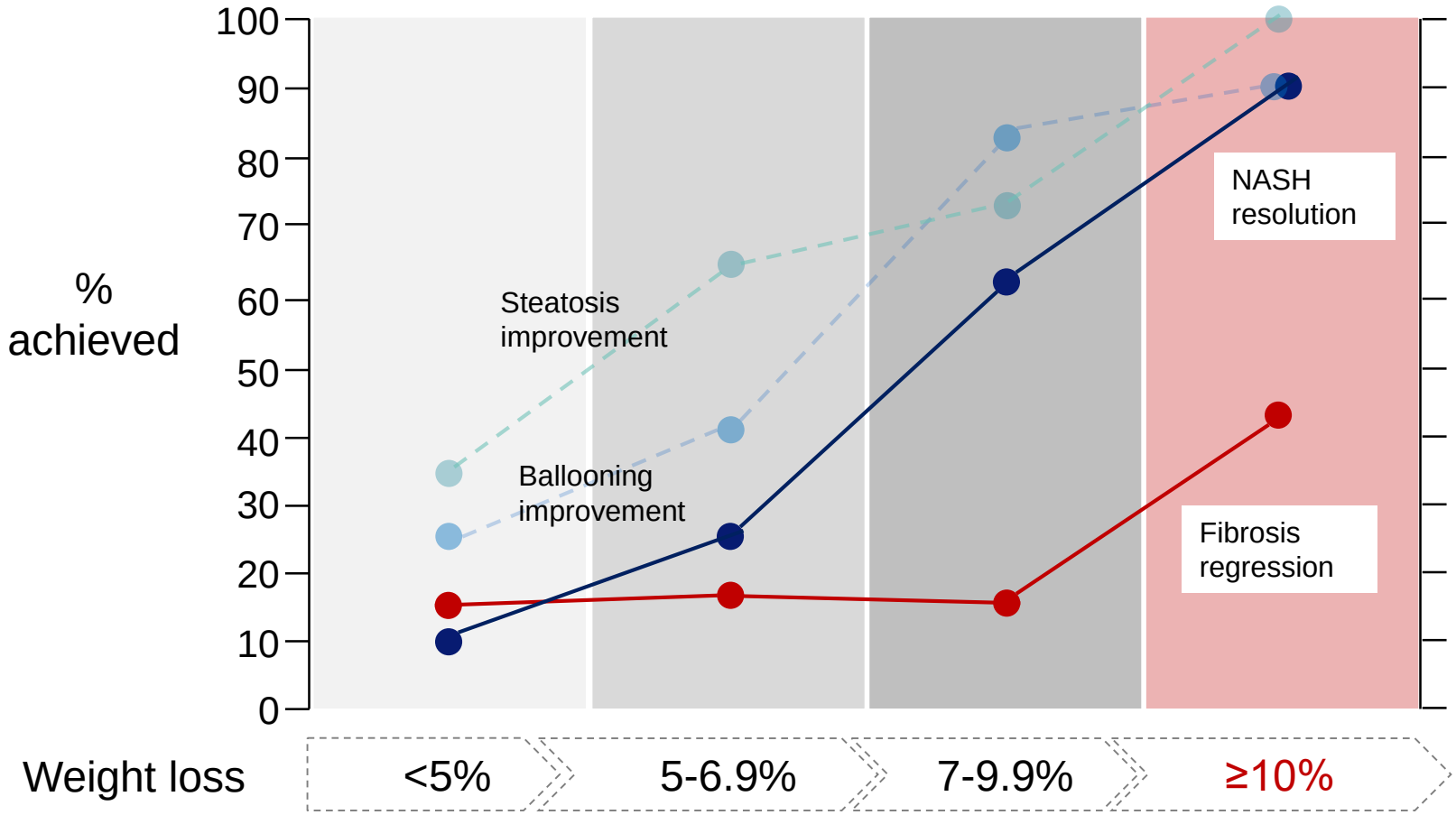
Substantial Body Weight Loss Blunts NASH Progression[1]

10% OR MORE WEIGHT LOSS MUST BE ACHIEVED



[1] *Promrat et al Hepatology 2010; Glass et al Dig Dis Sci 2015; Vilar-Gomez et al Gastroenterology 2015; Marchesini et al Hepatology 2016; Koutowkidis et al JAMA Intern Med 2019*

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GLP-1/Glucagon Receptor Dual Agonists

OPTIMIZED FOR NASH AND WEIGHT LOSS

GLP-1

blood glucose

appetite

inflammation

Indirect effects on liver

GLUCAGON

energy expenditure

adipose browning

lipolysis/ gluconeogenesis

mobilization of liver fat

Direct effects on liver

SIGNIFICANT REDUCTIONS IN

body weight

liver fat/cholesterol, inflammation, resulting fibrosis

blood glucose

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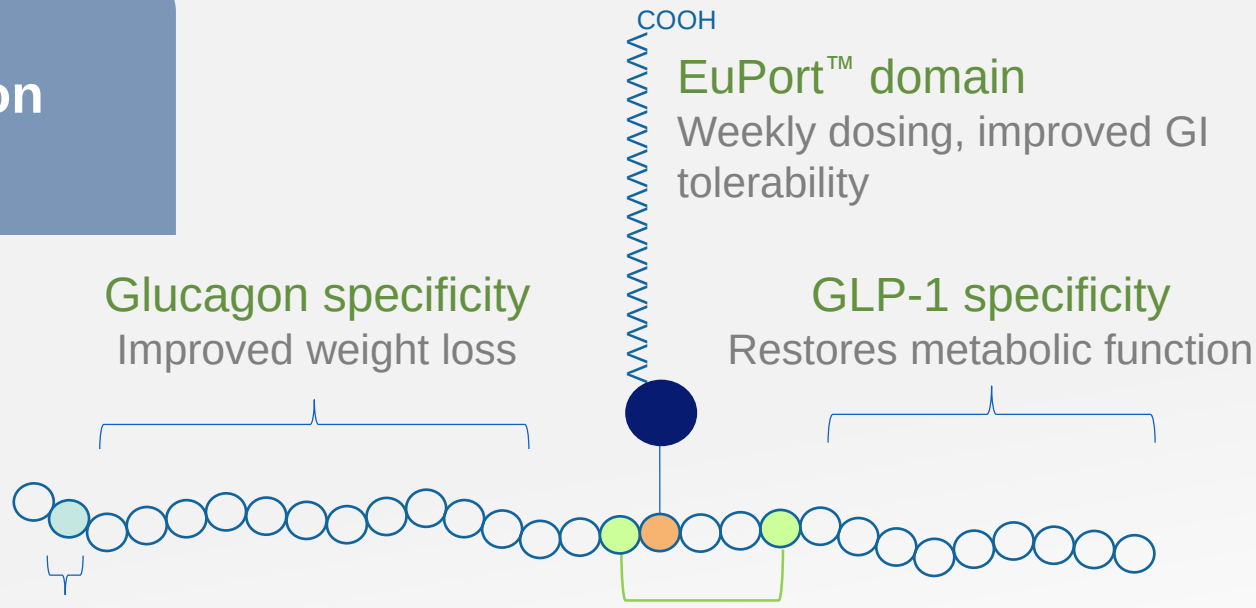
ALT-801

STRUCTURE IS KEY TO DIFFERENTIATION

Proprietary EuPort™ domain provides prolonged $t_{1/2}$ and reduced C_{max}

Balanced GLP-1:Glucagon Agonism



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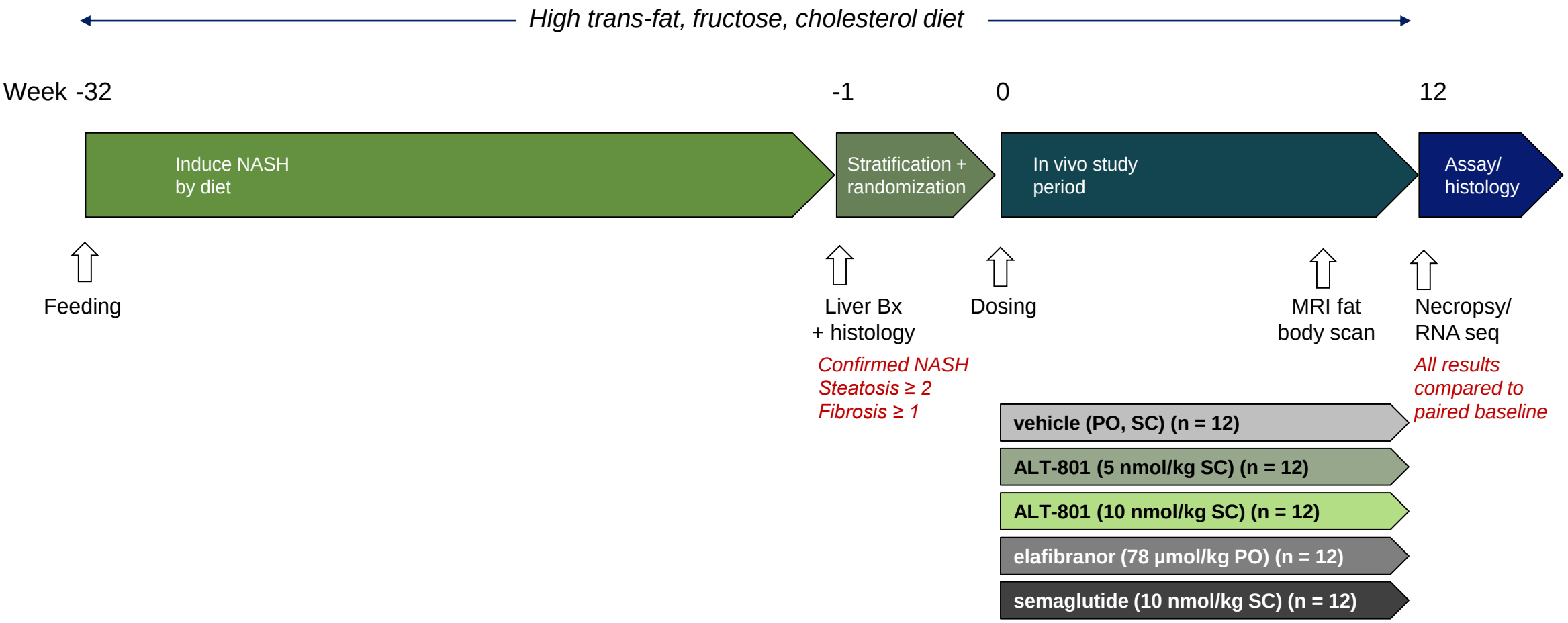
ALT-801
GUBRA AMYLIN NASH MODEL IN MALE C57BL/6J MICE



Hansen, HH, et al. (2017) Drug Disc Today ***22 (11)***: 1707-18

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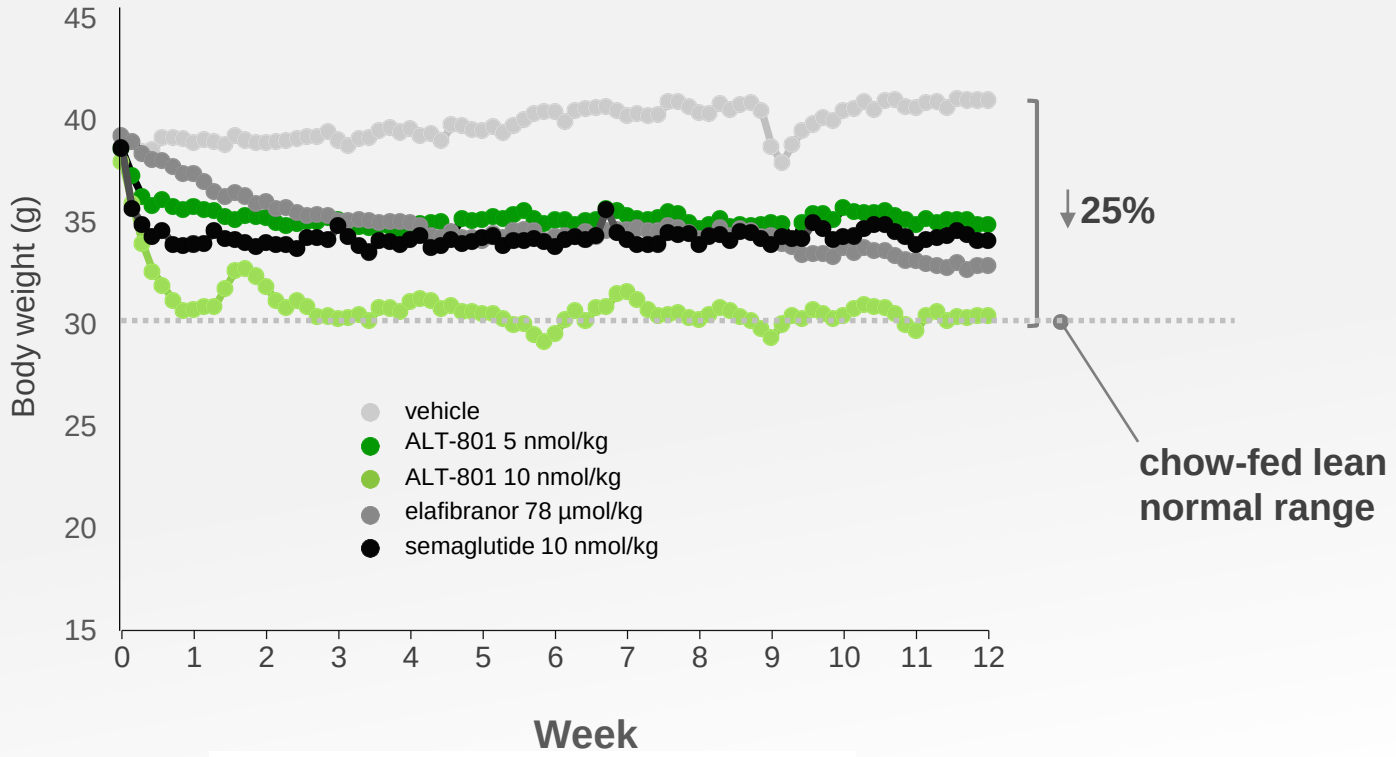
BODY WEIGHT RETURNS TO CHOW-FED LEAN NORMAL RANGE

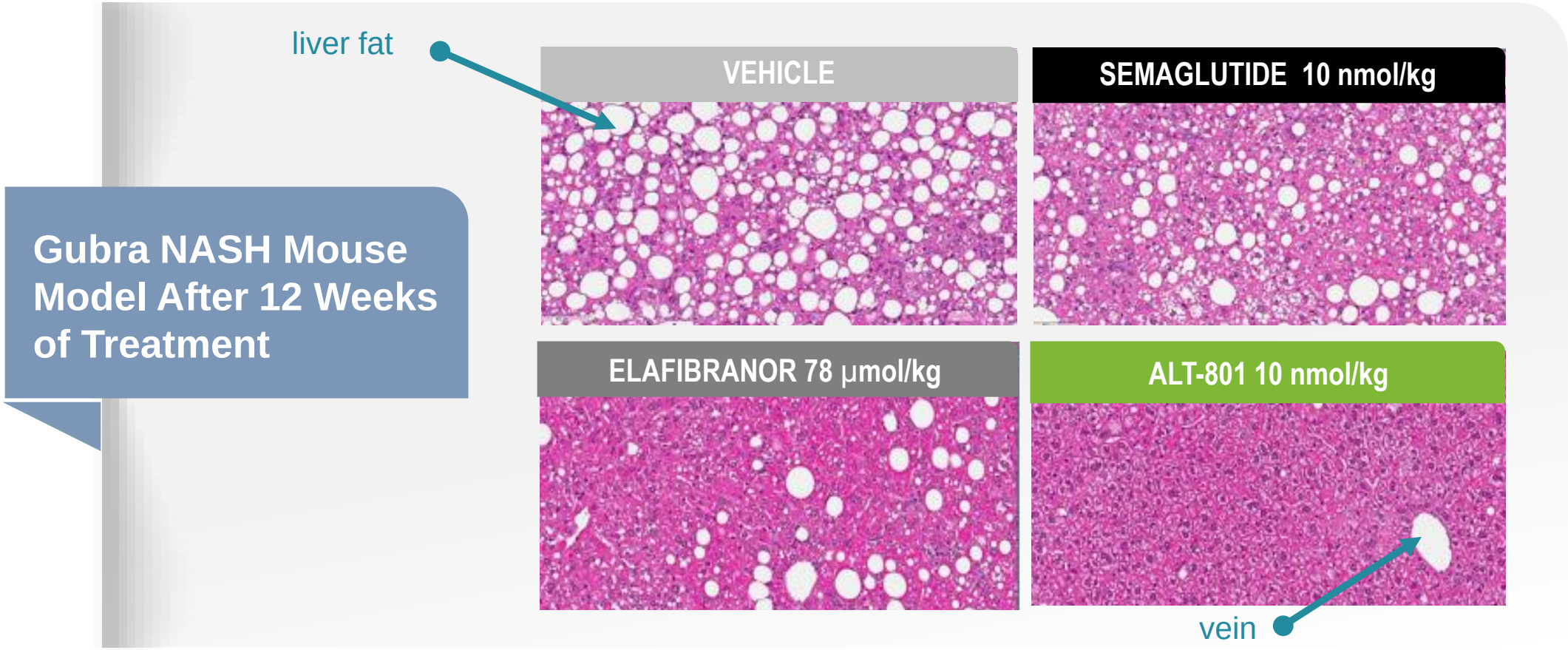
Gubra NASH Mouse Model After 12 Weeks of Treatment



ALT-801

REDUCTION IN LIVER FAT TO CHOW-FED LEAN NORMAL RANGE

Gubra NASH Mouse Model After 12 Weeks of Treatment



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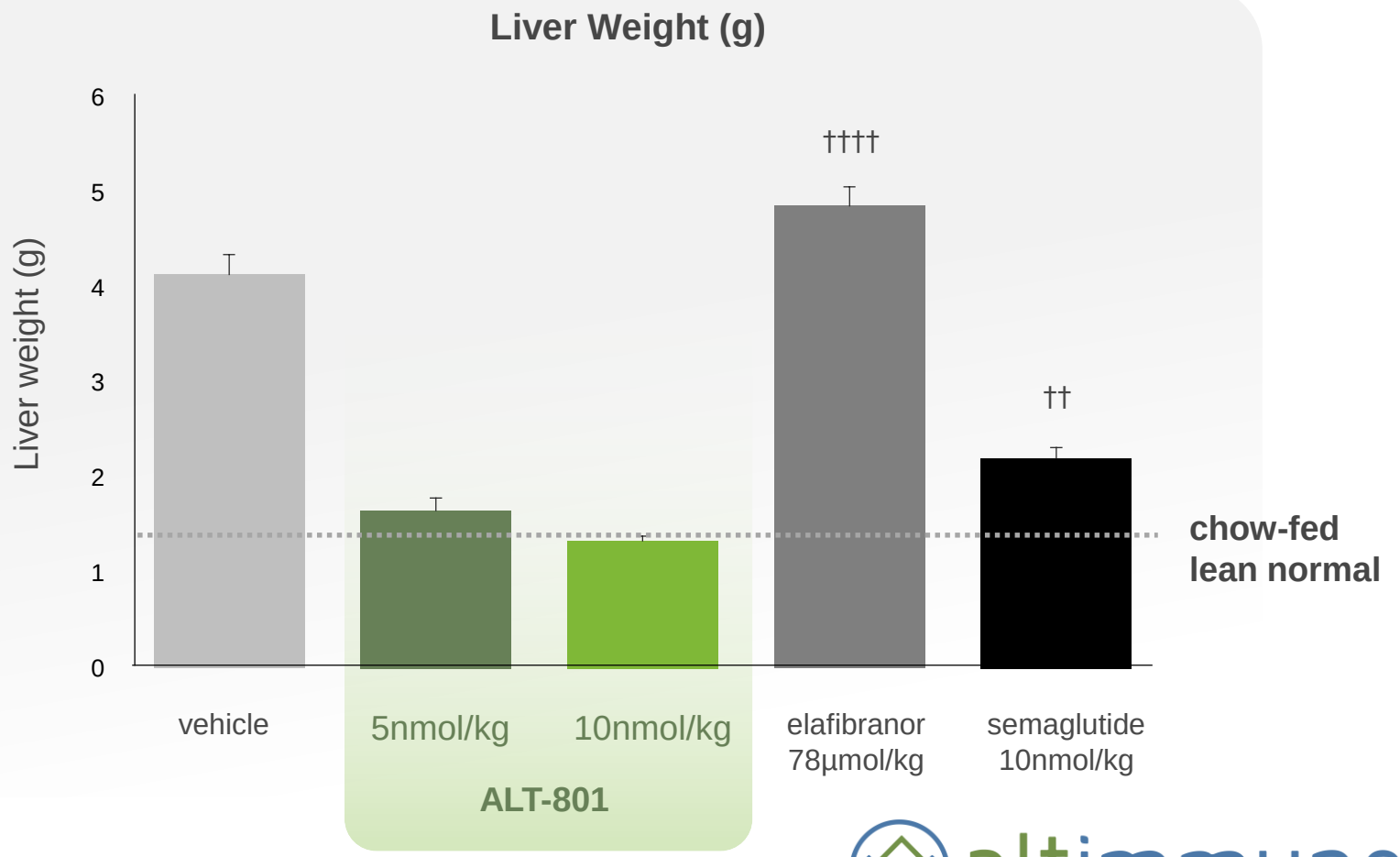
ALT-801
NORMALIZATION OF LIVER WEIGHT

Gubra NASH Mouse Model After 12 Weeks of Treatment



Mean (SE), 1-way ANOVA with Dunnett's adjustment for multiplicity
†† p < .01, ††† p < .001, ††††, p < .0001 vs. **ALT-801** 10 nmol/kg (n=11-12)

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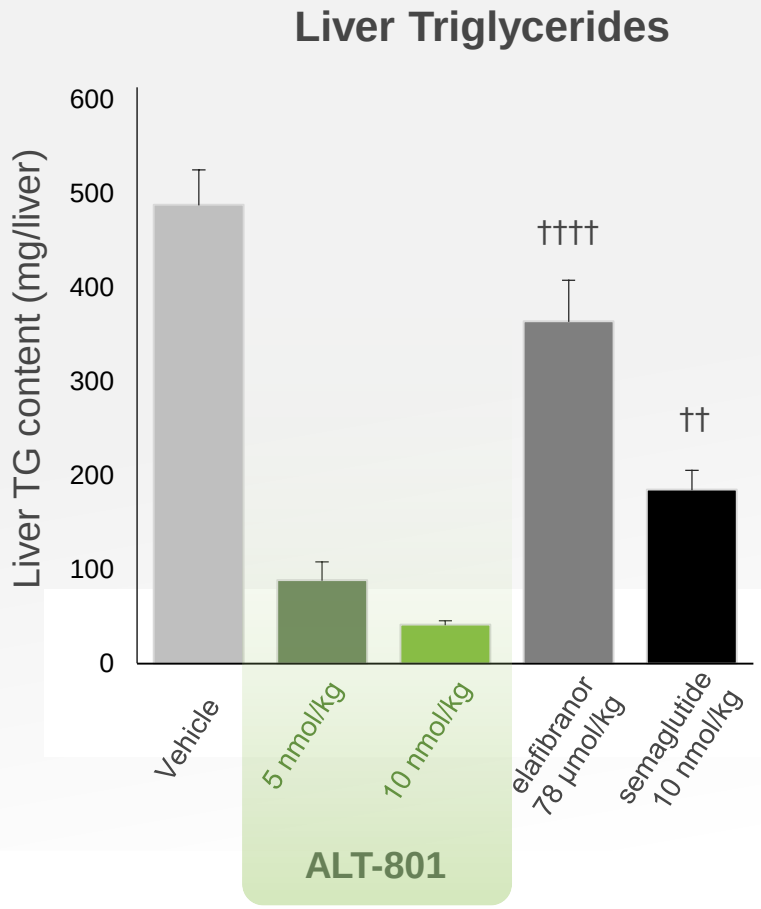
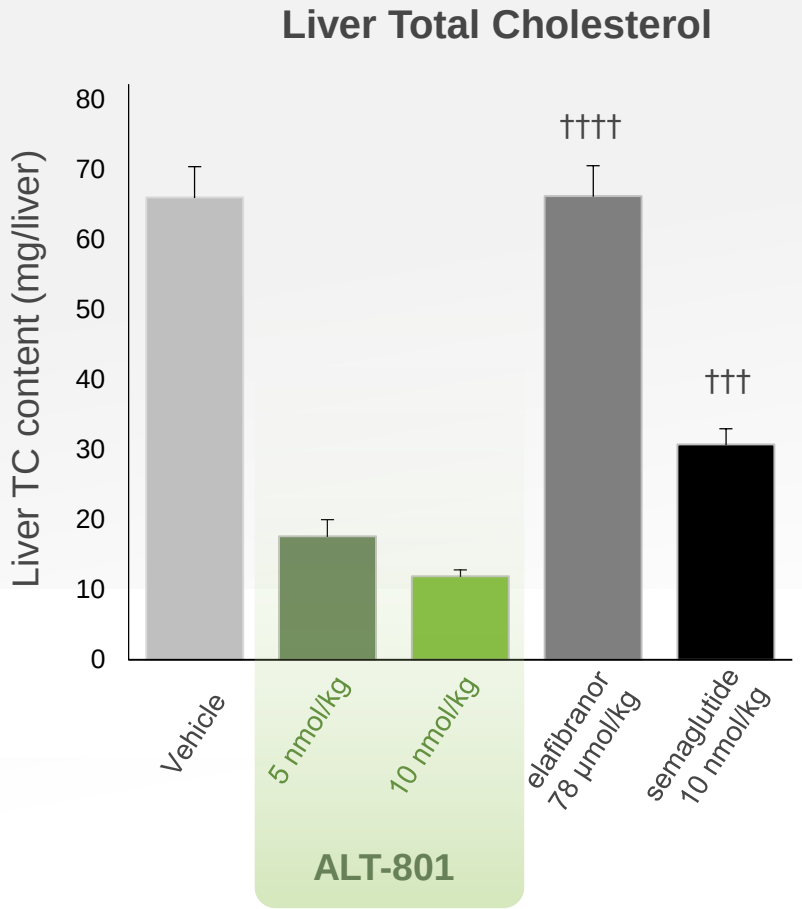
REDUCTIONS IN LIVER TRIGLYCERIDES (TG) AND TOTAL CHOLESTEROL (TC)

Gubra NASH Mouse Model After 12 Weeks of Treatment





Mean (SE), 1-way ANOVA with Dunnett's adjustment for multiplicity
†† p < .01, ††† p < .001, ††††, p < .0001 vs. **ALT-801** 10 nmol/kg (n=11-12)

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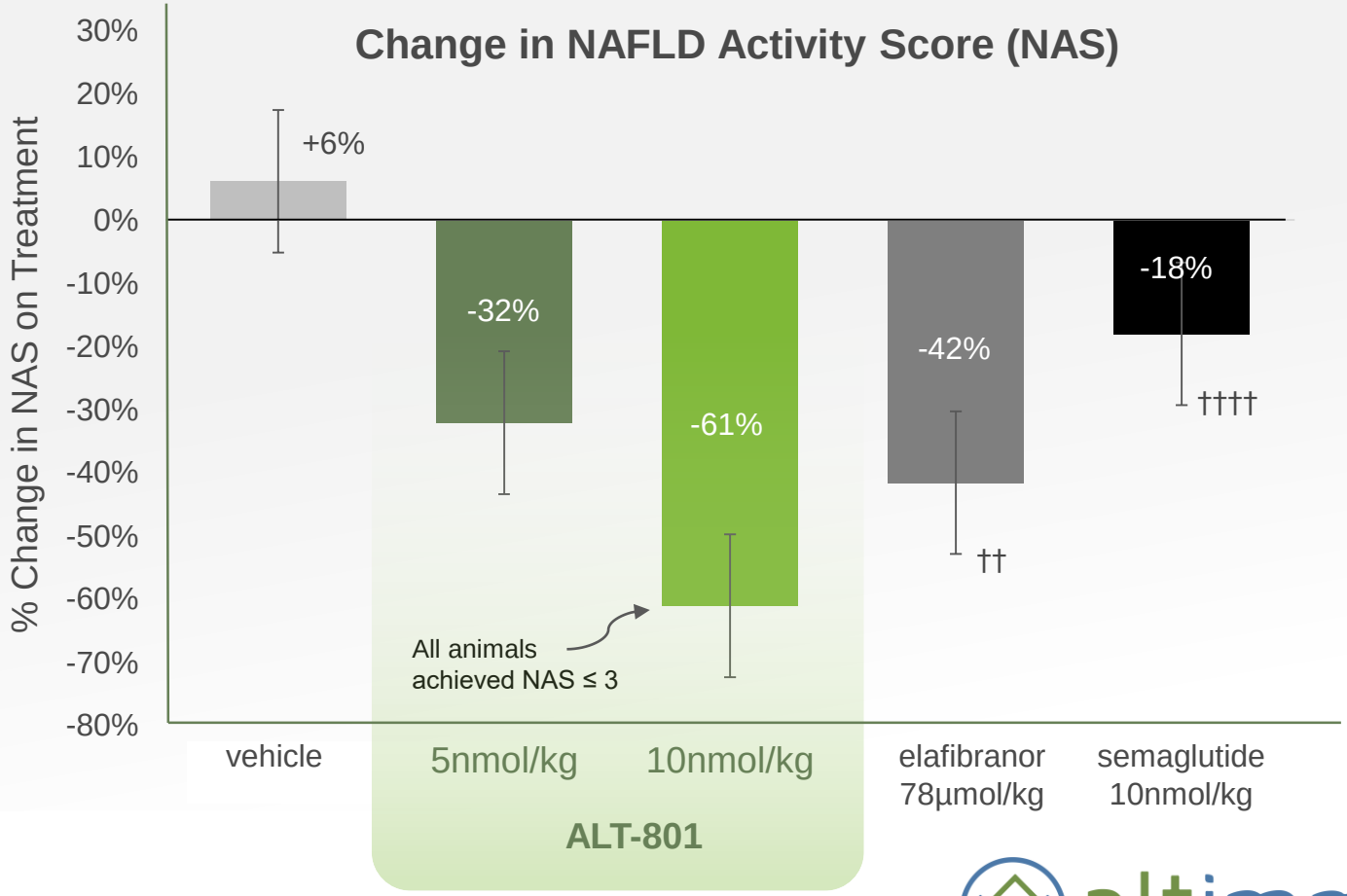
GREATER REDUCTION IN NAFLD ACTIVITY SCORE (NAS)

Gubra NASH Mouse Model After 12 Weeks of Treatment



Mean (SE), 1-way ANOVA with Dunnett's adjustment for multiplicity
†† p < .01, ††† p < .001, ††††, p < .0001 vs. ALT-801 10 nmol/kg (n=11-12)

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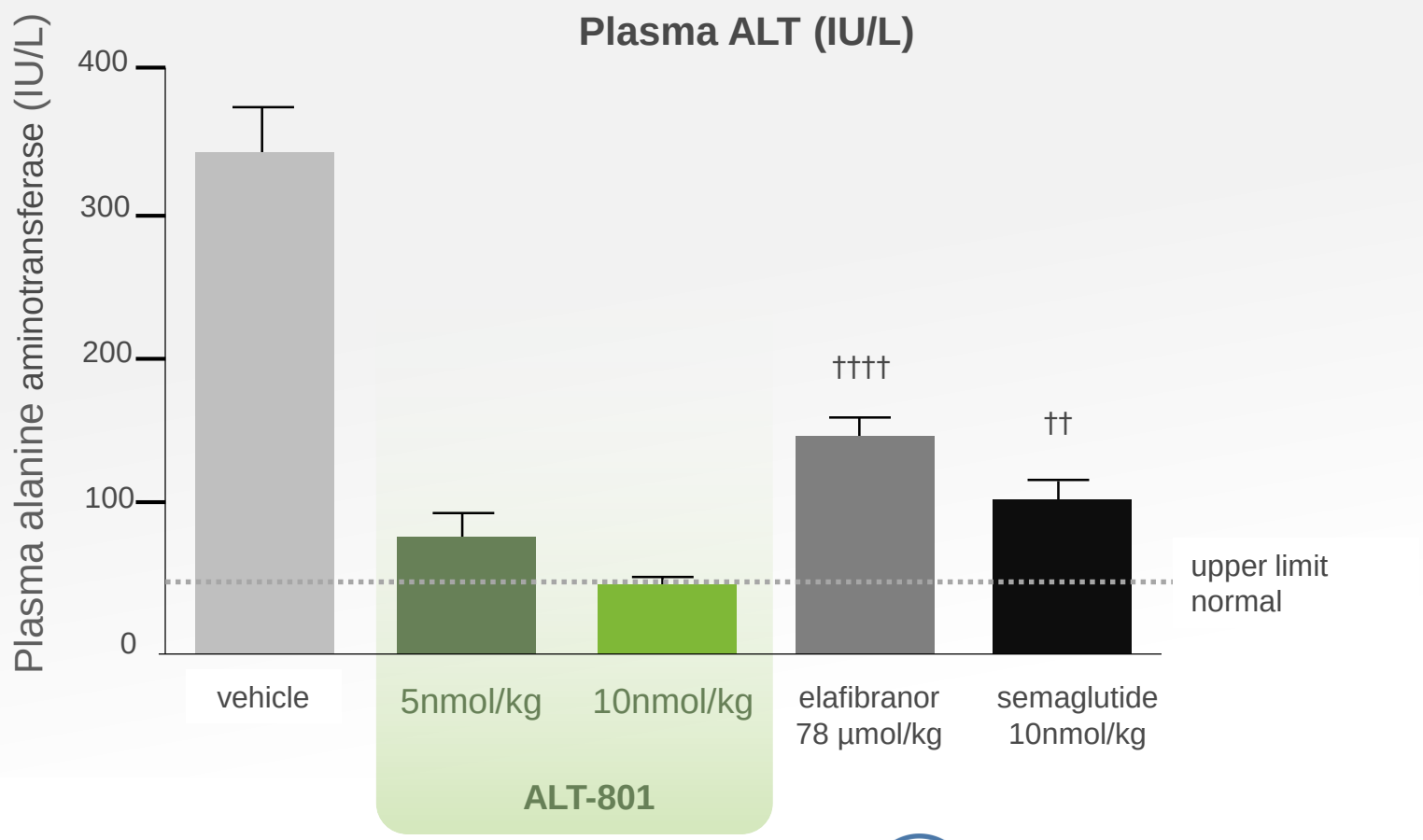
NORMALIZATION OF PLASMA ALT

Gubra NASH Mouse Model After 12 Weeks of Treatment



Mean (SE), 1-way ANOVA with Dunnett's adjustment for multiplicity
†† p < .01, ††† p < .001, ††††, p < .0001 vs. ALT-801 10 nmol/kg (n=11-12)

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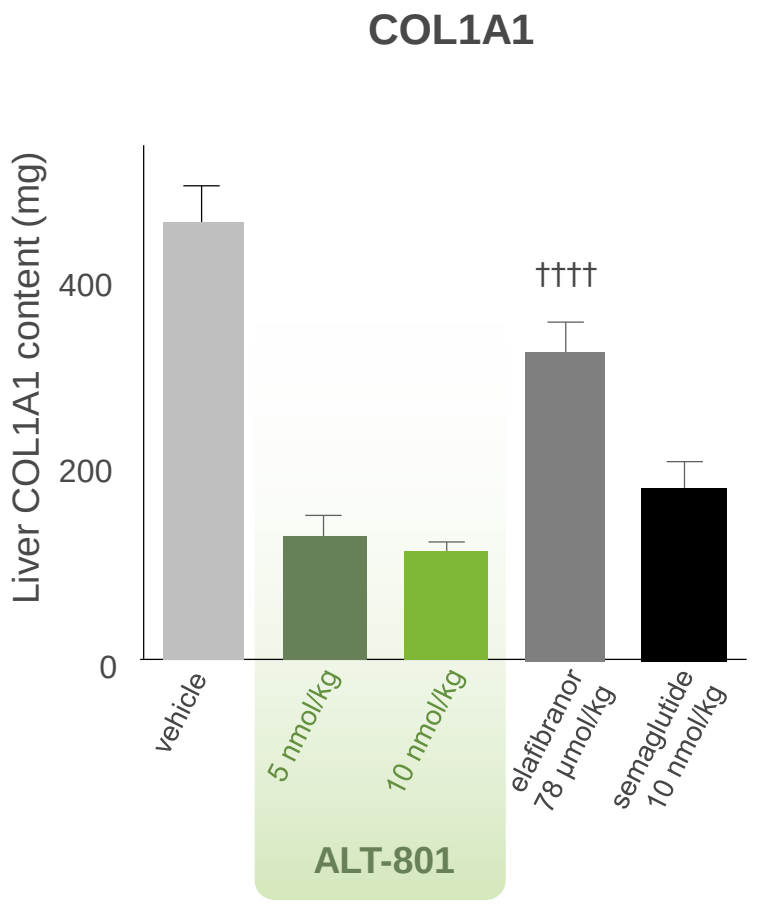
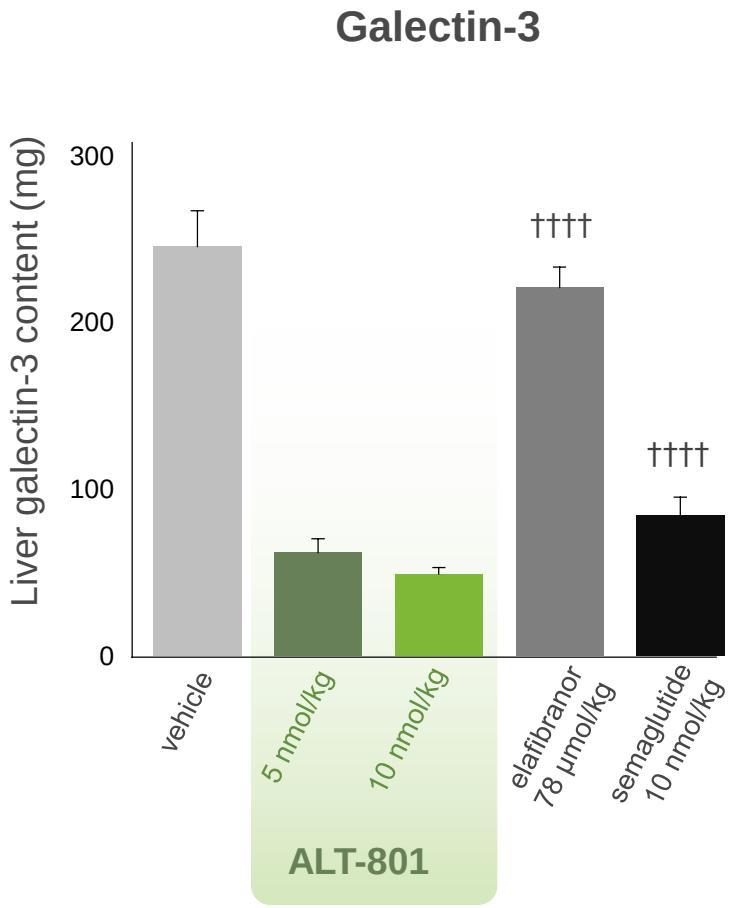
GREATER EFFECTS ON FIBROSIS

Gubra NASH Mouse Model After 12 Weeks of Treatment





Mean (SE), 1-way ANOVA with Dunnett's adjustment for multiplicity
†† p < .01, ††† p < .001, ††††, p < .0001 vs. **ALT-801** 10 nmol/kg (n=11-12)

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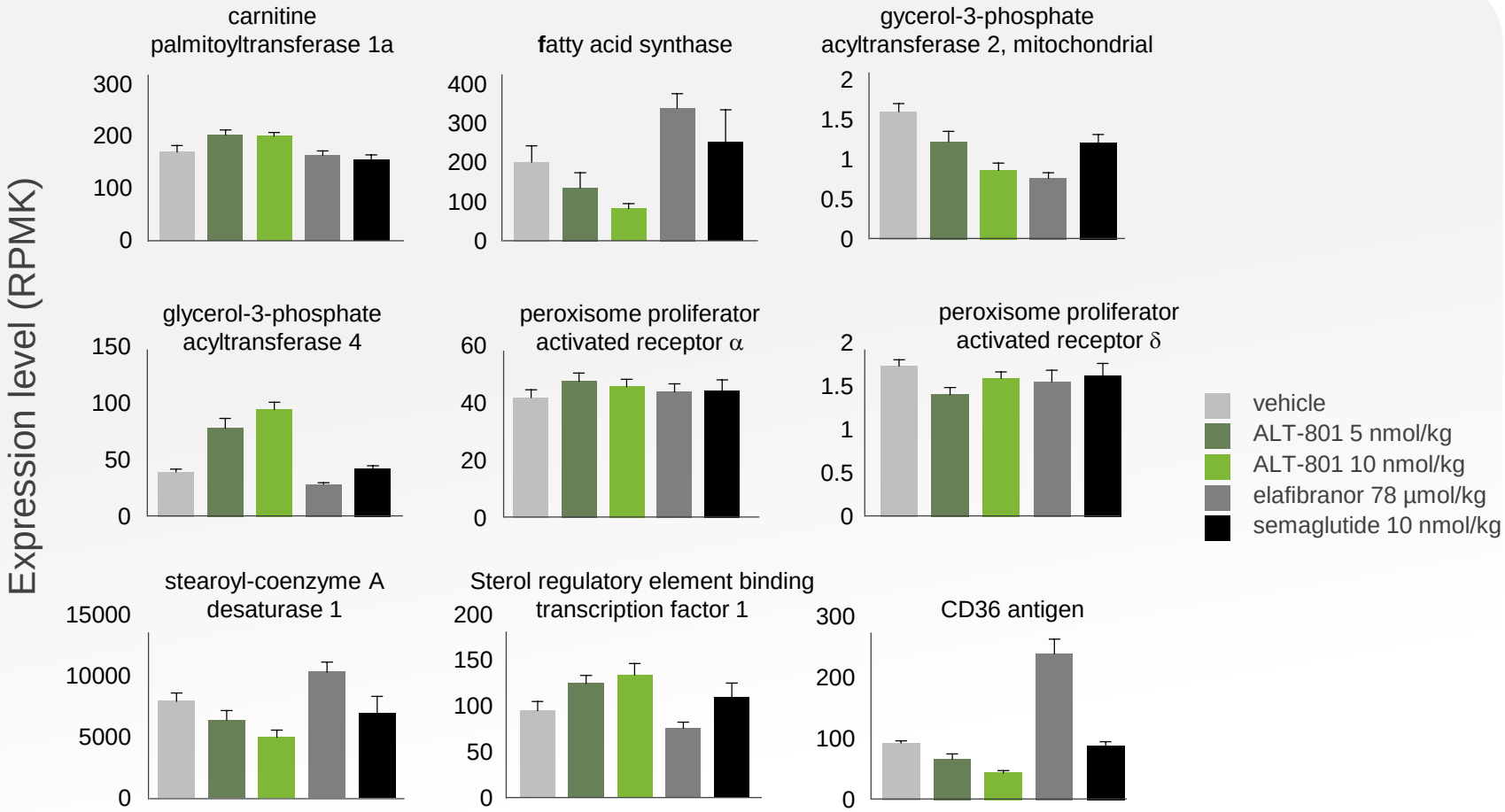
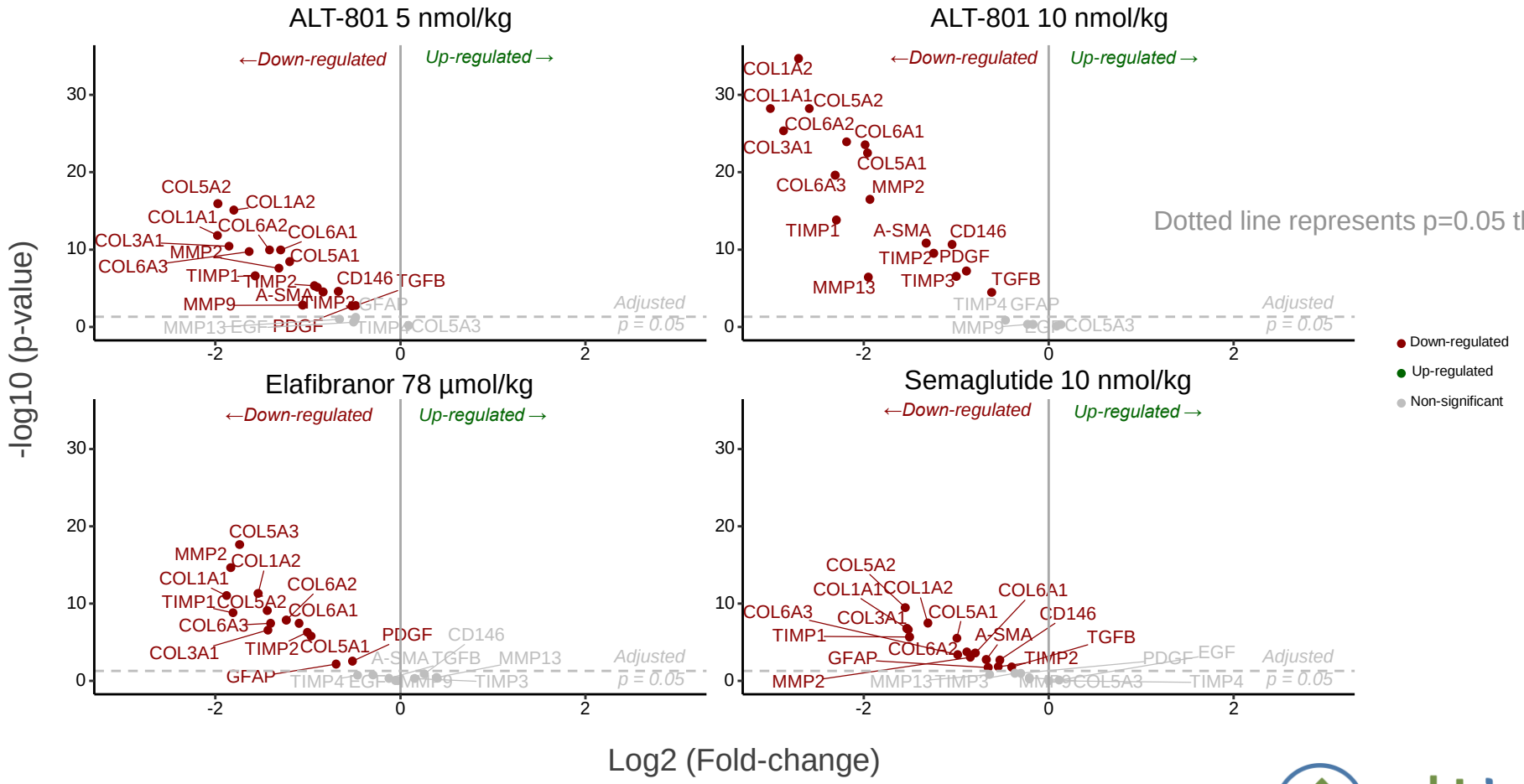
MODULATES GENES AFFECTING FAT METABOLISM AND TRANSPORT

Gubra NASH Mouse Model After 12 Weeks of Treatment

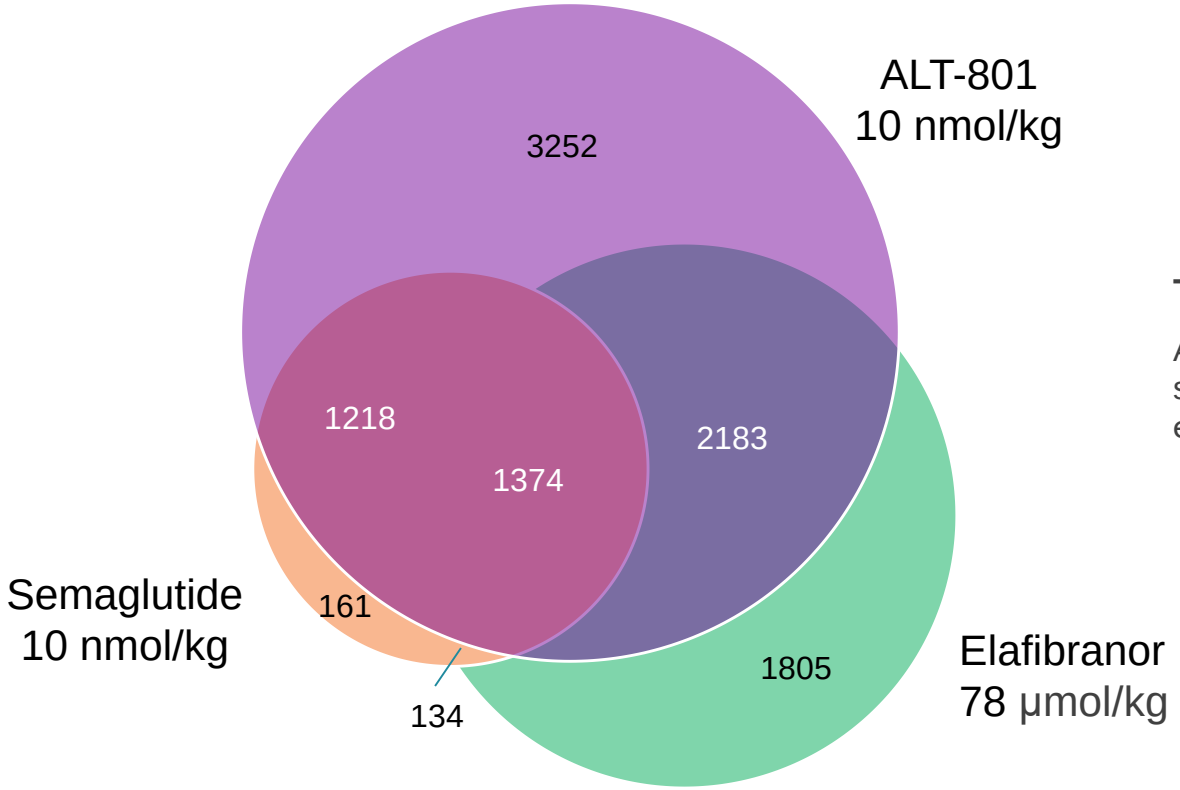


ALT-801

SUPPRESSION OF PRO-FIBROTIC STELLATE CELL GENES



ALT-801
DIFFERENTIALLY REGULATES ADDITIONAL PATHWAYS



Total regulated genes

ALT-801 10nmol/kg ~ 8,000
semaglutide 10nmol/kg ~ 2,800
elafibranor 78µmol/kg ~ 5,800

Visualization of the number of genes regulated by combinations of compounds. Values inside circles indicate the number of genes differentially expressed versus the vehicle group that are compound specific or shared between treatments.

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SUMMARY

- ALT-801 resulted in superior reductions in nearly all measured NASH parameters compared to semaglutide or elafibranor, returning many parameters to lean normal range:
  - Body and liver weight
  - NAS and ALT
  - Collagen (COL1A1 and galectin-3) content
  - Liver fat, cholesterol and triglycerides
- ALT-801 improved metabolic function and exhibited pleiotropic effects across multiple pathways involved in NASH
- ALT-801 resulted more profound suppression of genes associated with steatosis, inflammation and stellate cell fibrosis by RNA sequencing compared to elafibranor

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CONCLUSIONS

- The improvements of body weight, liver pathology and metabolic parameters in this NASH model highlight ALT-801 as an attractive new drug candidate for the treatment of NASH

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Thank You