Muscle-Preserving Weight Loss With RV-8451, a Novel, Oral Non-Peptide GLP-1 Receptor Agonist, in Diet-Induced Obese Non-Human Primates

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Rivus Pharmaceuticals, Charlottesville, VA

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Presenter Disclosure

Sol Collado, Ph.D.

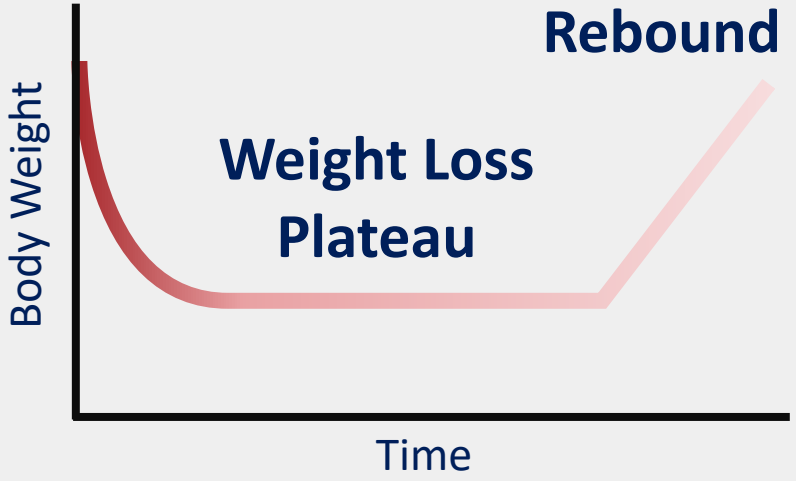
Executive Director, Rivus Pharmaceuticals

Employee: Rivus Pharmaceuticals

Stock/Shareholder: Rivus Pharmaceuticals

Current GLP-1RAs Have Persistent Limitations

Body Weight Trajectory on Current GLP-1RAs



Poor GI Tolerability

Limits dose escalation and real-world adherence

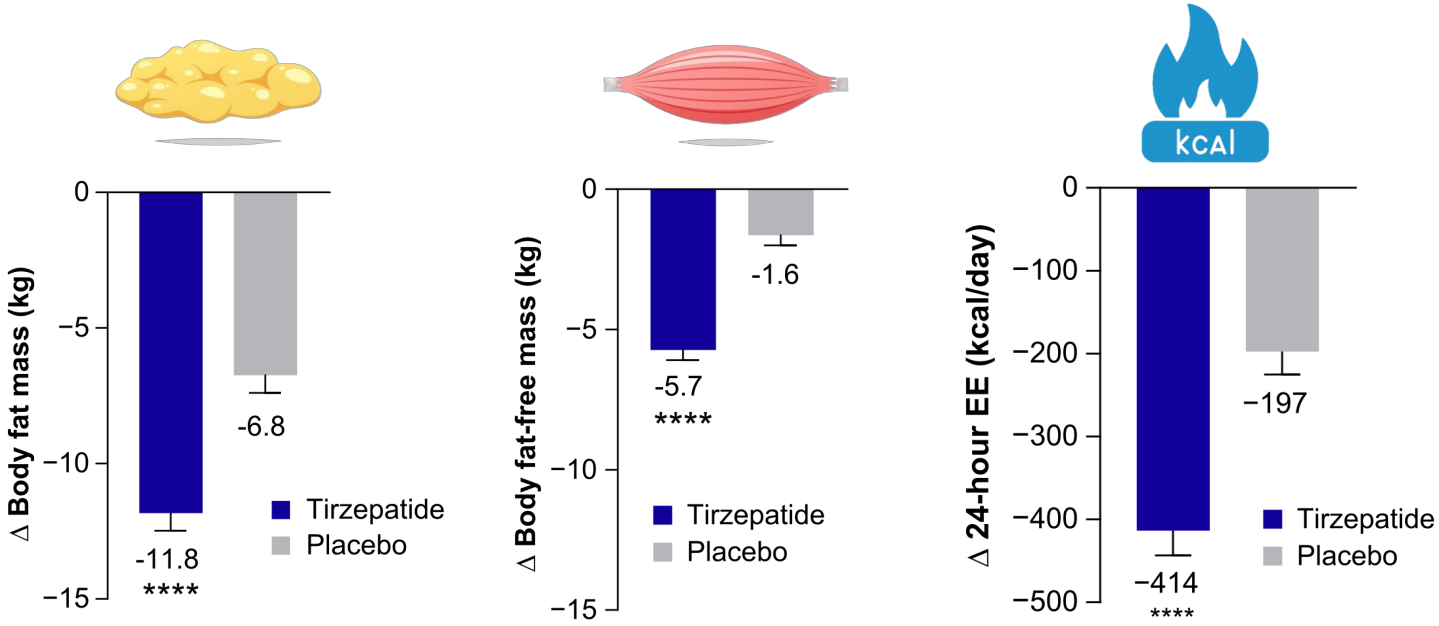
Loss of Lean Mass

Up to ~40% of weight lost is muscle

Metabolic Adaptation

Leads to weight plateau and rebound

GLP-1RA-Driven Fat-Free-Mass Loss Drives Down Energy Expenditure in Obese Subjects



Ravussin et al., 2025, Cell Metabolism 37

RV-8451: Muscle Preserving, Oral Non-Peptide GLP-1RA

Designed to address the key limitations of current GLP-1RA therapies

Muscle-Preserving

Selective fat loss with preservation of lean mass

Counters Metabolic Adaptation

For durable weight loss

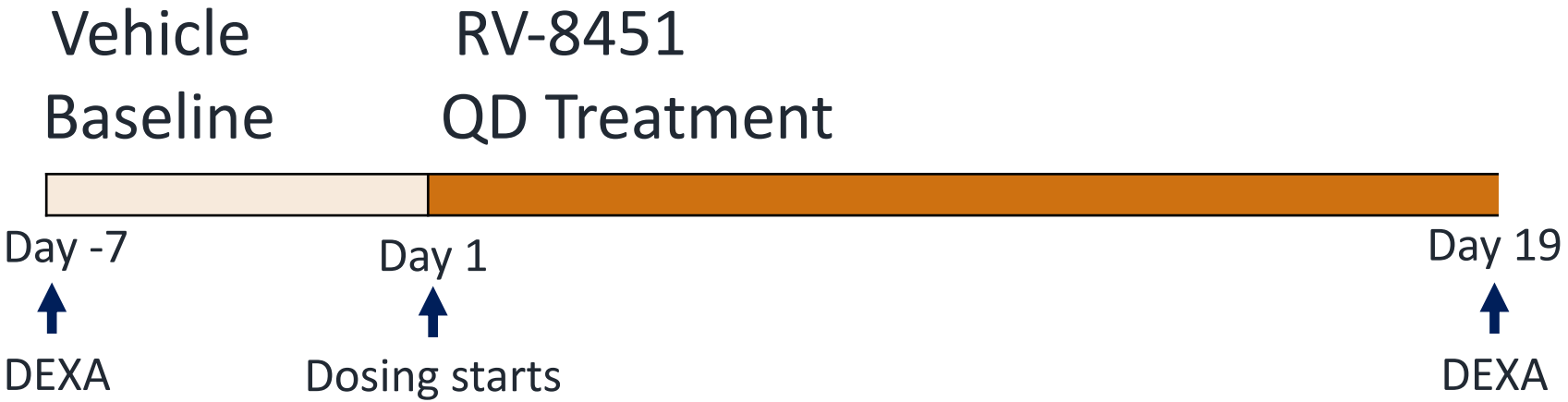
Oral, Non-Peptide

Chronic, convenient administration

RV-8451 Is a Novel GLP-1R Non-Peptide Agonist

	RV-8451	Orforglipron	Danuglipron
In vitro potency			
hGLP-1R cAMP, EC_{50}, nM	< 50	2	0.2
MkGLP-1R cAMP, EC_{50}, nM	< 2	< 1	< 1
hGLP-1R binding, K_i, nM	< 500	20	200
Cross species activity			
Human, NHP, rat, mouse, dog	+, +, -, -, -	+, +, -, -, -	+, +, -, -, -

Efficacy and Quality of Weight Loss of RV-8451 in DIO NHPs



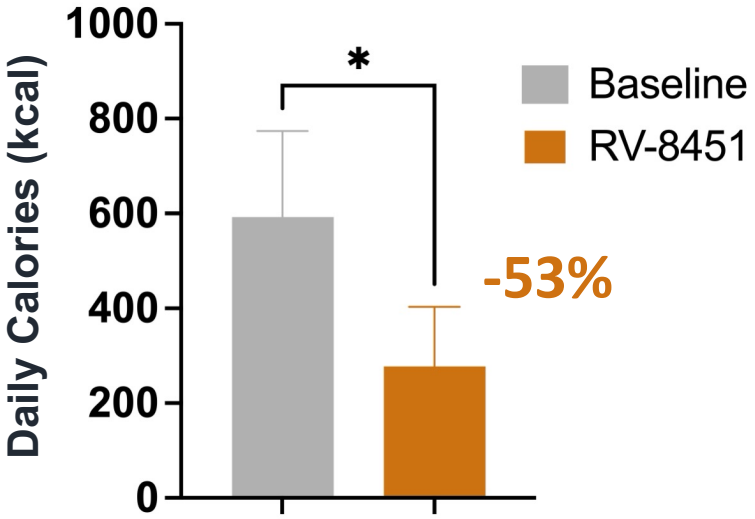
Endpoints:

- Daily bodyweight, caloric intake
- Body composition (Baseline vs End of Treatment, DEXA)

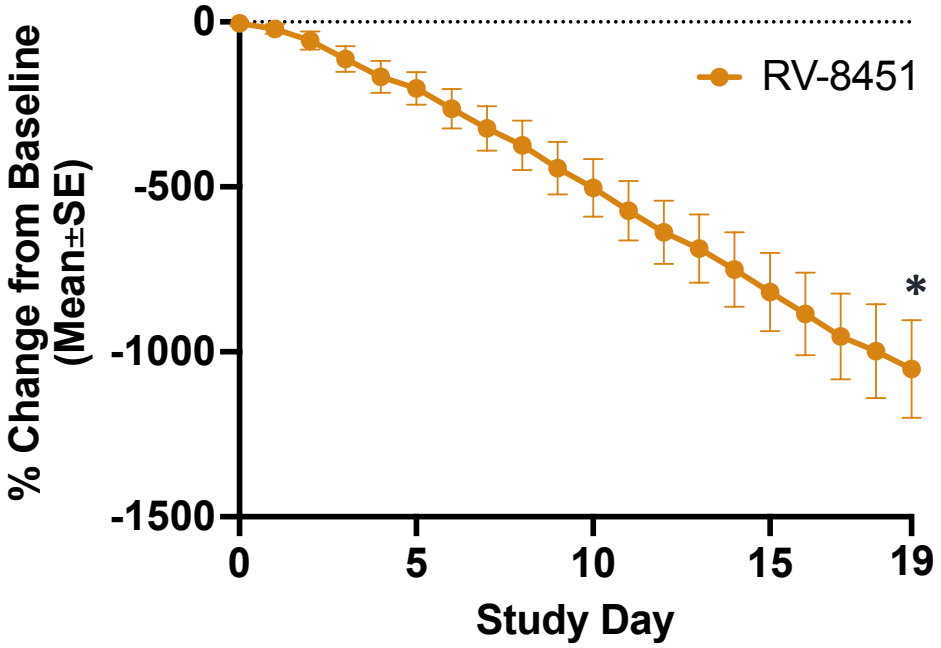
RV-8451 Significantly Reduces Daily Caloric Intake

DIO NHPs

Average Daily Caloric Intake



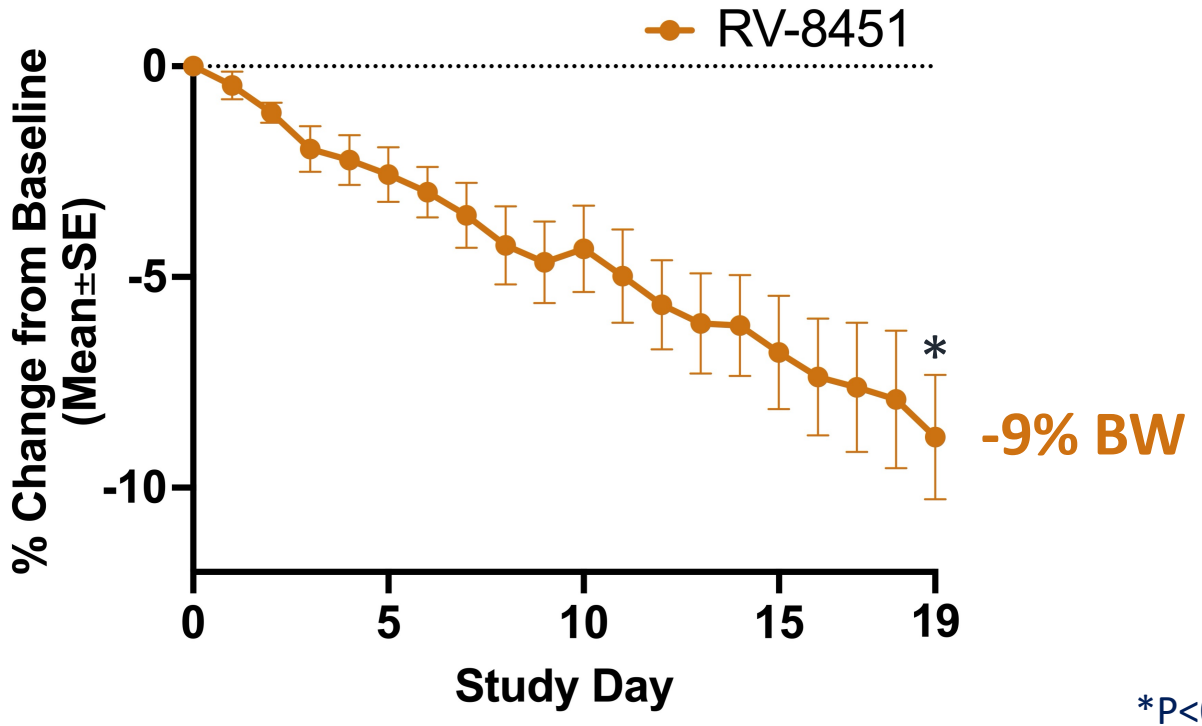
% Change in Cumulative Caloric Intake



*P<0.05 from baseline

RV-8451 Results in Significant Weight Loss at 19 Days

DIO NHPs

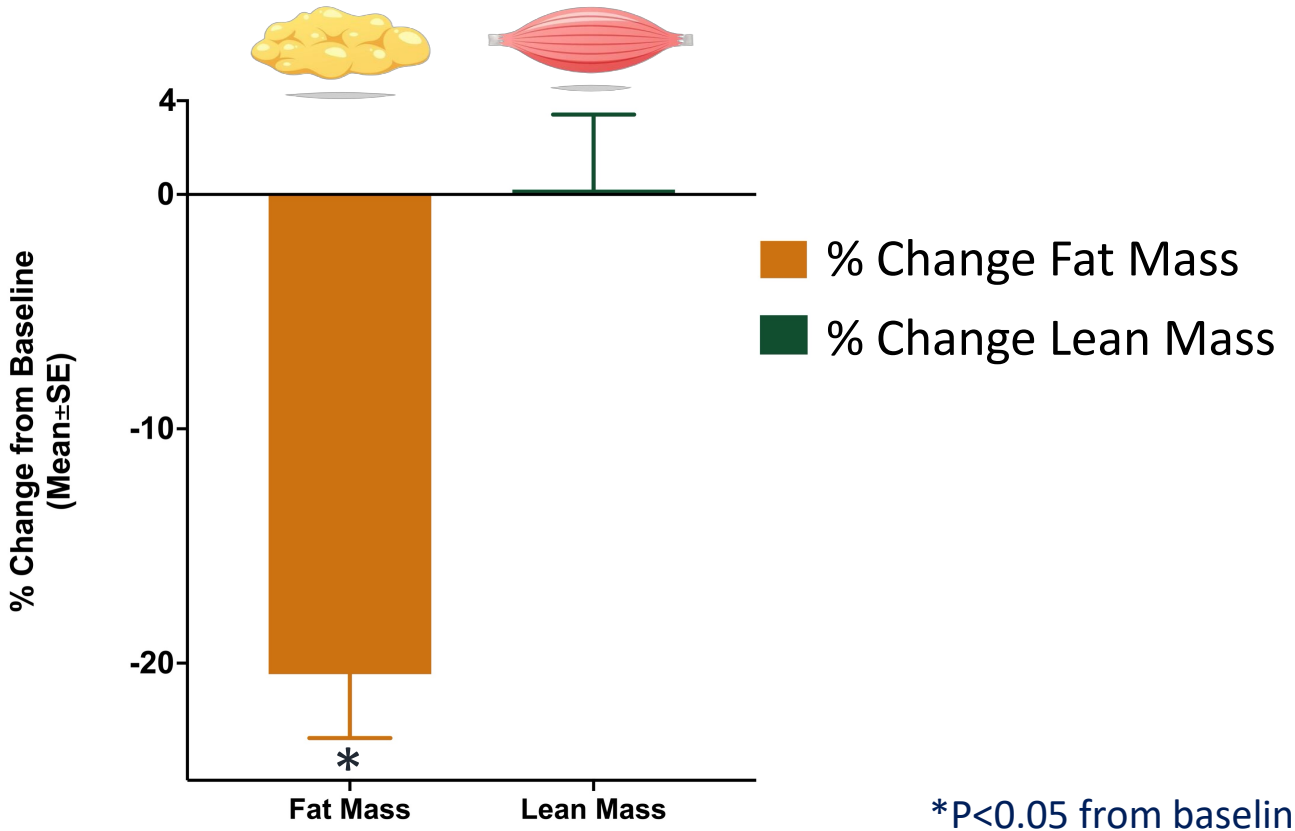


*P<0.05 from baseline

RV-8451 Induces Fat Loss While Preserving Muscle

DIO NHPs Day 19, Assessed by DEXA

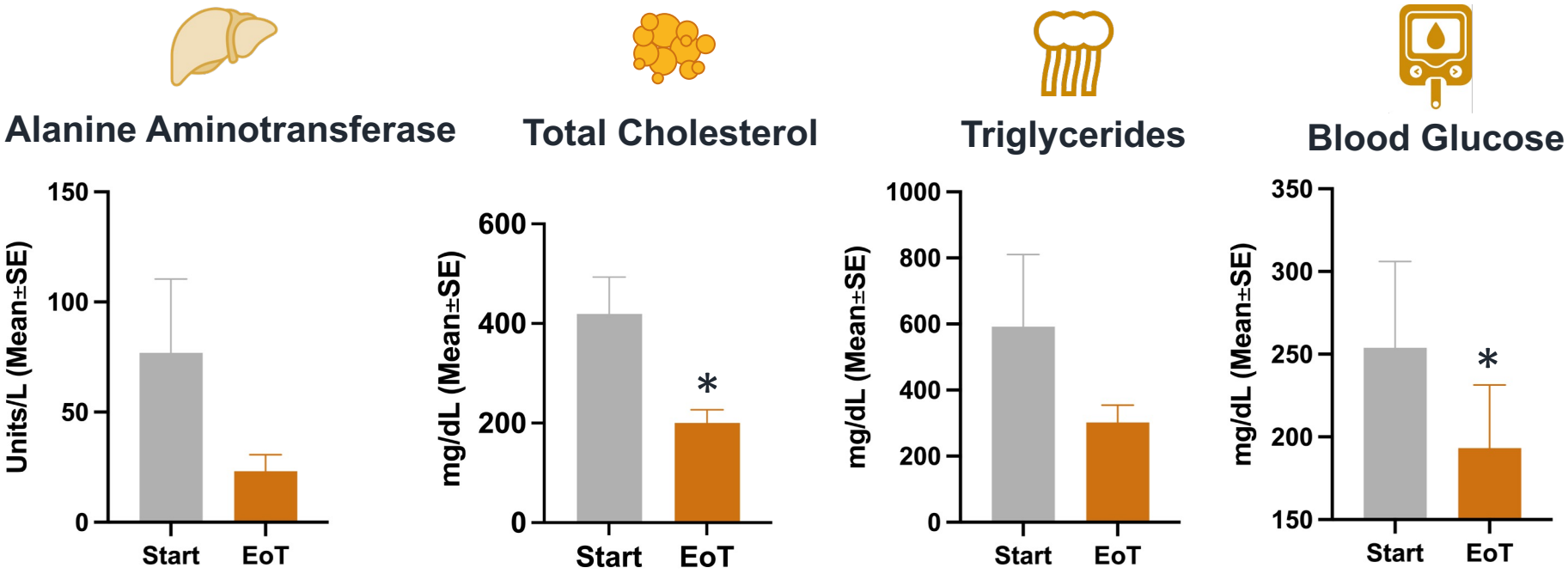
Percent Change from Baseline in Body Composition: Fat Mass & Lean Mass with RV-8451



*P<0.05 from baseline

RV-8451 Improves Metabolic Parameters

DIO NHPs, Day 19



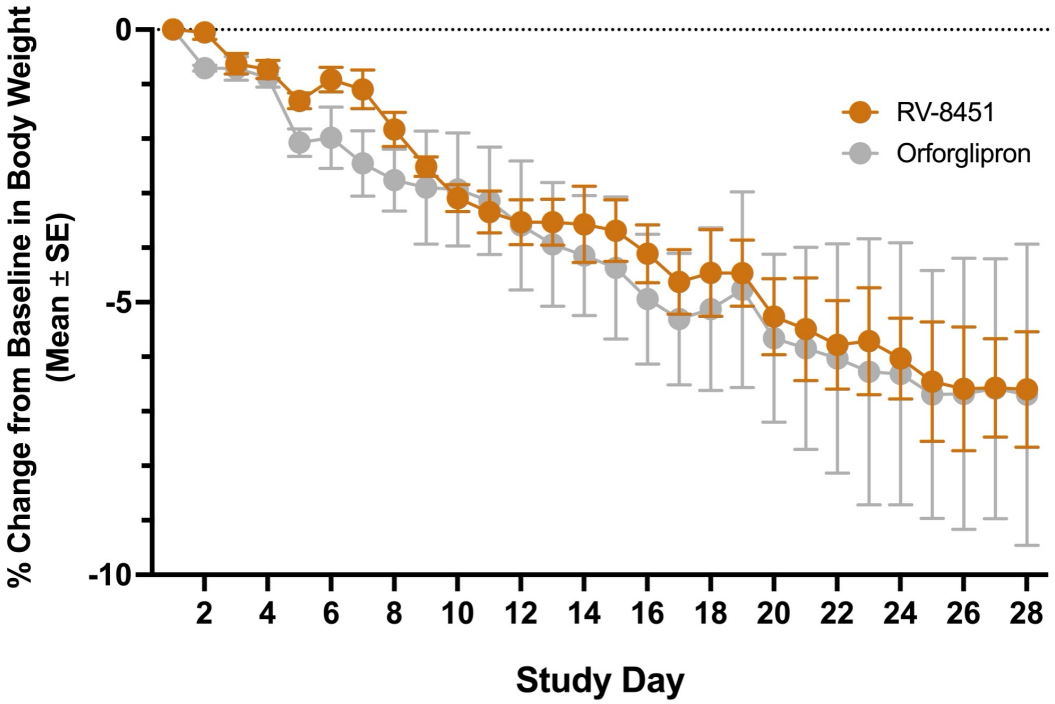
*P<0.05 from baseline

Head-to-Head Study Comparing Quality of Weight Loss Between RV-8451 and Orforglipron in DIO NHPs

- Selected doses to get the same pharmacological effect on caloric intake
- Endpoints: Daily bodyweight, and daily caloric intake, body composition (Baseline vs End of Treatment, DEXA)

RV-8451 Drives Similar Weight Loss to Orforglipron, Dose-Matched for Similar Reductions in Caloric Intake

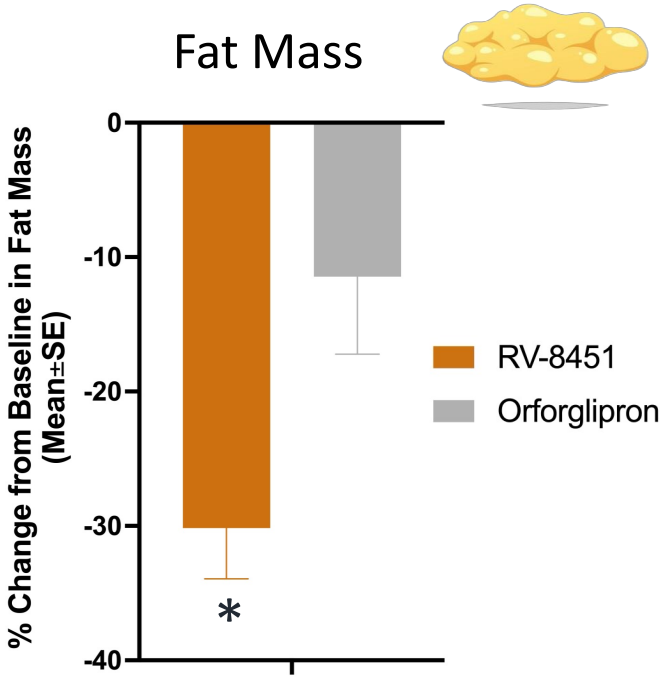
DIO NHPs, Assessed over 28 Days of Dosing

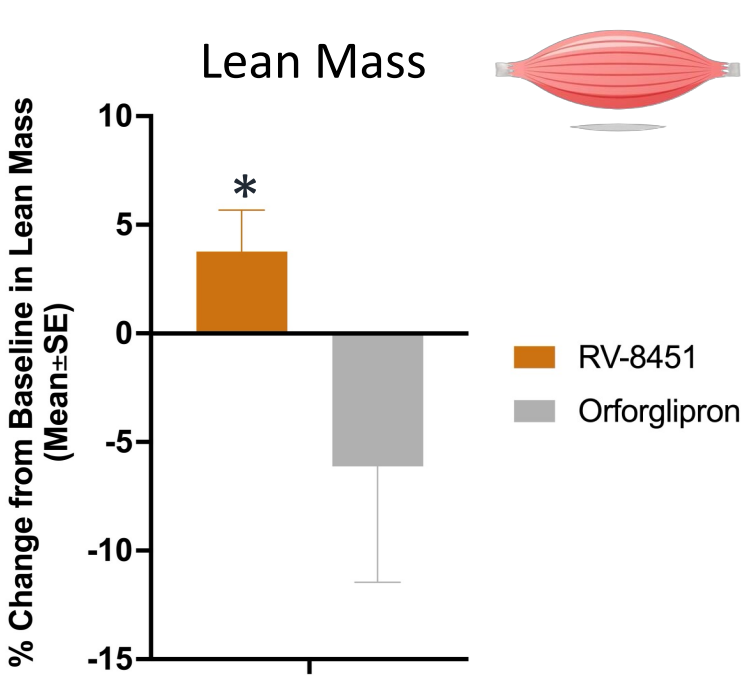


-7% BW

RV-8451 Delivered Higher Quality of Weight Loss Versus Orforglipron in DIO NHPs

Superior Reduction in Fat Mass with Lean Mass Preservation (DEXA, 28 days)

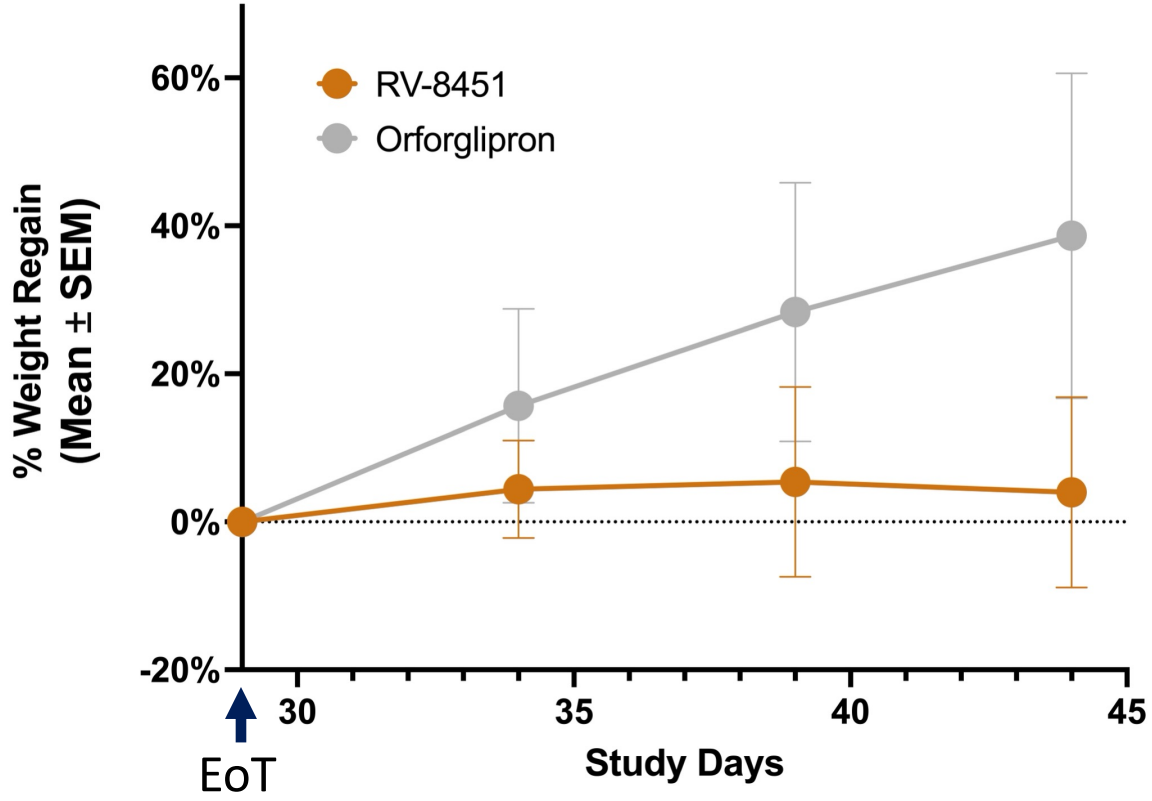




*P<0.05 from Orforglipron

RV-8451 Resulted in Sustained Weight Loss

DIO NHPs, Assessed for 15 Days following End of Treatment



RV-8451: Summary of Results in H2H NHP Study

-7%

Body weight change

28-day DIO NHP Study

-30%

Fat mass change (DEXA)

28-day DIO NHP Study

+4%

Lean mass change (DEXA)

28-day DIO NHP Study

=

Caloric intake reduction comparable to orforglipron

✓

Outperforms orforglipron in quality of weight loss and prevention of weight rebound

0

Drug-related GI adverse events

Across two independent NHP studies

Conclusions

- RV-8451 GLP-1RA oral monotherapy results in selective fat loss with full preservation of lean mass in DIO NHPs
- Reduction in caloric intake comparable to current GLP-1RAs
- Superior quality of weight loss compared to orforglipron with similar quantity of weight loss
- No drug-related GI adverse events observed; well-tolerated profile
- Results replicated in DIO hGLP-1R mice (Poster 2574-P)
- IND-enabling studies underway for planned Phase 1 trial

Acknowledgments

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Poster 2574-P

"Discovery of RV-8451, a Novel, Oral, Muscle-Preserving Small Molecule GLP1 Receptor Agonist"

Monday, June 8, 2026, 1:30 - 2:30 p.m. CT

Thank You

Questions & Discussion