



# Ascleptis Corporate Presentation

March 2026



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# Ascletis: Clinical-Stage Biotech With Complete and Differentiated Obesity Portfolio

Breadth of Ascletis' obesity medicines is competitive for a \$173.5B market<sup>1</sup>

- Hong Kong Stock Exchange listed biotech (1672.HK)
- Approximately 200 employees in discovery, clinical development, GMP manufacturing and administration
- All clinical studies conducted in the U.S.

4 clinical stage programs | 1 Phase III Start in 2026 | 7 Phase I Clinical Starts in 2026

## Best in Class/First in Class Small Molecule Clinical Programs

- Phase 3 ready Oral GLP-1RA
- Monthly SQ GLP-1RA (Ph2)
- Quarterly SQ GLP-1RA (Ph2 )
- Monthly SQ THRβ+incretin (Ph2 ready)
- Oral small mol amylin (IND 3Q2026)
- Oral small mol GIP RA (IND 4Q2026)

## Next Generation Ultra-Long-Acting Peptides (observed $t_{1/2} \geq 30$ days)

- Monthly SQ amylin RAs
- Monthly SQ amylin+GLP/GIP FDC
- Monthly SQ GLP-1/GIP RA
- Monthly SQ triple G RA
- Monthly SQ amylin+triple G FDC

## Enhanced Oral Bioavailability Peptides

- Daily/weekly oral amylin RA

## Three Underlying Platform Technologies for Continuous Innovation and Growth

- Artificial Intelligence-assisted Structure-Based Drug Discovery (AISBDD) technology
- Ultra-Long-Acting-Platform (ULAP) technology
- Peptide Oral Transport Enhancement Technology (POTENT)

1. GlobalData (Jan 28, 2025) estimates of global obesity market; \*\*RA: receptor agonist.

# Metabolic Diseases: Obesity - Small Molecules

Product (Modality)	Target	Indication	Commercial Rights	Discovery	IND-Enabling	Phase I	Phase II	Topline data and Est. Next Milestone
<b>ASC30</b> (Once-daily oral small molecule)	GLP-1R	Obesity	Global					<ul style="list-style-type: none"> <li>7.7% PBO-adjusted weight loss at week 13 with superior GI tolerability</li> <li>Phase III studies will start in the third quarter of 2026</li> </ul>
<b>ASC30</b> (Once-monthly subcutaneous small molecule)	GLP-1R	Obesity	Global					<ul style="list-style-type: none"> <li>24-week Ph2 with SQ depot formulation A1 achieved PBO-adjusted weight loss of 7.5% at week 16 after 3 monthly doses of 400 mg each.</li> </ul>
<b>ASC30</b> (Once-quarterly subcutaneous small molecule)	GLP-1R	Obesity maintenance	Global					<ul style="list-style-type: none"> <li>24-week Ph2 with SQ depot formulation A1 maintained weight loss for four months following the 3rd and final monthly dose of 400 mg</li> </ul>
<b>ASC47</b> (Adipose-targeted once-monthly subcutaneous small molecule)	THRβ	Obesity muscle preserving	Global					<ul style="list-style-type: none"> <li>56.2% greater efficacy with improved GI in combo with semaglutide</li> <li>Phase II start combo with ASC35 in 2026</li> </ul>
<b>ASC39</b> (Once-daily oral small molecule)	Amylin receptor	Obesity	Global					<ul style="list-style-type: none"> <li>Amylin-selective oral small molecule with eloralintide-like selectivity and efficacy</li> <li>FDA IND submission 3Q2026</li> </ul>
<b>ASC48</b> (Oral small molecule)	GIPR	Obesity	Global					<ul style="list-style-type: none"> <li>FDA IND submission 4Q2026</li> </ul>

# Metabolic Diseases: Obesity - Peptides

Product (Modality)	Target	Indication	Commercial Rights	Discovery	IND-Enabling	Phase I	Phase II	Topline data and Est. Next Milestone
<b>ASC36</b> (Once-monthly to once quarterly subcutaneous peptide)	Amylin receptor	Obesity	Global					<ul style="list-style-type: none"> <li>Half-life 6-fold longer than MET-233i</li> <li>32% and 91% greater relative efficacy in DIO rats vs eloralintide and petrelintide</li> <li>IND FDA submission 2Q2026</li> </ul>
<b>ASC36</b> (Oral peptide)	Amylin receptor	Obesity	Global					<ul style="list-style-type: none"> <li>Oral bioavailability of 6% to 8% at steady state in non-human primates</li> <li>FDA IND submission 2Q2026</li> </ul>
<b>ASC35</b> (Once-monthly subcutaneous peptide)	GLP-1R/GIPR	Obesity	Global					<ul style="list-style-type: none"> <li>Half-life 6-fold longer than tirzepatide</li> <li>FDA IND submission 2Q2026</li> </ul>
<b>ASC36_35 FDC</b> (Once-monthly subcutaneous peptides)	Amylin + GLP-1R/GIPR	Obesity	Global					<ul style="list-style-type: none"> <li>FDA IND submission 2Q2026</li> </ul>
<b>ASC37</b> (Once-monthly subcutaneous peptide)	GLP-1R/GIPR/GCGR	Obesity	Global					<ul style="list-style-type: none"> <li>FDA IND submission 3Q2026</li> </ul>
<b>ASC36_37 FDC</b> (Once-monthly subcutaneous peptides)	Amylin + GLP/GIP/GCG	Obesity	Global					<ul style="list-style-type: none"> <li>FDA IND submission 3Q2026</li> </ul>

# A Portfolio Built to Outperform Market Leaders

Ascletis' differentiations to compete for a \$173.5B market\*

## Current Market Leaders are Beatable

Oral small molecule GLP-1RA with suboptimal efficacy and tolerability

Life-long weekly injections

Tolerability issues

## Ascletis portfolio: Designed for Market Leadership

ASC30: BIC oral small molecule GLP-1RA

ASC30 and peptides: FIC monthly to quarterly SQ injections

ASC47\*\*+ incretin combo significantly improves GI tolerability of incretin mono

\* GlobalData (Jan 28, 2025) estimates of global obesity market. \*\* ASC47: Adipose-targeted THR $\beta$  selective agonist

ASC30 oral tablets once-daily  
(Orforglipron-validated Chugai scaffold)

# ASC30-202: 13-Week Oral Phase II Conducted in U.S. at 6 Sites

ASC30-202 (NCT07002905)- a Phase 2 trial to investigate the efficacy and safety of once-daily oral ASC30 oral tablets in adult participants with obesity or overweight with weight-related comorbidities

Participants(N=125)

## ■ Key Inclusion Criteria

Adults with

- Obesity: BMI:  $\geq 30.0$  kg/m<sup>2</sup> **OR**
- Overweight: BMI  $\geq 27.0$  kg/m<sup>2</sup> if accompanied by at least one weight-related comorbidity
- Stable body weight (less than 5% self-reported change within the previous 3 months)

## ■ Key Exclusion Criteria

- Diabetes (type 1 or type 2)
- Used prescription drugs that promote weight loss within 3 months prior to the first dose of IP.
- Prior or planned surgical treatment for obesity
- ALT or AST level  $\geq 1.5$ x ULN
- Total bilirubin level  $\geq 1.5$ x ULN

## ■ Titration scheme: every week

### Formulation 1: ASC30 Tablets (QD)

Formulation 1: ASC30 Tablets (QD)								
<i>Cohort 1</i>								
N=20	1 mg	2 mg	5 mg	10 mg	15 mg	20mg x 8 weeks		Follow-up
<i>Cohort 2</i>								
N=20	1 mg	2 mg	5 mg	10 mg	20 mg	40mg x 8 weeks		Follow-up
<i>Cohort 3</i>								
N=9	PBO	PBO	PBO	PBO	PBO	PBO		Follow-up

### Formulation 2: ASC30 Tablets A1 (QD)

Formulation 2: ASC30 Tablets A1 (QD)								
<i>Cohort 4</i>								
N=21	1 mg	2 mg	5 mg	10 mg	15 mg	20 mg	20mg x 7 weeks	Follow-up
<i>Cohort 5</i>								
N=20	1 mg	2 mg	5 mg	10 mg	20 mg	40 mg	40mg x 7 weeks	Follow-up
<i>Cohort 6</i>								
N=20	1 mg	2 mg	5 mg	10 mg	20 mg	40 mg	60mg x 7 weeks	Follow-up
<i>Cohort 7</i>								
N=15	PBO	PBO	PBO	PBO	PBO	PBO	PBO	Follow-up

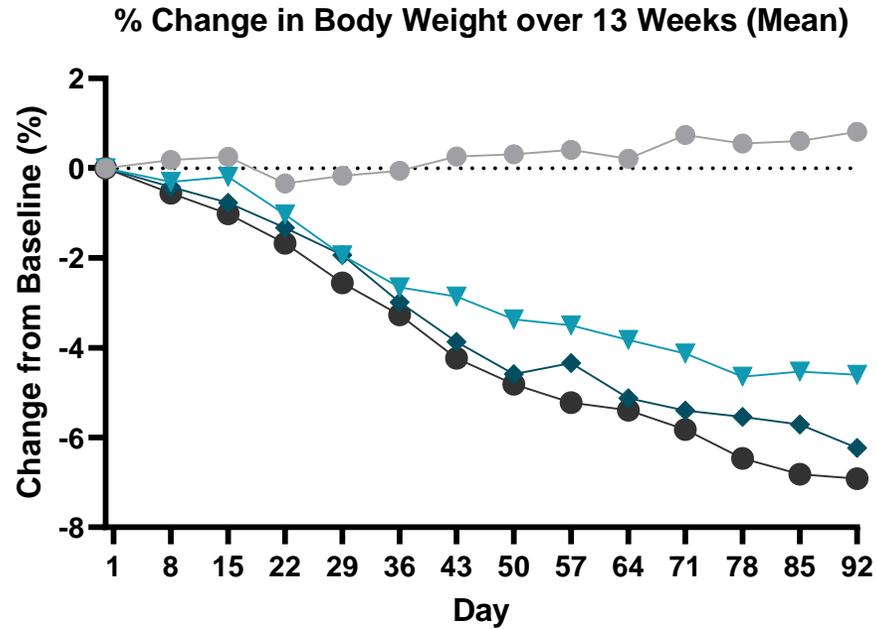
W1 | W2 | W3 | W4 | W5 | W6 | W7 – W13 | W14 – W15

Formulation 2: smaller pill size (300 mg pill contains 60 mg ASC30); suitable for co-formulation with our oral small molecule amylin ASC39

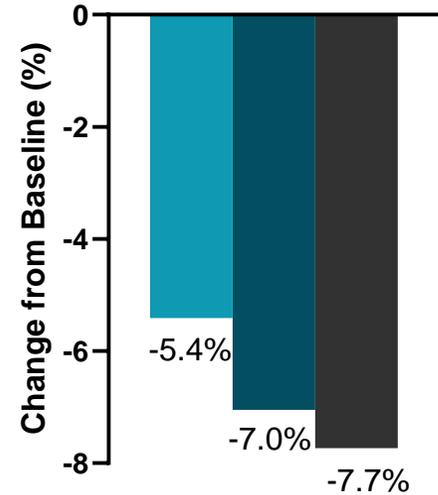
# ASC30-202: Baseline Demographics and Characteristics

Characteristics Mean(SD) or N(%)	Placebo N=24	ASC30 20mg N=41	ASC30 40mg N=40	ASC30 60mg N=20	Total N=125
<b>Age, years, mean</b>	45.9 (10.4)	49.0 (12.1)	45.7 (10.9)	46.7 (13.0)	47.0 (11.5)
<b>Weight, kg</b>	98.9 (20.0)	106.9 (24.4)	103.1 (22.7)	104.0 (15.2)	103.7 (21.7)
<b>Body mass index, kg/m<sup>2</sup></b>	36.2 (4.6)	38.6 (7.5)	37.6 (7.1)	37.2 (5.0)	37.6 (6.5)
<b>HbA1c, %</b>	5.5 (0.3)	5.5 (0.3)	5.6 (0.3)	5.4 (0.4)	5.5 (0.3)
<b>Systolic Blood pressure, mmHg</b>	122.6 (14.7)	120.1 (13.9)	119.1 (13.9)	122.2 (12.8)	120.6 (13.8)
<b>Diastolic Blood pressure, mmHg</b>	76.0 (10.2)	76.9 (8.2)	76.8 (7.3)	77.4 (8.6)	76.8 (8.3)
<b>Ethnicity (Hispanic or Latino)</b>	14 (58.3)	18 (43.9)	19 (47.5)	9 (45.0)	60 (48.0)

# ASC30 Demonstrated Dose-Dependent Weight loss



**PBO Adjusted % Change in Body Weight at Day 92 (Week 13)**



**% Change in Body Weight at Day 92 (Week 13)**

Percentage change	PBO	20mg ASC30	40mg ASC30	60mg ASC30
Mean(SE), %	0.8(0.6)	-4.6(1.0)	-6.2(1.2)	-6.9(0.9)
<i>p</i> vs PBO	-	<0.0001	<0.0001	<0.0001

# High-level weight loss comparison: ASC30 vs orforglipron

# ASC30 PBO-adjusted weight loss up to 7.7% with no plateau at 13 weeks

Cross-trial comparison	ASC30 13-week study			Orforglipron 36-week study <sup>1</sup>		Orforglipron ATTAIN-1 72-week study <sup>2</sup>	
Titration schedule	<b>Weekly</b> 1/2/5/10/15/20 mg	<b>Weekly</b> 1/2/5/10/20/40 mg	<b>Weekly</b> 1/2/5/10/20/40/60 mg	<b>Every two weeks</b> 3/6/8/12/24/36/45 mg		<b>Every four weeks</b> 1/3/6/12 mg	<b>every four weeks</b> 1/3/6/12/24/36 mg
Target dose	20 mg	40 mg	60 mg	45 mg		12 mg	36 mg
PBO adjusted weight loss from baseline	Week 13	Week 13	Week 13	Week 12	Week 36	Week 12	Week 72
	5.4%	<b>7.0%</b>	<b>7.7%</b>	<b>6.4%</b>	12.4%	4.5%	11.5%

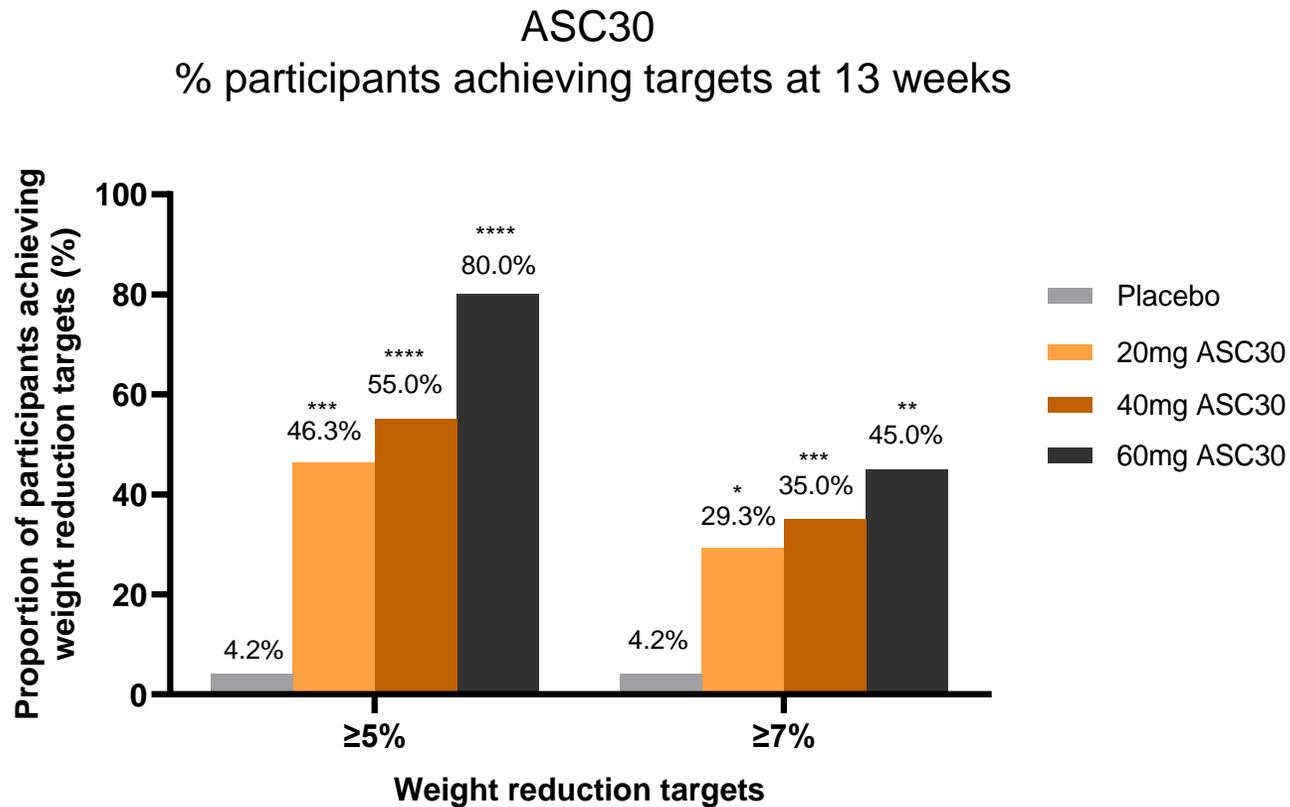
- ASC30 demonstrated dose-dependent weight losses and no plateau observed
- Orforglipron (OFG)'s weight loss at week 36 was doubled, compared to week 12.
- ASC30's weight loss is expected to double to ~15% as well

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

1. N Engl J Med 2023;389:877-88

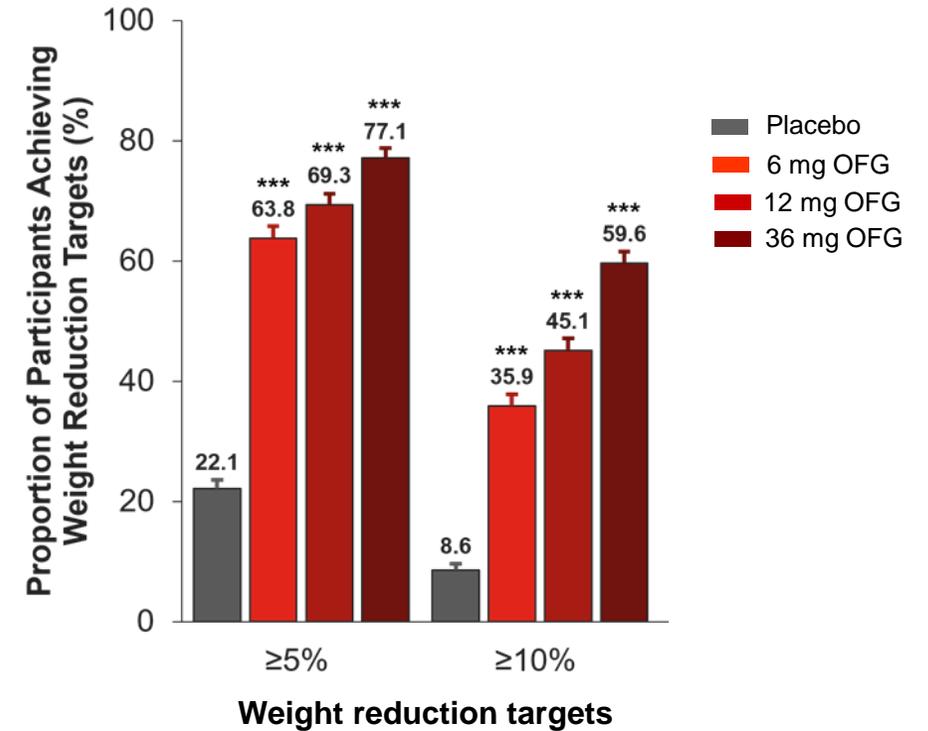
2. N Engl J Med. 2025;393:1796-1806

# % Participants achieving weight reduction targets is dose dependent



*p* vs PBO: \*\*\*\*  $p < 0.0001$ , \*\*\*  $p < 0.001$ , \*\*  $p < 0.01$ , \*  $p < 0.05$

**Orforglipron ATTAIN-1**  
% participants achieving targets at 72 weeks<sup>1</sup>



1. Eli Lilly presentation at ObesityWeek 2025

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# Cardiometabolic benefits

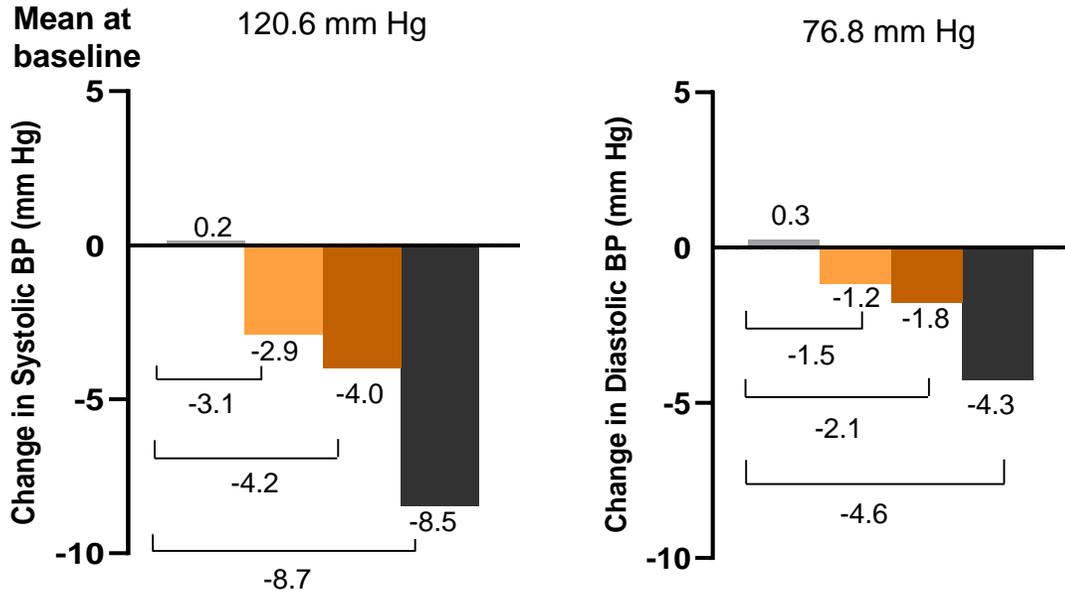
# Dose dependent blood pressure drop is consistent between ASC30 and OFG

## ASC30

Mean Change in Systolic/Diastolic Blood Pressure

### Systolic BP

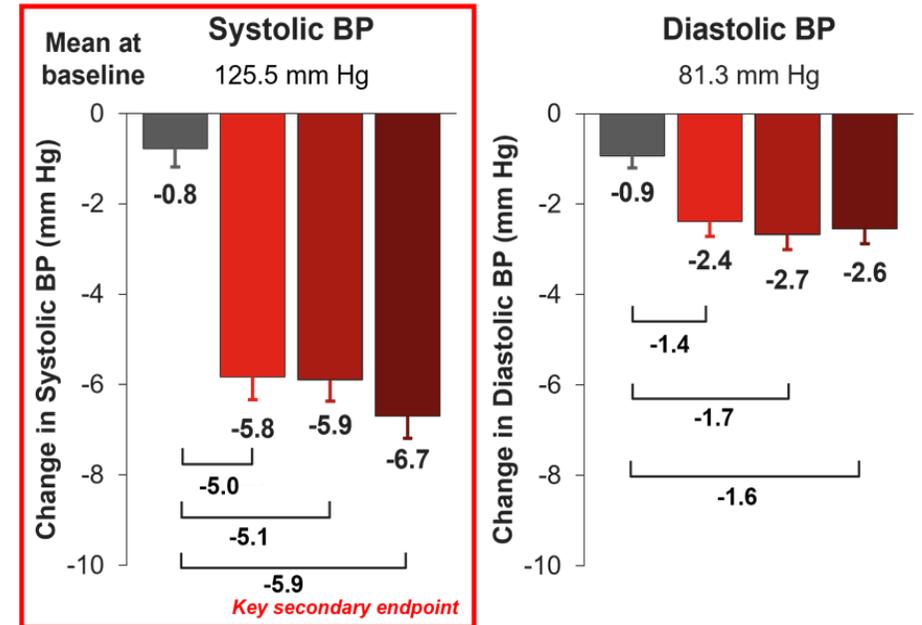
### Diastolic BP



- Placebo
- 20mg ASC30
- 40mg ASC30
- 60mg ASC30

## Orforglipron ATTAIN-1

Mean Change in Systolic/Diastolic Blood Pressure<sup>1</sup>



- Placebo
- 6 mg OFG
- 12 mg OFG
- 36 mg OFG

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1. Eli Lilly presentation at ObesityWeek 2025

# Concentrations of ASC30 increased with increasing doses

- Plasma samples were collected at pre-dose from day 1 to day 85 at one-week intervals
- At day 85, plasma samples were collected at 3 h and 6 h post-dose, in addition to samples collected at pre-dose
- Plasma concentrations of ASC30 increased with increasing doses from 20 mg, 40 mg to 60 mg.
- Higher concentrations of ASC30 correlated to more weight losses
- Phase II ASC30 concentration data are consistent with Phase I pharmacokinetic data

# ASC30 efficacy summary

- At 13 weeks, all three doses (20 mg, 40 mg and 60 mg) of ASC30 met the primary endpoint compared to placebo, demonstrating statistically significant and clinically meaningful weight loss.
- At the 13-week primary endpoint, ASC30 once-daily tablets showed dose-dependent placebo-adjusted mean body weight reductions of 5.4%, 7.0% and 7.7% for 20 mg, 40 mg and 60 mg, respectively.
  - No plateau was observed for weight loss
- % of patients achieving weight reduction targets (5% and 7%) was dose-dependent
- ASC30 attained reductions in known markers of cardiovascular risk,
  - Including total cholesterol, LDL-C, triglyceride, and systolic and diastolic blood pressure across all doses.
- Plasma concentrations of ASC30 increased with increasing doses.

# ASC30 GI tolerability

# ASC30 demonstrated a best-in-class GI tolerability profile

		ASC30 13-week study			
Titration schedule	Weekly				
Target dose	20 mg	40 mg	60 mg	PBO	
Vomiting	22%	25%	30%	4%	
Mild	12%	13%	20%	0	
Moderate	10%	13%	10%	4%	
Severe	0	0	0	0	
Nausea	49%	63%	40%	13%	
Diarrhea	15%	13%	20%	4%	
Constipation	12%	18%	10%	0	

Note: Percentages are rounded; totals may not be equal to sum exactly.

# High-level GI AE comparison: ASC30 vs orforglipron

# Vomiting rate of ASC30 titrated weekly was approximately half the rate observed with orforglipron titrated weekly

- GI AEs of ASC30 titrated weekly was comparable to published results of orforglipron titrated every four weeks in the Phase III ATTAIN-1 study

Cross-trial comparison	ASC30 13-week study			Orforglipron 12-week study <sup>1</sup>	Orforglipron ATTAIN-1 72-week study <sup>2</sup>
Titration schedule	Weekly			Weekly	Every four weeks
Target dose	20 mg	40 mg	60 mg	45 mg	36 mg
Vomiting	<b>22%</b>	<b>25%</b>	<b>30%</b>	<b>56%</b>	<b>24%</b>
Nausea	49%	63%	40%	78%	34%
Diarrhea	15%	13%	20%	11%	23%
Constipation	12%	18%	10%	Not published	25%

Of 125 patients in ASC30 13-week study, (1) all GI AEs were grade 1 (mild) and grade 2 (moderate) in severity and mostly occurred during the dose titration period; (2) there were no grade 3 (severe) or above AEs.

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

1. Diabetes Obes Metab. 2023;25:2642–2649  
2. N Engl J Med. 2025;393:1796-1806

# AEs in severity: ASC30 titrated weekly vs OFG titrated every four weeks

- Of 125 patients with **ASC30** titrated weekly across multiple U.S. sites
  - All GI AEs were grade 1 (mild) and grade 2 (moderate) in severity
  - Mostly occurred during the dose titration period
  - There were no grade 3 (severe) or above AEs
  - Only two SAEs (appendicitis and cholelithiasis) were reported and determined to be unrelated to the study drug according to the assessments by the Principal Investigators
- During 72-week study ATTAIN-1 with **orforglipron** titrated every four weeks<sup>1</sup>
  - Most GI adverse events (AEs) were grade 1 (mild) and grade 2 (moderate) in severity
  - Mostly occurred during the dose titration period
  - Grade 3 (severe) or above GI AEs were 1.4%, 2.6% and 3.4% for 6 mg, 12 mg and 36 mg OFG.
  - 1.2% SAE (cholelithiasis etc) rate was reported in orforglipron ATTAIN-1 study

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# Treatment discontinuation due to AE: ASC30 vs orforglipron

Titration schedule	Weekly				
ASC30 13-week study	20 mg	40 mg	60 mg	Placebo	Total
Treatment discontinuation due to AE	7.3%	7.5%	0.0%	0.0%	4.8%
Titration schedule	Weekly	Weekly or every three weeks	Every two weeks		
Orforglipron 36-week study <sup>1</sup>	24 mg	36 mg	45 mg	Placebo	Total
Treatment discontinuation due to AE	18.9%	15.5%	14.8%	2.0%	13.2%
Titration schedule	Every four weeks				
Orforglipron ATTAIN-1 72-week study <sup>2</sup>	6	12	36	Placebo	Total
Treatment discontinuation due to AE	5.3%	7.9%	10.3%	2.7%	6.3%

Treatment discontinuation due to AE rate of **ASC30 titrated weekly** to target dose was approximately half of treatment discontinuation due to AE rates observed with **orforglipron titrated weekly or every two or three weeks**.

# Hepatic safety signal: ASC30 vs orforglipron

## ■ **ASC30** - hepatic safety signal

- To date, ASC30 has been investigated in two Phase I and two Phase II clinical studies at multiple sites in the U.S in **340 participants** with obesity or overweight with at least one weight-related comorbidity.
- No hepatic safety signal was observed

## ■ **Orforglipron** - hepatic safety signal

- To date, orforglipron has been investigated in multiple ATTAIN and ACHIEVE clinical studies
- No hepatic safety signal was observed

# ALT and AST: ASC30 vs orfoglipron

	ASC30				Orfoglipron <sup>1</sup> ATTAIN-1			
	Placebo	ASC30 20 mg	ASC30 40 mg	ASC30 60 mg	Placebo	OFG 6 mg	OFG 12 mg	OFG 36 mg
<b>ALT, %</b>								
≥3x ULN	0	0	0	0	2.3%	2.9%	1.5%	3.1%
≥5x ULN	0	0	0	0	0.9%	0.8%	0.7%	1.3%
≥10x ULN	0	0	0	0	0.1%	0	0.3%	0.6%
<b>AST, %</b>								
≥3x ULN	0	0	0	0	1.0%	1.1%	0.6%	1.3%
≥5x ULN	0	0	0	0	0.3%	0.6%	0.1%	0.6%
≥10x ULN	0	0	0	0	0	0.1%	0	0.1%

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

1. Eli Lilly presentation at EASD 2025

# ASC30 safety and tolerability summary

- Vomiting rate of ASC30 titrated weekly to target dose was approximately **half** of the published vomiting rate observed with orforglipron titrated weekly
  - GI tolerability of ASC30 titrated weekly was comparable to published results of orforglipron titrated every four weeks in the Phase III ATTAIN-1 study
  - Given the significant improvement in GI tolerability seen with the GLP-1 agonist class when titration is slowed from weekly to every four weeks, we expect the GI tolerability of ASC30 tablets to be further improved in Phase III studies when titrated every four weeks.
- Treatment discontinuation due to AE rate of ASC30 titrated weekly to target dose was approximately **half** of the published treatment discontinuation due to AE rates observed with orforglipron titrated weekly or every two or three weeks
  - Treatment discontinuation due to AE rates of ASC30 titrated weekly was comparable to the published treatment discontinuation due to AE rates observed with orforglipron titrated every four weeks (ATTAIN-1)
- No hepatic safety signal observed and no elevations of ALT and AST

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

# ASC30 Once-Daily Oral Conclusions



ASC30 once-daily oral demonstrated dose-dependent placebo-adjusted body weight reductions up to **7.7%** at 13 weeks



Improvements in cardiometabolic parameters, including Lipids and blood pressure



**ASC30 titrated weekly** demonstrated comparable GI tolerability profile to **orforglipron titrated every four weeks**

**Phase II study suggests a potential best-in-class profile of ASC30 for both weight loss and GI tolerability**

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

We plan to submit these data to FDA and request an End-of-Phase II meeting in the second quarter of 2026

# ASC30 SQ Depot: Once Monthly Treatment and Once Quarterly Maintenance

# Observed $t_{1/2}$ of 18 days is NOT enough to support once-monthly dosing Pfizer/Metsera's MET097 phase III is once-weekly dosing<sup>1</sup>

Efficacy and Safety of **MET097** Once-Weekly in People With Overweight or Obesity (VESPER-4)

ClinicalTrials.gov ID: NCT07311850

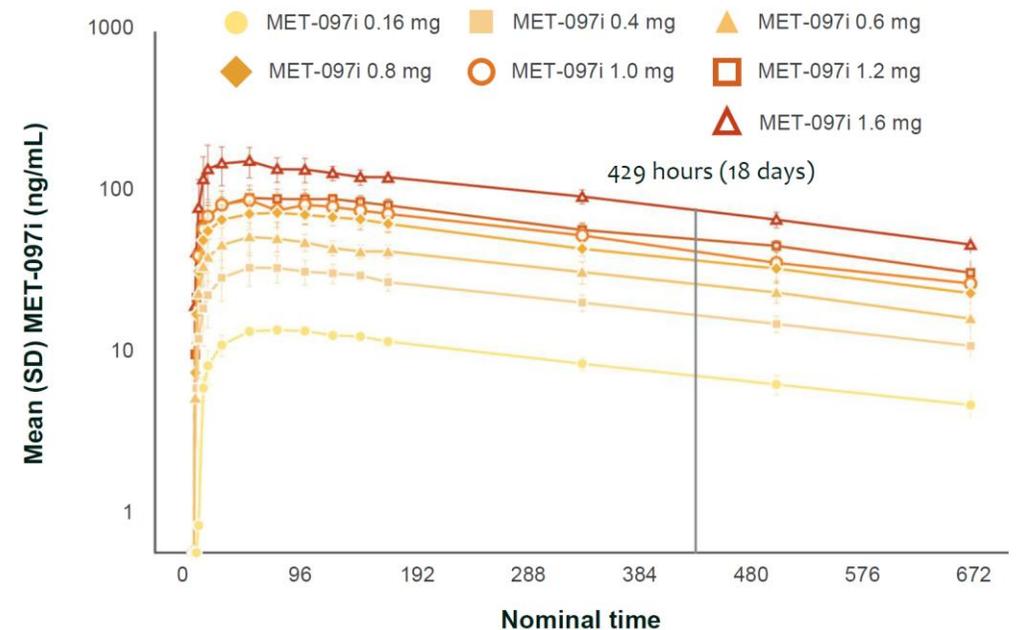
Sponsor: Metsera

Information provided by: Metsera (Responsible Party)

Last Update Posted: 2025-12-31

Official Title: Evaluating The Efficacy and Safety of **MET097**, a Fully-Biased, Ultra Long-Acting GLP-1RA, In People With Overweight or Obesity: A Phase 3, Multi-Center Randomized, Controlled Trial (VESPER-4)

## MET-097i OBSERVED HALF-LIFE<sup>1</sup> ~18 DAYS IN SAD



Ascletis' proprietary depot-based technology is able to achieve observed half-lives  $\geq 30$  days, supporting once-monthly dosing intervals

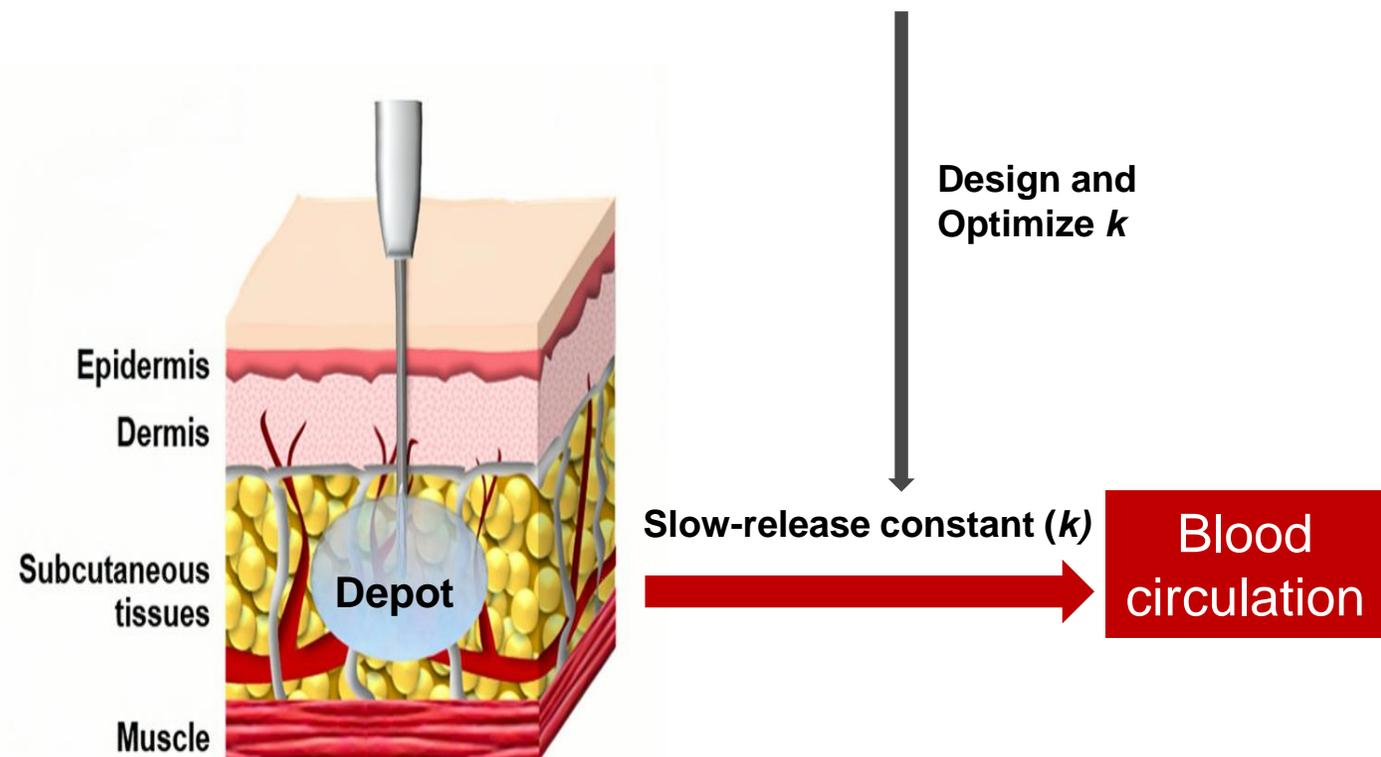
For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

1. www.clinicaltrials.gov

# Ultra-Long-Acting Platform (ULAP) Technology Validated Clinically and Commercially (Differentiated from commonly used albumin-based half-life extension technology)

- ULAP technology utilizes both non-lipid-based depot and lipid-based depot proprietary formulations
- Suitable for small molecules, peptides, antibodies, and proteins
- Allows continued optimization of release constant ( $k$ ) to achieve half-lives  $\geq 30$  days, supporting once-monthly and greater dosing intervals
- Albumin technology limited to 20 day half-life of albumin

## Ascletis' ULAP

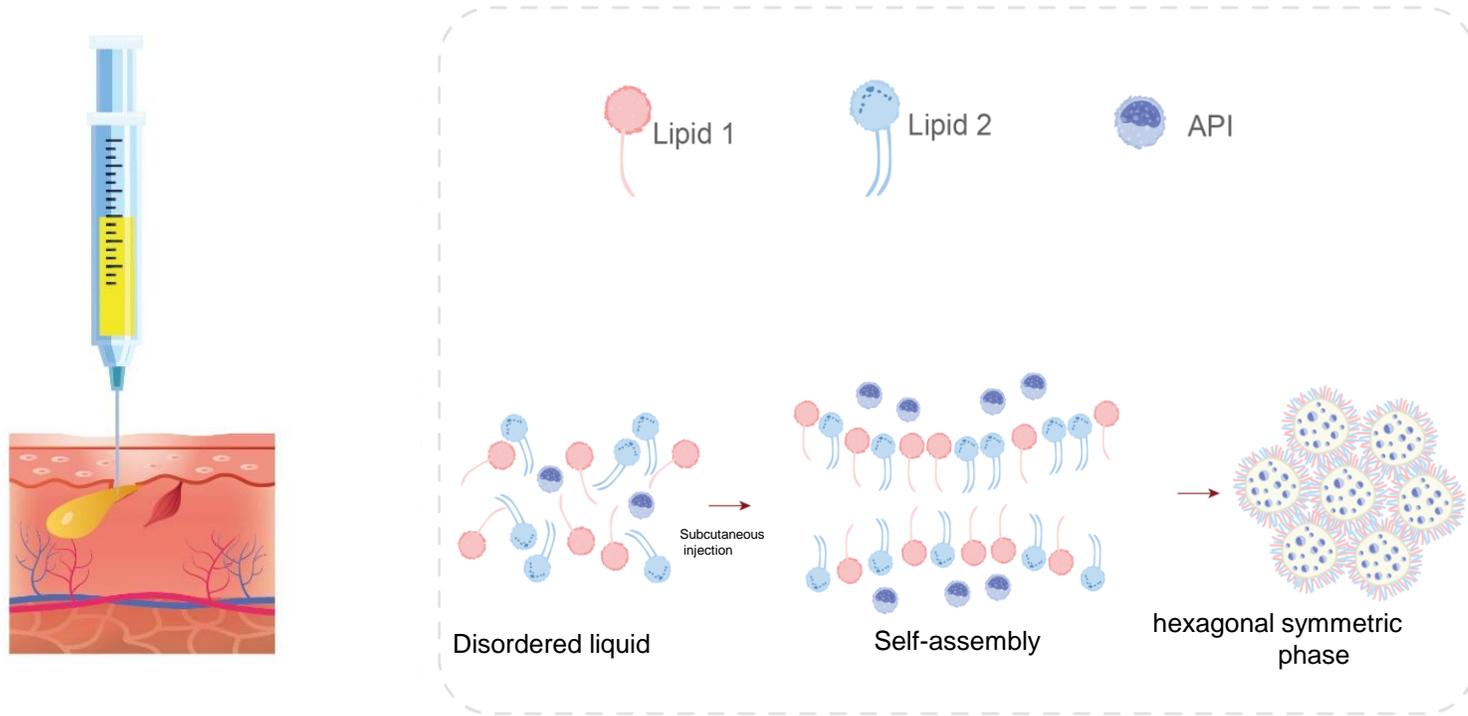


## Current Achievements and Validations

- Small Molecule GLP-1RA SQ: Half-life 46 days and 75 days in obese subjects
- Small Molecule Adipose Targeted THR $\beta$  SQ: Half life 40 days in obese subjects
- Small Molecule Integrase Inhibitor SQ: Half life 6 months in preclinical models
- Peptide (GLP-1R/GIPR) SQ: Half life ~6-fold longer than tirzepatide in NHP
- Peptides (amylin receptor) SQ: Half life ~6-fold longer than MET-233i in NHP

1. including both non-lipid-based depot and lipid-based depot

# Lipid-based Depot: Self-Assembly Lipid Depot



- The low-viscosity solution is composed of lipid 1, lipid 2, biocompatible organic solvents, and the active pharmaceutical ingredient(API). The low-viscosity solution can be easily administered into the subcutaneous tissue using a pre-filled pen (29G needle) or a syringe with a fine needle (29G).
- Once it enters the subcutaneous tissue and encounters an aqueous environment, the amphiphilic lipid molecules immediately undergo self-assembly, transforming the low-viscosity solution into a highly viscous depot, encapsulating the API.
- Under the action of enzymes in the tissue , the depot slowly degrades, releasing the API over one month or longer period.

Ultra-long-acting SQ depot **treatment/maintenance formulation** of  
small molecule GLP-1R agonist ASC30 in obese patients  
Observed  $t_{1/2}$  = 46-75 days

# ASC30 SQ Depot Formulations Have Longer Half-Lives Than Competitors' Peptide Drugs in Humans – Cross-Trial Comparison<sup>1</sup>

Except ASC30 SQ depot, all peptides below utilize albumin-dependent half-life extension technology, which limits half-life extension to the half-life of albumin (approximately 20 days)

	ASC30 SQ depot (small molecule GLP-1RA)	MET-097i	Petrelintide	Tirzepatide	Retatrutide	Semaglutide	MariTide
Human $t_{1/2}$ , days	46-75 <sup>2</sup>	18 <sup>2</sup>	10	5	6	7	14-15

<sup>1</sup>These are only a few representatives with available half-life data

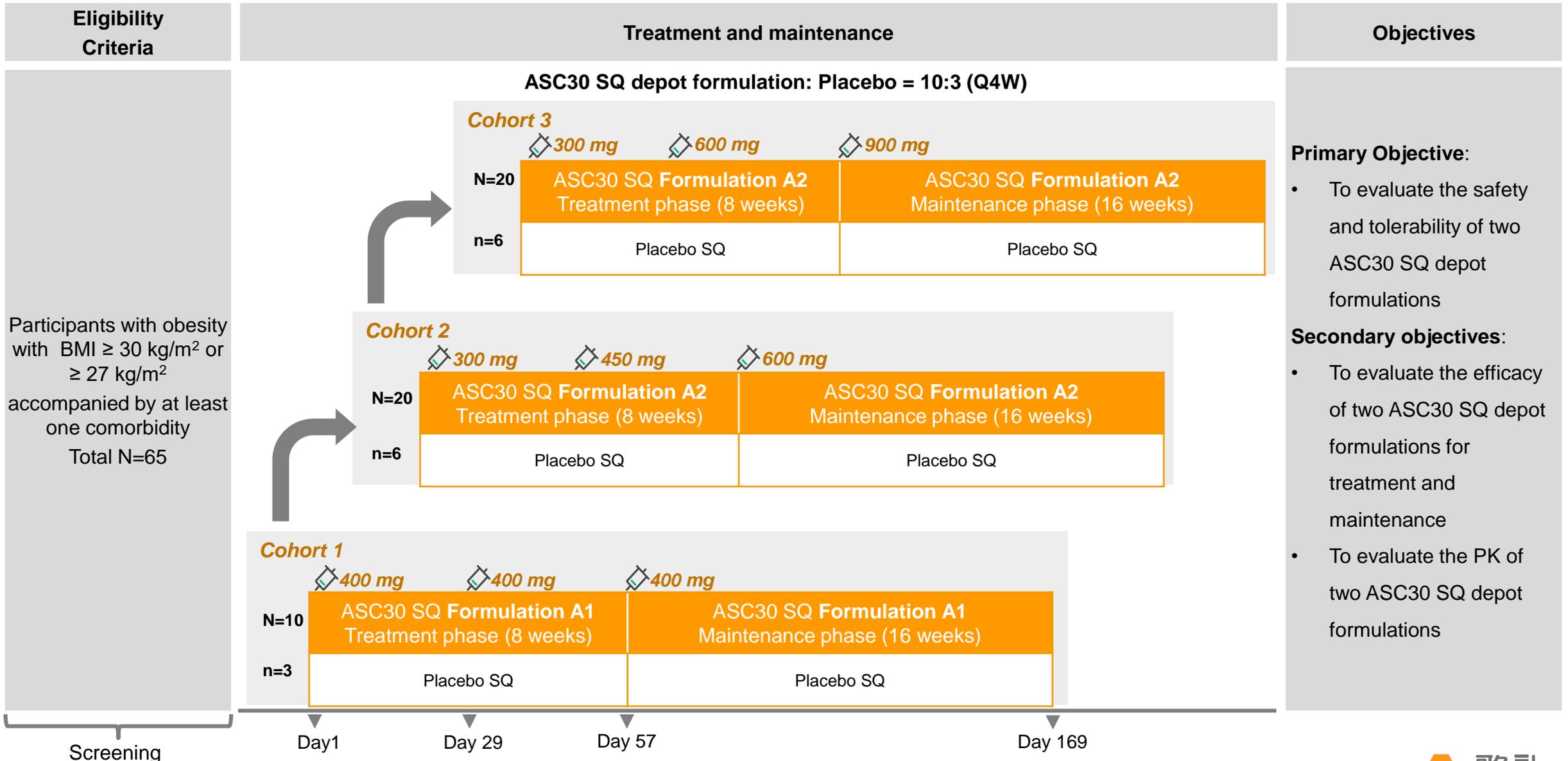
<sup>2</sup>Observed half-life

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

# ASC30 Treatment/Maintenance Formulation B: Excellent Tolerability

Category	ASC30 maintenance formulation 100 mg (N=8) n (%)	Placebo (N=16) n (%)
Number of participants reporting at least one AE	8 (100 %)	14 (87.5 %)
Number of participants reporting AEs by severity		
Grade 1	7 (87.5 %)	12 (75.0 %)
Grade 2	1 (12.5 %)	2 (12.5 %)
Grade 3	0 (0.0 %)	0 (0.0 %)
Grade 4	0 (0.0 %)	0 (0.0 %)
Number of participants reporting SAEs	0 (0.0 %)	0 (0.0 %)
Overall discontinuation	0 (0.0 %)	0 (0.0 %)
Common GI-related AEs		
Vomiting	0 (0.0 %)	0 (0.0 %)
Nausea	0 (0.0 %)	2 (12.5 %)
Diarrhea	1 (12.5 %)	1 (6.3 %)
Constipation	1 (12.5 %)	0 (0.0 %)
Abdominal pain	0 (0.0 %)	0 (0.0 %)

# U.S. Phase II, 24-Week Study for Ultra-Long-Acting Subcutaneous Depot Formulations of Small Molecule GLP-1R Agonist ASC30 for Obesity Treatment and Maintenance

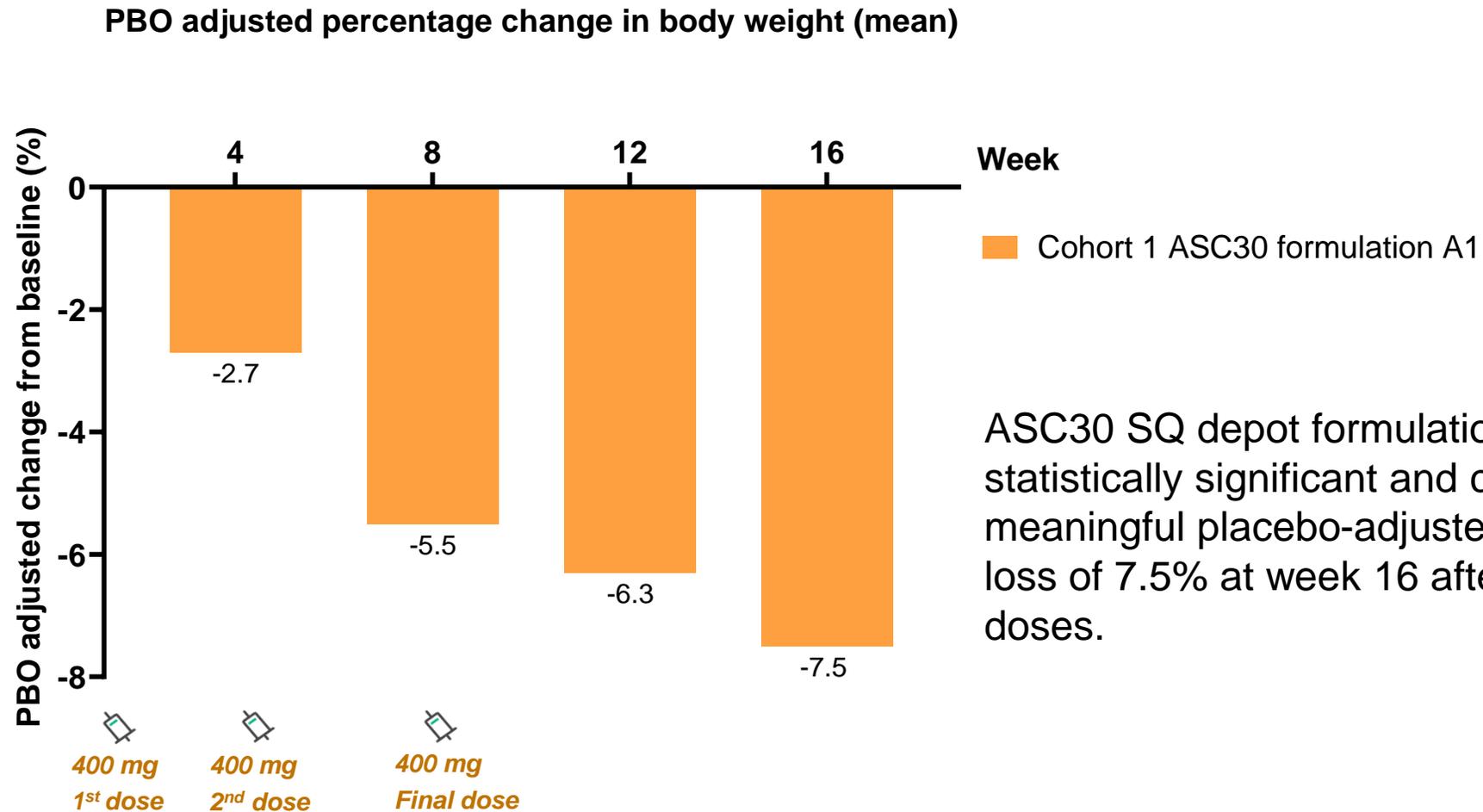


Q4W: once every four weeks

## Positive Topline Results from U.S. Phase II, 24-Week Study for Ultra-Long-Acting Subcutaneous Depot Formulations of ASC30 for Obesity Treatment and Maintenance

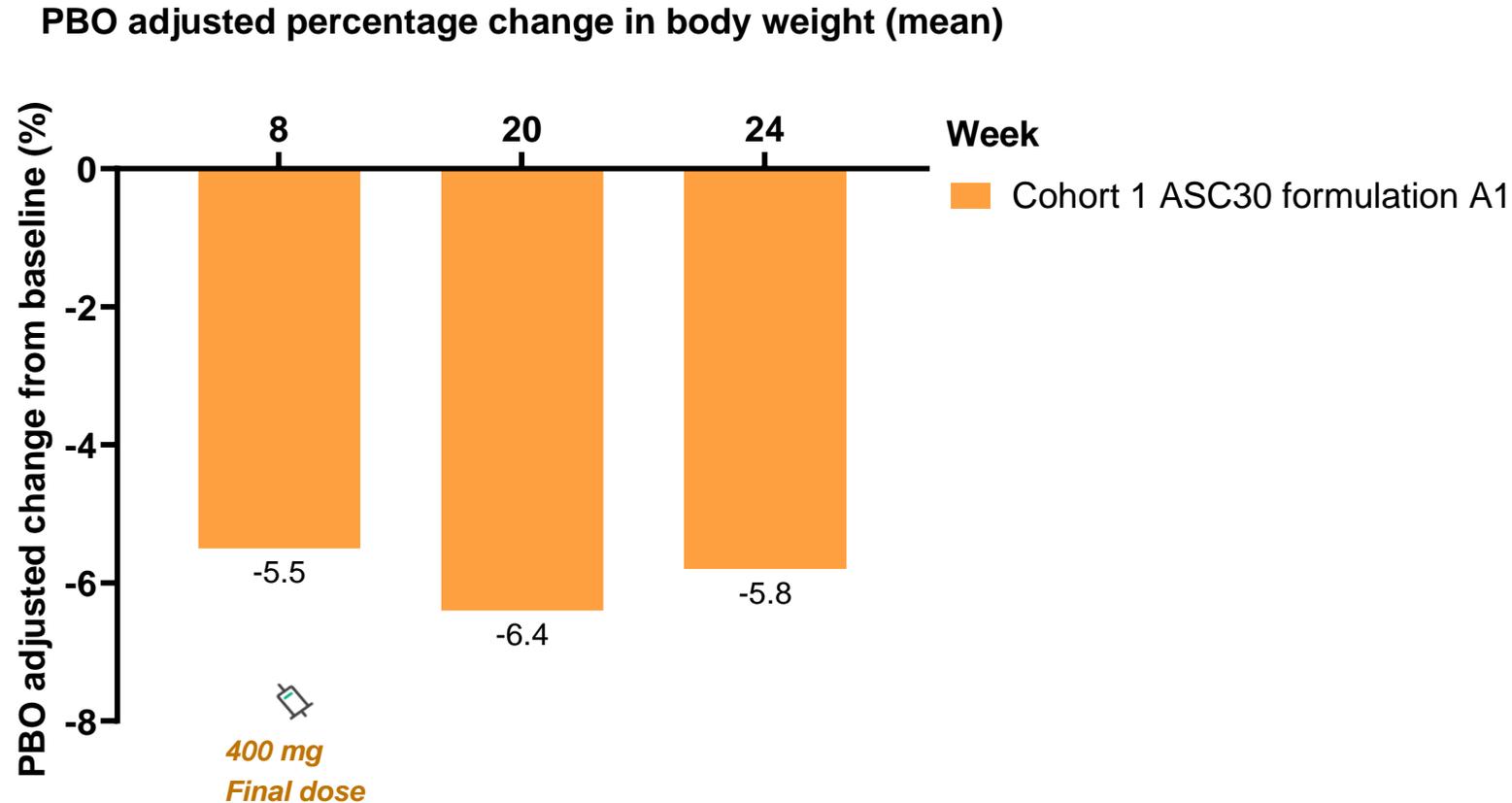
- ASC30 subcutaneous (SQ) depot formulation A1 achieved statistically significant and clinically meaningful placebo-adjusted mean weight loss of 7.5% at week 16 after three monthly doses.
- ASC30 SQ depot formulation A1 maintained weight loss for the four months following the third and final monthly dose, suggesting potential quarterly dosing as a maintenance therapy.
- ASC30 demonstrated a safety and tolerability profile consistent with the GLP-1 drug class.
- ASC30 SQ depot formulation A1 is the first GLP-1 to achieve drug class consistent weight loss with once-monthly injection without requiring lead-in weekly injections, and to maintain weight loss up to four months after the last dose.
- This competitive efficacy, combined with a well-tolerated safety profile of the long-acting formulation A1 of ASC30, reinforces our confidence in expanding clinical development program for both once-monthly treatment therapy and once-quarterly maintenance therapy.

ASC30 SQ depot formulation A1 can be dosed once monthly and potentially once every two months for the **treatment** of obesity without requiring a weekly lead-in dosing period



ASC30 SQ depot formulation A1 achieved statistically significant and clinically meaningful placebo-adjusted mean weight loss of 7.5% at week 16 after three monthly doses.

# ASC30 SQ depot formulation A1 has the potential to be an effective once-quarterly **maintenance** therapy for obesity



ASC30 SQ depot formulation A1 maintained weight loss for the four months following the third and final monthly dose of 400 mg

# ASC30 GLP-1: A Pipeline-in-a-Product

ASC30 GLP-1	Clinical Differentiation	Excellent GI Tolerability	Multiple Patient Types	Multiple Indications
Once-Daily oral tablet	Phase II superior weight loss and better GI tolerability vs. orforglipron	Half the vomiting rate of orforglipron	Afraid of injections	Obesity Diabetes MASH CVD
Once-Monthly SQ for treatment	46 to 75-Day observed $t_{1/2}$	Low GI side effects	Desire less frequent dosing for treatment	
Once-Quarterly SQ for maintenance	46 to 75-Day observed $t_{1/2}$	Low GI side effects	Desire less frequent dosing for maintenance	

# Oral Small Molecule Amylin Receptor Agonist ASC39 Demonstrated Eloralintide-like Amylin Selectivity and Efficacy in Preclinical Models

- In a head-to-head cyclic adenosine monophosphate (cAMP) activation assay vs. eloralintide, oral small molecule amylin receptor agonist ASC39 demonstrated similar selectivity and potency to that of eloralintide.  $EC_{50}$  for human amylin 1 receptor (hAMY1R) was 21.4 pM and 21.2 pM for ASC39 and eloralintide, respectively.  $EC_{50}$  for human calcitonin receptor (hCTR) was 846.1 pM and 1,350.8 pM for ASC39 and eloralintide, respectively. These data indicate ASC39 and eloralintide have similar selectivity for hAMY1R over hCTR.
- In a head-to-head diet-induced obese (DIO) rat study vs. eloralintide, efficacy of ASC39 oral dosing was comparable to that of eloralintide, demonstrating significant placebo adjusted weight loss of 6.6% and 5.6% for ASC39 and eloralintide, respectively.
- Submission of an Investigational New Drug Application (IND) to the U.S. Food and Drug Administration (FDA) for ASC39 oral tablets is expected in the third quarter of 2026.

Once-monthly peptides (observed  $t_{1/2} \geq 30$  days)  
(by proprietary depot-based technology - ULAP)

# Ascletis Strategy: once-monthly amylin receptor agonists as cornerstones (Observed $t_{1/2} \geq 30$ days)

## ■ ASC36 vs MET-233i

- *In vitro* activities against amylin and calcitonin receptors: consistent with MET-233i
- In NHP AUCs are 2-fold of MET-233i
- In NHP observed  $t_{1/2}$  in Ascletis ULAP proprietary formulation is 6-fold longer than MET-233i which has 19-day observed  $t_{1/2}$  in humans with its HALO technology
- Weight loss in DIO rats: consistent with MET-233i

## ■ Co-formulations developed with other once-monthly MOAs

- ASC36 (amylin) /ASC35 (GLP/GIP) co-formulation developed
- ASC36/ASC35 combo: 47% more weight loss than MET-233i/tirzepatide and 98% more weight loss than eloralintide/tirzepatide

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

# ASC36 and ASC35 have 6-fold longer $t_{1/2}$ than MET-233i and tirzepatide

Pharmacokinetic relationship between NHPs and humans is well established by multiple peptide agonists

	Tirzepatide GLP-1R/GIPR <sup>1</sup> (actual)		Semaglutide GLP-1R <sup>2</sup> (actual)		ASC36 amylin R		ASC35 GLP-1R/GIPR	
	NHP	Human	NHP	Human	NHP (actual)	Human (predicted)	NHP (actual)	Human (predicted)
Half-life (SQ injected)	56 h (2.3 days)	128 h (5.3 days)	54 h (2.3 days)	149 h (6.2 days)	32 days	74 days	14 days	32 days
Human to animal ratio	-	2.3 fold	-	2.8 fold	-	2.3 fold	-	2.3 fold

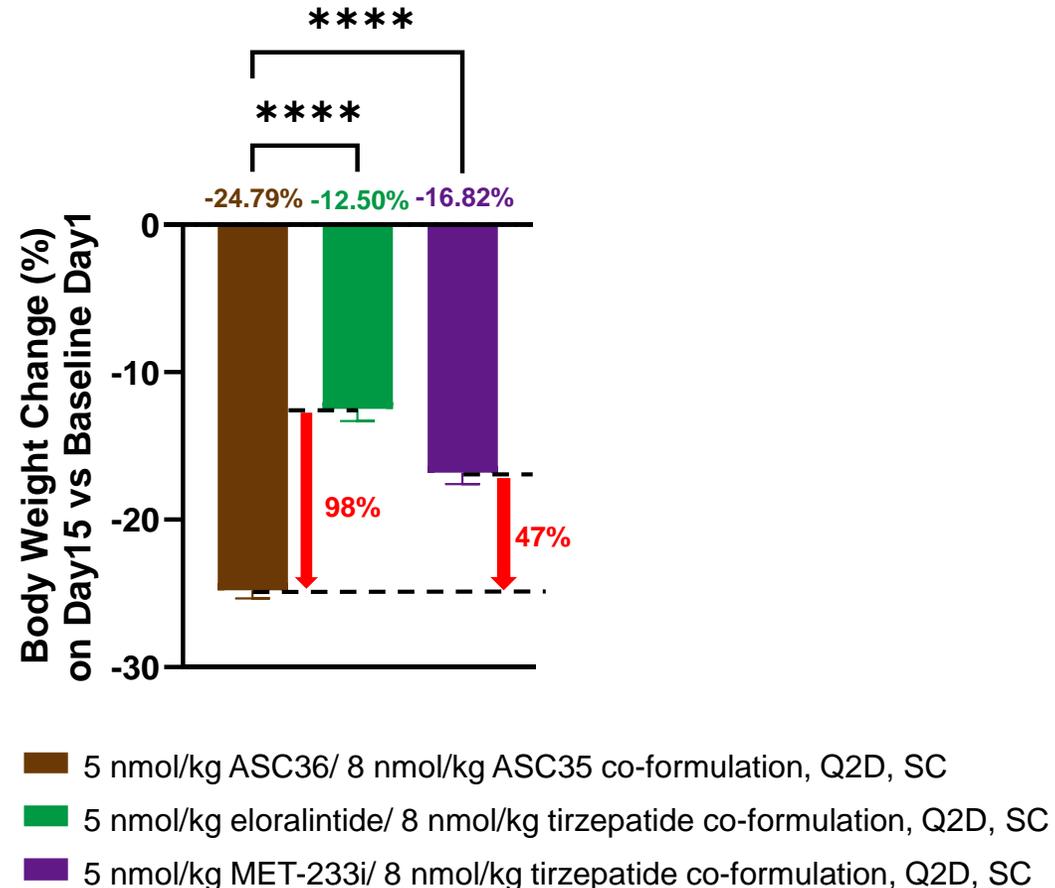
For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. The comparative data are extracted from the source indicated and has not been independently verified by the Company.

1. Jennifer A Martin et al, Absorption, distribution, metabolism, and excretion of tirzepatide in humans, rats, and monkeys, European Journal of Pharmaceutical Sciences 202 (2024) 106895,

<https://doi.org/10.1016/j.ejps.2024.106895>

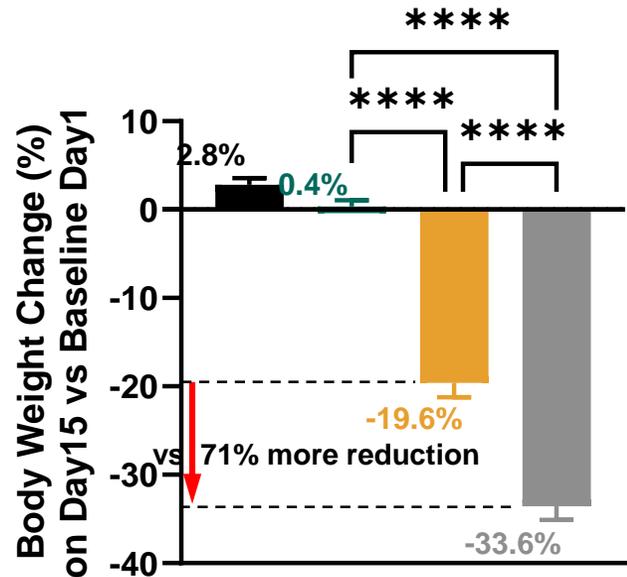
2. Semaglutide NDA package

# ASC36/ASC35 co-formulation demonstrated 98% more weight loss than eloralintide/ tirzepatide in DIO rat

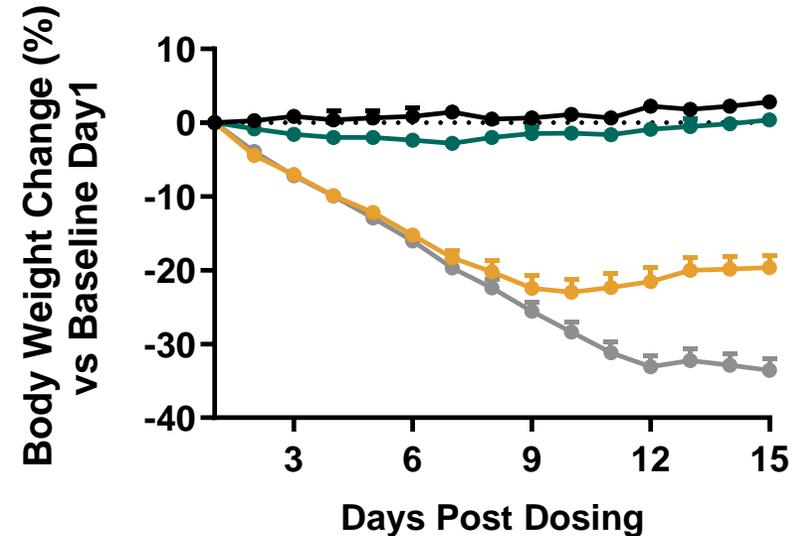


ASC36 monotherapy demonstrated 32% and 91% more weight loss than eloralintide and petrelintide in DIO rats

# ASC35 demonstrated approximately 71% greater relative body weight reduction compared to tirzepatide in a head-to-head diet-induced obese (DIO) mouse study



- Lean mice, Vehicle (SC, QD)
- DIO, Vehicle (SC, QD)
- DIO, Tirzepatide (3 nmol/kg, SC, QD)
- DIO, ASC35 (3 nmol/kg, SC, QD)



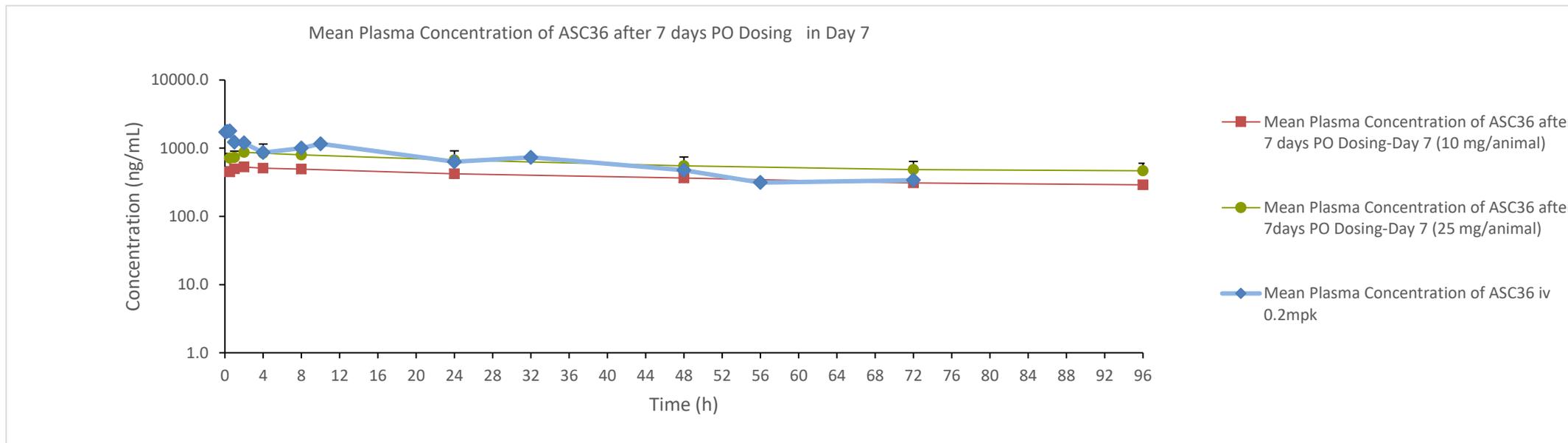
- Lean mice, Vehicle (SC, QD)
- DIO, Vehicle (SC, QD)
- DIO, Tirzepatide (3 nmol/kg, SC, QD)
- DIO, ASC35 (3 nmol/kg, SC, QD)

Note: One-way ANOVA test was used for multi-group univariate comparison. \*\*\*\*,  $p < 0.0001$ ;  $p < 0.05$  is considered statistically significant. GraphPad Prism 10 were used for data visualization. Data were presented as Mean  $\pm$  SEM, n=8.

# Peptide Oral Transport ENhancement Technology (POTENT)

- Impedes enzymatic degradation of peptides
- Increases gastrointestinal permeability of peptides
- Able to increase oral bioavailability of peptides to 3%-5% from <1%
- In NHPs, oral bioavailability of semaglutide in Ascleitis' POTENT formulation is 3-fold of oral bioavailability of semaglutide in FDA authorized SNAC formulation
- In NHPs, oral bioavailability of tirzepatide in Ascleitis' POTENT formulation is 9-fold of oral bioavailability of tirzepatide in SNAC formulation

# ASC36 oral tablets achieved absolute oral bioavailability of 6% to 8% at steady state, in NHP studies



## ASC36 pk summary after once-daily dosing for 7 days in monkeys

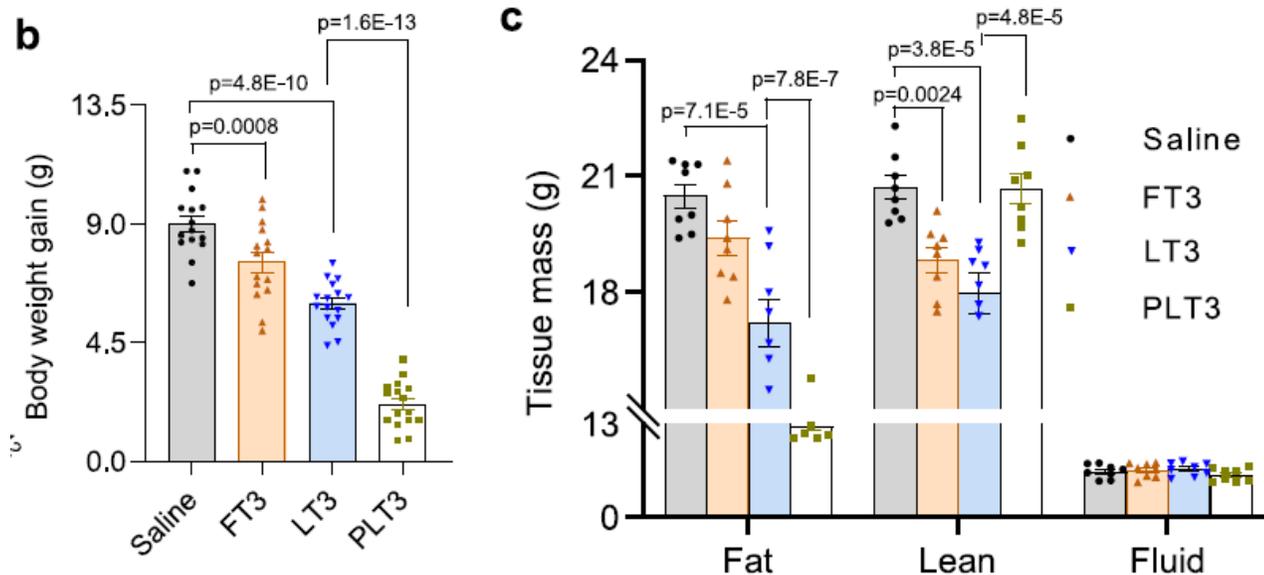
Group	Monkey	Administration	body weight (kg)	dose (mg/kg)	strength	AUC Inf (h*ng/mL)	AUC Inf (h*ng/mL) / (dose/bw)	F(%) (0-inf)	T <sub>1/2</sub> (h)
IV 0.2mpk	n=3	IV	2.7	0.2	/	60500	302698	100.0%	27.6
Oral after once-daily dosing for 7 days (10 mg ASC36 tablet)	n=3	PO	2.9	3.6	10 mg/tablet	85500	<b>24080</b>	<b>8%</b>	<b>116.0</b>
Oral after once-daily dosing for 7 days (25 mg ASC36 tablet)	n=3	PO	2.9	8.8	25 mg/tablet	161000	<b>18250</b>	<b>6%</b>	<b>167.0</b>

# ASC47 Adipose Targeted THR $\beta$ Once Monthly SQ

# Proof-of-Concept: Adipose-Targeted Triiodothyronine (T3) Therapy for Muscle-Preserving Weight Loss

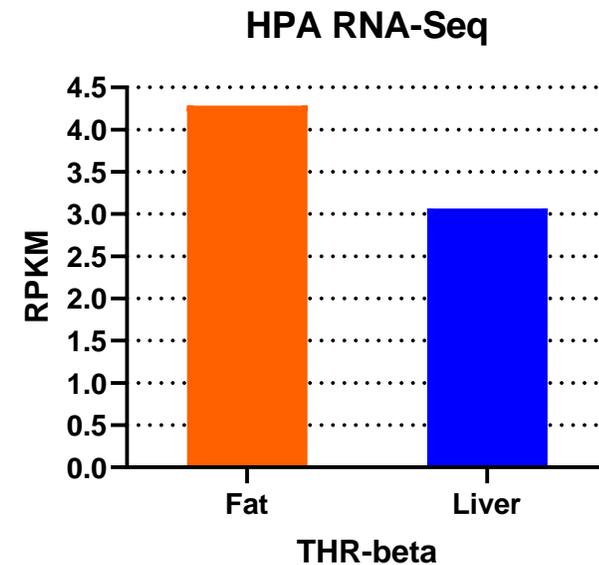
- Authors selectively delivered T3 to adipose tissues by *encapsulating T3 in liposomes modified with an adipose homing peptide (PLT3)*

- Mice treated with PLT3 are devoid of cardiac



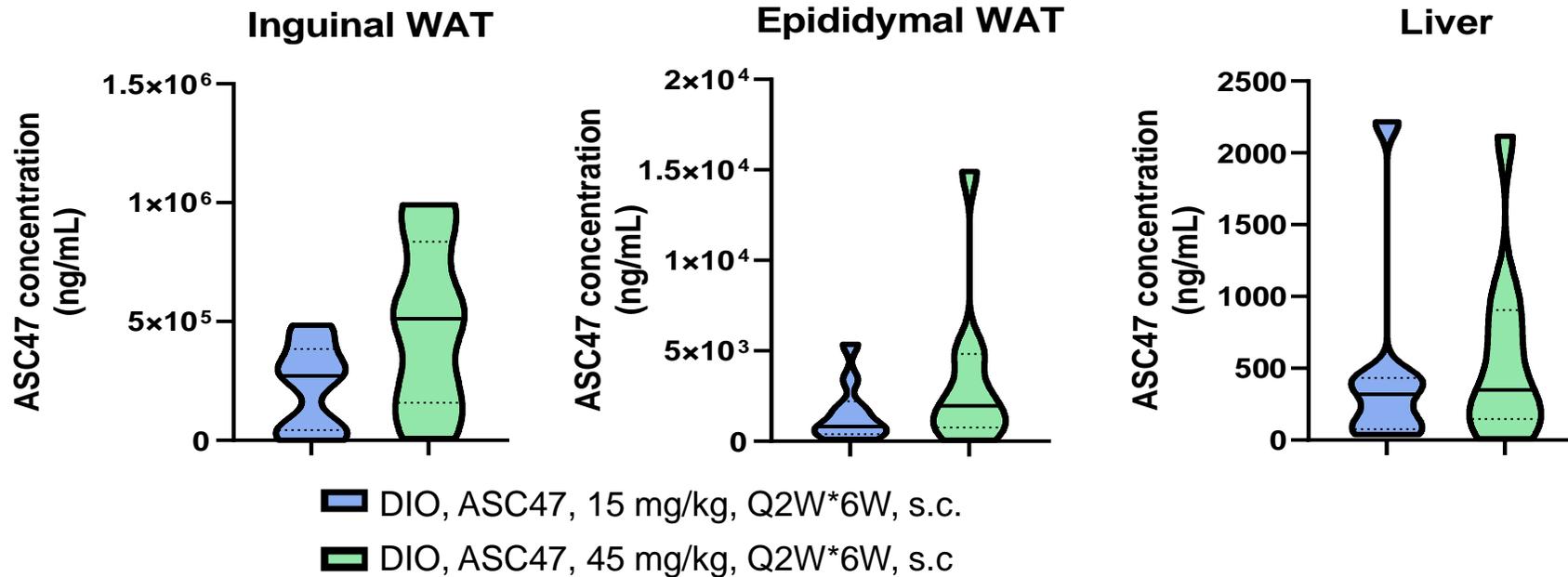
FT3: free T3;  
 LT3: T3-encapsulated liposomes without an adipose homing peptide;  
 PLT3: T3-encapsulated liposomes with an adipose homing peptide

THR-beta Highly Expressed in Human Adipose (fat) and Liver



<https://www.ncbi.nlm.nih.gov/gene/7068>

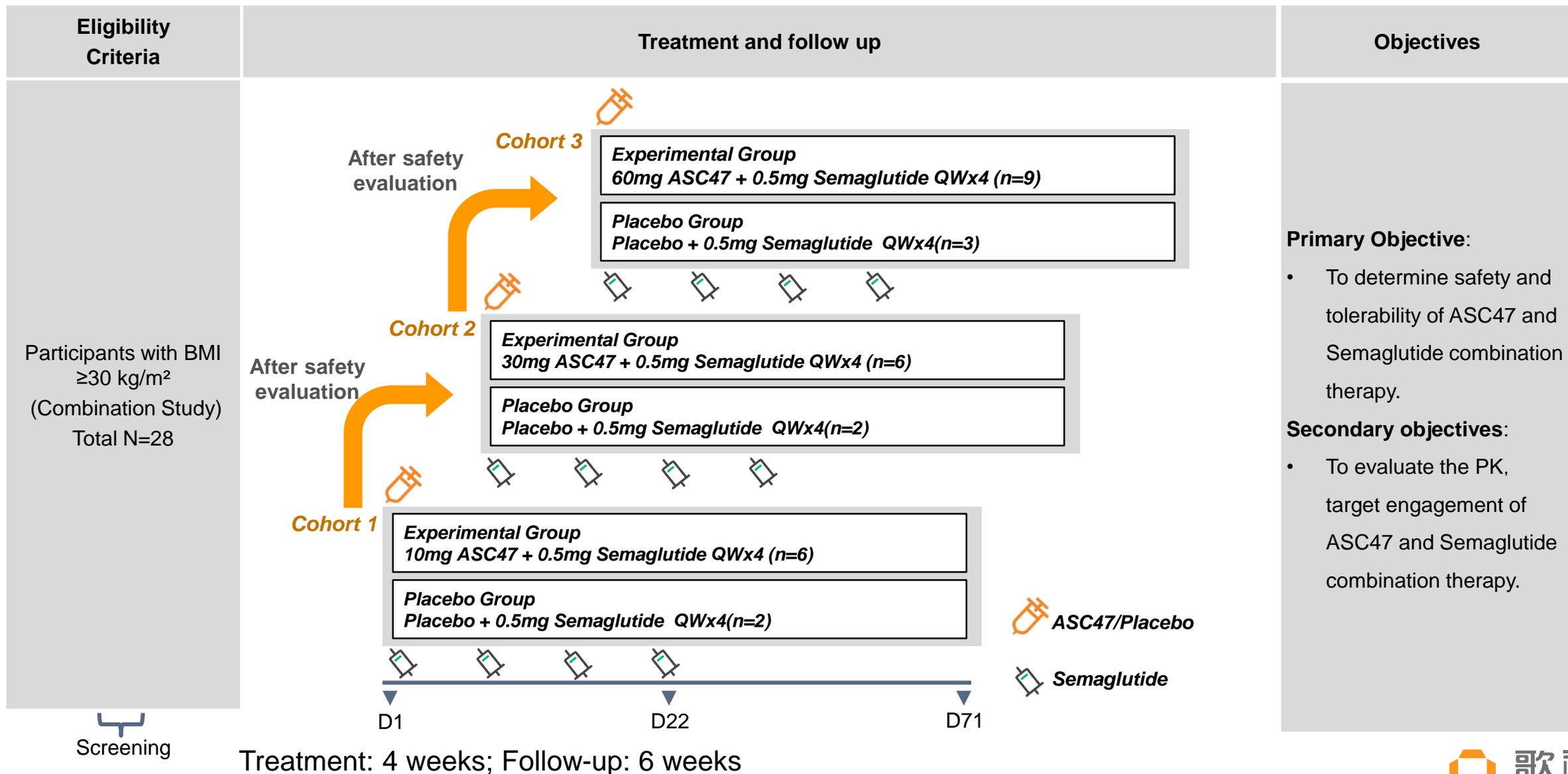
# ASC47 tissue distribution in DIO mice 2 weeks after SQ injection



Note:  
 1. The data were plotted as truncated violin plot (the black line was median).  
 2. N=10 in each group.

	ASC47 mean concentration (ng/g) (ASC47=15 mg/kg)	ASC47 mean concentration (ng/g) (ASC47=45 mg/kg)
Inguinal WAT	225,447	488,895
Epididymal WAT	1,545	3,384
Liver	487	585
Inguinal WAT to Liver Ratio	462.9	835.7
Epididymal WAT to Liver Ratio	3.2	5.8
Inguinal WAT to Epididymal WAT Ratio	145.9	144.5

# Single Dose ASC47 + 0.5mg Semaglutide in Obese Patients, U.S. Study



# ASC47 Significantly Increased the Efficacy of Semaglutide

- 30 mg ASC47 + semaglutide demonstrated 56.2% greater relative reduction in body weight in patients with obesity compared to semaglutide monotherapy
  - 60 mg ASC47 + semaglutide demonstrated 15.1% greater relative reduction in body weight in patients with obesity compared to semaglutide monotherapy
  - In a pooled patient analysis of 30 mg and 60 mg cohorts, ASC47 in combination with semaglutide demonstrated a 31.6% greater relative reduction in body weight compared to semaglutide monotherapy
- Human results were consistent with DIO mouse model, low dose ASC47 (3mg/kg, equivalent to 25 mg human dose) + semaglutide demonstrated **more** weight loss than high dose ASC47 (9 mg/kg, equivalent to 75 mg human dose) + semaglutide

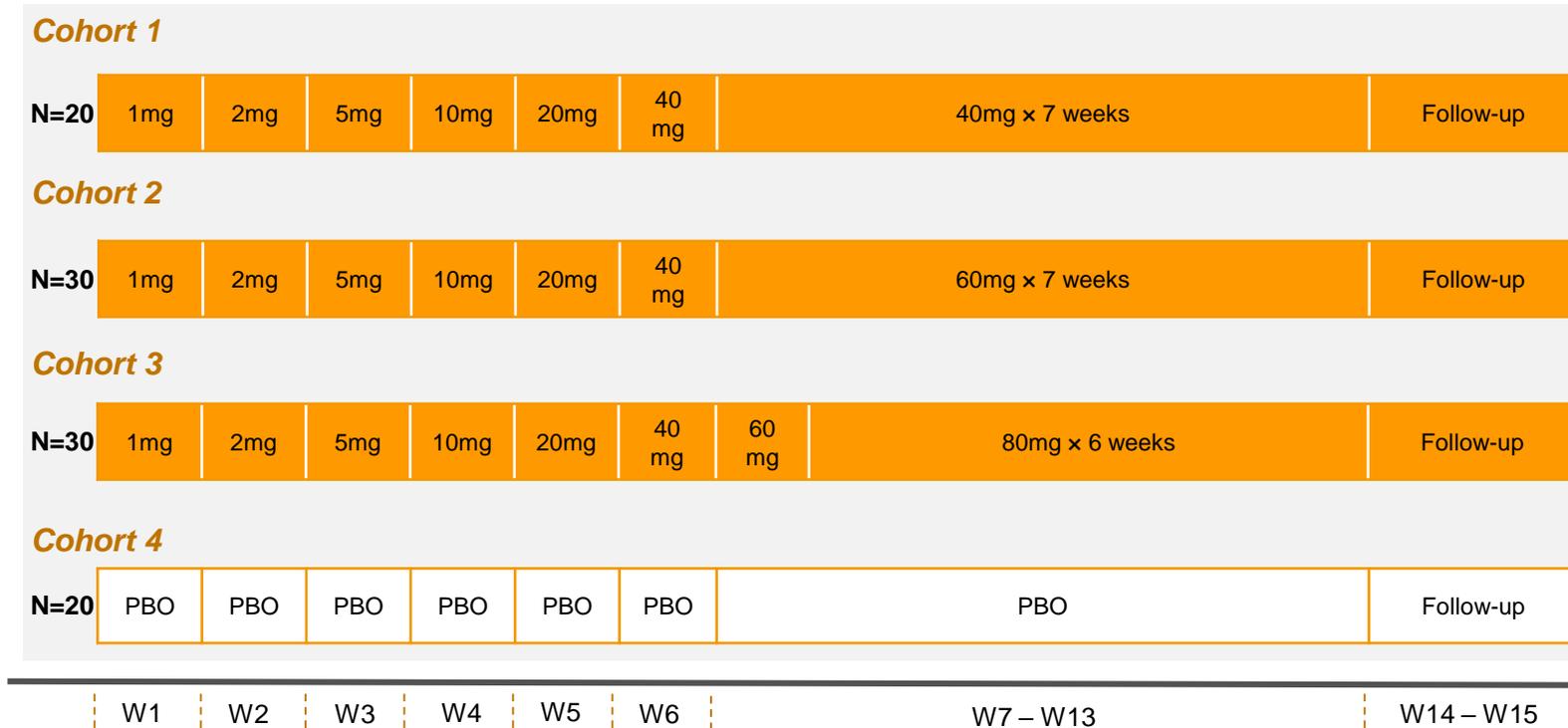
# ASC47 Significantly Improved the GI Tolerability of Semaglutide

Category	30 mg ASC47 + 0.5 mg semaglutide (N=6) n (%)	60 mg ASC47 +0.5 mg semaglutide (N=9) n (%)	30 mg/60 mg ASC47 + 0.5 mg semaglutide (N=15) n (%)	Placebo + 0.5 mg semaglutide (N=7) n (%)
Number of participants reporting at least one AE	6 (100.0%)	8 (88.9%)	14 (93.3%)	7 (100.0%)
Number of participants reporting SAEs	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Overall discontinuation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Number of participants reporting AEs by severity				
Grade 1	6 (100.0%)	4 (44.4%)	10 (66.6%)	6 (85.7%)
Grade 2	0 (0.0%)	4 (44.4%)	4 (26.7%)	1 (14.3%)
Grade 3	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Grade 4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Grade 5	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Common GI-related AEs				
Vomiting	<b>1 (16.7%)</b>	<b>0 (0.0%)</b>	<b>1 (6.7%)</b>	<b>4 (57.1%)</b>
Nausea	3 (50.0%)	1 (11.1%)	4 (26.7%)	3 (42.9%)
Diarrhea	0 (0.0%)	1 (11.1%)	1 (6.7%)	2 (28.6%)
Constipation	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Thyroid-related AEs				
Hypothyroidism	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Hyperthyroidism	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

ASC30 oral tablets once-daily for diabetes  
(Orforglipron-validated Chugai scaffold)

# ASC30-203: 13-Week Oral Phase II for diabetes at U.S. Sites

ASC30 tablets A1 : Placebo = 2:3:3:2 (QD)



- Enrollment began in January 2026.
- Primary endpoint: change from baseline in HbA1c up to 13 weeks.
- Secondary endpoints: (1) change from baseline in fasting blood glucose up to 13 weeks, (2) change from baseline in body weight up to 13 weeks and (3) safety and tolerability.
- Topline data are expected in the 3<sup>rd</sup> quarter of 2026.

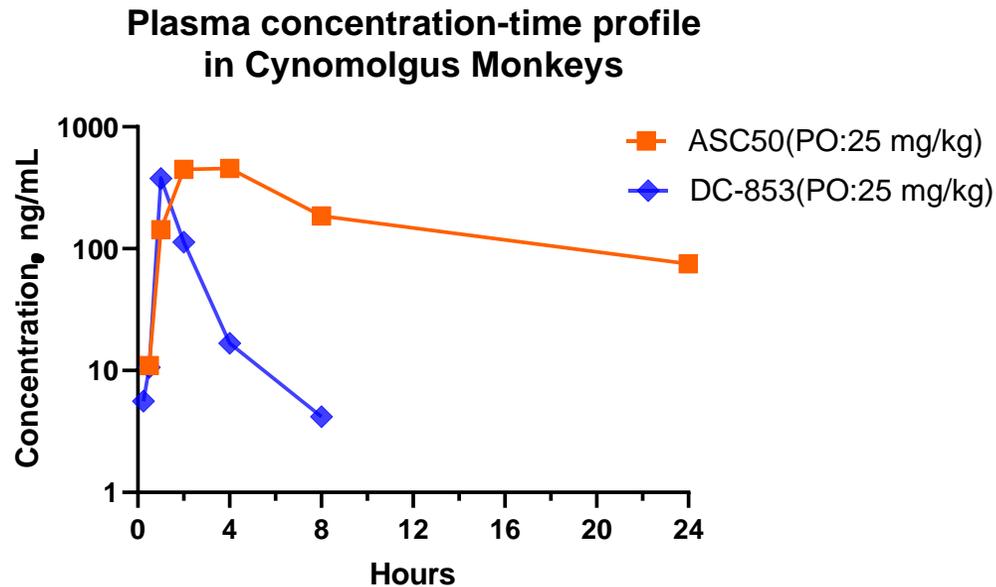
Immunology portfolio  
Oral small molecule IL-17 inhibitor: ASC50

# ASC50 Overview

- ASC50 is an in-house discovered novel scaffold vs LY4100511 (DC-853) oral small molecule IL-17 inhibitor for the treatment of auto-immune diseases
- Potentially best in class IL-17 oral small molecule inhibitor, supported by high oral exposure, a long half life and good efficacy in animals and humans
- Significantly better oral exposure, bioavailability
  - Oral exposure of ASC50 is 9 to 55-fold of DC-853 (phase 2 Lilly)
  - Oral bioavailability of ASC50 is 5 to 28-fold of DC-853
- Preclinical and clinical data support ASC50 as a once-daily low dose oral drug with potentially better efficacy vs. DC-853.
- Single Ascending Dose Phase I Clinical PK, PD (IL-17A) and safety data (10, 30 , 100, 200, 400, 600 mg) completed December 2025

# Pharmacokinetic (PK) profile of ASC50 and DC-853 in Cynomolgus Monkeys – Head-to-Head Study

## Oral exposure and bioavailability 9 and 5 fold of DC-853



	ASC50	DC-853
PK parameters	po: 25 mg/kg	po: 25 mg/kg
Cl/F, mL/min/kg	82.3	806.8
T <sub>1/2</sub> : h	8.7	1.40
T <sub>max</sub> : ng/mL	3.0	1.0
C <sub>max</sub> : ng/mL	493	376
AUC <sub>last</sub> : h*ng/mL	4,609	515
F :%	16.4	3.52

# ASC50 matches IL-17 Antibody Activity on IMQ-Induced Psoriasis Model in C57BL/6J Mice

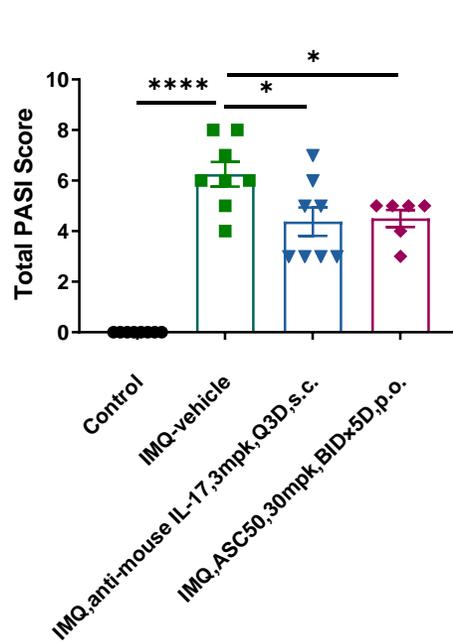


Figure 1. PASI Score of Dorsal Skin

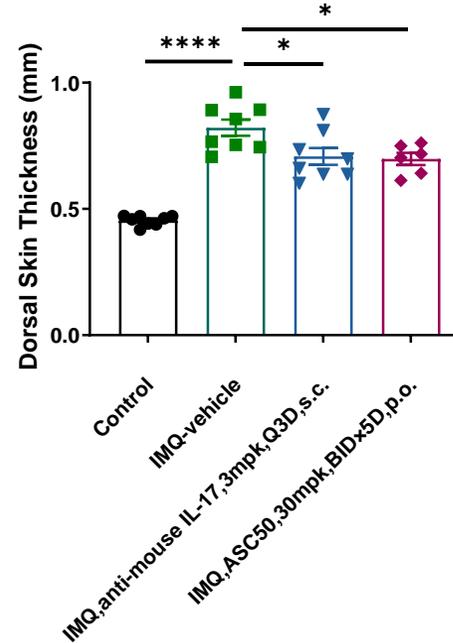


Figure 2. Dorsal Skin Thickness

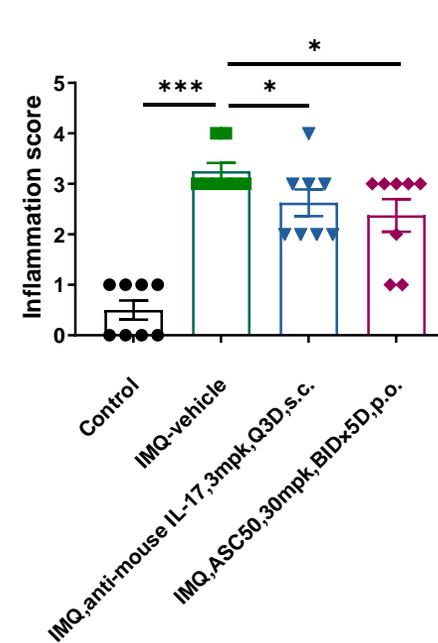


Figure 3. Inflammation Score

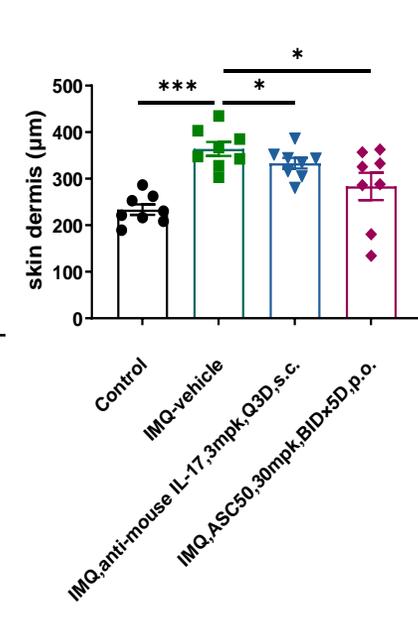


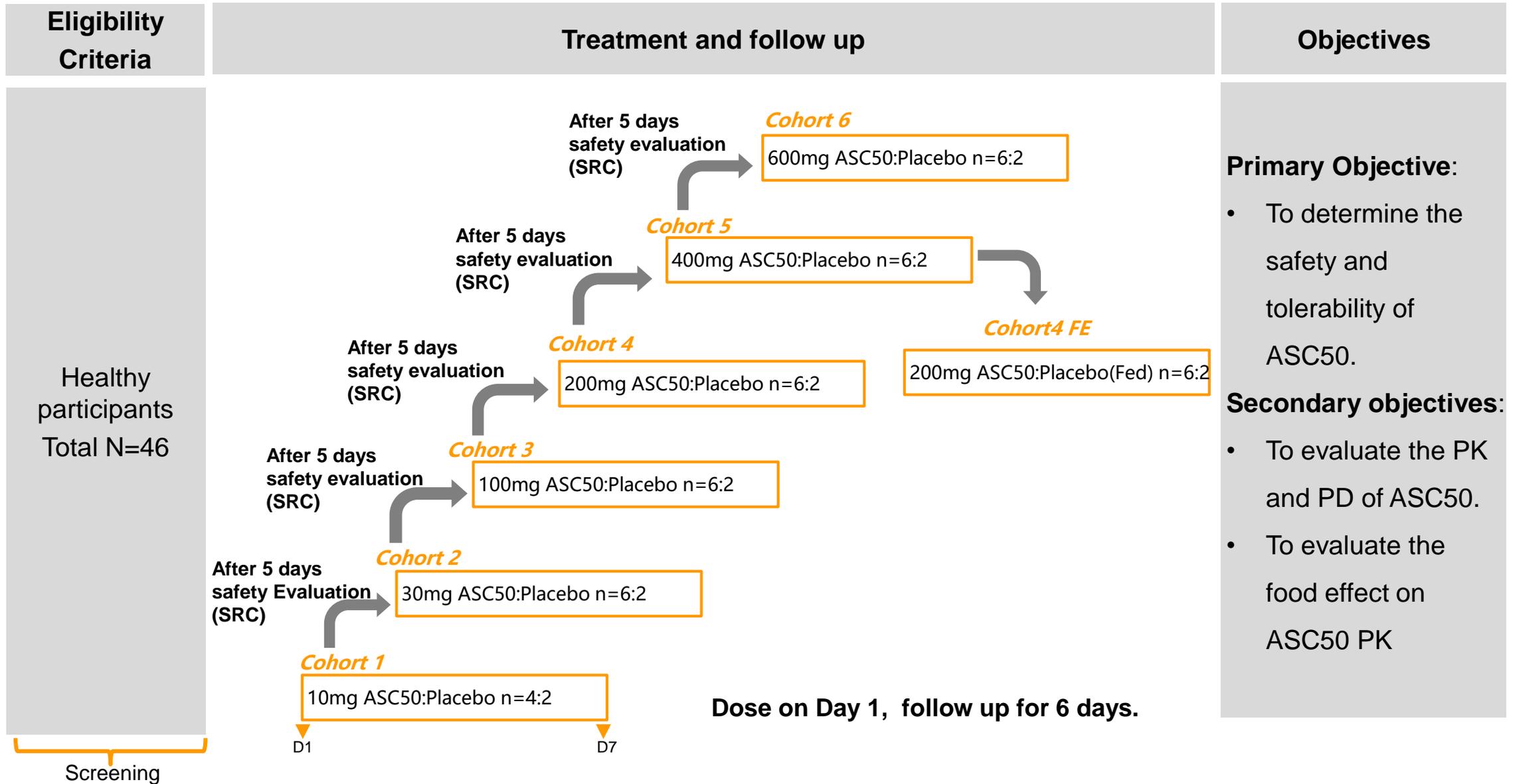
Figure 4. Skin Dermis Thickness (µm)

- ASC50 significantly decreased total PASI score of the dorsal skin on day 5 ( $P < 0.05$ ), significantly decreased dorsal skin thickness on day 5 ( $P < 0.05$ ), significantly decreased dorsal skin inflammation score and dermis thickness on day 5 ( $P < 0.05$ ).
- The data demonstrated that ASC50 can match the effect of an IL-17 monoclonal antibody<sup>1</sup> in an *in vivo* model of IL-17-driven inflammation.

<sup>1</sup> Cosentyx does not cross-react w/ mice IL-17, so a surrogate IL-17 monoclonal antibody with similar in vitro potencies against mouse IL-17 isoforms was used.

# ASC50 Phase I Clinical Study

# Part A: ASC50 Tablets Phase I Single Ascending Doses in US



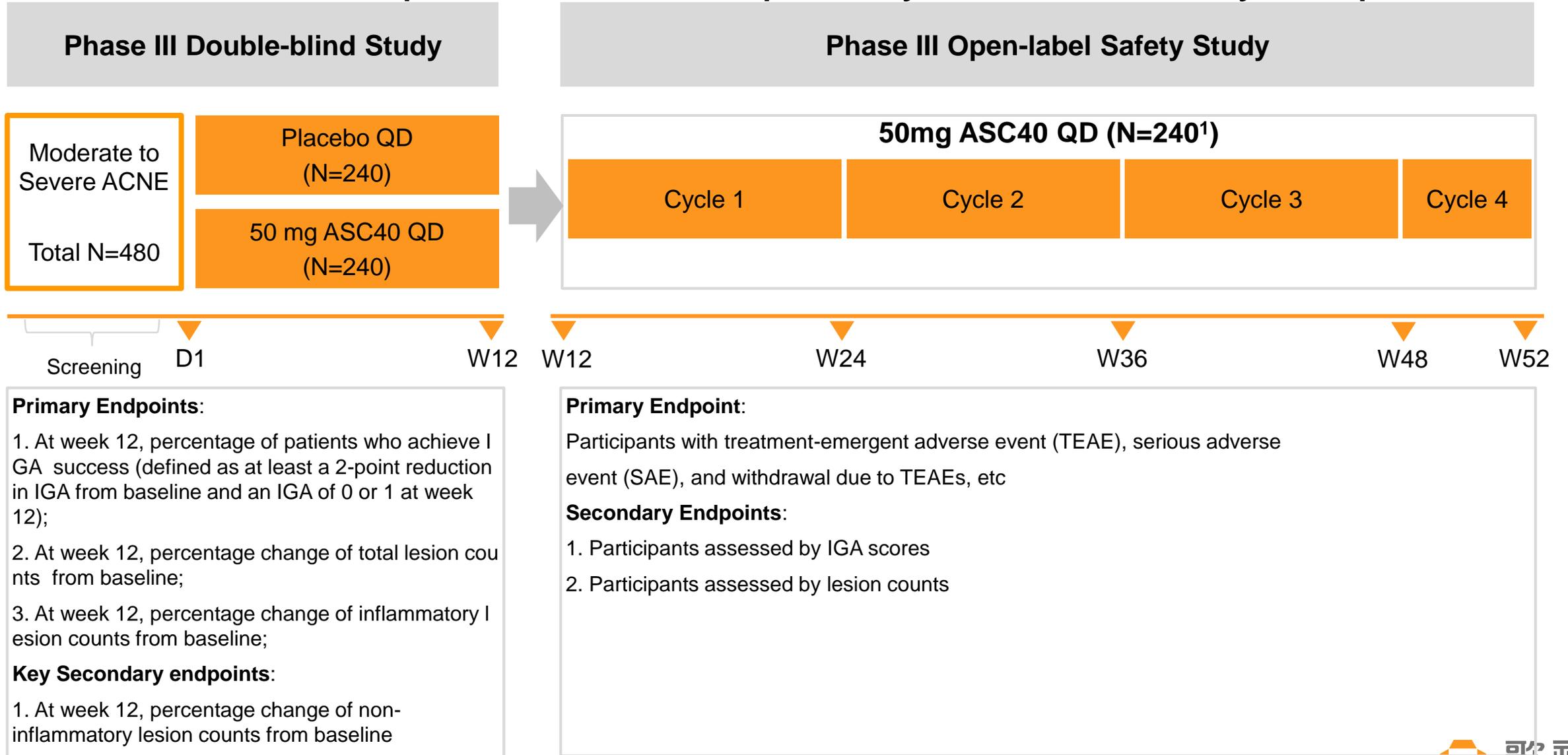
# ASC50 U.S. Phase I SAD study in healthy participants (Half-life up to 104 hours)

- **Elimination half-life** of ASC50 after a single oral dose was **43, 89, 91, 87, 104, and 85** hours for 10 mg, 30 mg, 100 mg, 200 mg, 400 mg, and 600 mg, respectively, supporting once-daily or potentially once-weekly oral dosing.
- ASC50 had strong target engagement after a single oral dose, indicated by elevated plasma IL-17A levels which continued until day 7 for higher doses of ASC50.
- ASC50 demonstrated a dose-proportional pharmacokinetic profile from 10 mg to 600 mg
- ASC50 was safe and well tolerated in the SAD study
  - All AEs were mild (Grade 1) and transient.
  - No SAEs were reported.
  - No discontinuation in the study.
  - No hepatic safety signal was detected.



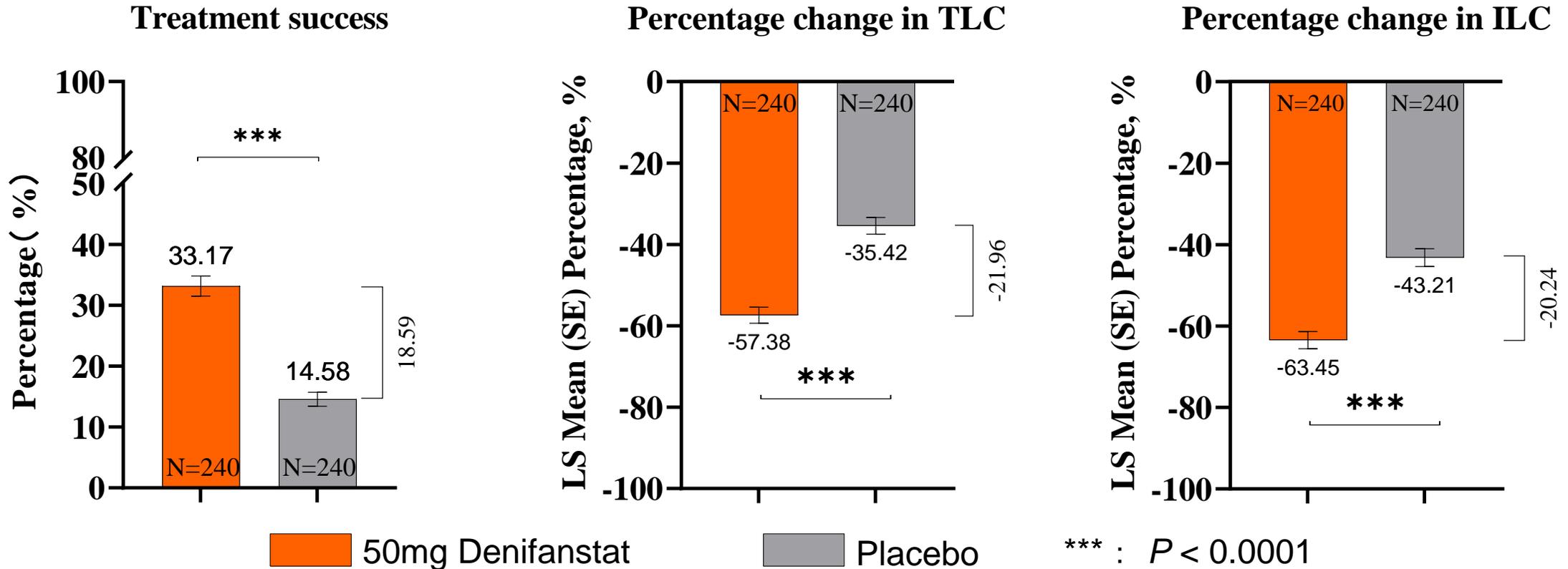
Exploratory indication  
First-in-class oral small molecule FASN inhibitor for  
acne:  
Denifanstat NDA accepted by China NMPA

# Denifanstat acne phase III met all primary and secondary endpoints



1. 240 patients from Phase III double-blind study

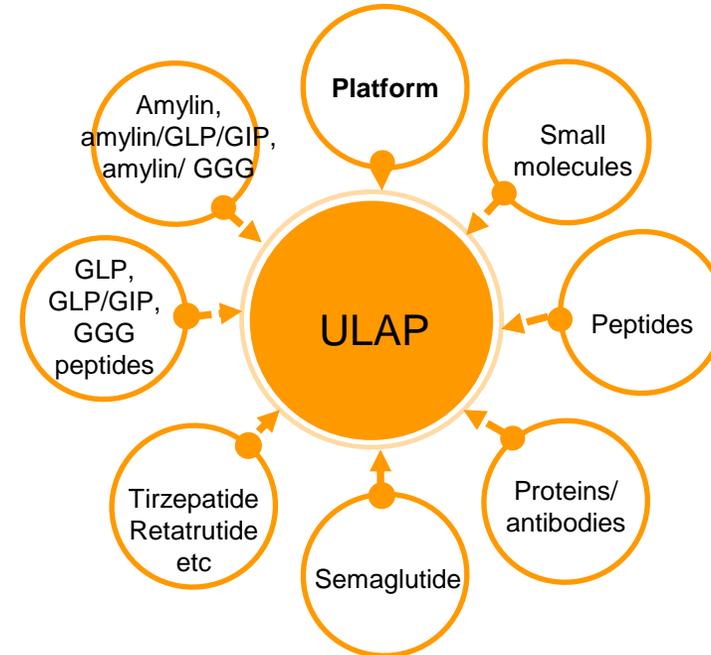
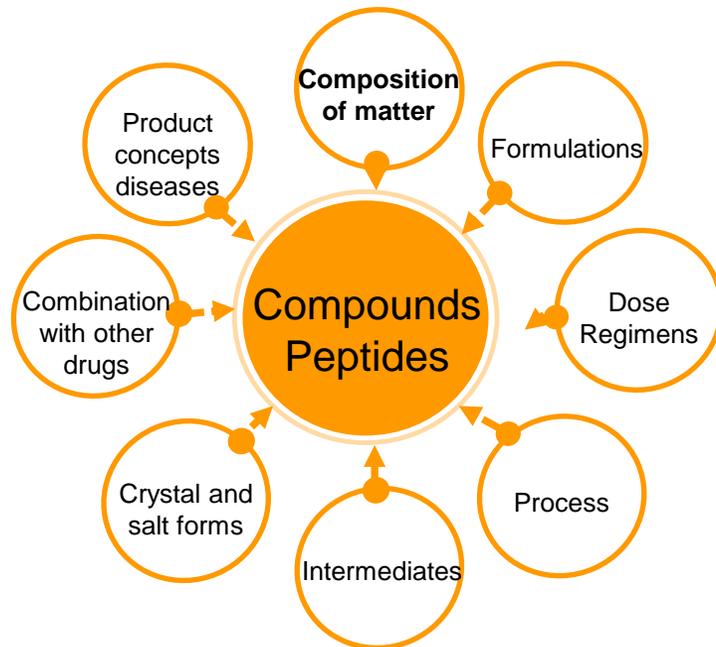
# Denifanstat met all primary efficacy endpoints (ITT analysis) and significantly improved moderate-to-severe acne compared with placebo



TLC: Total lesion count; NILC: Non inflammatory lesion count; ILC: Inflammatory lesion count; IGA: Investigator's global assessment; Treatment success:  $\geq 2$ -point reduction in IGA from baseline and an IGA of 0 or 1.

# Ascletis Portfolio: Multi-level Patent Protection

- ASC30 two composition of matter patents granted by USPTO (US12234236B1 & US12291530B1), protection until 2044, 2049 with extensions. Rest of world patent review pending
  - USPTO reviewed other patents or patent applications (such as Eli Lilly's and Hansoh's) published until end of April 2025 before granting Ascletis' patents
- ASC47 composition of matter patent pending Globally, protection until 2043, 2048 with extensions
- ASC35, ASC36, and ASC37 composition of matter patents filed, protection until 2045, 2050 with extensions
- ASC50 composition of matter patents filed, Protection until 2043, 2048
- Many patent applications filed globally covering formulations, synthetic processes, intermediates of synthetic processes, etc. for all compounds





# Thanks

Innovative cures liberate life to the fullest

