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Ascletis Metabolic Disease Portfolio

November 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[1]

- Hong Kong Stock Exchange listed biotech (1672.HK)
- Approximately 220 employees in discovery, clinical development, GMP manufacturing and administration
- **6 NMEs (3 small molecules and 3 peptides) and 15 assets. All clinical studies conducted in the U.S.**
- Sufficient cash on hand to support operations into 2029

1 Phase III in 2026 | 1 Phase II in 2026 | 9 Phase I in 2026

Best in Class/First in Class Small Molecule Programs

- **Phase III Oral small molecule GLP-1R agonist**
- **Oral small molecule amylin-selective agonist**
- Oral small molecule GIPR agonist
- GLP-1/GIP/amylin FDC
- GLP-1/GIP FDC

Next Generation Ultra-Long-Acting SQ peptides-observed $t_{1/2} \geq$ 30days

- Monthly/quarterly SQ **amylin** RA
- Monthly/quarterly SQ **amylin** + GLP-1/GIP FDC
- Monthly/quarterly SQ GLP-1/GIP RA
- Monthly/quarterly SQ triple G RA
- Monthly/quarterly SQ **amylin**+GGG FDC

Enhanced Oral Bioavailability Oral Peptides

- Weekly oral **amylin** RA
- Weekly oral **amylin** + GLP-1/GIP FDC
- Weekly oral GLP-1/GIP RA
- Weekly oral triple G RA
- Weekly oral **amylin** + GGG FDC

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.

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Metabolic Diseases – Oral Small Molecules

Product (Modality)	Target	Indication	Commercial Rights	Discovery	IND Enabling	Phase I	Phase II	Phase III	Topline data and Est. Next Milestone
ASC30 (Oral small molecule agonist)	GLP-1R	Obesity	Global						• Initiated global Phase III for ASC30 to enroll 4,600 people in U.S. and EU • Topline data expected in 3Q2028 • FDA NDA filing expected 2028 end
ASC30 (Oral small molecule agonist)	GLP-1R	Diabetes	Global						• U.S. Ph II data showed PBO-adjusted A1c reduction of 1.7% from baseline in diabetic patients at 12 weeks • Zero discontinuations due to GI AEs
ASC30_48 FDC (Oral small molecule dual agonist)	GLP-1R/GIPR	Obesity	Global						• FIC one-pill once-daily GLP-1/GIP dual agonist • 52% greater relative efficacy vs ASC30 • FDA IND filing 4Q2026
ASC30_48_39 FDC (Oral small molecule triple agonist)	GLP-1R/GIPR/ amylin receptor SARA	Obesity	Global						• FIC one-pill once-daily triple agonist • 120% greater relative efficacy vs oral dual agonist ASC30_39FDC • FDA IND filing 4Q2026
ASC39 (Oral small molecule agonist)	Amylin receptor SARA	Obesity	Global						• FIC oral small molecule SARA with eloralintide-like selectivity and efficacy • FDA IND filed and U.S. Ph I to be initiated Dec 2026
ASC30_39 FDC (Oral small molecule dual agonist)	GLP-1R/ amylin receptor SARA	Obesity	Global						• FIC one-pill once-daily GLP-1/SARA dual agonist • FDA IND filing 4Q2026

FDC: fixed-dose combination; SARA: selective amylin receptor agonist

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Metabolic Diseases - Once Monthly to Once-Quarterly Injectable Peptides

Product (Modality)	Target	Indication	Commercial Rights	Discovery	IND Enabling	Phase I	Phase II	Phase III	Topline data and Est. Next Milestone
ASC36i (Subcutaneous peptide agonist)	Amylin receptor	Obesity	Global						• Injectable lipid depot formulation has 6-fold half-life of eloralintide and MET-233i in NHP • 32% and 91% greater relative efficacy in DIO rats vs eloralintide and petrelintide • U.S. Phase I PK topline data expected at end of 2026
ASC36_35i FDC (Subcutaneous triple peptide agonist)	Amylin + GLP-1R/GIPR	Obesity	Global						• Injectable lipid depot formulation • 51% greater relative efficacy in DIO rats vs eloralintide + tirzepatide • U.S. Phase I PK topline data expected at end of 2026
ASC35i (Subcutaneous dual peptide agonist)	GLP-1R/GIPR	Obesity	Global						• Injectable lipid depot formulation has half-life 6-fold longer than tirzepatide in NHP • 71% greater relative efficacy in DIO mice vs tirzepatide • U.S. Phase I PK topline data expected at end of 2026
ASC37i (Subcutaneous triple peptide agonist)	GLP-1R/ GIPR/GCGR	Obesity	Global						• Injectable lipid depot formulation has half-life 7-fold longer than retatrutide in NHP • 88% greater relative WL in DIO mice vs TZP • FDA IND filed and U.S. Ph I to be initiated Dec 2026
ASC36_37i FDC (Subcutaneous quadruple peptide agonist)	Amylin + GLP-1R /GIPR/ GCGR	Obesity	Global						• Injectable lipid depot formulation • 69% greater relative efficacy in DIO rats vs ASC37 monotherapy • FDA IND filed and U.S. Ph I to be initiated Dec 2026

Both ASC35 and ASC37 were engineered to have 41 alpha amino acids, which qualifies them as biologics

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Metabolic Diseases - Once-Weekly Oral Peptides

Product (Modality)	Target	Indication	Commercial Rights	Discovery	IND Enabling	Phase I	Phase II	Phase III	Topline data and Est. Next Milestone
ASC36o (Oral peptide agonist)	Amylin receptor	Obesity	Global						• Tablet formulation half-life up to 7 days at steady state in non-human primate (NHP) • Oral bioavailability of 6% to 8% at steady state in NHP • U.S. Phase I PK topline data expected at end of 2026
ASC36_37o FDC (Oral quadruple peptide agonist)	Amylin + GLP-1R /GIPR/ GCGR	Obesity	Global						• Tablet formulation half-life up to 8.3 days for ASC36 and 4 days for ASC37 at steady state in NHP • Oral bioavailability of >10% for ASC36 and ≥ 9.1% for ASC37 at steady state in NHP • FDA IND submission 4Q2026
ASC36_35o FDC (Oral triple peptide agonist)	Amylin + GLP-1R/GIPR	Obesity	Global						• Tablet formulation half-life up to 8.8 days for ASC36 and 6.6 days for ASC35 at steady state in NHP • Oral bioavailability of ≥ 10% for ASC36 and ≥9.3% for ASC35 at steady state in NHP • FDA IND submission 4Q2026
ASC37o (Oral triple peptide agonist)	GLP-1R/ GIPR/GCGR	Obesity	Global						• Tablet formulation half-life up to 3.3 days at steady state in NHP • Oral bioavailability of 3.5% to 7.9% at steady state in NHP • FDA IND submission 4Q2026
ASC35o (Oral dual peptide agonist)	GLP-1R/GIPR	Obesity	Global						• Tablet formulation half-life 3.5 days in NHP • Oral bioavailability similar to ASC37o • FDA IND submission 4Q2026

Both ASC35 and ASC37 were engineered to have 41 alpha amino acids, which qualifies them as biologics

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Ascletis Obesity Portfolio - Small Molecules

Competitor	Ascletis	Ascletis Differentiation	Ascletis Development Status
Orforglipron (oral small molecule GLP-1)	ASC30 (oral small molecule GLP-1)	• Better GI tolerability to orforglipron • 15% weight loss (model-predicted) at week 72 vs 11.5% for orforglipron	Initiated global Phase III to enroll 4,600 people in U.S. and EU Topline data expected 3Q2028 FDA NDA filing expected end'28
	ASC30_48FDC (Oral small molecule GLP-1/GIP)	• First-in-class oral small molecule GLP-1/GIP dual agonist • 10.5% weight loss in non-human primates, 52% greater relative weight loss vs ASC30 monotherapy	FDA IND Filing 4Q2026
	ASC30_48_39FDC (oral small molecule GLP-1/GIP/amylin SARA)	• First-in-class oral small molecule GLP-1/GIP triple agonist • 15.2% weight loss in non-human primates, 120% greater relative weight loss vs ASC30_39FDC dual agonist	FDA IND Filing 4Q2026
ACCG-2671 (oral small molecule amylin DACRA)	ASC39 (oral small molecule amylin SARA)	• First-in-class amylin-selective oral small molecule agonist	FDA IND filed and U.S. Ph I to be initiated Dec 2026
Aleniglipron + ACCG-2671 (oral small molecule GLP-1/amylin DACRA, early preclinical stage)	ASC30_39FDC (oral small molecule GLP-1/amylin SARA)	• First-in-class GLP-1/amylin-selective oral small molecule dual agonist	FDA IND Filing 4Q2026

SARA: Selective amylin receptor agonist; DACRA: Dual amylin and calcitonin receptor agonist

Data Source: Pipeline information retrieved from official Eli Lilly and Structure Therapeutics websites.

Ascletis Obesity Portfolio - Injectable and Oral Peptides

Competitor	Ascletis	Ascletis Differentiation	Ascletis Development Status
Tirzepatide (SQ peptide GLP-1/GIP)	ASC35i (SQ peptide GLP-1/GIP)	• Once monthly to once-quarterly vs Lilly once weekly	U.S. Phase I Topline Ph I PK data end-2026
Eloralintide and Tirzepatide (amylin+GLP-1/GIP; four SQ injections per month)	ASC36_35i FDC (amylin+GLP-1/GIP; SQ injection)	• Once monthly to once-quarterly co-formulation	U.S. Phase I Topline Ph I PK data end-2026
	ASC36_37i FDC (amylin+GGG; SQ injection)	• Once monthly to once-quarterly co-formulation	FDA IND filed and U.S. Ph I to be initiated Dec 2026
Eloralintide (SQ peptide amylin, four injections per month)	ASC36i (SQ peptide amylin)	• Once monthly to once quarterly vs Lilly once weekly	U.S. Phase I Topline Ph I PK data end-2026
	ASC36o (oral peptide amylin)	• 10mg oral dose/week	U.S. Phase I Topline Ph I PK data end-2026
Retatrutide (SQ peptide triple G; four injection per monthly)	ASC37i (SQ peptide triple G)	• Once monthly to once quarterly vs Lilly once weekly	FDA IND filed and U.S. Ph I to be initiated Dec 2026
LY4086940 (oral peptide triple G)	ASC36_37o FDC (oral peptide amylin+ GGG)	• 25mg oral dose/week	FDA IND Filing 4Q2026

Data Source: Pipeline information retrieved from official Eli Lilly website.

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Oral Small Molecule GLP-1 ASC30 Global Phase III Studies Initiated

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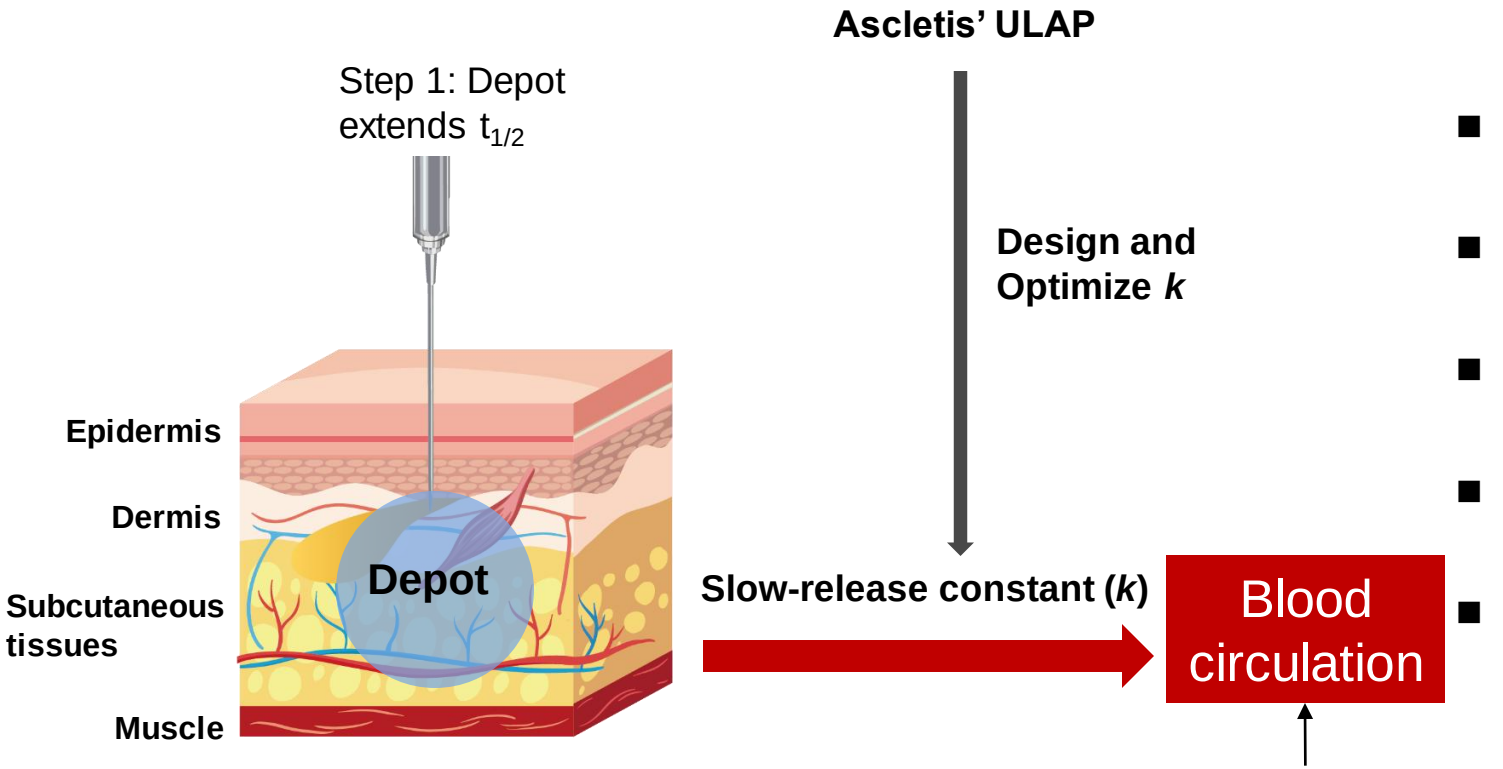
Two Global Phase III Studies for Oral SM GLP-1 ASC30 Initiated

- Two pivotal global Phase III trials (AURORA-1 NCT07743463 and AURORA-2 NCT07743450) will enroll approximately 4,600 participants with obesity or overweight in the U.S., Europe, and Canada.
- Topline data from the ASC30 Phase III program expected in the third quarter of 2028.
- U.S. FDA New Drug Application (NDA) filing expected by the end of 2028 and EMA Marketing Authorisation Application (MAA) filing expected in early 2029.
- If approved by the respective regulatory authorities, ASC30 is potentially the second oral small molecule GLP-1 approved in the U.S. and Europe after orforglipron.

Ascletis’ Ultra-Long-Acting Platform (ULAP) Technology for Once-Monthly to Once-Quarterly Peptides

Ultra-Long-Acting Platform (ULAP) Technology Validated Clinically and Commercially (ULAP extends $t_{1/2}$ by multiple fold beyond albumin-based $t_{1/2}$ extension technology)

- ULAP technology suitable for small molecules, peptides, antibodies, and proteins
- Proprietary depot-based technology[1] allows continued optimization of release constant (*k*) to achieve half-lives ≥ 30 days, supporting once-monthly and greater dosing intervals
- Albumin technology limited to 20 day half-life of albumin



Current Achievements and Validations

- Small Molecule GLP-1RA SQ: Half-life 46 days and 75 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 NHPs
- Peptide (amylin receptor) SQ: Half life ~6-fold longer than MET-233i in NHPs
- Peptide (GLP-1R/GIPR/GCGR) SQ: Half life ~7-fold longer than retatrutide in NHPs

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

Modified from www.nature.com/scientificreports | 7: 9613 | DOI:10.1038/s41598-017-10110-w

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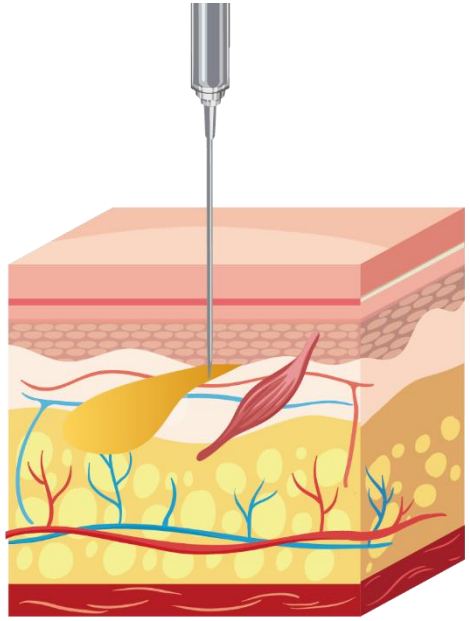
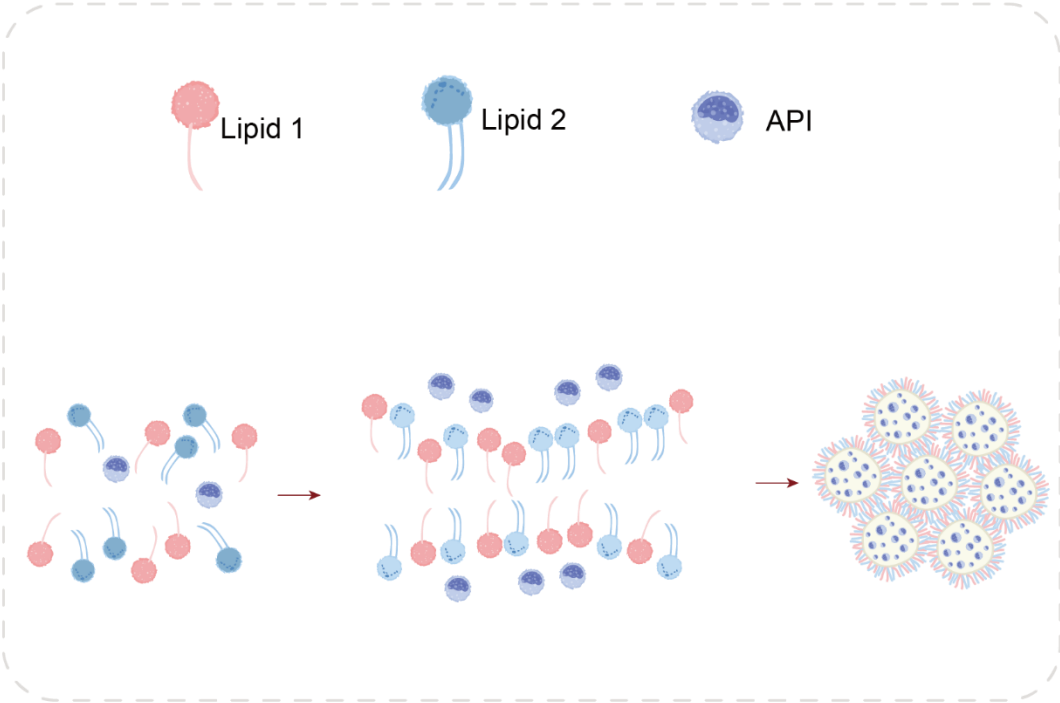
Lipid-Based Depot: Self-Assembling Lipid Depot (SALD)





- 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 a longer period.

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Monthly/Quarterly Formulation Screening and Selection Strategy and Criteria

- Use Ascletis' ULAP technology to design a lot of formulations

- All ULAP-designed formulations were screened in monkeys since we trust monkey PK data and SQ monkey $t_{1/2}$ to SQ human $t_{1/2}$ relationship is well established by SQ semaglutide and tirzepatide
  - Such formulation screening strategy is more expensive and time-consuming than conventional *in vitro/in vivo* screening plus modeling strategy → we trust monkey PK data more than anything else

- Clinical monthly/quarterly formulation selection key criteria
  - Monkey $t_{1/2}$ in Ascletis' monthly/quarterly formulations must be ≥ 5 to 6-fold of monkey $t_{1/2}$ for tirzepatide, eloralintide, MET-233i and retatrutide
  - Bioavailability of monthly/quarterly formulations in monkeys must be consistent with bioavailability of SQ semaglutide and tirzepatide in monkeys
  - Good stability at 2-8 °C and neutral pH
  - 29G needles can be used for SQ injection (worst case – 27G needles) - low viscosity
  - Solubility for peptides must at least 60-75 mg/mL
  - Manufacturing cost is the same as buffer-based formulations (such as QW semaglutide and tirzepatide formulations)

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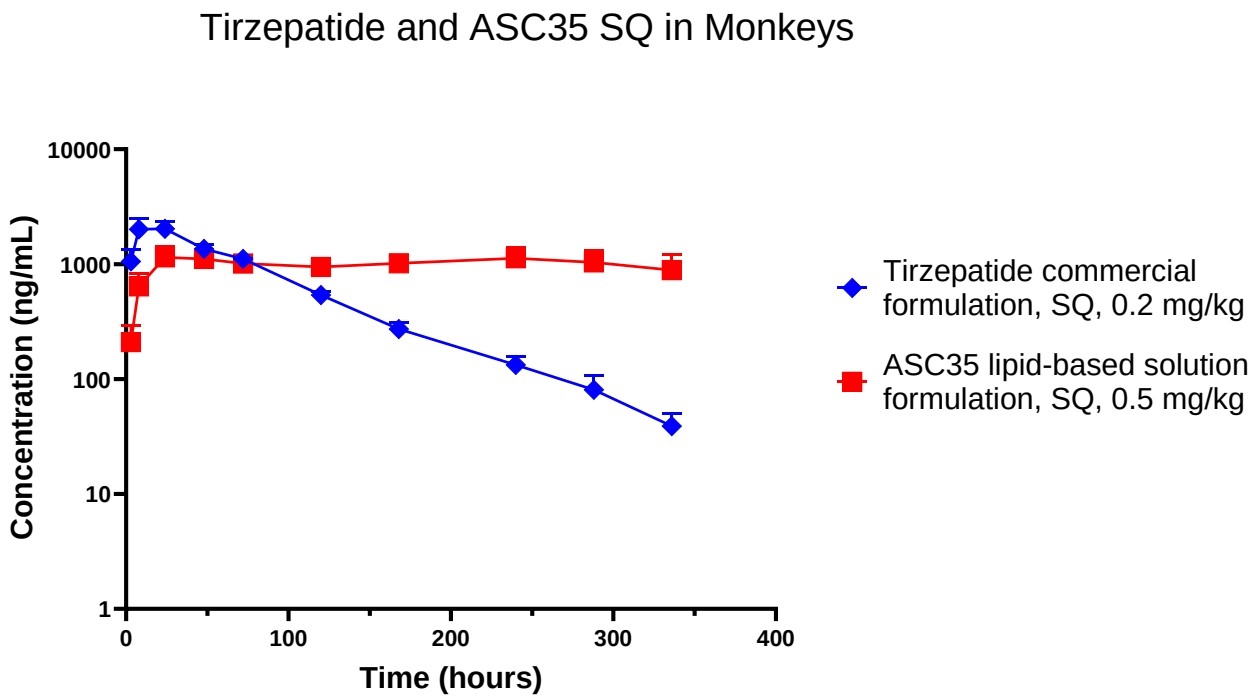
In Head-to-Head NHP Study, Average Observed Half-Life of ASC35 was Approximately 14 Days, 6-Fold Longer than Tirzepatide



Group	Monkey	Administration	dose (mg/kg)	$t_{1/2}$ (h)
Tirzepatide commercial formulation	n=3	SQ	0.2	57.1
ASC35 lipid-based solution formulation	n=3	SQ	0.5	328 (13.6 days)

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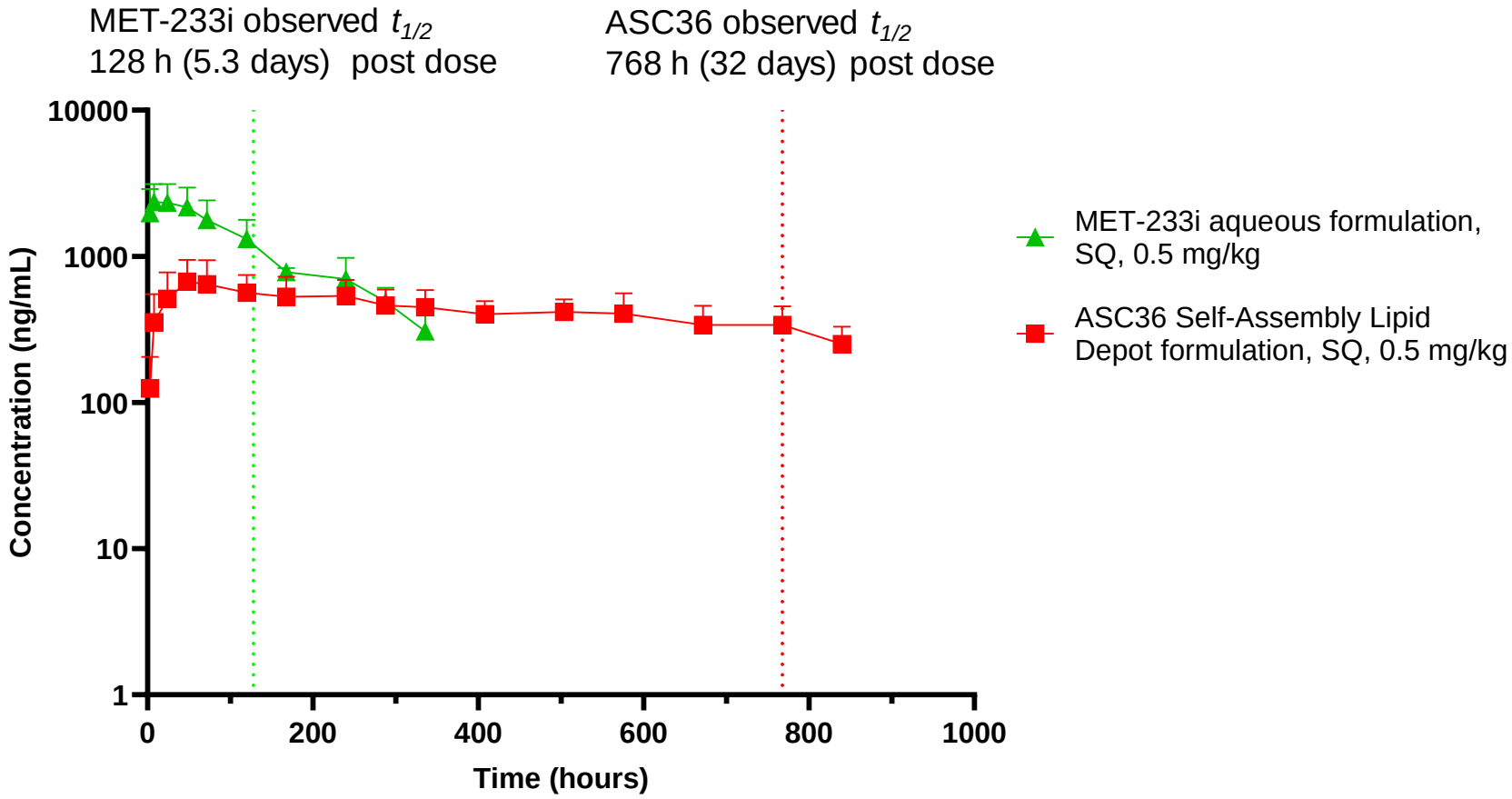
Ascletis Proprietary Self-Assembly Lipid Depot extends ASC36's $t_{1/2}$ to 6-Fold of MET-233i - Head-to-Head Study in NHPs



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ASC36i and ASC35 Self-Assembly Lipid Depot Formulations have 6-Fold Longer $t_{1/2}$ than MET-233i and Tirzepatide, Respectively

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

	Tirzepatide GLP-1R/GIPR[1] (actual)		Semaglutide GLP-1R[2] (actual)		ASC36 amylin R (Lipid-based formulation)		ASC35 GLP-1R/GIPR (Lipid-based formulation)	
	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

Ascletis Peptide Oral Transport ENhancement Technology (POTENT)

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 Ascletis' POTENT formulation is 3-fold of oral bioavailability of that of semaglutide in its commercial SNAC formulation
- In NHPs, oral bioavailability of tirzepatide in Ascletis' POTENT formulation is 9-fold of oral bioavailability of that of tirzepatide in SNAC formulation

Oral Bioavailability of Semaglutide with a POTENT Formulation is 3-Fold of Semaglutide with its Commercial SNAC Formulation[1]

Semaglutide tablet formulation developed utilizing POTENT technology

Group	Formulation	Monkey	body weight（kg）	dose (mg/kg)	$AUC_{0\text{-}72h}$ (ng*h/mL）	F(%)
IV dosing 0.2 mg/kg	0.2mg/ml Semaglutide, 20mM Citrate buffer solution (pH=7.0±0.2)	n=3	3.5	0.2	132,863	NA
Oral dosing after single dosing （One 14mg tablet per monkey）	Semaglutide commercial SNAC formulation[1], details: 14mg Semaglutide, 300mg SNAC, 80mg MCC, 8mg PVPK90, 9.7mg Magnesium stearate	n=3	2.9	4.8	29,165	0.92%
Oral dosing after single dosing （One 14mg tablet per monkey）	Ascletis' proprietary POTENT formulation	n=3	5.1	2.8	51,066	2.78%

[1] Extrapolated from Novo Nordisk's patents, FDA and Japanese regulatory filings

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Oral Bioavailability of Tirzepatide with a POTENT Formulation is 9-Fold of Tirzepatide with the SNAC Formulation[1]

Tirzepatide tablet formulation developed utilizing POTENT technology

Group	Formulation	Monkey	body weight（kg）	dose (mg/kg)	$AUC_{0\text{-}72h}$ (ng*h/mL）	F(%)
IV dosing 0.2 mg/kg	0.2mg/ml Tirzepatide, 20mM Citrate buffer solution (pH=7.0±0.2）	n=3	2.5	0.2	124,989	NA
Oral dosing after single dosing （One 14mg tablet per monkey）	14mg Tirzepatide, 300mg SNAC, 80mg MCC, 8mg PVPK90, 9.7mg Magnesium stearate	n=3	2.3	6.0	5,337	0.14%
Oral dosing after single dosing （One 14mg tablet per monkey）	Ascletis' proprietary POTENT formulation	n=3	4.3	3.3	27,480	1.29%

[1] Extrapolated from Novo Nordisk's patents, FDA and Japanese regulatory filings

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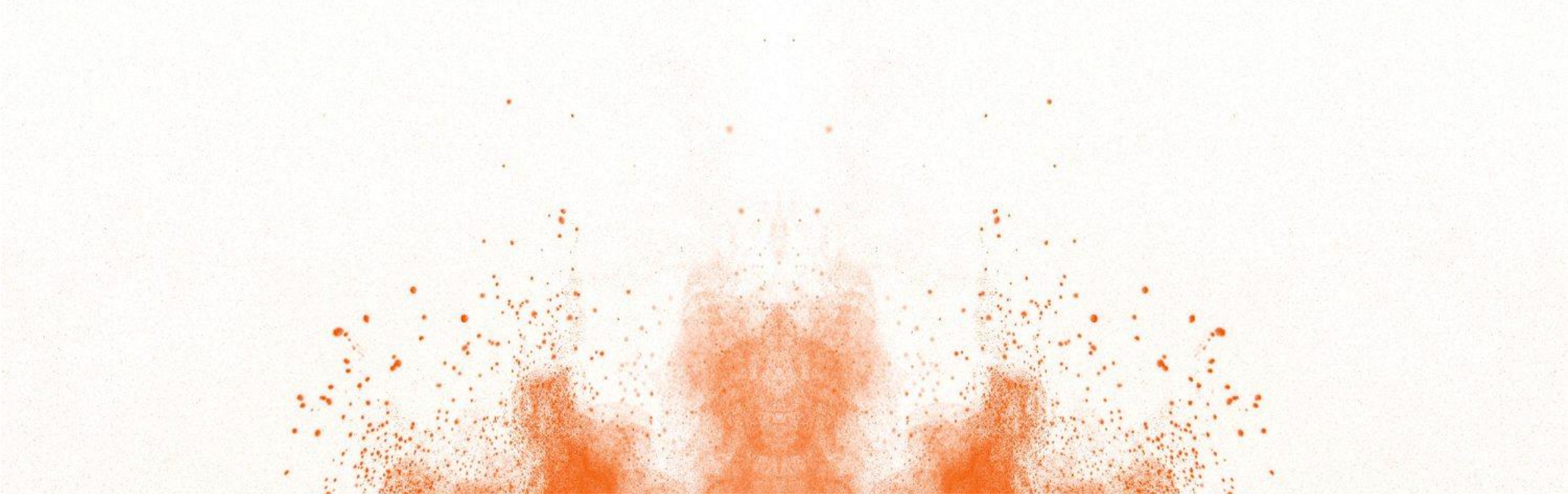
ASC36 Oral Tablets Achieved Absolute Oral Bioavailability of 6.0% to 8.0% in Non-Human Primates

ASC36 tablet formulation developed utilizing POTENT technology

Group	Monkey	body weight (kg)	dose (mg/kg)	$AUC_{0\text{-inf}}$ (ng*h/mL)	F(%)
IV dosing 0.2 mg/kg	n=3	2.7	0.2	60,540	NA
Oral dosing after once-daily dosing for 7 days (One 10mg ASC36 tablet per monkey)	n=3	2.9	3.6	85,532	8.0%
Oral dosing after once-daily dosing for 7 days (One 25mg ASC36 tablet per monkey)	n=3	2.9	8.8	161,367	6.0%



Thanks

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