UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of
the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): February 2, 2026

SKYE BIOSCIENCE, INC.
(Exact name of registrant as specified in its charter)

Nevada	**000-55136**	**45-0692882**
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

11250 El Camino Real, Suite 100, San Diego, CA 92130
(Address of principal executive offices)

(858) 410-0266
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligations of the registrant under any of the following provisions.

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
N/A	**N/A**	**N/A**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On February 2, 2026, the Company issued a press release announcing interim results from the combination cohort of the Company's Phase 2a extension study of nimacimab. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference and the Company's updated Investor Presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference. The Investor Presentation will also be available under the “Media & Investors” page of the Company’s website.

The information in Item 7.01 of this Current Report on Form 8-K, including the information in the press release and the Investor Presentation attached as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K, is furnished pursuant to Item 7.01 of Form 8-K and shall not be deemed “filed” for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section. Furthermore, the information in Item 7.01 of this Current Report on Form 8-K, including the information in the press release and the Investor Presentation attached as Exhibits 99.1 and 99.2 to this Current Report on Form 8-K, shall not be deemed to be incorporated by reference in the filings of the Company under the Exchange Act or the Securities Act of 1933, as amended.

Item 8.01 Other Events.

On February 2, 2026, the Company reported the following interim results from the combination cohort of its Phase 2a extension study:

- 19 participants in the combination cohorts completed week 26 and were eligible for the extension study, which continued in a blinded manner for 26 weeks, maintaining their original treatment assignment (10 nimacimab plus semaglutide; 9 placebo plus semaglutide). An additional 22 participants completed week 26 and were either ineligible for the extension or chose not to join the extension study and continued on post-treatment follow-up (11 nimacimab plus semaglutide; 11 placebo plus semaglutide).
- Of the 10 participants in the nimacimab plus semaglutide arm who joined the extension study, the mean weight loss at 26 weeks was 14.4%. 7 participants completed the additional 26 weeks of treatment and lost an additional 7.9% of weight, resulting in a mean weight loss of 22.3% after 52 weeks of treatment. The combination therapy remained safe and well tolerated. No SAEs or AESIs were reported during the extension period.
- Of the 9 participants in the placebo plus semaglutide arm that joined the extension study, mean weight loss at 26 weeks was -13.9%. 7 participants completed treatment of the additional 26 weeks and lost an additional -5.8% of weight during the extension period, resulting in a mean weight loss of -19.7% after 52 weeks of treatment.

Full topline reporting of the CBeyond Phase 2a extension data including nimacimab monotherapy data and 13-week off-therapy follow-up is expected to take place in Q3 2026.

The Company expects its current capital to fund projected operations and key clinical milestones into the fourth quarter of 2026, including topline data from the Phase 2a extension study of nimacimab and certain manufacturing and clinical activities, initial manufacturing runs needed to enable a subsequent trial, and planning activities, but excluding the anticipated clinical cost of a proposed Phase 2b study to evaluate higher doses of nimacimab and support combination development and additional anticipated drug manufacturing costs to resupply any such Phase 2b study. Additionally, the Company is evaluating potential further extensions of the Phase 2a study to evaluate higher doses of nimacimab.

FORWARD LOOKING STATEMENTS

This Current Report on Form 8-K includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this Current Report on Form 8-K other than statements of historical fact should be considered forward-looking statements, including, without limitation, statements relating to: the initiation, design and timeline of future clinical studies for nimacimab in obesity to evaluate higher doses of nimacimab; further extensions of the Phase 2a study; the expected timing for reporting topline data from the Phase 2a extension study; and the Company's cash runway. When used herein, words including "anticipate," "believe," "can," "continue," "could," "designed," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "planning," "possible," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. All forward-looking statements are based upon the Company's current expectations and various assumptions. The Company believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. The Company may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important risks and uncertainties, including, without limitation, the initiation and design of any future clinical trials will be impacted by the Company's capital resources, the Company's ability to obtain additional sources of capital, program considerations and potentially other factors outside the Company's control; the potential for additional weight loss after 26 weeks may not ultimately be observed; there is no guarantee that higher dosing of nimacimab will achieve increased efficacy, and likewise it is possible that higher dosing will produce adversely different safety and tolerability results than those observed to date; the Company's dependence on third parties in connection with product manufacturing; research and preclinical and clinical testing; the Company's ability to advance, obtain regulatory approval of and ultimately commercialize nimacimab; competitive products or approaches limiting the commercial value of nimacimab; the timing and results of preclinical and clinical trials; the Company's ability to fund development activities and achieve development goals; the impact of any global pandemics, inflation, supply chain issues, government shutdowns, high interest rates, adverse regulatory changes; the Company's ability to protect its intellectual property; risks associated with the Company's common stock and the other important factors discussed under the caption "Risk Factors" in the Company's filings with the Securities and Exchange Commission, including in its Annual Report on Form 10-K for the year ended December 31, 2024, which are accessible on the SEC's website at www.sec.gov and the Investors section of the Company's website. Any such forward-looking statements represent management's estimates as of the date of this Current Report on Form 8-K. While the Company may elect to update such forward-looking statements at some point in the future, except as required by law, it disclaims any obligation to do so, even if subsequent events cause the Company's views to change. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this Current Report on Form 8-K.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press release of Skye Bioscience, Inc. dated February 2, 2026
99.2	Investor Presentation
104	Cover Page Interactive Data File (embedded within the inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

SKYE BIOSCIENCE, INC.

Dated: February 2, 2026

/s/ Punit Dhillon

Name: Punit Dhillon

Title: Chief Executive Officer

Skye Reports Positive CBeyond Phase 2a Extension Interim Study Results for Nimacimab in Combination With Semaglutide

- *22.3% total weight loss at 52 weeks with nimacimab (200 mg dose) + semaglutide (2.4 mg) combination — no plateau observed, suggesting potential for further efficacy beyond one year and at higher nimacimab doses*
- *Weight regain during treatment interruption reduced by over 50% — nimacimab + semaglutide cohort regained only 17.8% of lost weight vs. 37.3% for semaglutide alone during 13-week off-therapy follow-up, demonstrating durability advantage*
- *Strong safety and tolerability profile maintained — no serious adverse events or adverse events of special interest reported during the 52-week extension period*

SAN DIEGO, CA – February 2, 2026 – Skye Bioscience, Inc. (Nasdaq: SKYE) ("Skye") a clinical-stage biotechnology company focused on unlocking new therapeutic pathways for obesity and other metabolic health disorders, today announced interim 52-week data from the combination therapy arms in the extension phase of the Phase 2a CBeyond™ proof-of-concept study of nimacimab, its peripherally-restricted CB1 inhibitor antibody.

CBeyond Extension Study Design and Interim Data Summary

The blinded extension of the CBeyond study for combination cohorts was opened in May 2025 for participants assigned to either nimacimab plus semaglutide or placebo plus semaglutide arms. Eligible patients completed 26 weeks of treatment and were precluded from being off therapy for longer than 4 weeks. In total, 19 participants in the combination cohorts who completed week 26 were eligible for and elected to enroll in the extension study. The extension continued in a blinded manner for an additional 26 weeks, maintaining their original treatment assignment (10 nimacimab plus semaglutide; 9 placebo plus semaglutide). An additional 22 participants completed week 26 and were either ineligible for the extension or chose not to join the extension study and continued for 13 weeks on post-treatment follow-up (11 nimacimab plus semaglutide; 11 placebo plus semaglutide).

Of the 10 participants in the nimacimab plus semaglutide arm who joined the extension study, the mean weight loss at 26 weeks was 14.4%. Seven (7) participants completed the additional 26 weeks of treatment and lost an additional 7.9% of weight, resulting in a mean weight loss of 22.3% after 52 weeks of treatment with no weight loss plateau observed. The combination therapy continued to demonstrate safety and was well tolerated at the tested doses. No serious adverse events or adverse events of special interest were reported during the extension period.

Of the 9 participants in the placebo plus semaglutide arm that joined the extension study, mean weight loss at 26 weeks was 13.9%. Seven (7) participants completed treatment of the additional 26 weeks and lost an additional 5.8% of weight during the extension period, resulting in a mean weight loss of 19.7% after 52 weeks of treatment.

In October 2025, Skye reported top-line 26-week data from CBeyond showing that the nimacimab and semaglutide combination cohort achieved clinically meaningful weight loss compared with semaglutide alone (-13.2% vs -10.25%, p=0.0372, mITT), with no plateau observed.

CBeyond Interim Results – Combination Arm

Treatment	Group (N)	% WL at 26 Weeks	% WL at 52 Weeks	% Weight Regain at 13-Week Follow-up
Nimacimab + Semaglutide	All Participants (21)	-13.6%		
	Combo -> Combo (10)	-14.4%	-22.3%	
	Combo -> Follow-up (11)	-12.9%		17.8%
Placebo + Semaglutide	All Participants (20)	-10.4%		
	Semaglutide -> Semaglutide (9)	-13.9%	-19.7%	
	Semaglutide -> Follow-up (11)	-7.5%		37.3%

“Compared to other combination treatments, we believe 22.3% weight loss with no observed plateau at 52 weeks is clinically meaningful and commercially competitive, and is comparable to other combinations that have been evaluated,” said Puneet Arora, MD, FACE, Chief Medical Officer of Skye. “These results suggest that we could see even more weight loss with treatment beyond 52 weeks. We also expect even deeper weight loss with more optimized dosing of nimacimab in potential future clinical trials. Importantly, the interim data showed that the combination treatment remains safe and tolerable at the tested doses.”

Weight Regain During CBeyond Off-therapy Follow-Up Period

The participants treated with nimacimab + semaglutide that continued to the 13-week off-therapy follow-up regained only 17.8% of the total weight loss at 26 weeks, which represents a greater than 50% mitigation of weight rebound. In comparison, semaglutide treatment alone demonstrated a weight regain of 37.3% from the weight lost at 26 weeks, indicating a potential durable response to treatment.

“Today’s interim data reinforces our vision to build a leading platform that is distinct yet complementary and able to intensify incretin outcomes and help patients achieve more durable metabolic benefit,” said Punit Dhillon, Chief Executive Officer of Skye. “We believe nimacimab’s attributes complement GLP-1 therapy through peripheral CB1 inhibition, with the potential to deepen weight loss and mitigate rebound during treatment interruptions. Our focus now is characterizing peripheral drug exposure at higher doses, dose selection, and developing plans to advance a Phase 2b program to rigorously reproduce the combination effect at scale, and optimize dose and regimen, with a goal of positioning nimacimab as a potential differentiated long-term option in obesity and related metabolic diseases.”

Full topline reporting of the CBeyond Phase 2a extension data, including nimacimab monotherapy data and 13-week off-therapy follow-up, is expected in Q3 2026.

About Nimacimab

Nimacimab is a potential first-in-class, peripherally-restricted monoclonal antibody inhibitor of the CB1 receptor. Unlike previous CB1-targeting drugs, nimacimab is designed to avoid central nervous system penetration, potentially limiting neuropsychiatric side effects seen

with small-molecule antagonists. As a non-incretin, non-peptide agent, nimacimab acts independently of the GLP-1 pathway and has also demonstrated additive or complementary effects in combination with incretin-based therapies in preclinical and clinical studies.

Skye Bioscience

Skye is focused on unlocking new therapeutic pathways for metabolic health through the development of next-generation molecules that modulate G-protein coupled receptors. Skye's strategy leverages biologic targets with substantial human proof of mechanism for the development of first-in-class therapeutics with clinical and commercial differentiation. Skye is conducting a Phase 2a clinical trial (ClinicalTrials.gov: NCT06577090) in obesity for nimacimab, a negative allosteric modulating antibody that peripherally inhibits CB1. This study is also assessing the combination of nimacimab and a GLP-1R agonist (Wegovy®). For more information, please visit: www.skyebioscience.com. Connect with us on X and LinkedIn.

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FORWARD LOOKING STATEMENTS

This press release includes “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release other than statements of historical fact should be considered forward-looking statements, including, without limitation, statements relating to: the potential for higher dosing of nimacimab to achieve increased efficacy; the potential for the combination of nimacimab and semaglutide to deepen weight loss and mitigate weight rebound; the potential for future weight loss beyond 52 weeks; plans to advance nimacimab into the next stage of development to optimize dosing; future clinical development of nimacimab, including the initiation and design of any future clinical trials; the expected timing for reporting topline data from the Phase 2a extension study; the ability of nimacimab to drive weight loss without neuropsychiatric and other adverse events; the potential for nimacimab to be a first-in-class drug; the potential for Skye to develop a leading orthogonal platform to intensify incretin outcomes and help patients achieve more durable metabolic benefit; the commercially competitive nature of nimacimab combined with semaglutide; and the potential for nimacimab to be a long term option in obesity and related metabolic diseases. When used

herein, words including “anticipate,” “believe,” “can,” “continue,” “could,” “designed,” “estimate,” “expect,” “forecast,” “goal,” “intend,” “may,” “might,” “plan,” “planning,” “possible,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. All forward-looking statements are based upon Skye’s current expectations and various assumptions. Skye believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. Skye may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important risks and uncertainties, including, without limitation, the initiation and design of any future clinical trials will be impacted by Skye’s capital resources, Skye’s ability to obtain additional sources of capital needed to run an additional Phase 2 clinical trial, program considerations and potentially other factors outside the Skye’s control; the potential for additional weight loss after 52 weeks may not ultimately be observed; there is no guarantee that higher dosing of nimacimab will achieve increased efficacy, and likewise it is possible that higher dosing will produce adversely different safety and tolerability results than those observed to date; Skye’s dependence on third parties in connection with product manufacturing; research and preclinical and clinical testing; Skye’s ability to advance, obtain regulatory approval of and ultimately commercialize nimacimab, competitive products or approaches limiting the commercial value of nimacimab; the timing and results of preclinical and clinical trials; Skye’s ability to fund development activities and achieve development goals; the impact of any global pandemics, inflation, supply chain issues, government shutdowns, high interest rates, adverse regulatory changes; Skye’s ability to protect its intellectual property; risks associated with Skye’s common stock and the other important factors discussed under the caption “Risk Factors” in Skye’s filings with the Securities and Exchange Commission, including in its Annual Report on Form 10-K for the year ended December 31, 2024, which are accessible on the SEC’s website at www.sec.gov and the Investors section of Skye’s website. Any such forward-looking statements represent management’s estimates as of the date of this press release. While Skye may elect to update such forward-looking statements at some point in the future, except as required by law, it disclaims any obligation to do so, even if subsequent events cause Skye’s views to change. These forward-looking statements should not be relied upon as representing Skye’s views as of any date subsequent to the date of this press release.

Nasdaq: SKYE

February 2026

Developing Innovative Medicines to Treat Obesity and Other Metabolic Diseases

Disclaimer and Important Information for Investors

This presentation ("Presentation") has been prepared solely for general information purposes by or on behalf of Skye Bioscience, Inc. (together with its subsidiaries and affiliates, "Skye"). Any discussion of the potential use or expected success of our product candidates is subject to our product candidates being approved by regulatory authorities.

Cautionary Language Regarding Forward-Looking Statements

This Presentation includes "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. The Company intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act of 1933, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. All statements contained in this Presentation other than statements of historical fact should be considered forward-looking statements, including, without limitation, statements relating to: Skye's future plans and prospects; inferences or conclusions from our preclinical data; statements relating to any expectations regarding the efficacy and therapeutic potential of nimacimab as a monotherapy or in combination with semaglutide or other incretin drugs, including efficacy at higher doses based on preclinical data; the potential for future weight loss beyond 52 weeks; the timing of receipt and disclosure of data from Skye's clinical trials; the planned timing of Skye's anticipated milestones for nimacimab; the Company's cash runway; future clinical development of nimacimab, including the Phase 2a extension and a potential Phase 2b clinical trial; and the regulatory strategy for nimacimab. When used herein, words including "anticipate," "believe," "can," "continue," "could," "designed," "estimate," "expect," "forecast," "goal," "intend," "may," "might," "plan," "planning," "possible," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements use these words or expressions. All forward-looking statements are based upon the Company's current expectations and various assumptions. The Company believes there is a reasonable basis for its expectations and beliefs, but they are inherently uncertain. The Company may not realize its expectations, and its beliefs may not prove correct. Actual results could differ materially from those described or implied by such forward-looking statements as a result of various important risks and uncertainties, including, without limitation, the Company may not proceed into a next Phase 2 clinical trial for nimacimab, including due to capital constraints and program considerations; the indicated trajectory of continuing weight loss at 52 weeks may not ultimately be observed; it is possible that higher dosing will produce adversely different safety and tolerability results than those observed to date; the Company's dependence on third parties in connection with product manufacturing; research and preclinical and clinical testing; the Company's ability to advance, obtain regulatory approval of and ultimately commercialize nimacimab, competitive products or approaches limiting the commercial value of nimacimab; the timing and results of preclinical and clinical trials; the Company's ability to fund development activities and achieve development goals; the impact of any global pandemics, inflation, supply chain issues, government shutdowns, high interest rates, adverse regulatory changes; the Company's ability to protect its intellectual property; risks associated with the Company's common stock and the other important factors discussed under the caption "Risk Factors" in the Company's filings with the Securities and Exchange Commission, including in its Annual Report on Form 10-K for the year ended December 31, 2024, which are accessible on the SEC's website at www.sec.gov and the Investors section of the Company's website. Any such forward-looking statements represent management's estimates as of the date of this Presentation. While the Company may elect to update such forward-looking statements at some point in the future, except as required by law, it disclaims any obligation to do so, even if subsequent events cause the Company's views to change. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this Presentation.

Industry and Market Data, and Third-Party Reports

The views and statements provided in this Presentation are based on information derived from Skye's internal estimates and research, studies, publications, surveys and other information provided by third parties and also from publicly available sources. In this Presentation, Skye relies on, and refers to, publicly available information and statistics regarding market participants in the sector in which Skye competes and other industry data. Any comparison of Skye to any other entity assumes the reliability of the information available to Skye. Skye has not independently verified the accuracy or completeness of these sources. Certain information contained in this Presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources. Skye has not independently verified, and makes no representation as to, the adequacy, fairness, accuracy or completeness of any information obtained from third-party sources. All of the market data included in this Presentation involves a number of assumptions and limitations, and there can be no guarantee as to the accuracy or reliability of such assumptions.

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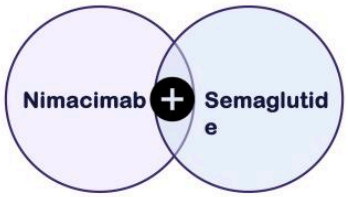
Executive Summary

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

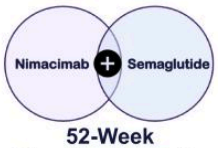


Additive Weight Loss

Improved Durability of Weight Loss

Favorable Tolerability Profile

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



52-Week Combination Data

High-Dose Rationale

ENHANZE

High-Dose Feasibility

FDA

Regulatory Alignment

Commercial Scalability

Attractive Target Product Profile

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Investment Thesis

Nimacimab: complementary, not competitive – potential scalable add-on to enhance incretin therapy

- **Additive efficacy on top of GLP-1s:**
  13% weight-loss at 26 weeks, which was significantly better than semaglutide alone (p=0.03) in the Phase 2a study; 22.3% total weight loss at 52 weeks based on interim Phase 2a extension study data, with no plateau observed at 52 weeks.

- **Durable & quality weight loss:**
  Lower post-treatment rebound (~17.8% combo vs. ~37.3% semaglutide-alone) and a favorable body-composition profile (increases fat loss by 37% compared to semaglutide alone) in Phase 2a study supporting potential use for maintenance after incretins and minimizing impact of weight regain.

- **Safe combo, titration-free:**
  No additive GI burden and 0% neuropsychiatric AEs in the combo arm in Phase 2a study; enables potential straightforward combination use across the incretin class.

- **Potential differentiated mechanism in a crowded indication; potential first in class combination profile:**
  In a crowded incretin landscape, peripheral CB1 mechanism provides potential differentiation that we believe is complementary to incretins.

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Nimacimab Target Product Profile (TPP)

Opportunity across multiple treatment settings that adds clinically meaningful weight loss on top of GLP-1 therapy without adding tolerability burden and designed for chronic use.

In combination with incretin-based therapies, HCPs have told us they believe nimacimab will be most appropriate for patients requiring significant weight loss

Highest-priority candidates for combo nimacimab (with GLP-1 based therapy)

- **Severe obesity** (e.g., BMI ≥40 kg/m² or BMI ≥35 kg/m² with comorbidities) requiring greater total weight reduction (often ≥20% goal)
- **Incretin "plateau":** patients with attenuated incremental weight loss after sustained therapy where further dose escalation of incretin alone yields diminishing benefit
- **Inadequate response to incretin alone:** patients not meeting treatment goals despite adherence (e.g., ≤10% weight loss on GLP-1 therapy)
- **Dose-limiting tolerability:** patients unable to reach/maintain maximal incretin dose due to GI intolerance or other adverse effects

TPP

- **Target Efficacy:** +5-8% weight loss on top of incretin-based therapy.
- **Target Safety/Tolerability:** No meaningful increase in GI burden when combined with incretin-based therapy; No neuropsychiatric signal
- **Target Dosing & Delivery:** Ideally subcutaneous QM dosing, or QW dosing of nimacimab with co-administration of incretin-based therapy.
- **Target Durability:** Minimal weight regain following treatment discontinuation allowing for potential treatment cycling.

HCP: Healthcare Provider
AOM: Anti-obesity Medication
Source: Primary Market Research (N=10 Endocrinologists, N=14 PCPs)

Presentation Overview

1.0 Nimacimab Overview – A Highly Peripherally-restricted CB1-inhibiting Antibody

2.0 CBeyond Extension Data Review – 52-week Combination Data

2.1 CBeyond – What We Learned

3.0 CBeyond^2 – Phase 2b Adaptive Design Dose Ranging Study

3.1 Regulatory Strategy – Combination Approval, Monotherapy Opportunity

4.0 Financial Overview and Team

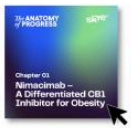
1.0

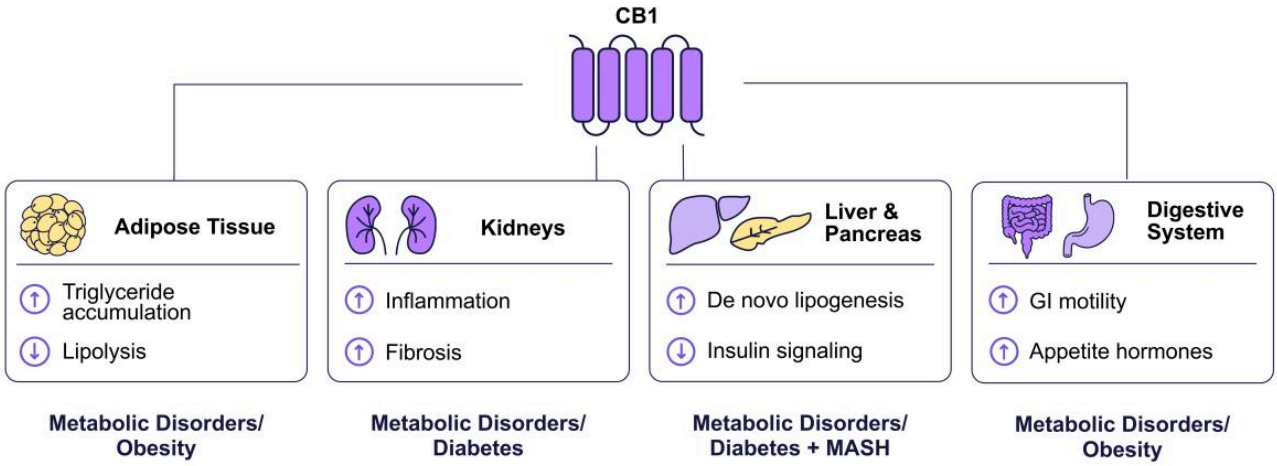
Nimacimab

A Highly Peripherally-restricted CB1-inhibiting Antibody that Stands Apart from Small–molecule **CB1 Inhibitors**

Peripheral CB1 Signaling: Metabolic-focused Targets

Active CB1 engagement promotes inflammation, fibrosis, and metabolic dysfunction; blocking peripheral CB1 can potentially reverse negatively-trending pathologies





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Nimacimab: Peripherally-restricted CB1-inhibiting Antibody

Long Half-life	• Stable antibody with half-life of 18-21 days (potential Q2W or monthly dosing) • Single mutation in the hinge region that prevents antibody Fab exchange
Exclusion from Brain	• Multiple NHP studies: background levels in CNS/brain (even at high doses) • No accumulation of antibody in CNS/brain despite multiple weekly doses • NOAEL > 75 mg/kg. MTD not reached
Differentiated Inhibitor	• Functions as both an **antagonist** and an **inverse agonist** • Binds allosteric site and non-competitively inhibits CB1, independent of agonist
Potential Safe & Effective Drug	• Achieve ~7x peripheral CB1 inhibition while ~600x below CB1 inhibition in brain • Allosteric binding maintains peripheral CB1 inhibition with increased endocannabinoids • Supports a favorable therapeutic index to safely and effectively treat obesity

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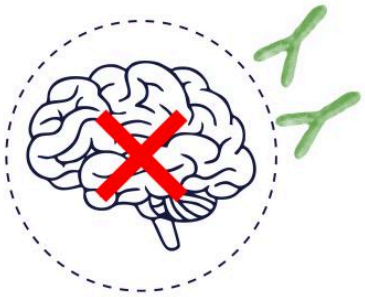
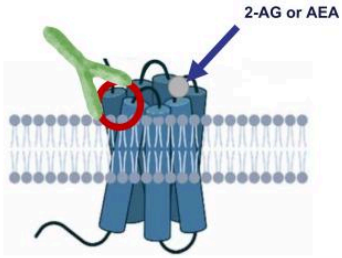
Nimacimab's Potential Differentiation from Small Molecule CB1 Inhibitors

Peripheral Restriction



Significantly less brain penetration than small molecules currently in development

Negative Allosteric Modulator



Unlike small molecules currently in development, **nimacimab retains potency** even in the presence of competition

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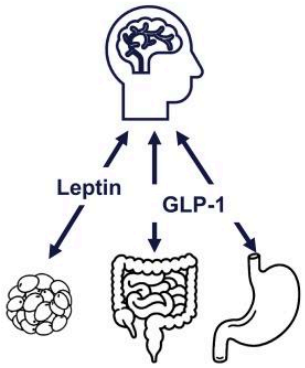
Four Mechanistic Pillars of Nimacimab

01

Peripheral Modulation of Appetite Regulating Hormones



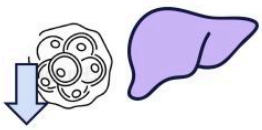
02

Improvement and Restoration of Glycemic Control

Reduced fasting insulin and improved glucose control

03

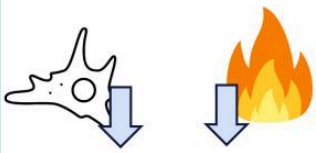
Enhanced Lipid Metabolism



Decreased steatosis and serum cholesterol

04

Reduction of Obesity-Induced Inflammation



Decreased inflammation and fibrotic markers

skye

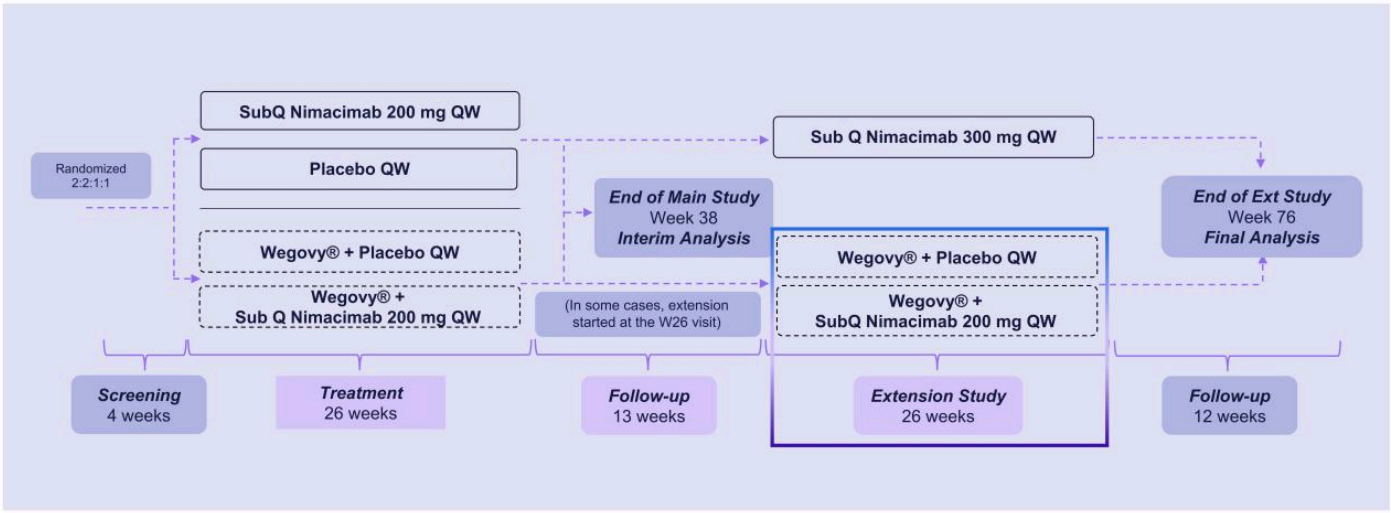
2.0

Review of Interim Extension Study: 52-Week Combination Data

CBeyond

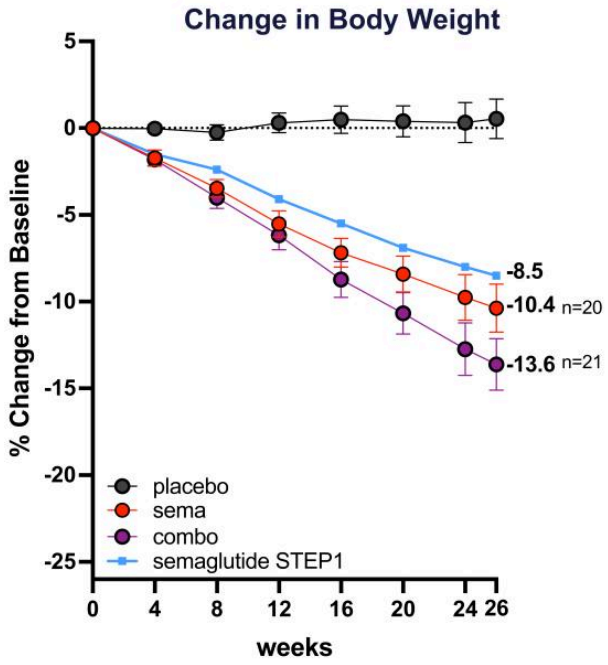
CBeyond Phase 2a Clinical Trial Design for Proof of Concept

Monotherapy and combination arms: weight loss, safety/tolerability, body composition, biomarkers



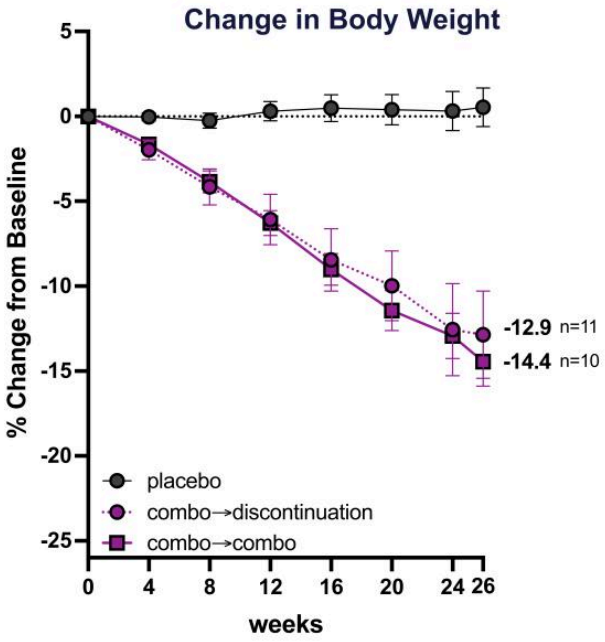
Initial 26-week treatment period completed; 26-week extension study ongoing

Nimacimab + Semaglutide Performed Better Than Semaglutide Alone



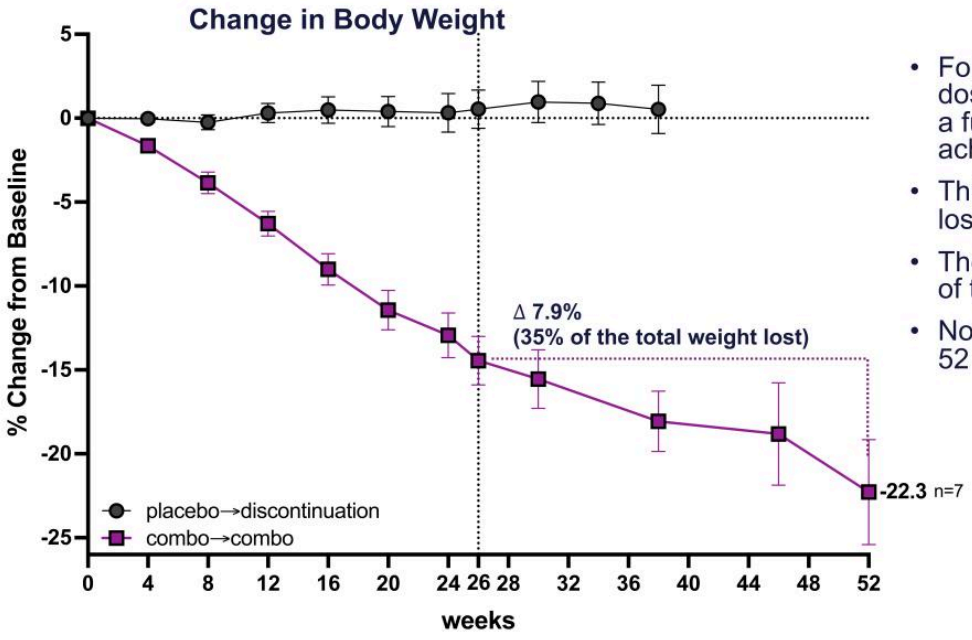
- Combination of nimacimab + semaglutide resulted in a 30% increase compared to semaglutide alone in CBeyond at 26 weeks.
- Semaglutide alone and combination groups in CBeyond outperformed historical semaglutide data (STEP-1).

Combination Subjects Similar between Extension and Follow-up Groups



- 10 subjects on active combination (nimacimab + semaglutide) rolled over to extension
- 11 subjects on the nimacimab + semaglutide combination therapy went into off therapy follow up
- There was minimal difference between the two groups in weight loss achieved at 26-weeks.
- We believe this suggests that the extension therapy subset is representative of the larger cohort of subjects on the combination treatment

Combination Group Demonstrated 22.3% Weight Loss at 52-Weeks



- Following an additional 26-weeks of dosing of nimacimab + semaglutide, a further 7.9% weight loss was achieved
- This represents 35% of total weight loss over 52-weeks.
- The total weight loss after 52 weeks of treatment was 22.3%
- No plateau in weight loss seen at 52 weeks

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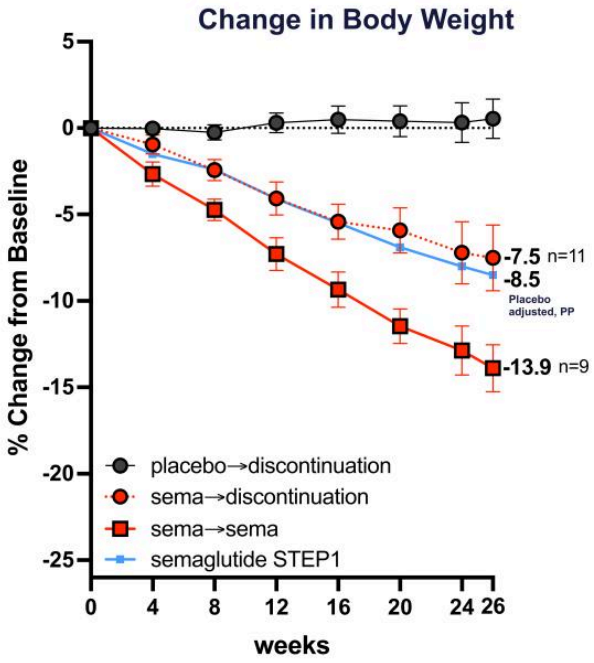
Semaglutide Subjects Were Different Between Extension and Follow-Up



- 9 subjects in the semaglutide alone (with placebo) arm enrolled in the extension study.
- 11 subjects in the semaglutide arm went into off therapy follow
- There was a marked difference in weight loss between these two groups at week 26 (85% greater weigh loss in the extension subset)
- This suggest that subset in extension treatment was not representative of the larger cohort and also differs from the historical response to semaglutide
- Subjects who were doing well on semaglutide chose to participate in the extension study
- This subset is a self-selected high-responder population (i.e. Super Responders).

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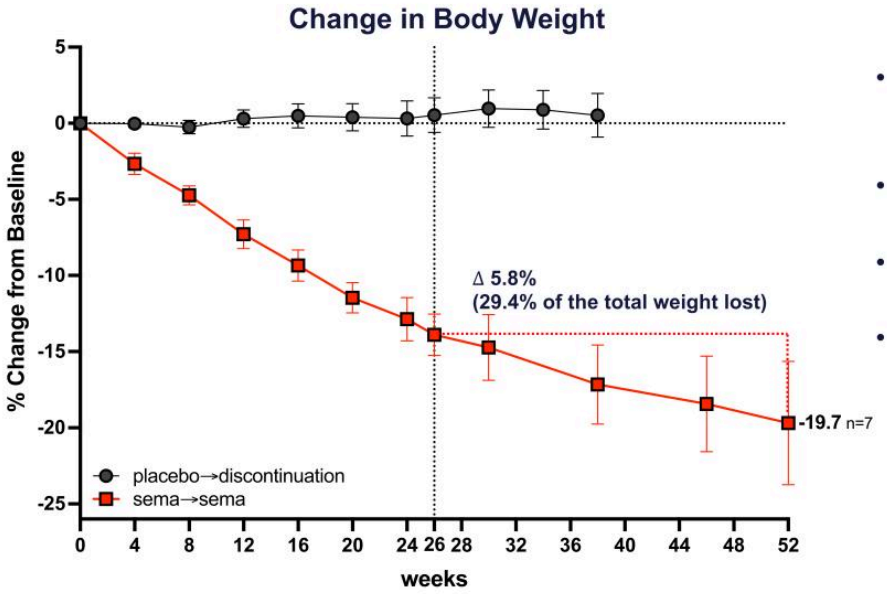
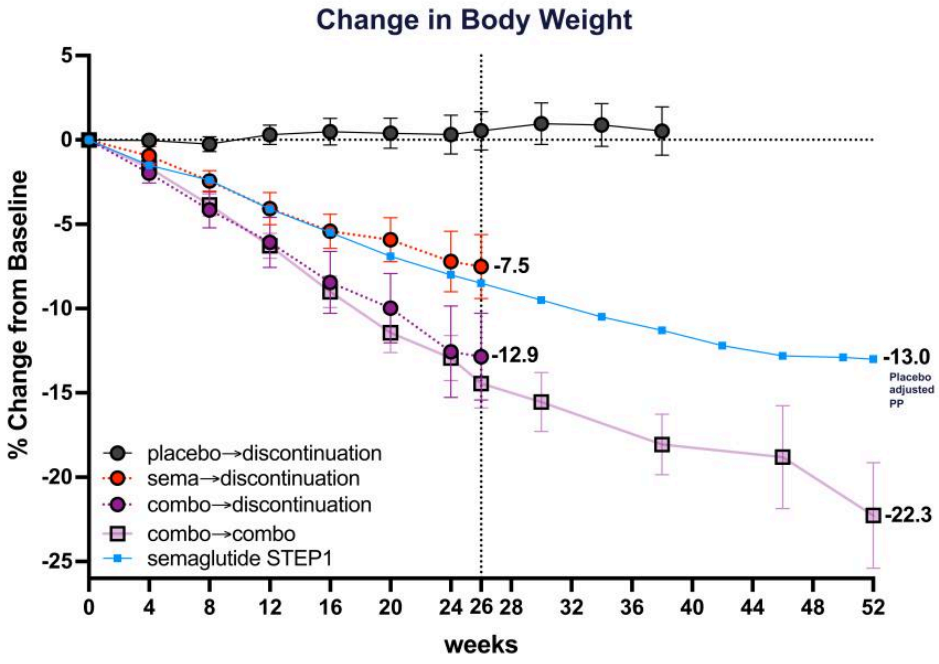
Semaglutide Group Demonstrated a 19.7% Weight Loss at 52-Weeks



- Following an additional 26-weeks of dosing of semaglutide + placebo, a further 5.8% weight loss was achieved.
- The additional 5.8% represents 29.4% of total weight loss over 52-weeks.
- The total weight loss after 52 weeks of treatment was 19.7%.
- This “Super Responder” population performed better than historical semaglutide.

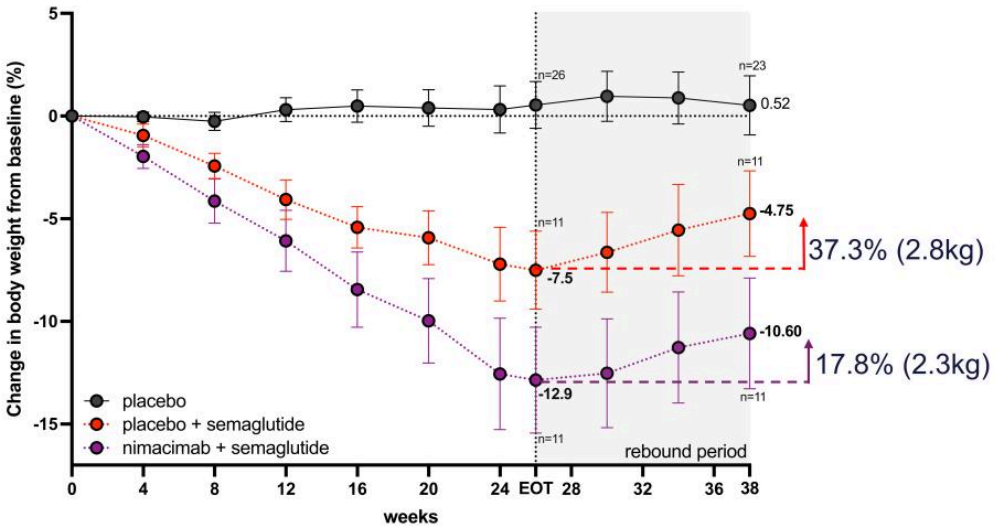
Nimacimab Converts Patients to “Super Responders”



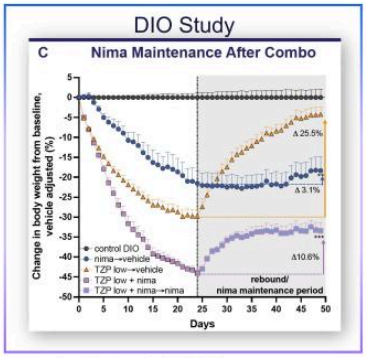
- Unusually high frequency of sema ‘super-responders’ makes it challenging to differentiate the combo effect
- Sema discontinuation group closely mirrors the STEP-1 trajectory
- Both combination cohorts closely track with the more active efficacy curves
- Thus in a larger trial, we would expect the sema cohort to closely follow the STEP-1 curve while the combination cohort **would be expected to sustain ~20–23% weight loss**

Nimacimab Reduces Weight Regain

Off-Therapy follow up for 13 weeks after the last dose



Off therapy follow up for 13 weeks after the last dose showed a significantly reduced rebound in weight in patients treated with combination therapy versus semaglutide



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.

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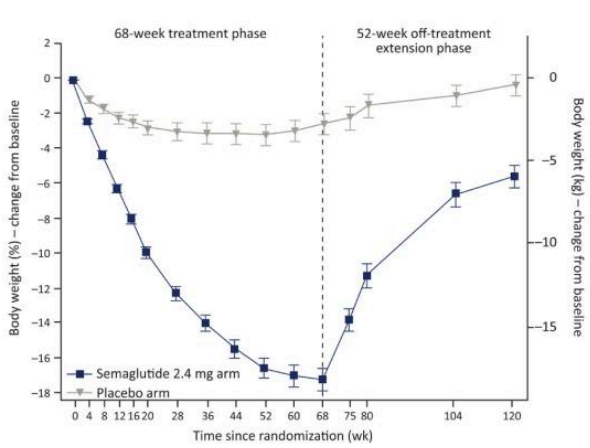
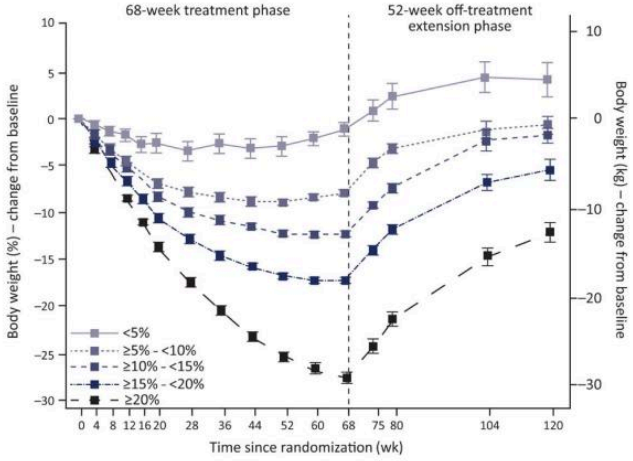
Typical Semaglutide Rebound Profile

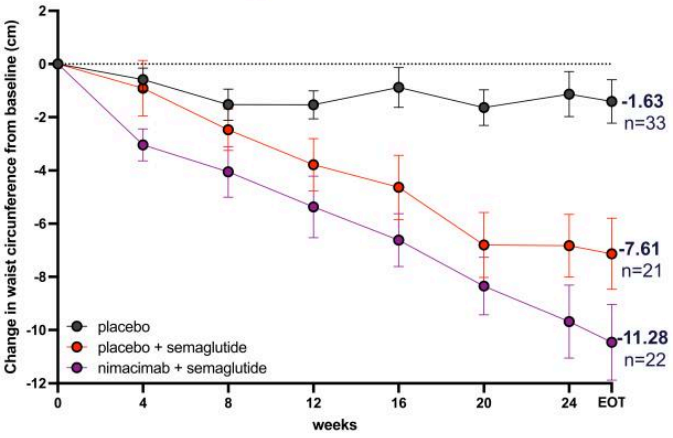




Wilding *et al.*, 2022. *Weight regain and cardiometabolic effects after withdrawal of semaglutide: The STEP 1 trial extension*

Lean to Fat Mass Ratio and Waist Circumference Improve with Nimacimab-Semaglutide Combination

Change in Waist Circumference



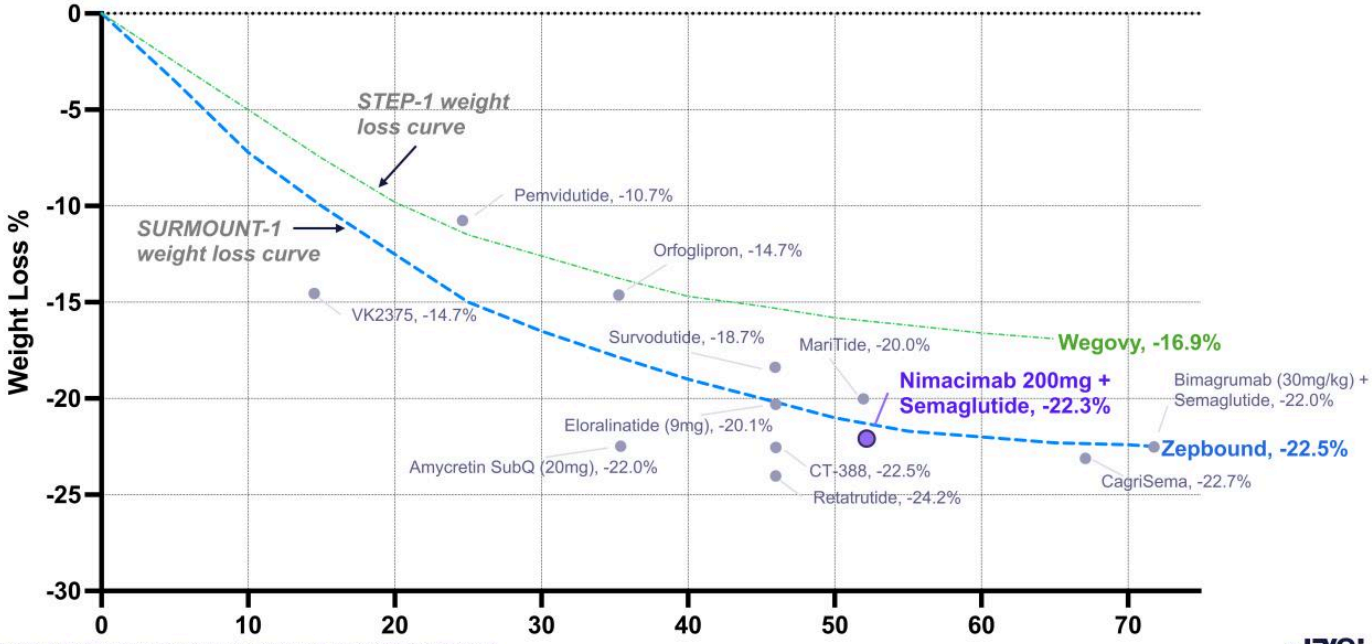
Nimacimab + semaglutide treatment results in a significant additional decrease in waist circumference

Change in Lean to Fat Mass Ratio with Weight Loss (Dexa scan)

	Placebo + Semaglutide	Nimacimab 200 mg + Semaglutide
	n=20	n=25
Mean baseline lean to fat mass ratio (SD)	1.15 (0.296)	1.06 (0.216)
Mean Week 26 lean to fat mass ratio (SD)	1.32 (0.312)	1.30 (0.463)
Least-squares mean change from baseline (SE)* (95% CI)	**0.13 (0.038) (0.1, 0.2)**	**0.26 (0.037) (0.2, 0.3)**
Least-squares mean difference from semaglutide (SE) (95% CI), P-value		**0.13 (0.051) (0.0, 0.2), p= 0.0126**

Nimacimab + semaglutide increases weight loss by ~30% & fat loss by 37% compared to semaglutide alone

Nimacimab + Semaglutide Better Than, Or Comparable To, Other Combinations With No Plateau at 52 Weeks



MariTide: Phase 2, 16% ITT at highest dose, placebo 1.2%; Cagrisema: 68 weeks, 22.7% PP and 20.4% ITT; Tirzepatide: 72W, ITT 20.9% vs 3.4%, PP 22.5% vs 2.4% at highest dose; Retatrutide: Phase 2 24.2% at 48 weeks, TRIUMPH4 ITT 23.7%, PP 28.7% W68; Survodutide: Phase 2 14.9% at 46 weeks, "upto 19%" likely PP highest dose

Summary and Conclusions

- We believe semaglutide-alone group self-selected for a “Super Responder” population which elected to continue enrollment in the 26-week extension study and showed continued weight loss beyond what is typically seen with semaglutide therapy alone.
- Nimacimab has demonstrated the ability to increase weight loss when combined with semaglutide by converting patients to “Super Responders”.
- Combination of nimacimab + semaglutide continued to demonstrate safe and tolerable profile at tested doses, similar to semaglutide-alone.
- Weight loss of 22.3% with no evidence of plateau is comparable to other combination therapies at 52 weeks.

skye

2.1

What We Learned From CBeyond

Dosing Strategy and Rationale

What We Learned from CBeyond Regarding Dosing

Data from CBeyond, together with our preclinical models, suggests:

1. Concentration in the serum does not equal concentration in the tissues, and achieving a higher serum concentration and steady-state sooner through a loading dose can potentially improve response.

2. Nimacimab can be dosed significantly higher and drive additional weight loss as both a monotherapy and in combination with semaglutide.

3. Compliance and retention are priorities for the success of the next study. We intend to include weekly on-site visits for dosing and implement highly competitive retention programs.

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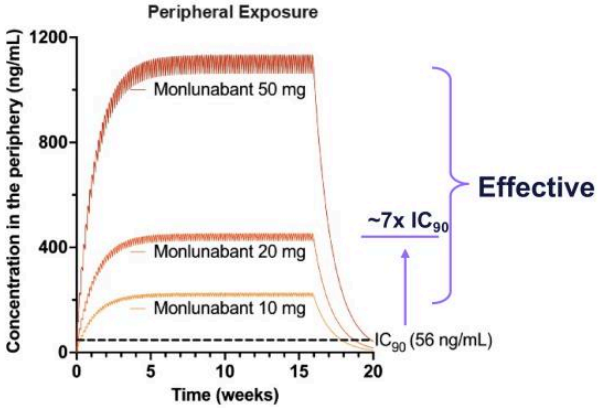
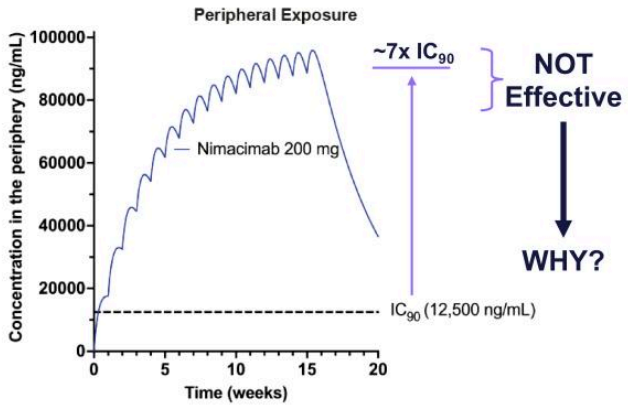
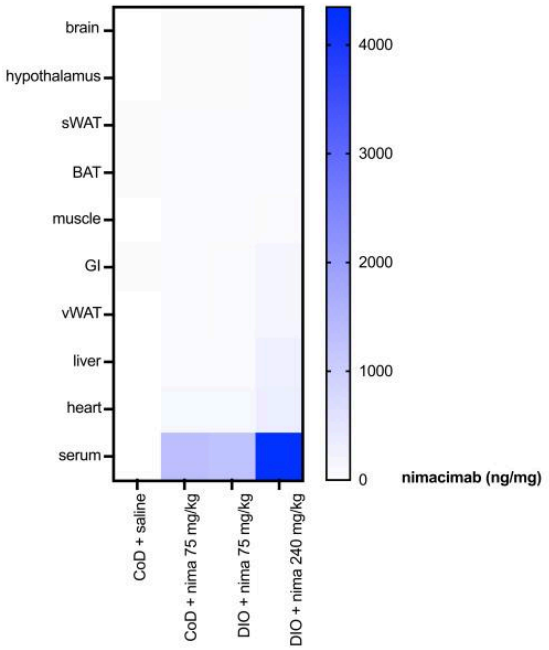
Initial rationale for CBeyond Dosing

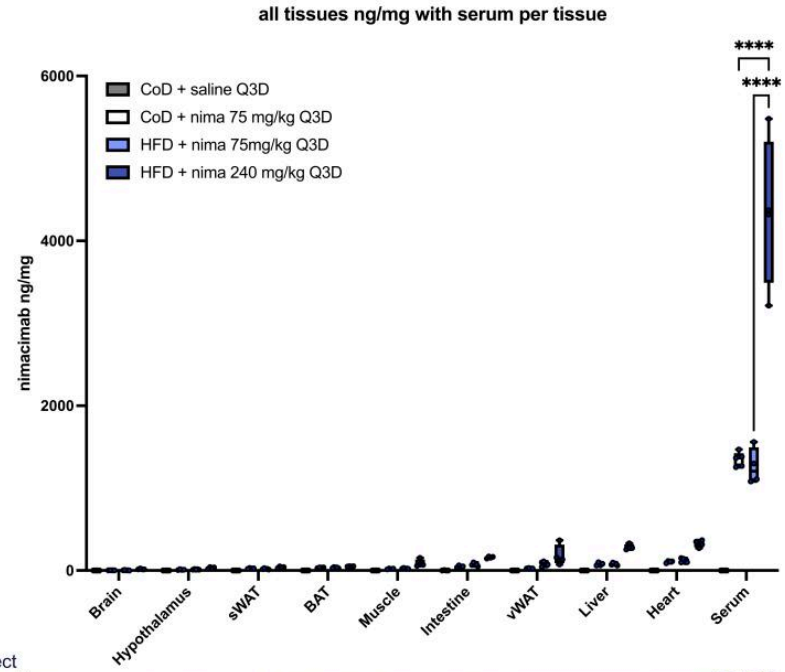
- Before pharmacodynamic data (clinical weight loss or DIO model), Skye developed clinical PK models (Ph1 data) to understand dosing options
- IC_{90} (serum) was used as a surrogate for target engagement
- Similar IC_{90} at $C_{max, ss}$ with 20mg monlunabant and 200mg nimacimab





Nimacimab biodistribution in lean and obese mice

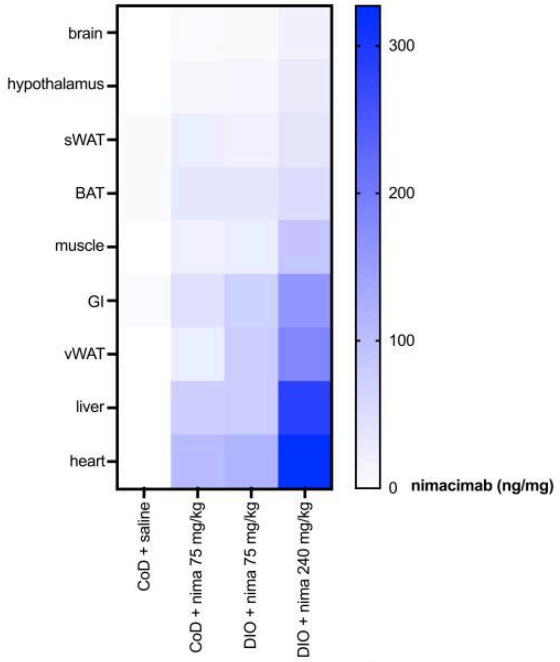


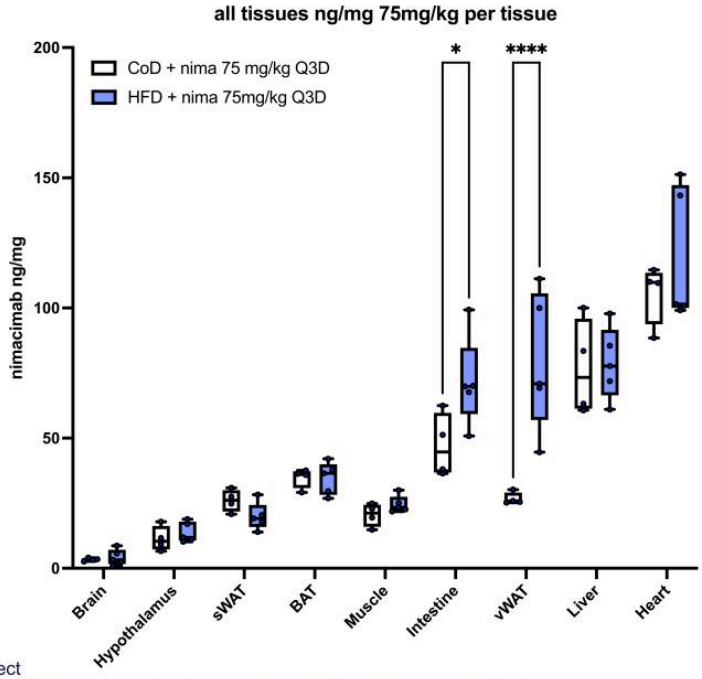


Human IgG ELISA kit (Ray Biotech, catalog# ELH-IGG) was used to detect nimacimab in tissue homogenates. Results are reported as ng of nimacimab/mg of tissue. N=4-5 per group.

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.

Beyond the Serum: CB1 Inhibition in Peripheral Tissues

Small molecule vs antibody-based CB1 inhibitors demonstrate differential distribution in peripheral tissues

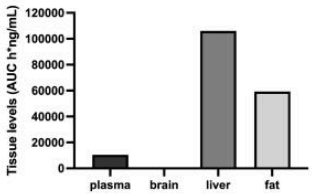
Small molecule

"S-MRI-1867 exhibited high exposure in most tissues, with concentrations ranging from 2 to 31 times greater than in plasma"

Adapted from Padilha EC. et. al. Biomed Pharmacother. 2023 Dec;168:115178

"Tissue distribution of Rimonabant preferentially accumulated in the liver and the adipose tissue"

Muller T. et. al. Int J Mol Sci. 2022 Mar 8;23(6):2923

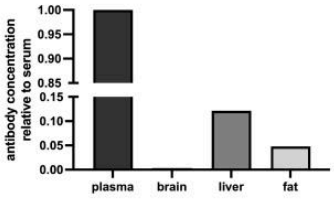


Parameter	Plasma	Brain	Liver	Fat
Tissue/Plasma AUC_{0-last} Ratio -		0.05	10	6

Antibody

Antibody distribution into tissues is ~4–16% of the plasma concentration for most tissues

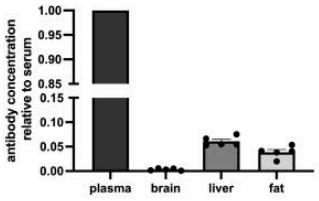
Shah, D. K., & Betts, A. M. *mAbs*, 2013 *5*(2), 297–305



Parameter	Plasma	Brain	Liver	Fat
Tissue/Plasma Ratio	1	0.0035	0.12	0.048

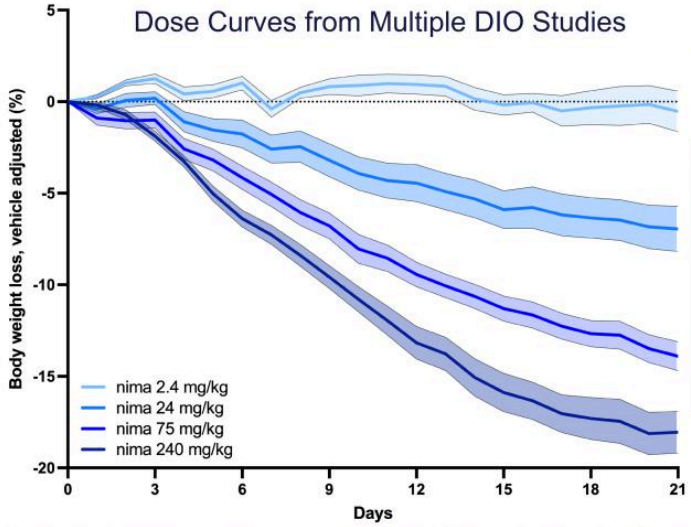
Skye BioD mouse data*

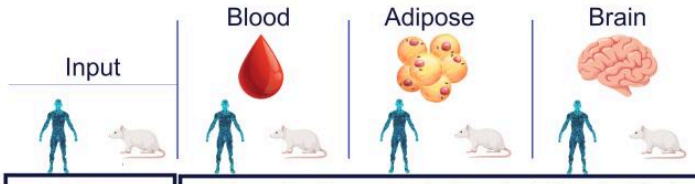
*this is data from the previous slide – ratios are derived tissue vs serum



Parameter	Plasma	Brain	Liver	Fat
Tissue/Plasma Ratio	1	0.003	0.06	0.04

Compartmental Analysis: Activity associated with CB1 inhibition in peripheral tissue

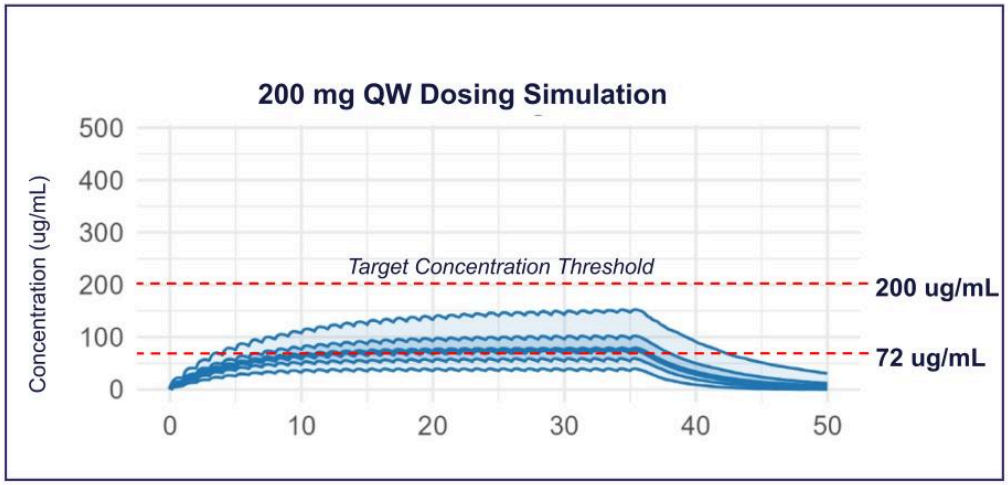




dose		nimacimab concentration (relative to IC_{90})					
200 mg dose	24 mg/kg	7.3x	6.4x	0.4x	0.3x	0.03x	0.02x
600 mg dose	75 mg/kg	22x	20x	1.1x	0.9x	0.1x	0.1x

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).

200 mg QW CBeyond Dosing Did Not Achieve Significant Concentrations in the Serum



- While 200 mg QW achieved median serum exposures of at least 7x over IC90; however, this dose proved to be sub-optimal.
- Higher dosing strategies need to be evaluated to achieve median serum concentrations of at least 200 ug/mL
- Based on our toxicity data, we believe we can evaluate multiple higher concentrations without safety concern.

How Much Higher Can Nimacimab Be Safely Dosed?

Nimacimab NOAEL based on 26-week NHP study is 75mg/kg

Phase 2b Simulations: Limiting toxicity assessment

Considering the human equivalent dose (HED) from the FDA guidance:

$$HED = 75\frac{mg}{kg} \cdot \frac{5.5\ kg}{100\ kg}^{0.33}$$

$28.8\ \frac{mg}{kg}$ in humans

In a 100 kg human the equivalent NOAEL dose is 2880mg

Table 1: Conversion of Animal Doses to Human Equivalent Doses Based on Body Surface Area

Species	To Convert Animal Dose in mg/kg to Dose in mg/m^2, Multiply by k_m	To Convert Animal Dose in mg/kg to HED[a] in mg/kg, Either:	
		Divide Animal Dose By	Multiply Animal Dose By
Human	37	---	---
Child (20 kg)[b]	25	---	---
Mouse	3	12.3	0.08
Hamster	5	7.4	0.13
Rat	6	6.2	0.16
Ferret	7	5.3	0.19
Guinea pig	8	4.6	0.22
Rabbit	12	3.1	0.32
Dog	20	1.8	0.54
Primates:			
Monkeys[c]	12	3.1	0.32
Marmoset	6	6.2	0.16
Squirrel monkey	7	5.3	0.19
Baboon	20	1.8	0.54
Micro-pig	27	1.4	0.73
Mini-pig	35	1.1	0.95

[a] Assumes 60 kg human. For species not listed or for weights outside the standard ranges, HED can be calculated from the following formula:
HED = animal dose in mg/kg x (animal weight in kg/human weight in kg)$^{0.33}$.

[b] This k_m value is provided for reference only since healthy children will rarely be volunteers for phase 1 trials.

[c] For example, cynomolgus, rhesus, and stumptail.

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Modeling NHP Toxicity Study Provides Guidance for Potential Nimacimab Dosing Regimens

- Skye has conducted two non-human primate toxicology studies both establishing 75mg/kg as NOAEL dose.
    1. **26-Week Subcutaneous Dosing (N=9)**
    2. **4-Week IV Dosing (N=10)**

	Cmax	Weekly AUC
26-Week SubQ Study	2150 ug/mL	~305,000 ug*h/mL
4-Week IV Study	2500 ug/mL	~375,000 ug*h/mL

- Direct concentration comparisons (e.g. Cmax and AUC) in non-human primate PK is highly predictive of human PK due to species similarities (S6 ICH Guidance).

- Using these data, we evaluated multiple doses determine safety of potential clinical doses.

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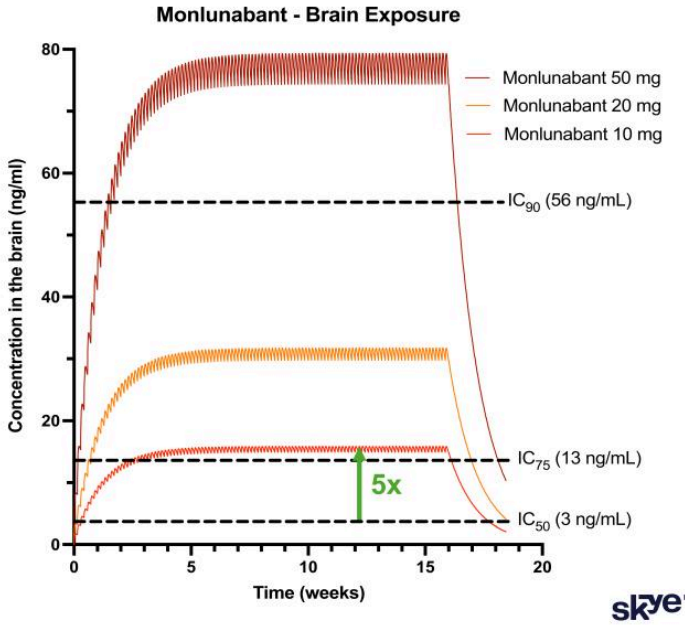
Monlunabant's Dose Dependent Increase in Brain Leads to Dose Dependent Increase in Neuropsychiatric Adverse Events

- Monlunbant's Phase 2a 16-week data demonstrated a dose dependent increase in neuropsychiatric side effects (Knop et al.).
- Neuropsychiatric adverse events were identified even at the lowest dose (10mg QD)
- Our modeling demonstrates that with each increasing dose, the concentration gets closer to IC_{90}, with the highest dose exceeding IC_{90}.
- **At the lowest dose of 10mg, monlunbant is already 5x above the IC_{50}**



References: Crater *et al*, 2023; Liu *et al*, 2021; Knop *et al*, 2025; Braga *et al.*, 2025

Nimacimab Has Wide Safety Margin in the Brain

- Modeling of brain exposure for **nimacimab (antibody)** shows a significantly better safety margin than **monlunabant (small molecule)**.
- Wang et al., demonstrates brain (CSF) to serum concentration ratios are between 0.1%-0.2% for antibodies.
- NHP studies of nimacimab demonstrate brain to serum ratio as low as 0.01%.
- Modeling for best case (0.01% brain:serum) and worst case (0.1% brain:serum), scenarios demonstrates that nimacimab is still significantly below the IC_{50} in the brain.

References: Phase 1 biodistribution study – internal data; NHP biodistribution study – internal data; NHP toxicology study – internal data; Fjord-Larsen *et al.*, 2021; Wang *et al.*, 2018

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3.0

Clinical Strategy

Phase 2 Adaptive Design Dose-Ranging Study

Path to the Potential Phase 3 Pivotal Studies

CBeyond 2

Phase 2b

An adaptive study designed to optimize combination therapy doses +
Define individual contributions of nimacimab and semaglutide

Part A
Monotherapy Dose Selection

Evaluate 3 doses of nimacimab as a single agent against placebo

Select 2 doses for combination therapy based on safety and efficacy

Part B
Combination Dose Optimization

Test the 2 selected doses, from Part A in combination with semaglutide versus semaglutide alone

CBeyond 3

Phase 3
Pivotal Studies

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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

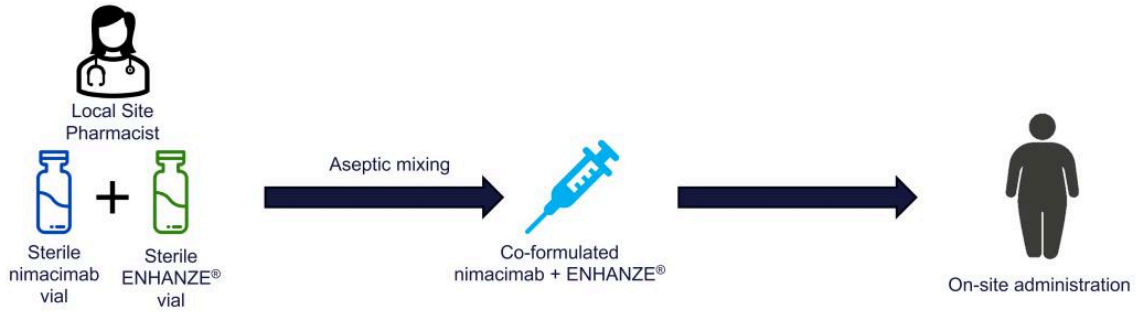

Improved absorption


Increased bioavailability

skye

“Mix-and-Deliver” Approach – Ensuring Compliance

- In the potential Phase 2b study, all patients will be required to visit the site for their weekly injections.
- These mandatory weekly visits are intended to ensure compliance, while also allowing for ENHANZE® and nimacimab to be co-formulated on-site prior to injection.
- This “mix-and-deliver” approach will reduce need for co-formulation development prior to Phase 2b study start.
- Compatibility and in-use stability (CIUS) studies will be completed to support ‘mix-and-deliver’ approach to use the co-formulated product as a Category 1 Compounded Sterile Preparation.



Positive Part A Enables Broader Clinical Pipeline & Commercial Opportunity

Pipeline Expansion with Additional Combo Opportunities

CBeyond

Phase 2b

An adaptive study designed to optimize combination therapy doses +
Define individual contributions of nimacimab and semaglutide

Part A
Monotherapy Dose Selection

Evaluate 3 doses of nimacimab as a single agent against placebo

Part B
Sema Combination Dose Optimization

2 selected doses, based on safety and efficacy will be tested in combination with semaglutide versus semaglutide alone

Planned

Future

***New* Phase 2b**
TRZ Combination Study

2 selected doses, may be tested in combination with terzepatide versus terzepatide alone

skye

3.1

Regulatory Strategy
Combination Approval, Monotherapy Opportunity

Combination Regulatory Strategy

- Phase 2b adaptive design is meant to satisfy the FDA's requirement to evaluate contribution of parts between nimacimab and semaglutide.
- If acceptable, we believe the pivotal Phase 3 design may only require a two-arm study comparing combination of nimacimab + semaglutide versus placebo.
- There is precedent for a similar approach as QSYMIA was approved by the FDA on the basis of studies evaluating the combination of phentermine + topiramate versus placebo.

skye

Monotherapy Opportunities

- We believe nimacimab has opportunity to fill gaps in the 2nd line therapy space after patients fail NuSH therapies (i.e. GLP1, GLP1/GIP, or amylin).
- If nimacimab alone can demonstrate at least +8% pbo-adjusted weight loss then it could be an ideal 2nd line therapy
- Alternatively, nimacimab has the potential as a maintenance therapy, using a similar regulatory path to orlistat (Xenical).
- Xenical Label:

----------INDICATIONS AND USAGE----------

- XENICAL is a reversible inhibitor of gastrointestinal lipases indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet. (1)
- XENICAL is also indicated to reduce the risk for weight regain after prior weight loss. (1)

skye

4.0

Financial Overview and Team

Selected Financial Figures & Metrics

- $107M in equity capital raised since August 2023 (no new equity financing issuances since March 2024 PIPE)
- Supported by top-tier specialist life science investors
- Cash runway into Q4 2026, excludes: the clinical cost of any potential Phase 2b study and the CMC cost to resupply such Phase 2b study
- Ongoing strategic investments in scaling manufacturing, operations, R&D, and advancing the clinical pipeline

Stock Information

Listed: Nasdaq	SKYE
Stock Price[1]	$1.01
Shares Outstanding[2]	32.1M
Shares Fully Diluted[2]	47.9M
Cash, Cash Equivalents & Short-term Investments [3]	$35.3M
Market Cap (inclusive of PFWs)[1]	$40.1M
Avg. 3-Mo. Daily Trading Volume[3]	858K

[1] Jan 30, 2026 [2] Nov 11, 2025 [3] Sep 30, 2025

Leadership

Contributed to commercialization of 40+ drugs/diagnostics, led high-value strategic transactions, and co-founded multiple companies

Executive Management

Punit Dhillon
President & CEO

Kaitlyn Arsenault, CPA
Chief Financial Officer

Tu Diep, MSc
Chief Operating Officer

Chris Twitty, PhD
Chief Scientific Officer

Puneet Arora, MD
Chief Medical Officer

Brennen Brodersen, JD
General Counsel

Board of Directors

Paul Grayson
Chairman of Skye BOD; Pres./CEO, Radionetics

Annalisa Jenkins, MBBS, FRCP
Managing Director, Annalisa Jenkins LLC

Deborah Charych, PhD
Co-founder and ex-CTO, RayzeBio

Andy Schwab
Managing Partner, 5AM Ventures

Karen Smith, MD, PhD, MBA, LLM
Global pharma/biotech exec and C-suite advisor

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THANK YOU

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Spotlight

CBeyond

The ANATOMY of PROGRESS
EXAMINING PERIPHERAL CB1 INHIBITION IN METABOLIC HEALTH

skye Obesity