March 10, 2026

2025 Q4 Financial Results & Business Update

Nasdaq: SKYE

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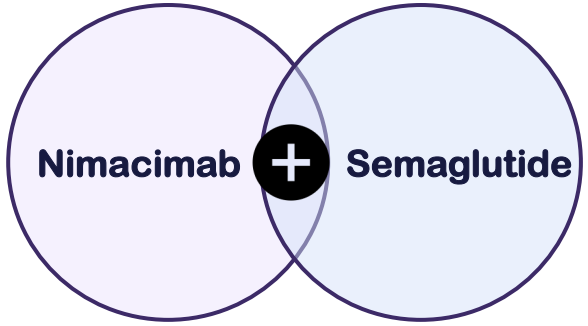
Executive Summary

Accomplishments since Q3 2025 Update

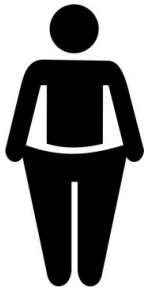
CBeyond

CBeyond data established potential path for combination strategy with existing incretin therapies



☑ **Additive Weight Loss**

New Clinical Data

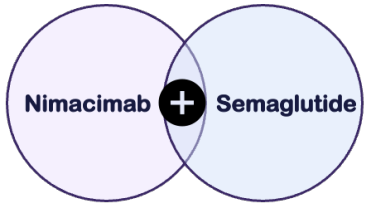


☑ **Improved Durability of Weight Loss**

☑ **Favorable Tolerability Profile**

Skye has developed a robust strategy to support a combination strategy for nimacimab + semaglutide that has the potential to provide a compelling new therapeutic option for patients.

Execution



52-Week Combination Data

High-Dose Rationale

ENHANZE®

High-Dose Feasibility

FDA

Regulatory Alignment

Commercial Scalability

Attractive Target Product Profile

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What Has Objectively Changed in the CB1 Field

Since launching nimacimab in obesity, Skye has delivered a series of field-firsts for peripheral CB1

1 FIELD FIRST

First-in-class modality

Allosteric GPCR antibody designed for peripheral CB1 inhibition to improve energy metabolism while minimizing brain exposure.

2 CLINICAL FIRST

First human obesity program with clean safety

First clinical obesity program to evaluate a CB1 monoclonal antibody and create a direct readout for the mechanism without any neuropsychiatric events.

3 COMBINATION FIRST

First CB1 + GLP-1 dataset

First reported clinical test of a CB1 mechanism in combination with a GLP-1, establishing proof of combination activity.

R&D INFRASTRUCTURE

Human-CB1 knock-in DIO workflow + quantitative biodistribution + APC Platform

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CBeyond: Three Primary Learnings

Meaningful combo efficacy, clean safety, and a clear dosing path

CBeyond

LEARNING 1

Meaningful combination signal

+3.0%

incremental weight loss vs semaglutide alone at 26-weeks

22.3%

mean weight loss at 52 weeks, with no plateau observed

- Significant waist circumference improvement
- Improved lean-to-fat mass ratio

LEARNING 2

Clean safety and tolerability

0

nimacimab-associated neuropsychiatric signal through 52- weeks

No additive GI burden

with semaglutide

- Combination-ready at tested exposure

LEARNING 3

Solvable development variable

200 mg

weekly monotherapy underexposed peripheral tissues

Next step: higher exposure

- Higher-dose expansion study underway
- ENHANZE supports higher-exposure SC delivery

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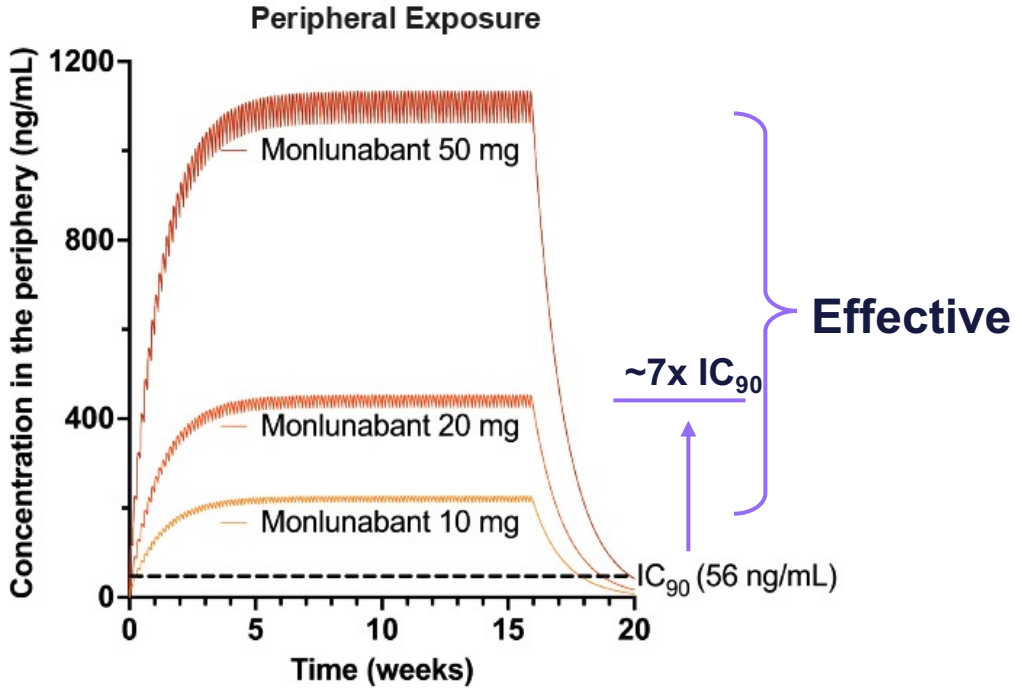
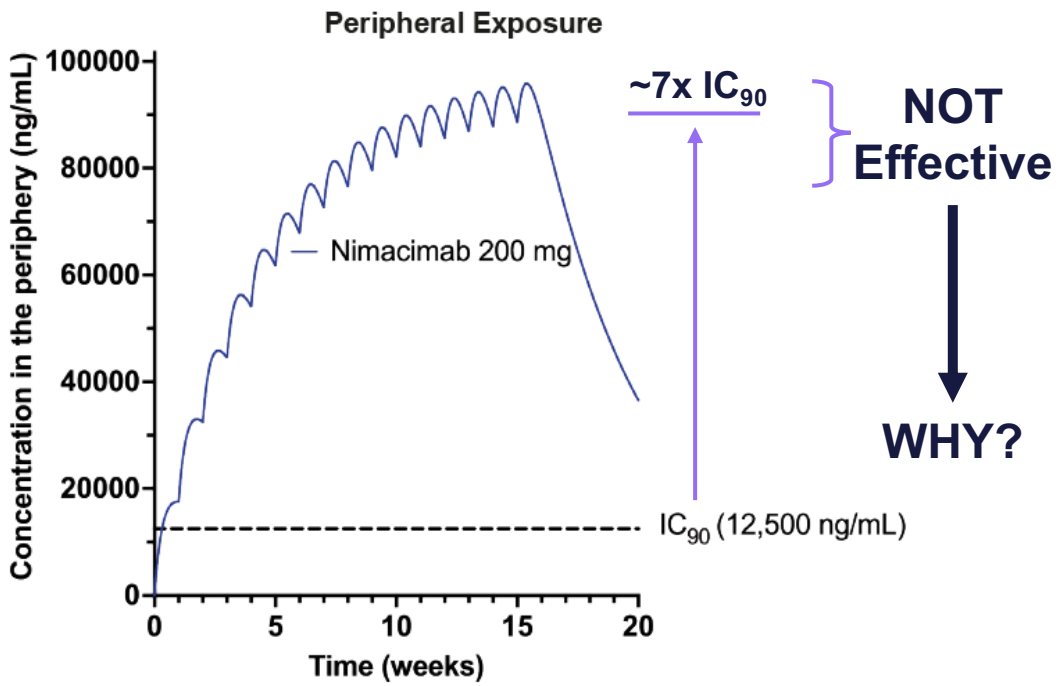
Dosing Rationale

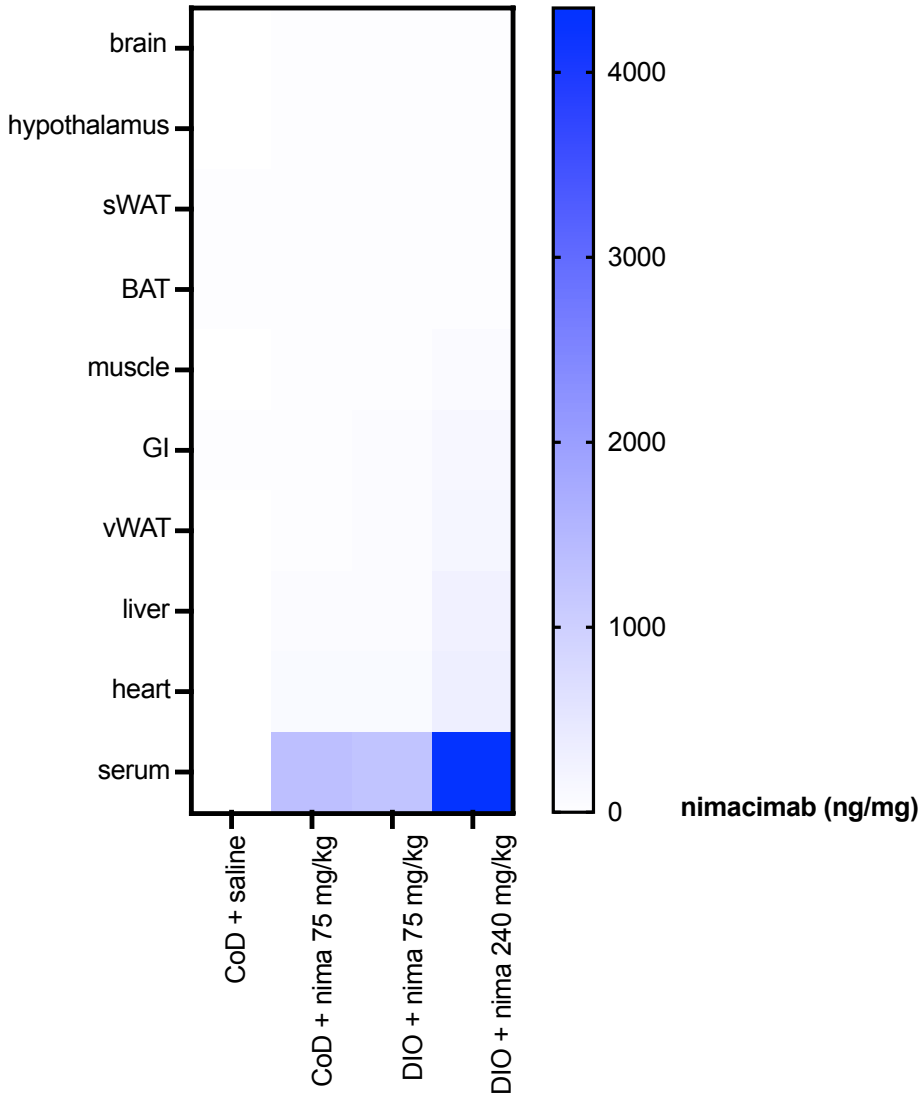
Initial rationale for CBeyond dosing

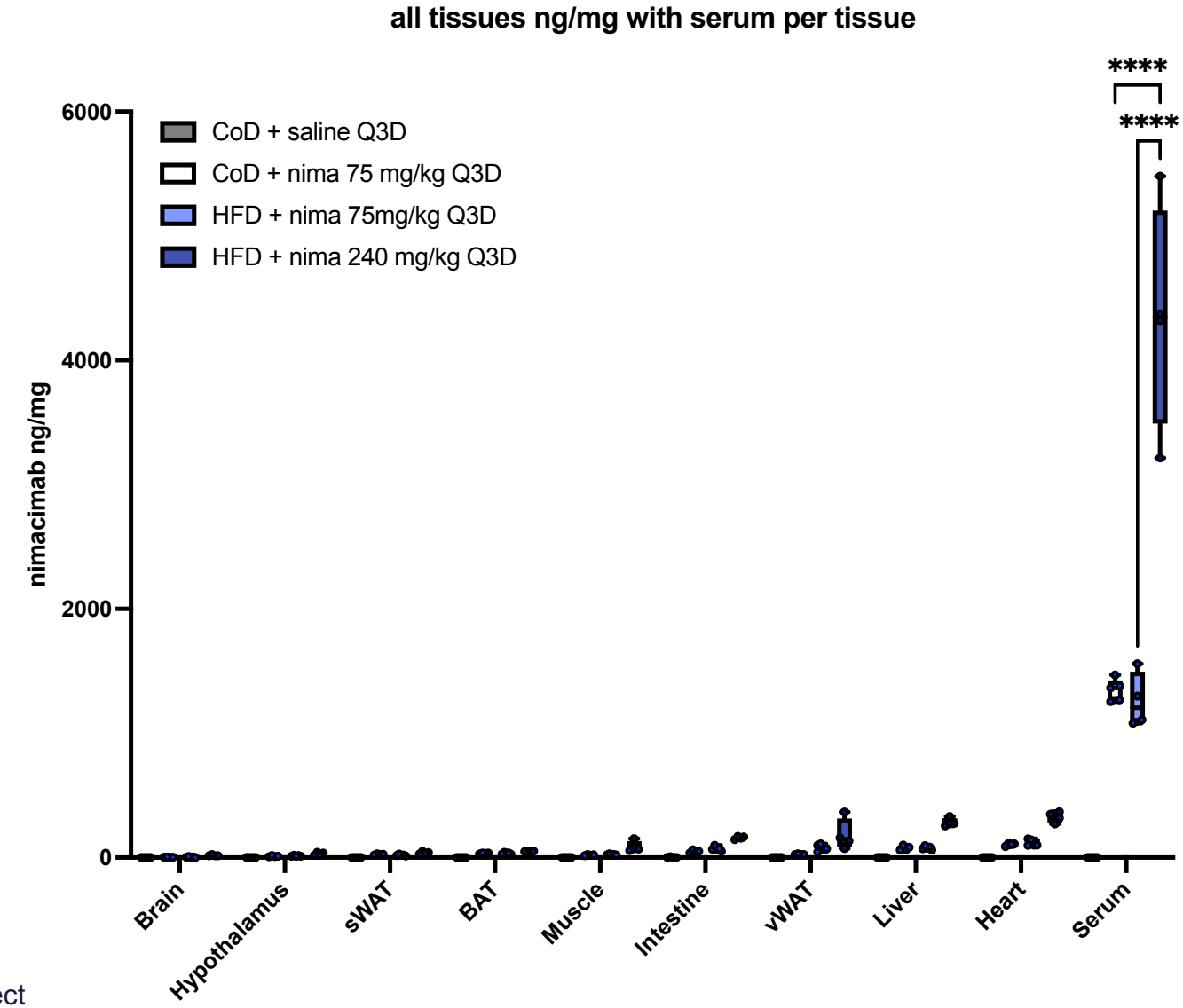
- Before pharmacodynamic data (clinical weight loss or DIO model), Skye developed clinical PK models (Phase 1 data) to understand dosing options
- IC_{90} (serum) was used as a surrogate for target engagement
- Similar IC_{90} at $C_{max, ss}$ with 20mg monlunabant and 200mg nimacimab





Nimacimab biodistribution in lean and obese mice

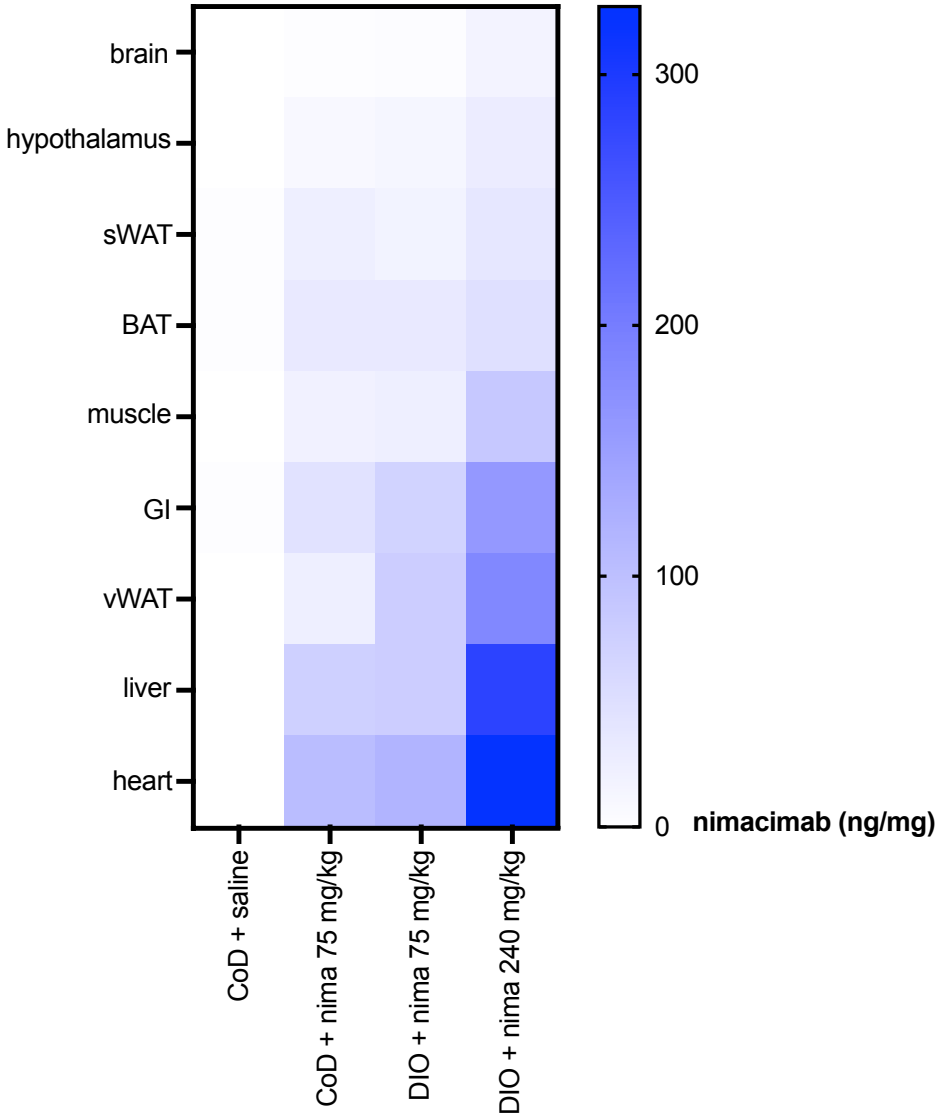


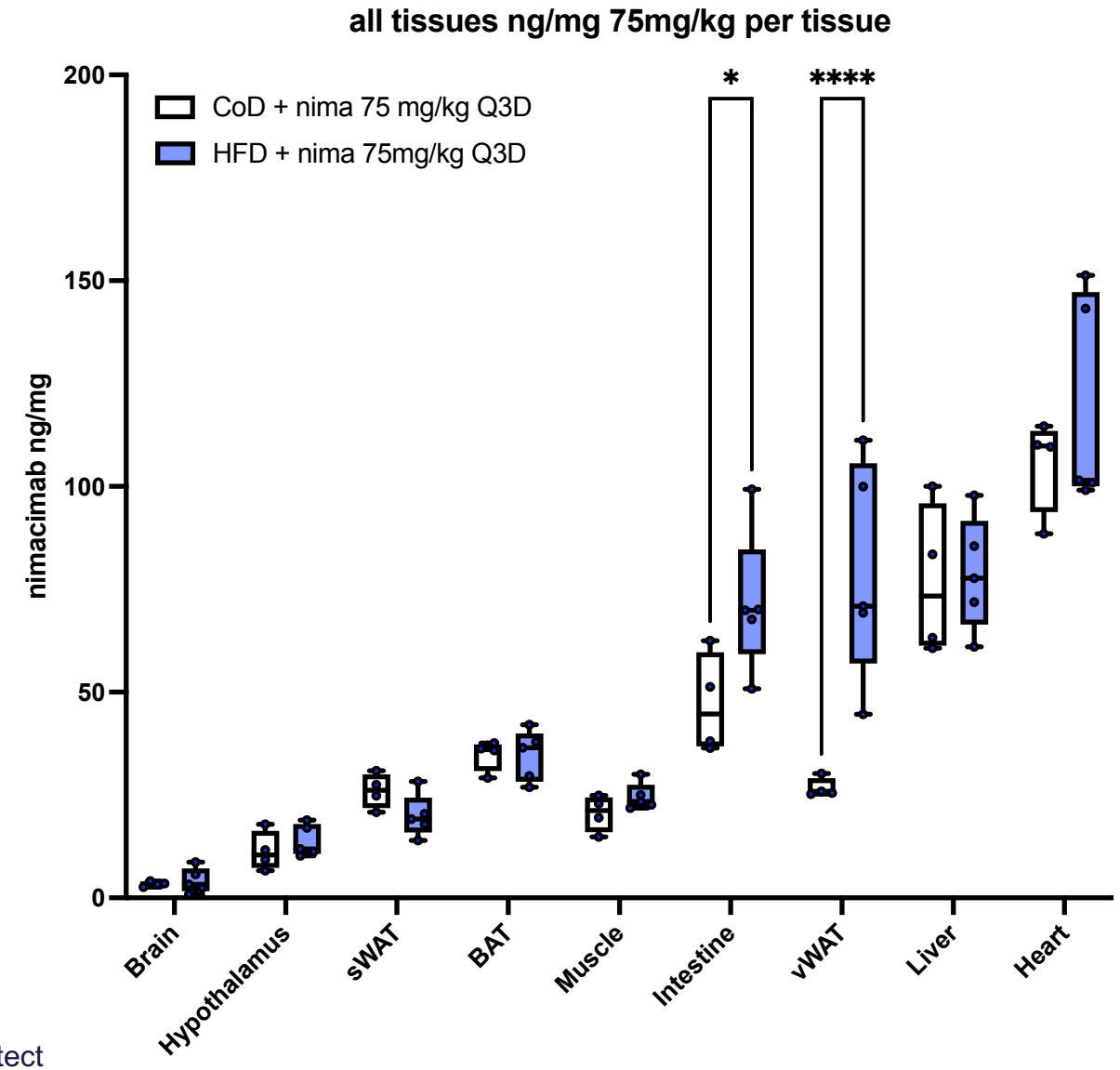


Human IgG ELISA kit (Ray Biotech, catalog# ELH-IGG) was used to detect nimacimab in tissue homogenates. Results are reported as ng of nimacimab/mg of tissue. N=4-5 per group.

2-way ANOVA followed by Tukey's multiple comparison tests per tissue.

Nimacimab tissue biodistribution in lean and obese mice

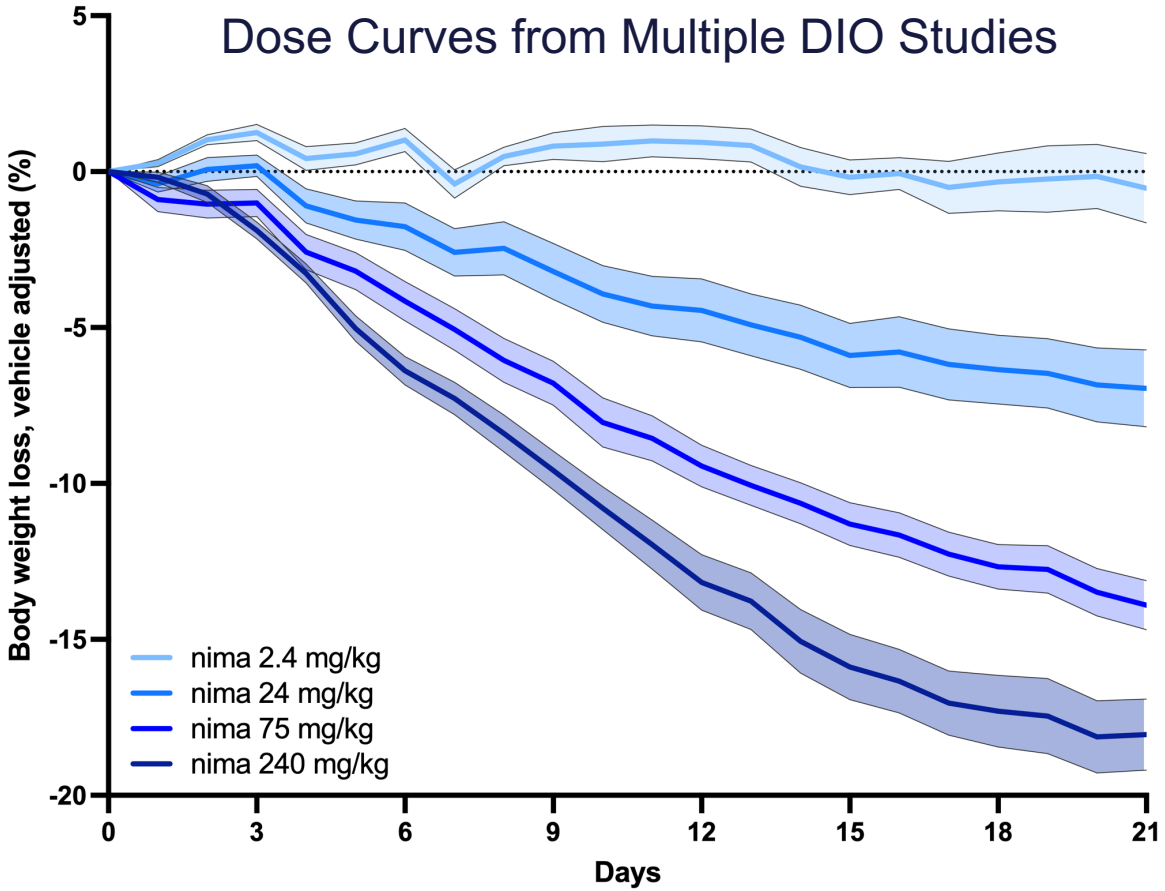


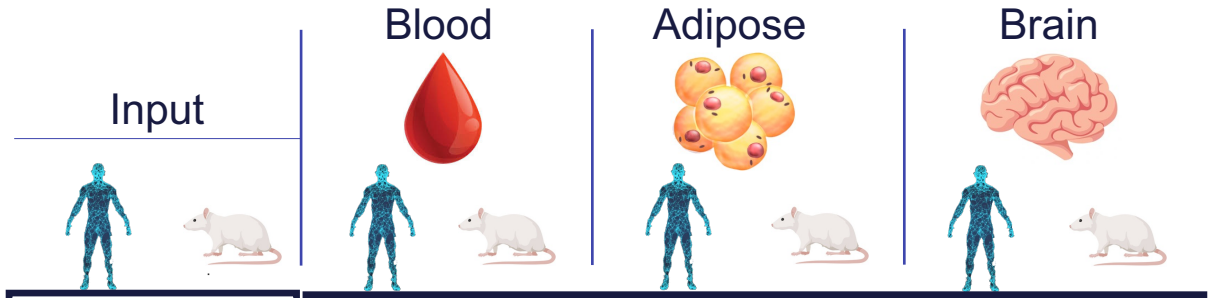


Human IgG ELISA kit (Ray Biotech, catalog# ELH-IGG) was used to detect nimacimab in tissue homogenates. Results are reported as ng of nimacimab/mg of tissue. N=4-5 per group.

2-way ANOVA followed by Tukey's multiple comparison tests per tissue.

Compartmental analysis: Efficacy requires CB1 inhibition in peripheral tissue

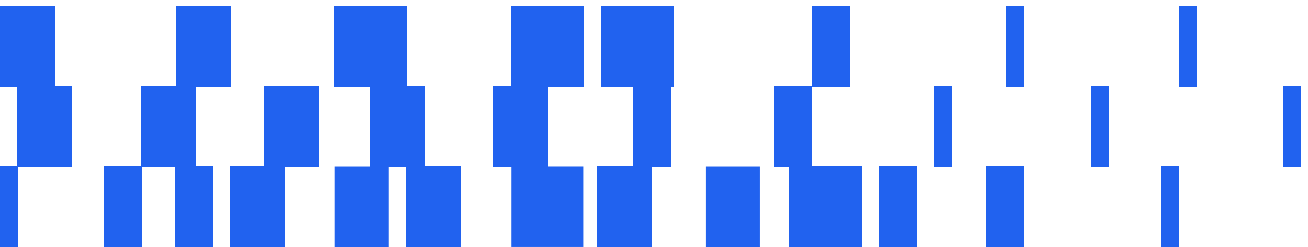




dose		nimacimab concentration (relative to IC_{90})					
200 mg dose	24 mg/kg	7.3x	6.4x	0.4x	0.3x	0.03x	0.02x
600 mg dose	75 mg/kg	22x	20x	1.1x	0.9x	0.1x	0.1x

Nimacimab concentration in serum based on Ctrough at week 26 (human Ph1) and day 24 (DIO mouse). Concentration in adipose tissue used serum:adipose ratio derived from NHP bioD study and published human data (human) and Skye bioD DIO data (mouse). Concentration in brain used serum:brain ratio derived from more conservative published human data (human) and Skye bioD DIO data (mouse).

CBeyond Expansion Study and Next Steps



CBeyond

CBeyond Expansion Study / Part C / IV Dosing

Cohort 2
Randomized 3:1 to either
- Nimacimab 600 mg, QW, IV (n=6), equivalent to ~1000 mg SC
- Matched placebo, QW, IV (n=2)

Safe to Proceed to Cohort 2 following Cohort Review Committee safety review of the first 4 participants in Cohort 1 completed 4 weeks of treatment

Cohort 1
Randomized 3:1 to either
- Nimacimab 400 mg, QW, IV (n=6), equivalent to ~600 mg SC
- Matched placebo, QW, IV (n=2)

Within each cohort

Screening Period (4 weeks) → **Treatment Period (15 weeks: 16 doses)** → **Follow-up Period (12 weeks)**

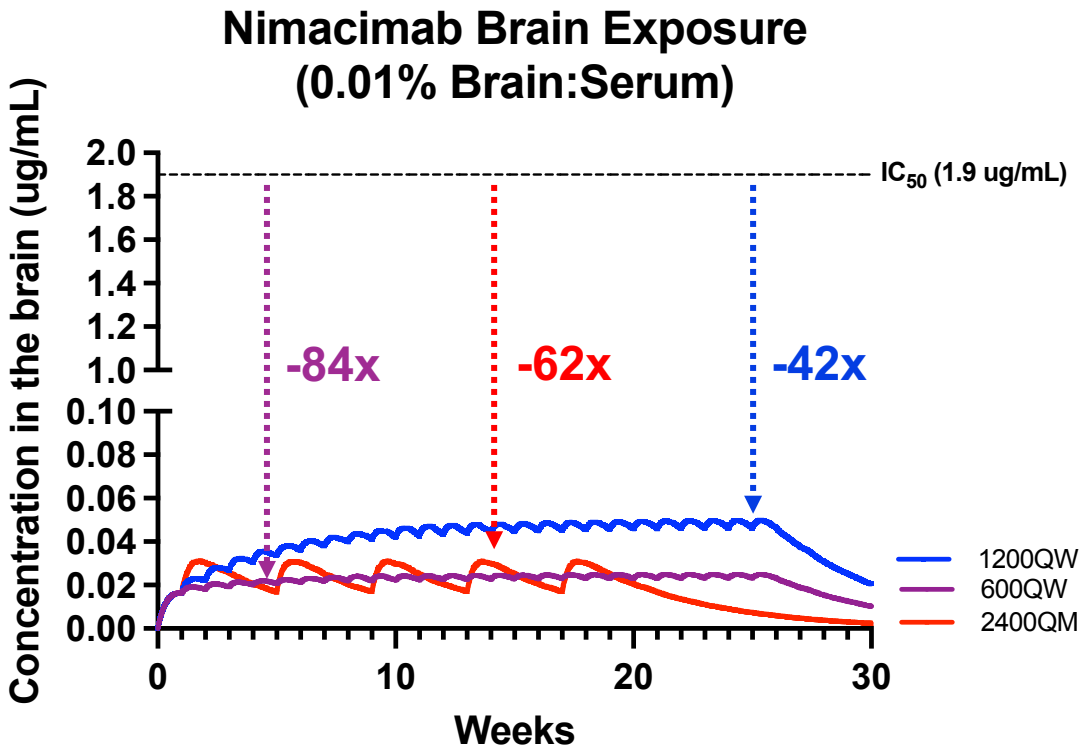
Superior Exclusion of CB1 Inhibitor from Brain; No Neuropsychiatric Side Effects

Cyno	Day 1 (post 1st dose)	Day 8 (post 2nd dose)	Day 15 (post 3rd dose)
CSF/Serum 3 mg/kg IV q1w	BLQ	<0.02%	<0.02%

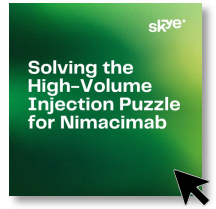
Cyno	9 hours
CSF/Serum 40 mg/kg IV	0.01%

Rhesus	48 hours
CSF/Plasma	0.05%
Prefrontal Cortex/Plasma	0.83%
Cerebellum/Plasma	0.84%
Liver/Plasma	16.44%

- *Tissues harvested without perfusion*
- *Tissue to plasma assuming 1 mL = 1 g*



Achieving Large Volume Dose Administration with ENHANZE®



- Skye has established a global collaboration and licensing agreement with Halozyme Therapeutics to evaluate the co-formulation of nimacimab with ENHANZE® (rHuPH20).

- ENHANZE® is an enzyme that degrades hyaluronan by cleaving B-1,4 linkage between N-acetyl glucosamine and glucuronic acid.

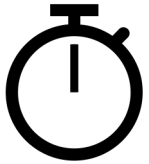
What it does:

ENHANZE® creates temporary space for SC fluid dispersion; reduces tissue backpressure.

How it works:

ENHANZE® works rapidly, locally and transiently in SC space; HA is naturally restored in 1-2 days

Large volume injection up to 10-12 mL



Reduced administration time

Increased patient preference

Improved absorption

Increased bioavailability

Nimacimab Lifecycle Management

High Concentration Development

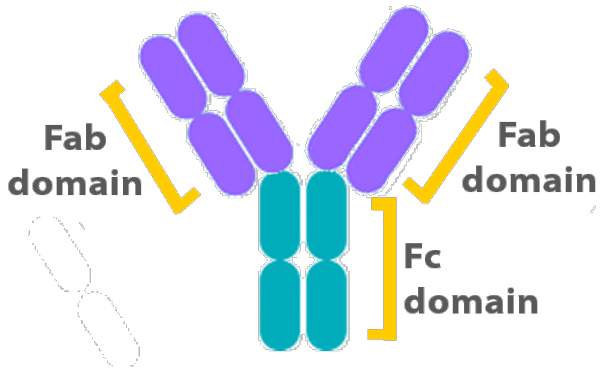
	Concentration	Injection Volume (600 mg QW dose)
Current Formulation	100 mg/mL	6 mL
	125 mg/mL	5 mL
	150 mg/mL	4 mL
Next Generation Formulation	200 mg/mL	3 mL
	250 mg/mL	2.4 mL

Current Concentration

Current formulation of nimacimab has ability to increase concentration without need for significant change to manufacturing process and can be implemented in advance of Phase 3.

Next generation formulations with concentrations +200 mg/mL could further reduce COGS.

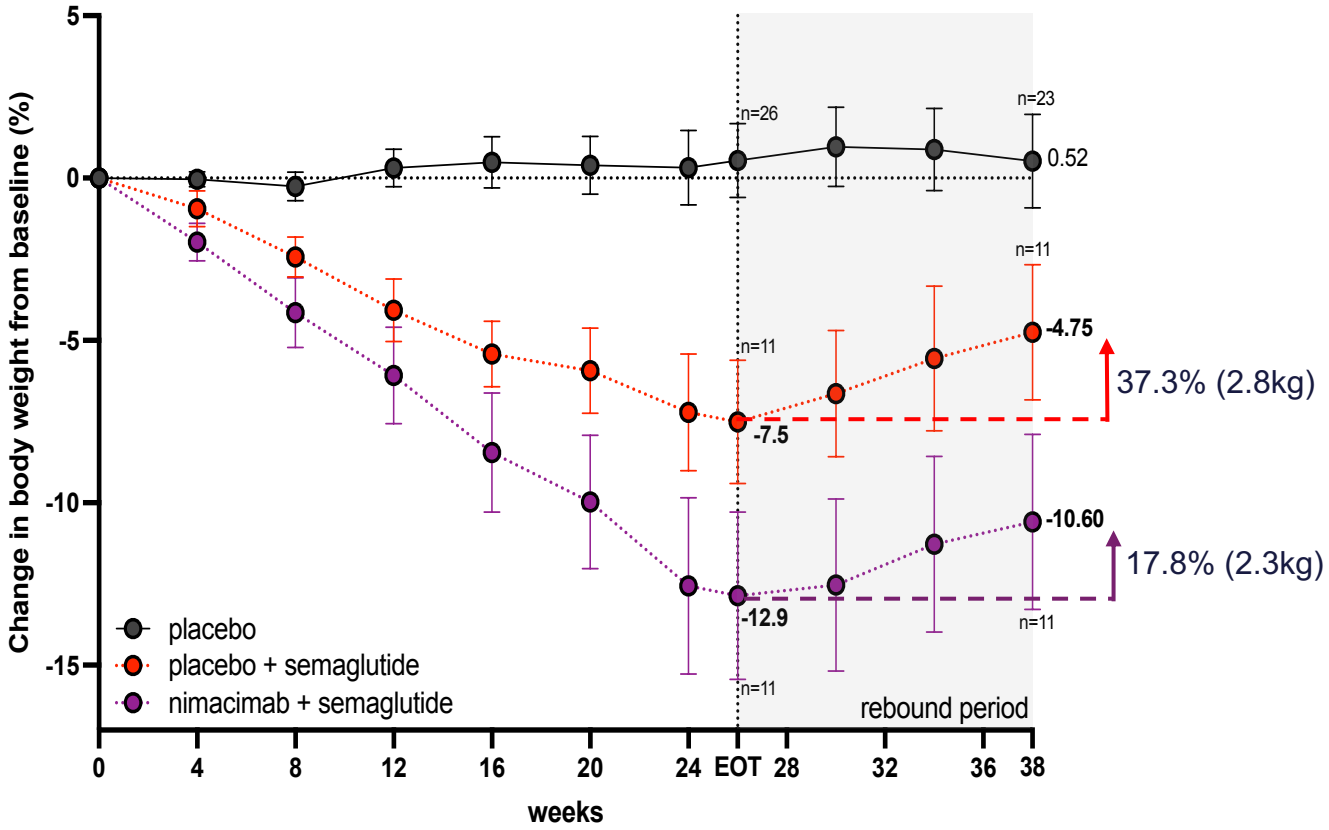
Half-Life Extension



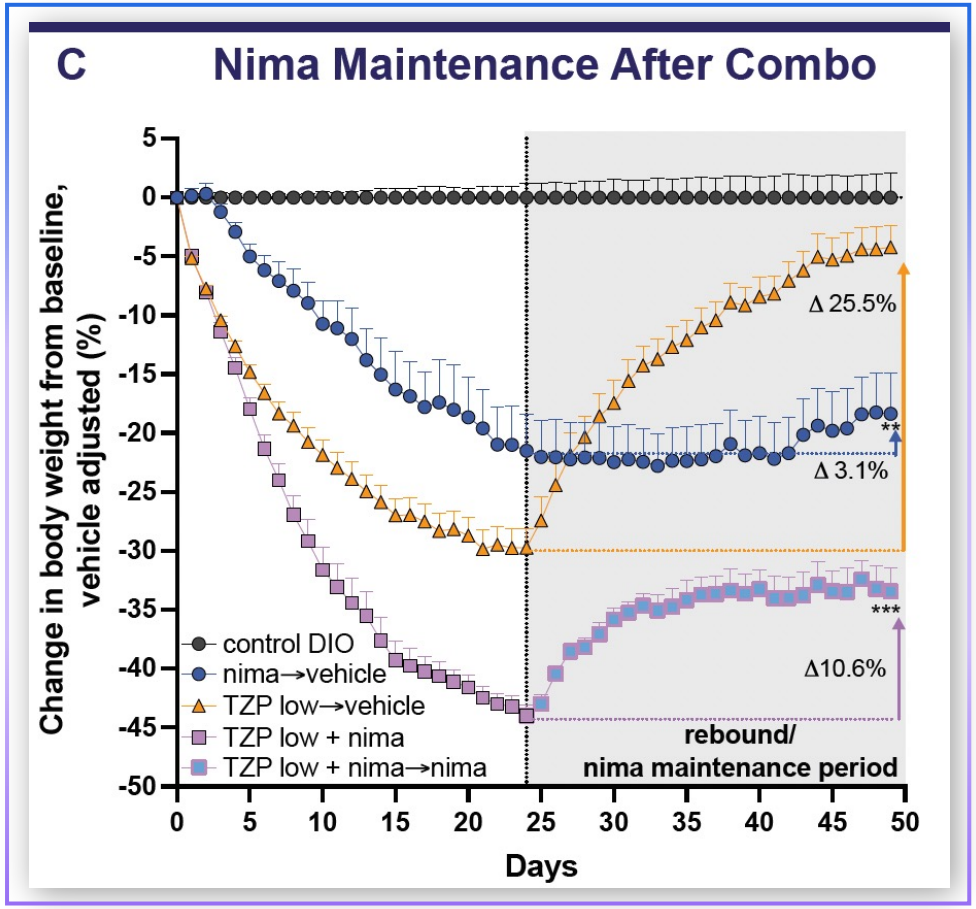
2nd generation nimacimab with Fc-domain modifications may improve half-life and potentially reduce COGS by allowing for reduced dose, or less frequent dosing.

This would be a 2nd generation product that could be commercialized post-first approval of nimacimab.

Nimacimab Reduces Weight Regain
Off-Therapy follow up for 13 weeks after the last dose



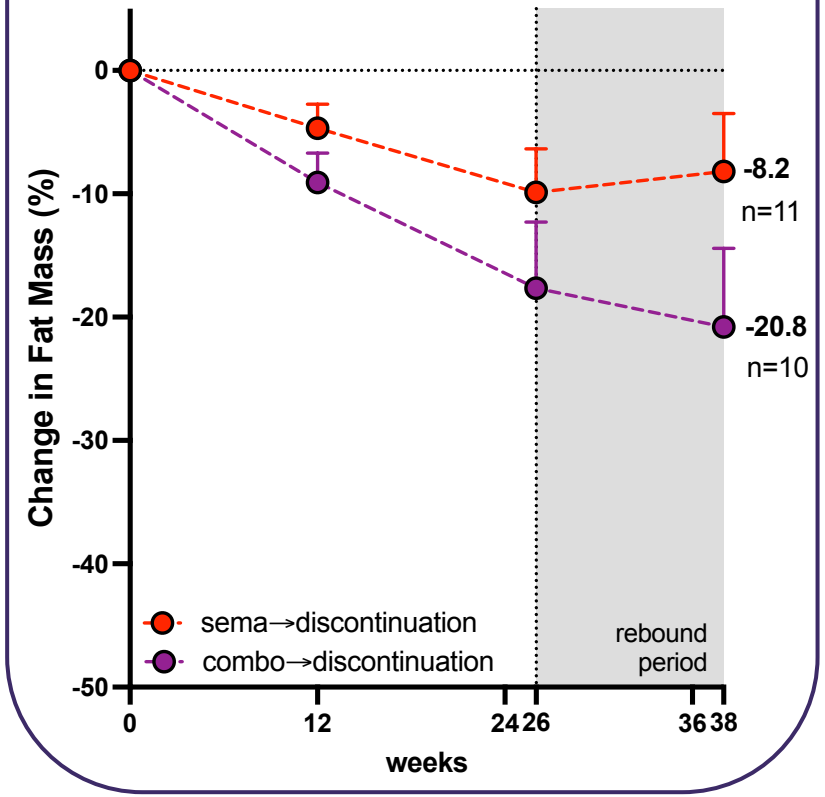
DIO Study



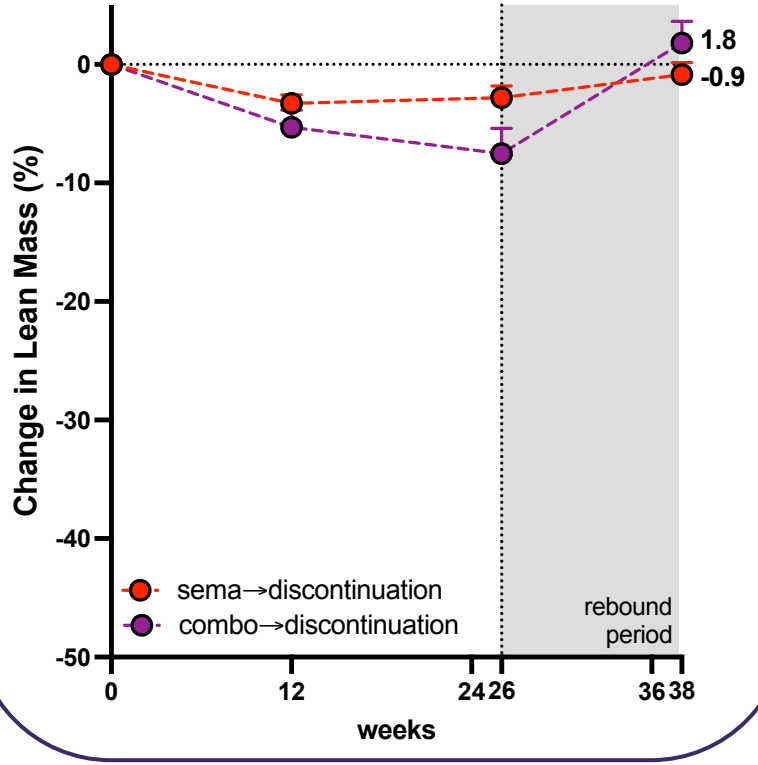
Inclusion criteria: patients must have completed at least 75% of treatment and have at least one follow-up visit three or more weeks after week 26/EOT.
Data is reported as mean ± SEM. 2-way ANOVA followed by Tukey's multiple comparison tests, reporting significance vs placebo at week 38 and EOT.
Rebound data is interim data from off-therapy follow-up.

Differentiated Body Composition Through 13-Week Follow-up

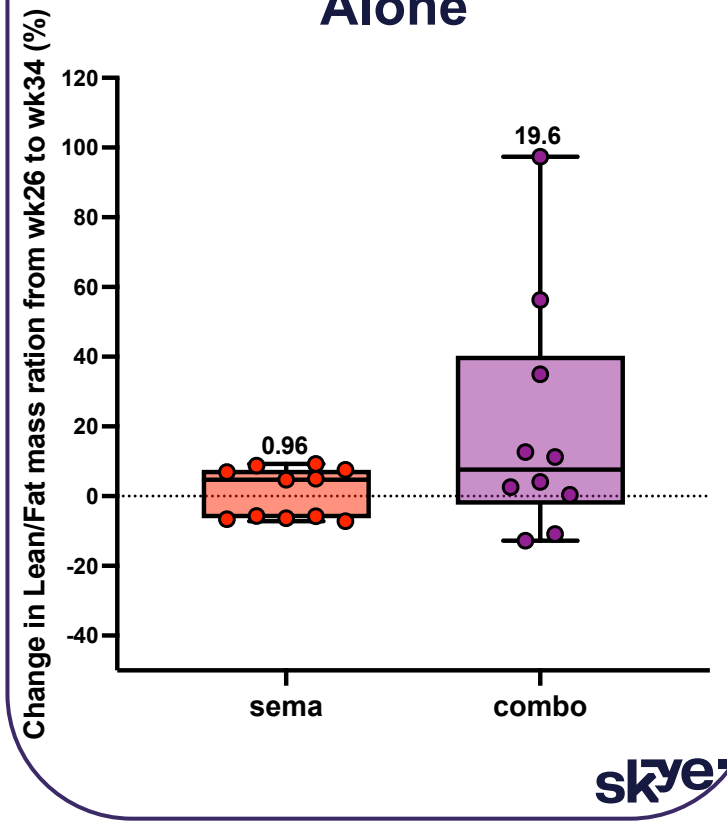
Combo Group Maintains Fat Mass During Follow-Up Period



Combo Group Gains Lean Mass During Follow-Up Period

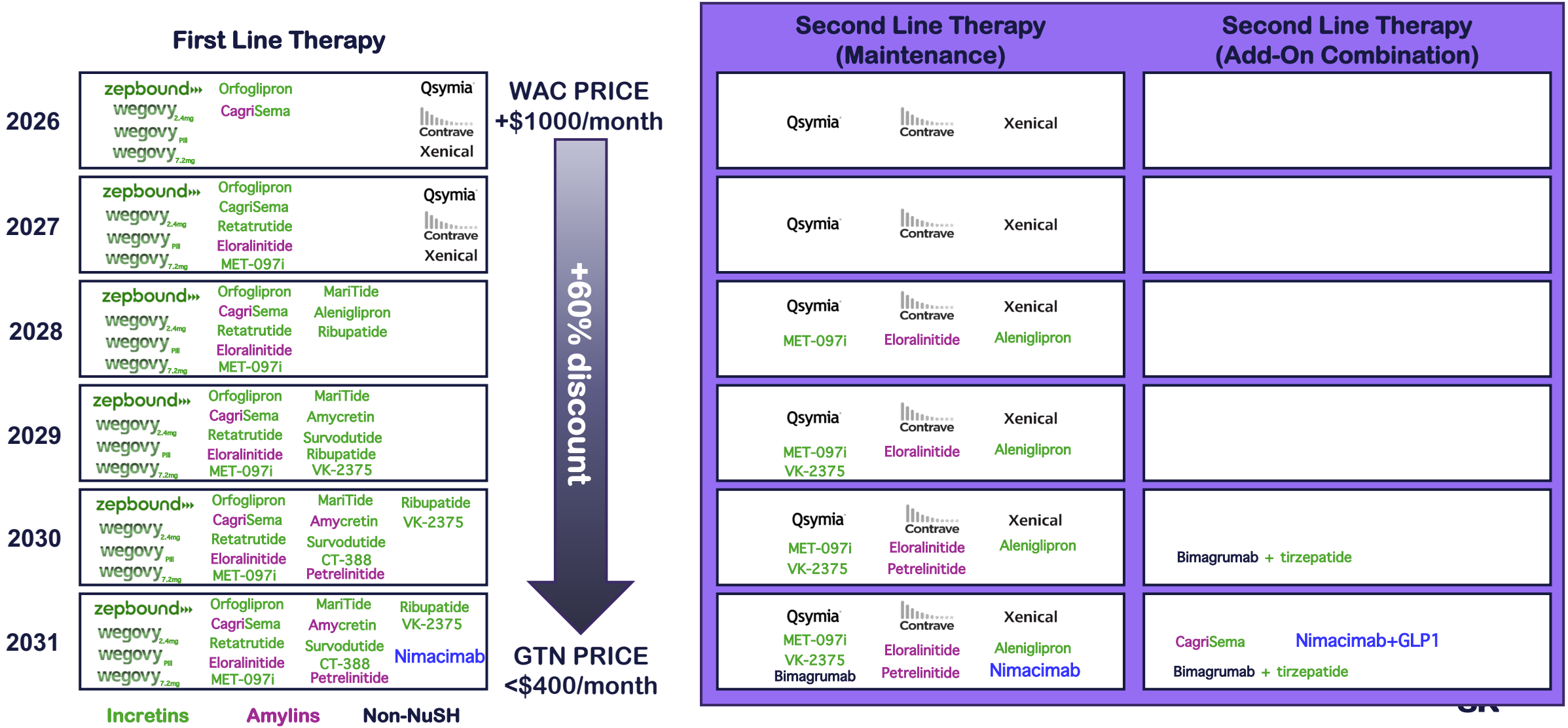


Lean to Fat Mass Ratio Improves Compared to Sema Alone



Crowded 1L Space with Significant Price Compression

- NuSH drugs will dominate the 1L setting, but it will become increasingly competitive with less room for profit margin.
- The 2L setting has significant opportunity with few non-NuSH drugs available, or being developed.



Nimacimab Complimentary, Not Competitive to GLP-1s

Maintenance rationale for late comer GLP1s is to protect the patient base; nimacimab improves persistence and durability of 1L GLP1s

WHY THEY DO IT

Maintenance is a rational same-class play

Lower-risk

regulatory + commercial defense

- Chronic-use precedent is already established
- Studies start in responders already on backbone
- Oral, monthly, COGS, or flex-dose convenience can still create value

WHY IT IS HARD FOR INCRETINS

Hard to win the true add-on slot

≥5%

pivotal semaglutide-adjusted delta

- Dose step-down is retention, not superiority
- Same-class agents will struggle to obtain add-on therapy to label
- Price compression with GLP1s is an advantage for nimacimab

WHY NIMACIMAB WINS

Orthogonal add-on, not another incretin

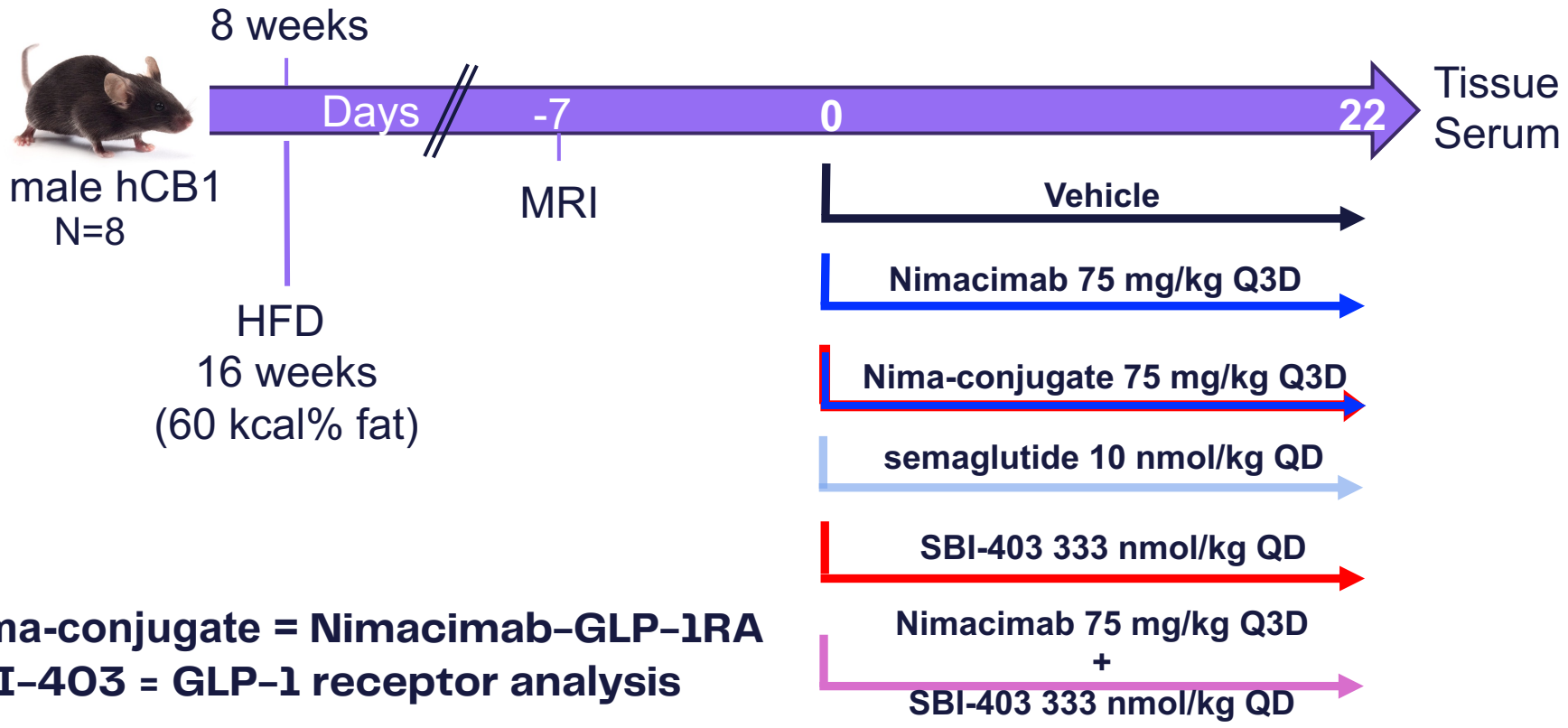
2L white space

for GLP-1 experienced patients

- Augments tirzepatide / semaglutide instead of trying to replace them
- Targets plateaued, titration-limited, or intolerant patients
- More differentiated than same-class maintenance plays

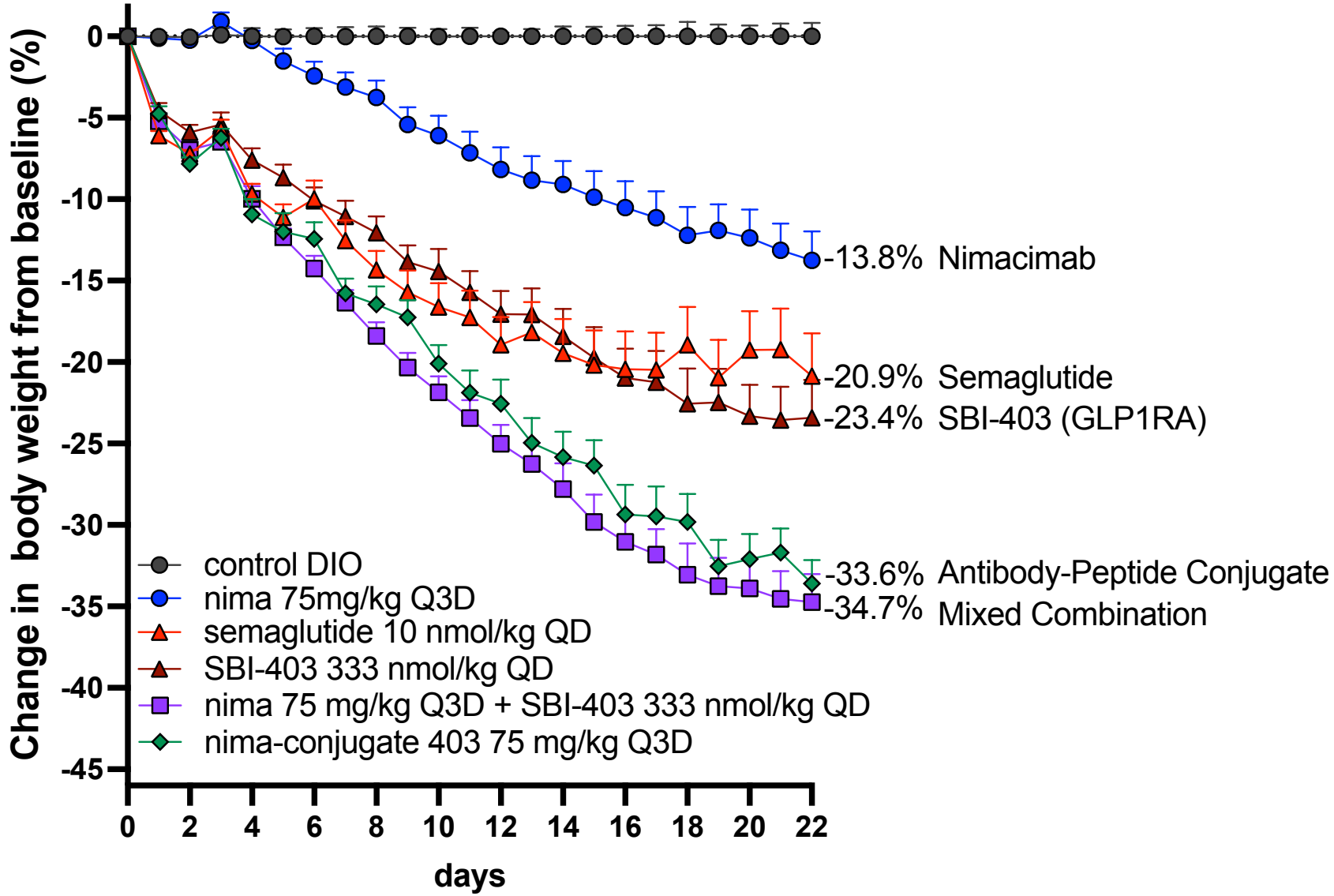
Antibody Peptide Conjugation (APC) Program

Study Design:
Testing Efficacy of Nima-GLP-1RA (Antibody-Peptide-Conjugate) in a DIO model

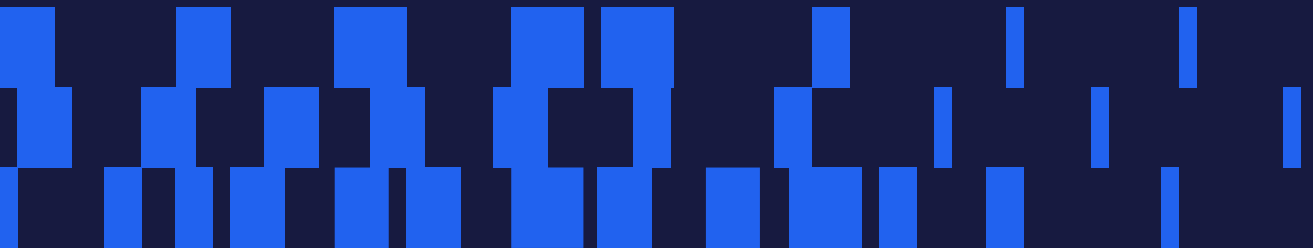


Nima-conjugate = Nimacimab–GLP–1RA
SBI–403 = GLP–1 receptor analysis

APC demonstrates similar efficacy of combination dosing



Closing Remarks



Key Takeaways

CBeyond

- **CBeyond Expansion Study Initiated**
- **Differentiated Mechanism of Weight Regain**
- **Proof-of-Principle for APC Program**
- **Phase 2b Study to Demonstrate Competitive TPP and Development Path**

Why Is This Important?

This study will generate safety and PK data at higher exposures, which we intend to take forward in future clinical trials.

Body composition data demonstrates that fat mass loss is maintained even after 13-weeks of being off-treatment. Supports hypothesis that nimacimab is a differentiated and orthogonal mechanism to GLP-1s making it ideal for combination treatment.

A proprietary unimolecular dual mechanism biologic designed to simplify dosing.

Advancing Phase 2b study design and TPP to demonstrate clinically meaningful additional weight loss in GLP-1 experienced adults.

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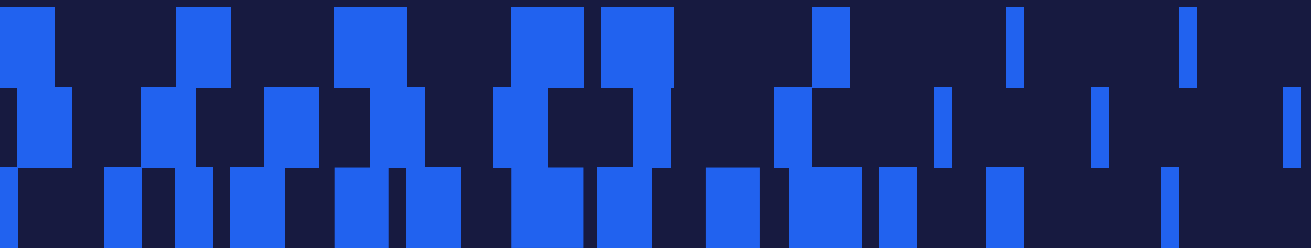
Anticipated Catalysts Through 2026

Q1 2026	Q2 2026	Q4 2026
✓ CBeyond Interim Extension Data	❑ Expansion Study Cohort 2 initiates enrollment	❑ Topline Clinical Data from Expansion Study
✓ FDA Type C Meeting Minutes	❑ Expansion Study Enrollment Complete for Cohort 1 and 2	❑ Phase 2b Final Study Design
❑ Launch CBeyond Expansion Study (Part C)	❑ Preclinical Bioconjugation Data	
❑ Compatibility and In-Use study complete with ENHANZE	❑ Feasibility study complete on high concentration program	

Clinical Regulatory Preclinical CMC

Q&A



Thank You

11250 El Camino Real, Suite 100
San Diego, CA 92130

Please learn more or contact us at:

ir@skyebioscience.com

+1 (858) 410-0266

Spotlight

CBeyond

The ANATOMY of PROGRESS
EXAMINING PERIPHERAL CB1 INHIBITION IN METABOLIC HEALTH

skye Obesity