



Asclepis Pharma(HK.1672)

Corporate Presentation

Sept 29th 2024



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Contents

- Overview
- Pipeline Highlights
- Summary & Outlook



Overview

Differentiated, competitive R&D pipeline

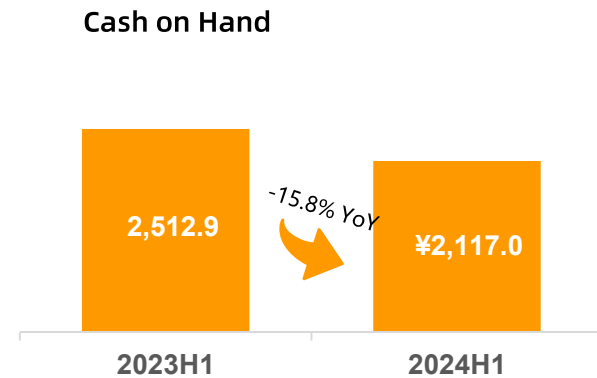
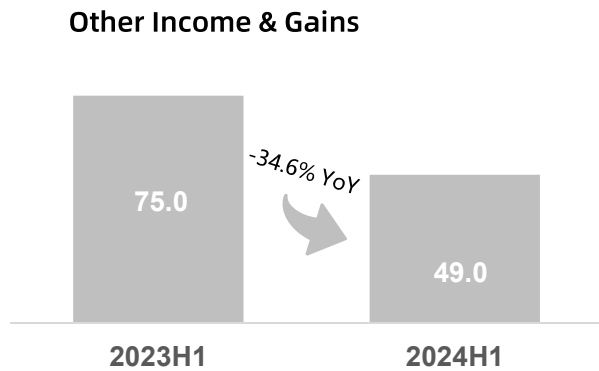
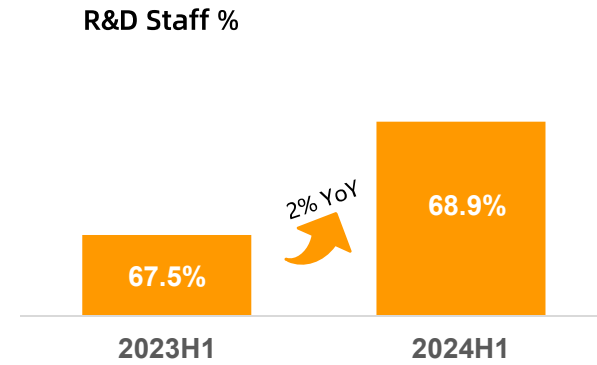
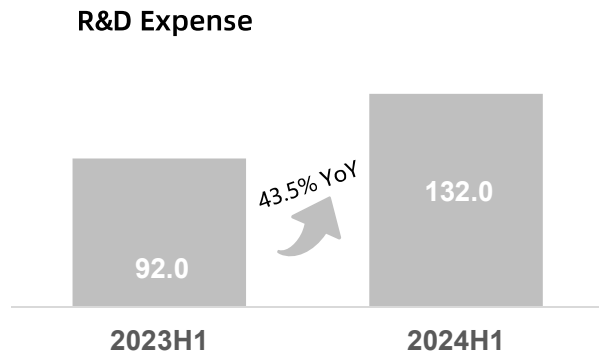
Therapeutical Area	Product (Modality)	Target	Indication	Commercial Rights	Pre-IND	IND	Phase I	Phase II	Phase III
Metabolic Diseases	ASC30 (Once-monthly subcutaneous small molecule)	GLP-1R	Obesity	Global	[Progress bar]				
	ASC30(Oral small molecule)	GLP-1R	Obesity	Global	[Progress bar]				
	ASC40 (Oral small molecule)	FASN	MASH	Greater China ¹	<i>U.S. FDA Fast Track</i>				
	ASC41 (Oral small molecule)	THRβ	MASH	Global	[Progress bar]				
Viral Diseases	ASC22(Subcutaneous mAb)	PD-L1	CHB functional cure	Global ²	[Progress bar]				
Cancer	ASC40(Oral small molecule)+ Bevacizumab	FASN+ VEGF	Recurrent glioblastoma	Greater China ¹	[Progress bar]				
	ASC61(Oral small molecule)	PD-L1	Advanced solid tumors	Global	[Progress bar]				
Exploratory Indications	ASC40 (Oral small molecule)	FASN	ACNE	Greater China ¹	[Progress bar]				

Notes::

1. ASC40 is licensed from Sagimet Biosciences Inc. for the exclusive rights in the Greater China.
2. ASC22 is licensed from Suzhou Alphamab Co.,Ltd for the worldwide exclusive rights.

Sufficient Cash Supports Our Continuous Efforts on R&D Capabilities

mm RMB

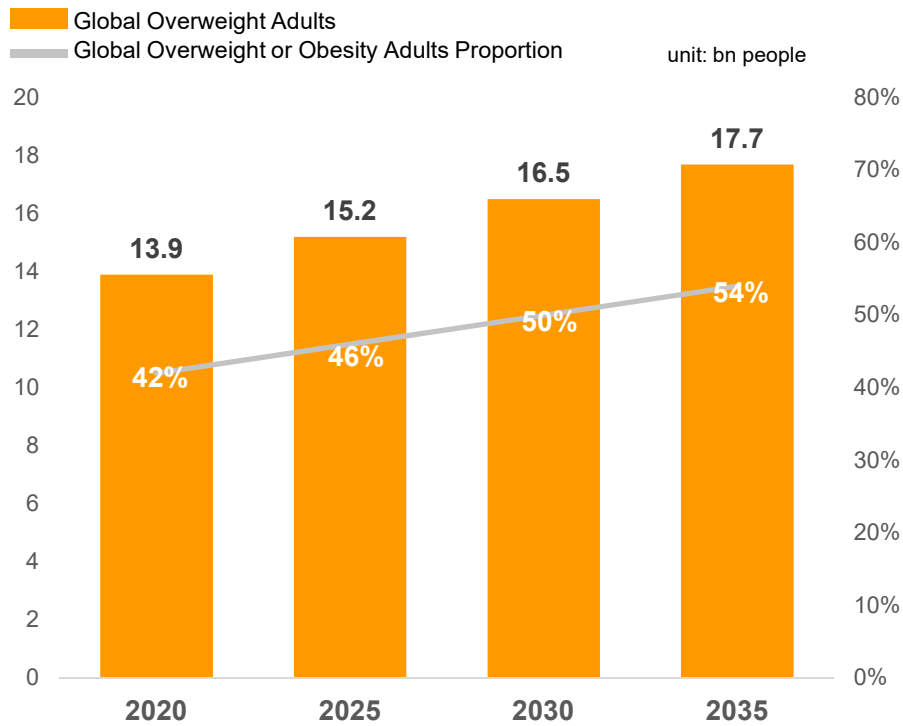




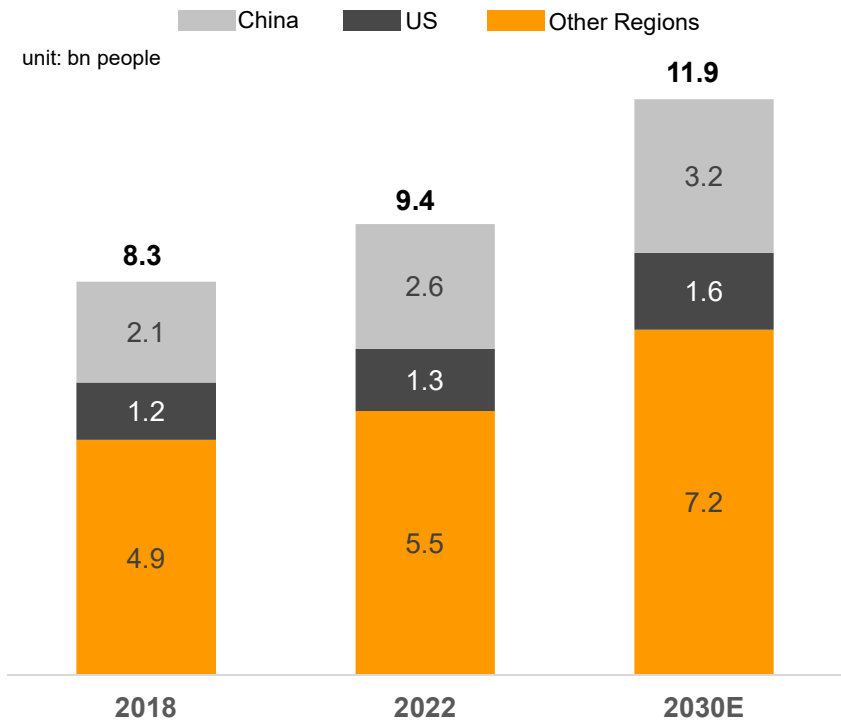
Pipeline Highlights--Obesity

Number of Overweight and Obesity: on the Rise

WOF Forecast for Global Overweight and Obesity^[1]



WHO: China & US are the key regions for new obesity patients^[2]



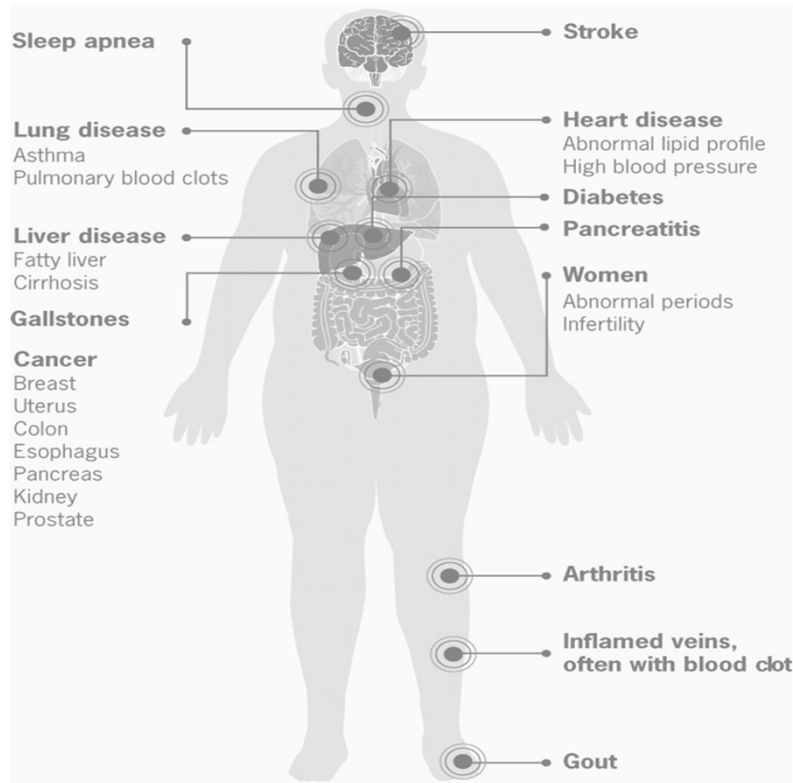
Goldman Sachs^[3] expects anti-obesity drug market could grow to \$100 billion by 2030

Obesity: BMI ≥30 kg/m² Overweight: BMI ≥25 to 30 kg/m²

1. World Obesity Federation. World Obesity Atlas 2024 <https://data.worldobesity.org/publications/WOF-Obesity-Atlas-v7.pdf>
2. WHO, CIC
3. <https://www.goldmansachs.com/insights/articles/anti-obesity-drug-market>

Obesity is highly correlated with the occurrence of various diseases GLP-1 drugs emerging with huge potential

Obesity is highly correlated with various diseases



Multiple factors driving rapid growth of GLP-1 drug

Increase of patients with diabetes and obesity

Globally, the number of patients with type 2 diabetes and obesity is rising, which directly results in the growth of GLP-1 drug demand

Superior drug efficacy

GLP-1 drugs not only have the effect of lowering blood sugar, but also help with weight loss. Compared to traditional treatment drugs, GLP-1 drugs do not increase the risk of hypoglycemia or cause weight gain, which gives them significant advantages in efficacy

Exploration of new indications

In addition to diabetes and weight loss, GLP-1 shows therapeutic potential in cardiovascular disease, MASH, chronic kidney disease (CKD) and Alzheimer's disease (AD), which provides a new growth point for the GLP-1 drug market

Formulation technology advancement

The development of long-acting GLP-1 drugs and oral GLP-1 drugs, has improved patient compliance and further promoted market development

ASC30, Small Molecule GLP-1R Agonist, for Both Once-Monthly Subcutaneous Injection and Once-Daily Oral Tablet for the Treatment of Obesity



Excellent Preclinical Data

- ASC30 is two- to threefold more potent, *in vitro*, than orforglipron and stimulated significantly greater insulin secretion when compared with orforglipron in non-human primates (NHPs).
- ASC30 single dose subcutaneous injection demonstrated sustained weight loss over one month in NHPs supporting once-monthly administration in humans.
- ASC30 oral once-daily dosing demonstrated sustained weight loss in NHPs supporting once-daily oral administration in humans.



In-house R&D

- ASC30 is the first and only small molecule GLP-1 receptor (GLP-1R) agonist that can be dosed once-monthly subcutaneously and once-daily orally to treat obesity.
- ASC30 is a new molecular entity (NME), with U.S. and global compound patent protection until 2044.



Lower Costs and Better Availability

- ASC30 offers both once-monthly injection and once-daily oral dosing options, significantly improving the convenience of dosing.
- Small molecule products have lower production costs and thus better availability.



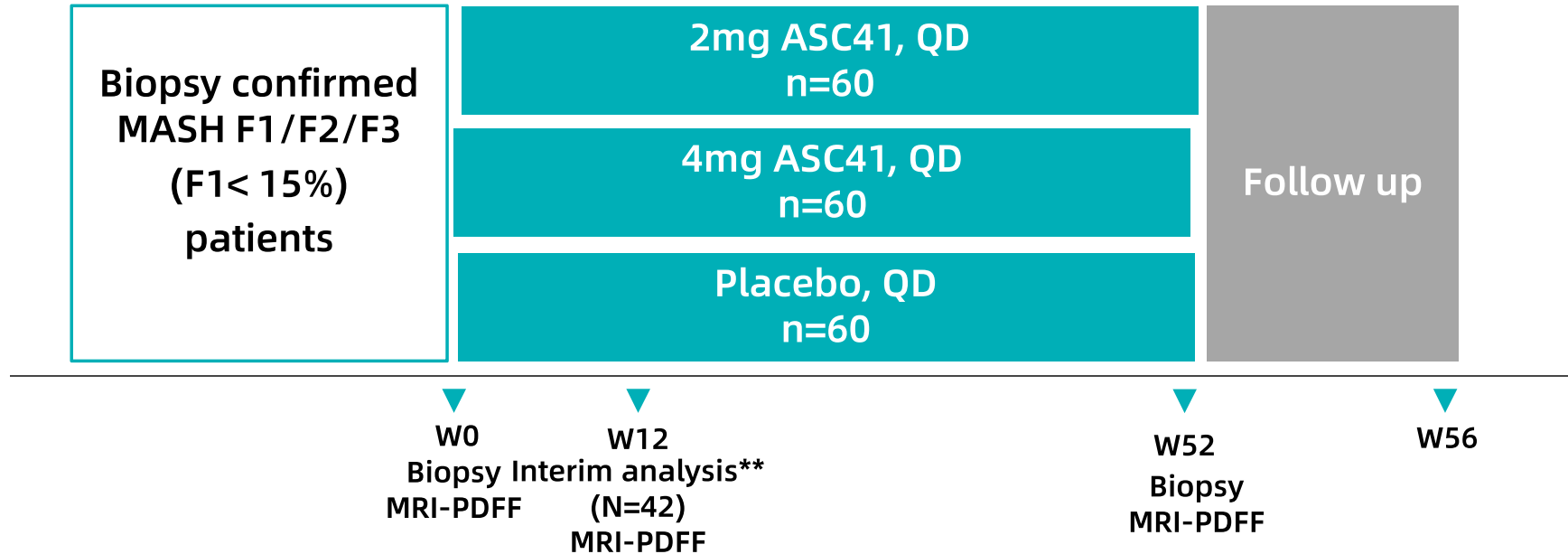
Two Ongoing U.S. Phase I Clinical Trials

- Both ASC30 Phase I Clinical Trials have completed initial dosing.
- Topline data from ongoing U.S. Phase I clinical trials of ASC30 are expected in first quarter 2025.



Pipeline Highlights--MASH

ASC41: 52-week Phase II Study in Biopsy-confirmed MASH patients*



Primary Objective

To evaluate the efficacy of ASC41 tablet in biopsy-confirmed noncirrhotic NASH patients by a histological reduction in NAS ≥ 2 points that results from reduction of necro-inflammation (inflammation or ballooning) without worsening fibrosis.

Secondary objectives

1. NASH resolution;
2. Fibrosis improvement.

*Phase II study protocol was agreed by both US FDA and China NMPA

**Pre-specified interim analysis conducted when 42 patients completed 12-week treatment of ASC41/placebo.

Summary of Interim Week 12 Data from 52-Week ASC41 Tablet Study

■ Mean liver fat reduction

Up to **68.2%** mean liver fat reduction from baseline in biopsy-confirmed NASH patients receiving 12-week treatment of ASC41 tablet

■ ALT Reduction

At Week 12, placebo-adjusted mean reductions in alanine aminotransferase (ALT) from baseline was up to **37.8%**

■ Safety

Adverse events (AEs), including gastrointestinal (GI)-related AEs, were similar among the cohorts receiving ASC41 tablet treatment versus the placebo

■ Respond Rate

Up to **93.3%** patients achieved at least a 30% relative reduction in liver fat after 12-week treatment

■ AST Reduction

At Week 12, placebo-adjusted mean reductions in AST from baseline was up to **41.5%**

■ Lipids Decrease

At Week 12, placebo-adjusted mean reductions in LDL-C, TC and TG from baseline were up to

27.7%, 23.4%

and **46.5%**, respectively

Reduction in Liver Fat Content from Baseline at Week 12 by MRI-PDFF

	Placebo (n = 14)	ASC41 Tablet	
		2 mg, QD (n = 13)	4 mg, QD (n = 15)
Mean baseline liver fat content	18.2%	17.8%	18.9%
Mean relative change in liver fat content from baseline	-13.1%	-55.0% (p = 0.0001 vs placebo)	-68.2% (p < 0.0001 vs placebo)
Median relative change in liver fat content from baseline	-5.8%	-48.8%	-70.1%
Percentage of patients achieving ≥ 30% relative reduction in liver fat content from baseline	21.4%	92.3% (p = 0.0002 vs placebo)	93.3% (p < 0.0001 vs placebo)
Percentage of patients achieving ≥ 50% relative reduction in liver fat content from baseline*	21.4%	46.2% (p = 0.24)	86.7% (p = 0.0004)
Percentage of patients achieving normalized liver fat (≤5% absolute liver fat content)*	0.0%	30.8% (p = 0.16)	66.7% (p = 0.0017)

≥ 30% reductions in liver fat content is highly associated with patients achieving histologic improvement in MASH

Stine JG, Munaganuru N, Barnard A, et al. Clin Gastroenterol Hepatol. 2021;19(11):2274-2283.e5. doi:10.1016/j.cgh.2020.08.061



Statistically Significant, Clinically Meaningful Reductions in ALT & AST at Week 12 Differentiate ASC41 from Other THR β Agonists In Development

	Placebo (n = 14)	ASC41 Tablet	
		2 mg, QD (n = 13)	4 mg, QD (n = 15)
ALT			
Mean baseline ALT	77.6 U/L	65.9 U/L	84.8 U/L
Mean relative change in ALT from baseline*	5.2%	-8.5% (p = 0.61)	-32.6% (p = 0.0051)
Percentage of patients achieving mean ALT decrease > 17 U/L*	21.4%	30.8% (p = 0.68)	73.3% (p = 0.0052)
AST			
Mean baseline AST	47.9 U/L	44.2 U/L	53.8 U/L
Mean relative change in AST from baseline*	17.3%	-3.6% (p = 0.67)	-24.2% (p = 0.041)

Decline in ALT in MASH patients is associated with improvement in liver histology

*p-value vs placebo

Reduction in Lipids from Baseline at Week 12

	Placebo (n = 14)	ASC41 Tablet	
		2 mg, QD (n = 13)	4 mg, QD (n = 15)
LDL-C, mean change from baseline	4.3%	-19.4% (p = 0.0002 vs placebo)	-23.4% (p < 0.0001 vs placebo)
TC, mean change from baseline	3.4%	-16.8% (p < 0.0001 vs placebo)	-20.0% (p < 0.0001 vs placebo)
TG, mean change from baseline	3.9%	-30.6% (p = 0.0001 vs placebo)	-42.6% (p < 0.0001 vs placebo)

- HDL-C remained unchanged from baseline among the cohorts receiving ASC41 tablet treatment or placebo.
- Reductions in these lipids improve a patient's overall cardiometabolic profile and may reduce the risk of cardiovascular-related events.

Safety and Tolerability

	Placebo (n = 14)	ASC41 Tablet	
		2 mg, QD (n = 13)	4 mg, QD (n = 15)
TEAEs [1] Number of subjects (%)	13(92.9%)	13(100%)	15(100%)
Drug-related TEAEs [2]	6(42.9%)	7(53.9%)	7(46.7%)
Grade 1	6(42.9%)	7(53.9%)	7(46.7%)
Drug-related GI AEs	2(14.3%)	3(23.1%)	1(6.7%)
Nausea	0(0.0%)	0(0.0%)	0(0.0%)
Vomiting	0(0.0%)	0(0.0%)	0(0.0%)
Diarrhea	1(7.1%)	3(23.1%)	1(6.7%)
Abdominal distension	1(7.1%)	0(0.0%)	0(0.0%)
Abdominal pain (upper)	0(0.0%)	0(0.0%)	0(0.0%)
Constipation	0(0.0%)	0(0.0%)	0(0.0%)
Dyspepsia	0(0.0%)	0(0.0%)	0(0.0%)
Frequent bowel movements	0(0.0%)	0(0.0%)	0(0.0%)

- Levels of thyroid axis hormones, including thyroid stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4) were relatively unchanged from baseline among the cohorts receiving ASC41 tablet treatment versus the placebo.
- Changes in vital signs and electrocardiogram (ECG) were similar among patients receiving ASC41 tablet treatment versus placebo.

[1]Data as of November 22, 2023;[2] Deemed by investigator as possibly, probably, or definitely related to study drug

Favorable Reduction in Liver Inflammatory Biomarkers Compared to other THR β Agonists at 12 Weeks

Placebo-adjusted mean reductions in liver inflammatory biomarkers from baseline at Week 12	ASC41 tablet, stable at room temperature	Resmetirom tablet ^[1] , stable at room temperature	VK2809 Capsule ^[2] , stable only under refrigeration	Tern-501 ^[3] , formulation and storage condition unknown
ALT	Up to 37.8% (Statistically significant difference vs placebo)	No statistically significant difference vs placebo	Similar to placebo	Similar to placebo
AST	Up to 41.5% (Statistically significant difference vs placebo)	No statistically significant difference vs placebo	Similar to placebo	Similar to placebo

[1] Week 12 data from 36-week phase 2 and 52-week phase 3

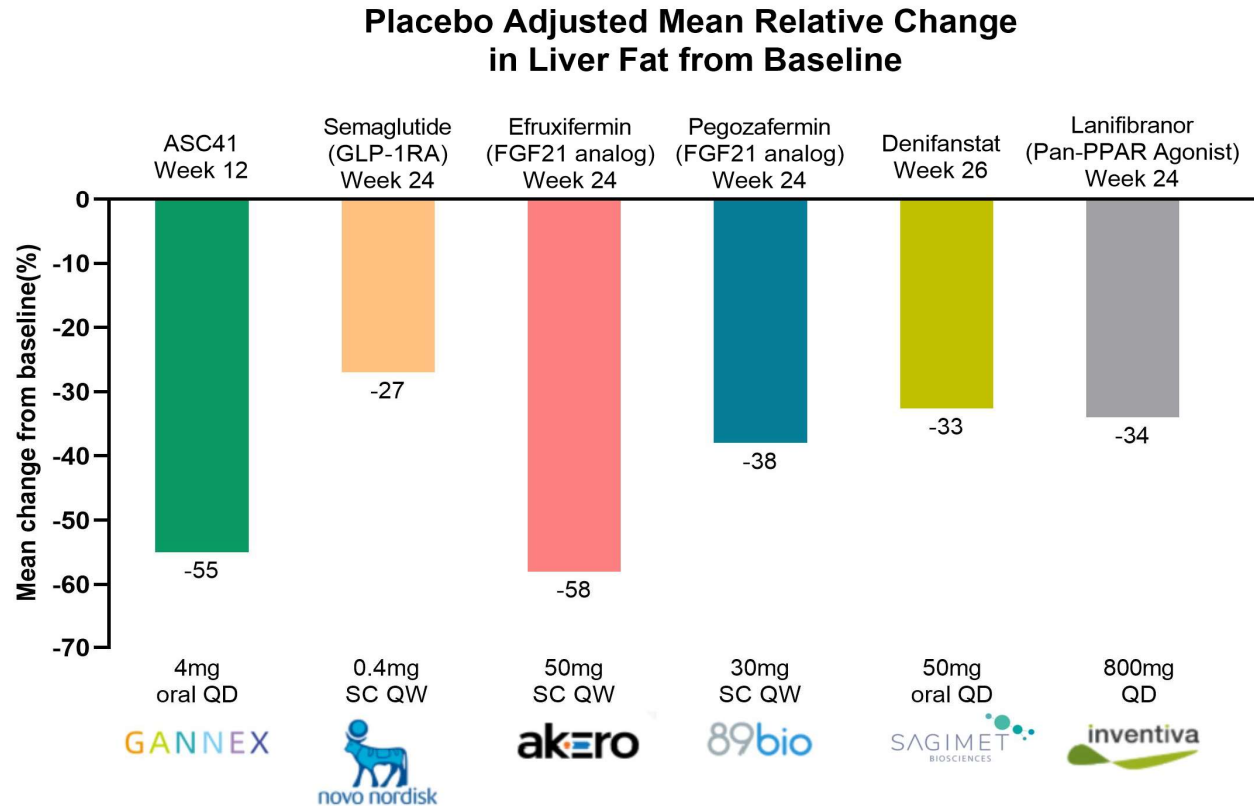
[2] Viking press release, May 2023

[3] Terns press release, August 2023

Favorable Safety Profile Compared to other THR β Agonists

	ASC41 tablet		Resmetirom tablet Phase III		VK2809 Capsule		Tern-501	
	Placebo (n = 14)	2mg/4mg QD (n=28)	Placebo (n = 321)	100mg QD (n=323)	Placebo (n = 65)	10mg QOD (n=61)	Placebo (n =24)	6mg QD (n=22)
TEAEs Number of subjects(%)	13(92.9%)	28(100%)	269(92.2%)	296 (91.6%)	47(72.3%)	54(88.5%)	NA	NA
Drug-related TEAEs	6(42.9%)	14(50%)	86 (26.8%)	134(41.5%)	22(33.8%)	23(37.7%)	NA	NA
Drug-related TEAEs leading to study discontinuation	0(0.0%)	1(3.6%)	8 (2.5%)	22 (6.8%)	5(7.7%)	5(8.2%)	1(4.2%)	1(4.5%)
Drug-related GI AEs	2(14.3%)	4(14.3%)	NA	NA	12(18.5%)	7(11.5%)	2(8.3%)	2(9.1%)
Nausea	0(0.0%)	0(0.0%)	40 (12.5%)	62 (19.2%)	5(7.7%)	3(4.9%)	0(0.0%)	0(0.0%)
Diarrhea	1(7.1%)	4(14.3%)	50 (15.6%)	109(33.7%)	2(3.1%)	3(4.9%)	1(4.2%)	1(4.5%)
Vomiting	0(0.0%)	0(0.0%)	17 (5.3%)	35 (10.8%)	NA	NA	1(4.2%)	0(0.0%)
Abdominal distension	1(7.1%)	0(0.0%)	NA	NA	NA	NA	0(0.0%)	0(0.0%)

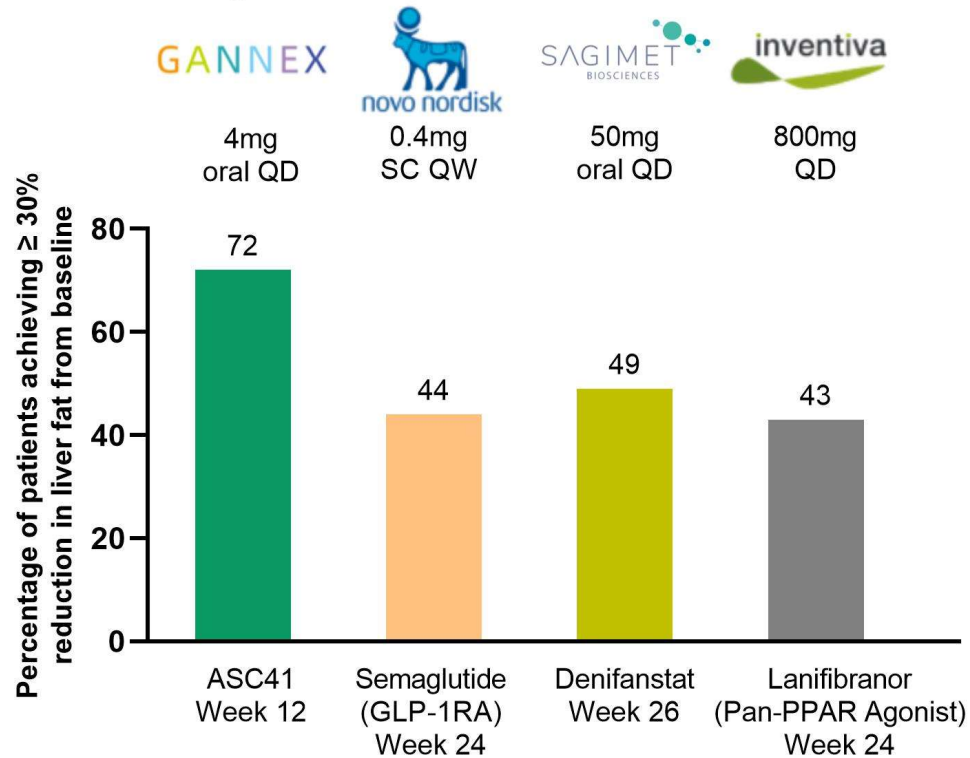
ASC41 vs GLP-1, FGF21, FASN and PPAR: Liver Fat Reduction



1. Semaglutide: Flint, A., et al. [J] Aliment Pharmacol Ther, (2021), DOI: 10.1111/apt.16608;
2. Efruxifermin: Stephen A. Harrison., et al. AASLD 2022 Abstract #39094;
3. Pegzofermin: <https://ir.89bio.com/news-releases/news-release-details/89bios-phase-2b-enliven-trial-pegzofermin-non-alcoholic>;
4. Denifanstat: Rohit Loomba, et al. EASL 2023 Abstract #OS-061;
5. Lanifibranor: <https://inventivapharma.com/wp-content/uploads/2023/06/IVA-Topline-results-lanifibranor-in-T2D-and-NAFLD-06282023.pdf>

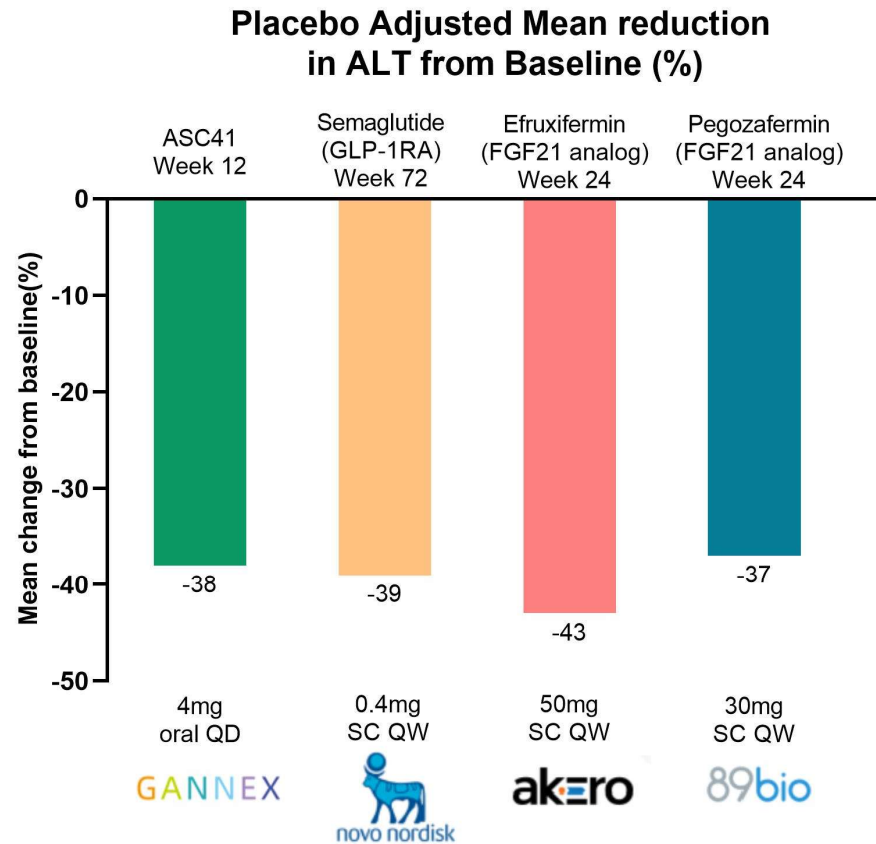
ASC41 vs GLP-1, FASN and PPAR: $\geq 30\%$ Liver Fat Reduction

Placebo Adjusted Percentage of patients achieving $\geq 30\%$ reduction in liver fat from baseline



1. Semaglutide: Flint, A., et al. [J] Aliment Pharmacol Ther, (2021). DOI: 10.1111/apt.16608;
2. Denifanstat: Rohit Loomba, et al. EASL 2023 Abstract #OS-061;
3. Lanifibranor: <https://inventivapharma.com/wp-content/uploads/2023/06/IVA-Topline-results-lanifibranor-in-T2D-and-NAFLD-06282023.pdf>

ASC41 vs GLP-1 and FGF21: Reduction in ALT



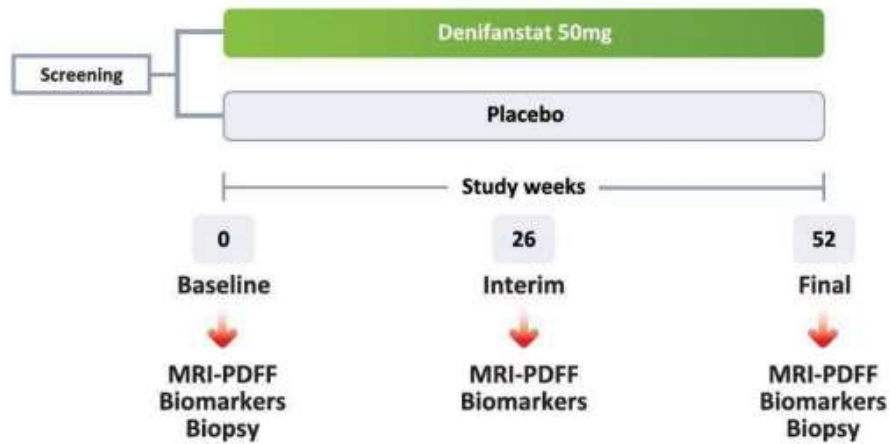
1. Semaglutide: Newsome, P. N., et al. [J] N Engl J Med, (2021). DOI: 10.1056/NEJMoa2028395;
2. Efruxifermin: Stephen A. Harrison., et al. AASLD 2022 Abstract #39094;
3. Pegozafermin: <https://ir.89bio.com/news-releases/news-release-details/89bios-phase-2b-enliven-trial-pegozafermin-non-alcoholic>;

Patents of ASC41

	Application Date	Publication Number	Patents Applied	Patents Authorized	Pending
Formulation Patent (Tablet)	2020/3/27	US20210308155A1 (U.S.) CN115427022A (China) WO2021190624A1 (PCT)	U.S., China and Globally	U.S.	China and Globally
Crystal Patent	2020/9/30	CN114315902A (China) WO2022067602A1 (Globally)	China and Globally	\	China and Globally
Synthesis Patent	2020/2/18	US11292805B2 (U.S.) US20220332738A1 (U.S.) CN113336792A (China)	U.S. and China	U.S.	China
Composition Patent	2021/7/6	WO2023280152A1 (PCT)	U.S., China and Globally	\	U.S., China

ASC40(FASN)MASH | Phase IIb Clinical Trial Design

FASCINATE-2 Phase 2b trial design



- Biopsy confirmed F2-F3 NASH patients
- 52 weeks, 2:1 50mg or placebo, double-blind

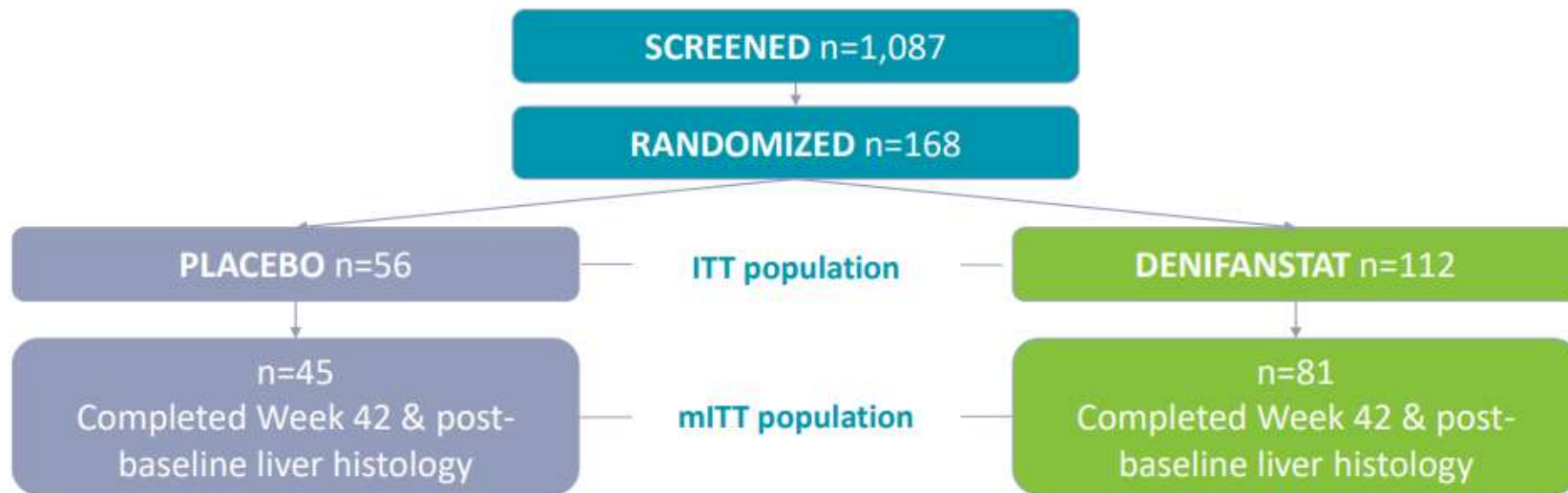
Primary endpoints

- NAS ≥ 2 points improvement w/o worsening of fibrosis OR
- NASH resolution + NAS ≥ 2 improvement w/o worsening of fibrosis

Other selected endpoints

- Improvement in liver fibrosis ≥ 1 stage without worsening of NASH (Bx)
- Digital AI pathology
- MRI-PDFF: absolute decrease, % change from baseline, % pts $\geq 30\%$ reduction from baseline (responders)

ASC40(FASN) MASH | Phase IIb Screening and Randomization



ASC40 MASH Phase IIb Baseline Characteristics Typical F2/F3 MASH Population

Parameter	Placebo, n=45	Denifanstat, n=81
Age, years	59.6 (+/- 10.9)	56.1 (+/- 10.8)
Sex, female	27 (60%)	48 (59%)
Race, White	41 (91%)	73 (90%)
Ethnicity, Hispanic or Latino	15 (33%)	27 (33%)
BMI, kg/m ²	36.5 (+/- 6.7)	34.6 (+/- 6.1)
Type 2 diabetes	27 (60%)	55 (68%)
ALT (alanine aminotransferase) U/L	67 (+/- 33)	57 (+/- 29)
AST (aspartate aminotransferase) U/L	52 (+/- 27)	48 (+/- 29)
Liver Fat Content (MRI-PDFF), %	19.0 (+/- 7.0)	16.6 (+/- 7.1)
Baseline liver biopsy NAS ≥ 5	34 (76%)	63 (78%)
Baseline liver biopsy F2/F3	22 (49%) / 23 (51%)	34 (42%) / 47 (58%)
Statin (at baseline)	21 (47%)	38 (47%)
GLP1-RA (at baseline)	4 (9%)	12 (15%)
LDL, mg/dL	103 (+/- 39)	96 (+/- 34)
Triglycerides, mg/dL	153 (+/- 67)	173 (+/- 79)
ELF (Enhanced Liver Fibrosis) Score	9.8 (+/- 0.8)	9.6 (+/- 0.8)
FAST (Fibroscan AST) Score	0.6 (0.19)	0.6 (0.20)

ASC40 MASH Phase IIb Biopsy Results

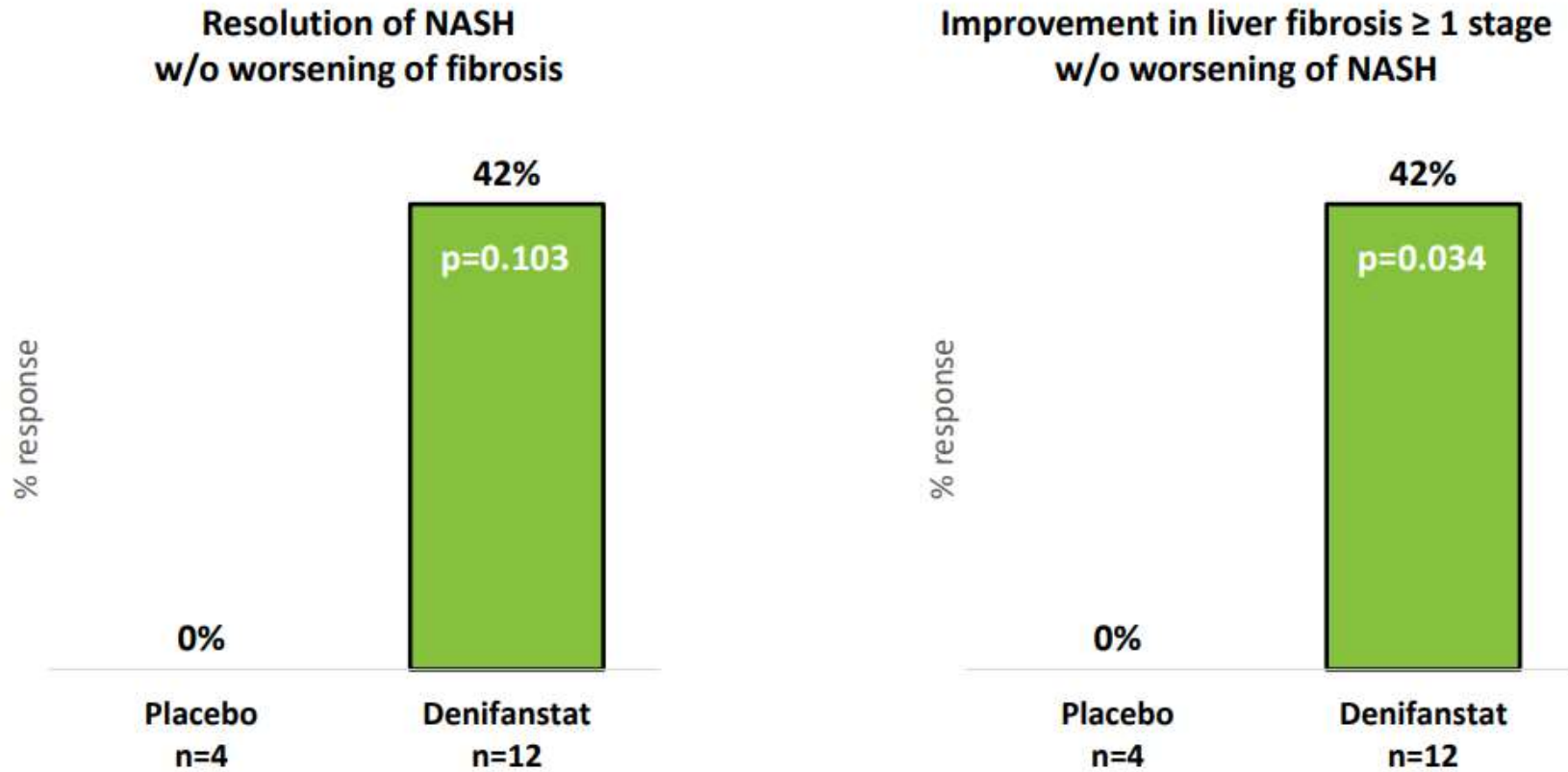
	Placebo (n=45)	ASC40 50 mg (n=81)	Placebo adjusted	<i>P value</i>
Primary Endpoints				
MASH resolution + NAS \geq 2 improvement w/o worsening of fibrosis	13%	36%	23%	0.0022
NAS \geq 2 points improvement* w/o worsening of fibrosis	20%	52%	32%	0.0001
Other Endpoints				
Improvement in liver fibrosis \geq 1 stage w/o worsening of MASH	18%	41%	23%	0.0051
Resolution of MASH w/o worsening of fibrosis	16%	38%	22%	0.0021
AI Digital Pathology (qFibrosis)**	0.1	-0.3	-0.4	0.0023
ALT % from baseline	-17.2%	-30.5%	-13.3%	0.0300
MRI-PDFF respond rate (>30% reduction)	21%	65%	44%	<0.0001
FibroScan AST (FAST) 评分	-0.1	-0.3	-0.2	<0.0001
LDL-C (mg/dL)***	-9.1	-19.1	-10.0	--

* \geq 1-point improvement in ballooning or inflammation.

**least squares mean. HistolIndex platform. mITT population.

***For LDL-c, baseline > 100 mg/dL.

MASH Patient Subset on Stable GLP1-RA at Baseline: Liver Biopsy ASC40 Improves MASH Resolution and Fibrosis



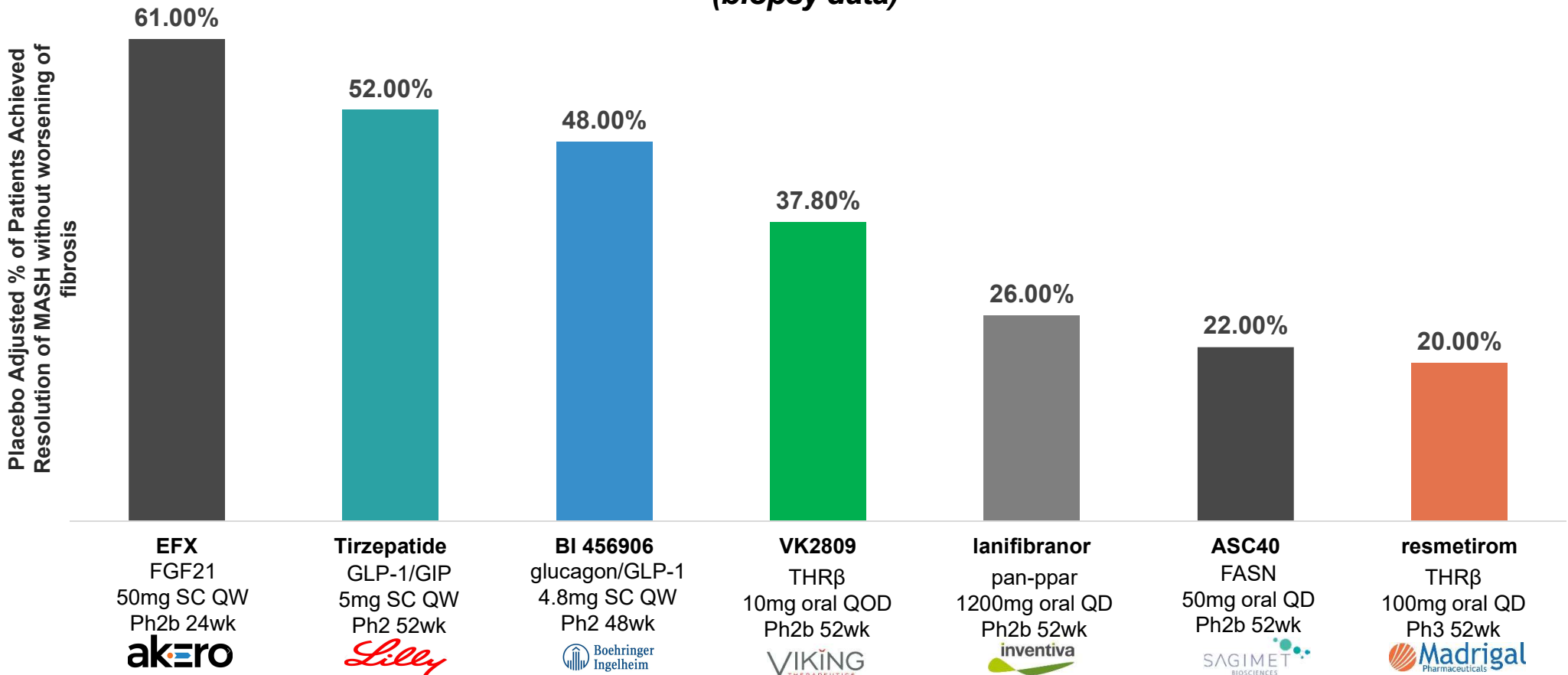
ASC40(FASN)MASH | Phase IIb Safety Profile

Parameter	Placebo n=56	Denifanstat N=112
Any TEAE (treatment emergent adverse event)	45 (80.4%)	96 (85.7%)
TEAE related to study drug	20 (35.7%)	51 (45.5%)
Most common TEAE related to study drug in ≥5% of patients by system organ class		
eye disorders	9 (16.1%)	17 (15.2%)
gastrointestinal disorders	5 (8.9%)	13 (11.6%)
skin and subcutaneous tissue disorders	4 (7.1%)	25 (22.3%)
TEAE leading to study drug discontinuation	3 (5.4%)	22 (19.6%)
TEAE with CTCAE Grade 3 (Severe) or higher*	3 (5.4%)	13 (11.6%)
SAE (none related to treatment)	3 (5.4%)	13 (11.6%)
Fatal TEAE	0	0

* No treatment-related AE was Grade 3 or higher

Comparison of MASH Candidates (Not Head to Head)

Placebo Adjusted % of Patients Achieved Resolution of MASH without worsening of fibrosis (biopsy data)



1. Per protocol, <https://ir.akerotx.com/news-releases/news-release-details/akero-therapeutics-presents-poster-and-late-breaking-oral>

2. ITT, <https://www.nejm.org/doi/full/10.1056/NEJMoa2401943>

3. mITT, <https://www.nejm.org/doi/full/10.1056/NEJMoa2401755>

4. ITT, <https://ir.vikingtherapeutics.com/2024-06-04-Viking-Therapeutics-Announces-Positive-52-Week-Histologic-Data-from-Phase-2b-VOYAGE-Study-of-VK2809-in-Patients-with-Biopsy-Confirmed-Non-Alcoholic-Steatohepatitis-MASH>

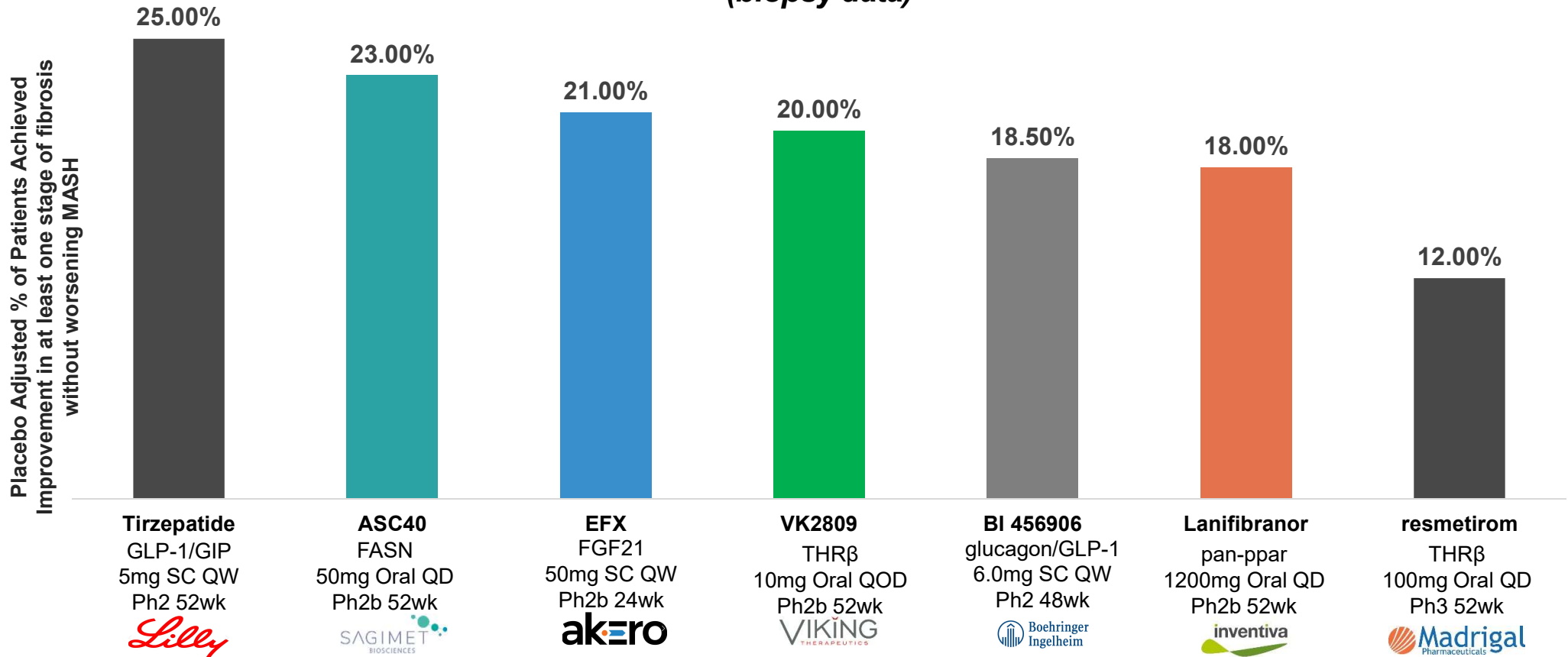
5. ITT, <https://inventivapharma.com/wp-content/uploads/2024/04/04-Inventiva-Presentation-ENG-04032024-2.pdf>

6. mITT, <https://ir.sagimet.com/news-releases/news-release-details/sagimet-biosciences-announces-positive-topline-results-phase-2b>

7. mITT, <https://ir.madrigalpharma.com/news-releases/news-release-details/madrigal-announces-positive-topline-results-pivotal-phase-3>

Comparison of MASH Candidates (Not Head to Head)

Placebo Adjusted % of Patients Achieved Improvement in at least one stage of fibrosis without worsening MASH (biopsy data)



1.ITT, <https://www.nejm.org/doi/full/10.1056/NEJMoa2401943>

2.mITT, <https://ir.sagimet.com/news-releases/news-release-details/sagimet-biosciences-announces-positive-topline-results-phase-2b>



3.Per protocol, <https://ir.akerotx.com/news-releases/news-release-details/akero-therapeutics-presents-poster-and-late-breaking-oral>

4.IIT, <https://ir.vikingtherapeutics.com/2024-06-04-Viking-Therapeutics-Announces-Positive-52-Week-Histologic-Data-from-Phase-2b-VOYAGE-Study-of-VK2809-in-Patients-with-Biopsy-Confirmed-Non-Alcoholic-Steatohepatitis-MASH>

5.mITT, <https://www.nejm.org/doi/full/10.1056/NEJMoa2401755>

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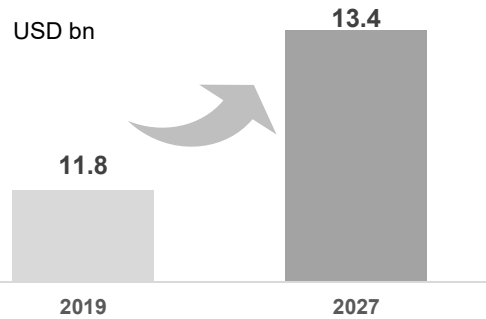
7.mITT, <https://ir.madrigalpharma.com/news-releases/news-release-details/madrigal-announces-positive-topline-results-pivotal-phase-3>



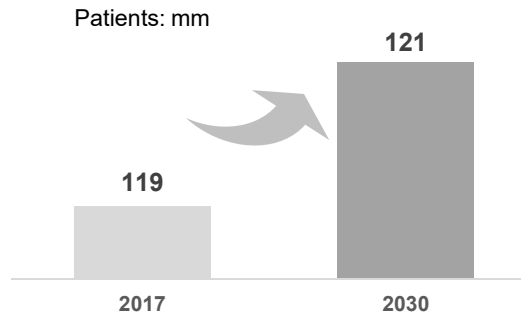
Pipeline Highlights--Acne

Acne: the Eighth Most Prevalent Disease with 640+ mm Patients Globally

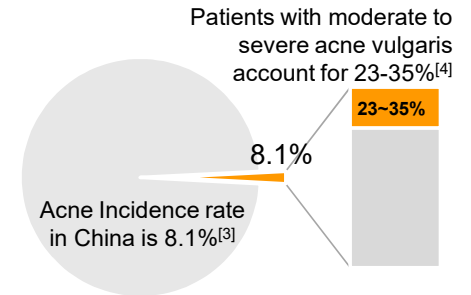
Global Acne Market Forecast^[1]



Acne Patients Growth in China^[2]



High Prevalence in China



Multiple Factors Contribute to the Incidence Rise^[2]

- Work and life pressure
 - High sugar, spicy and greasy diet
 - Pollution
 - Unhealthy lifestyle
- endocrine disorder
 - excessive sebum production
 - inflammation

Limitations of Current Treatment

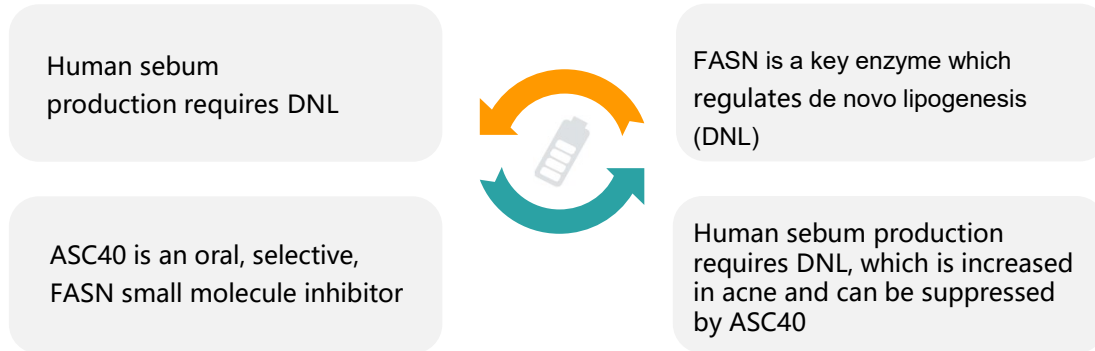
- **Oral antibiotics** antibiotic resistance^[5] Side effects including GI reactions /rash/liver damage
- **Oral isotretinoin** ^[5] Over 10 kinds of side effects^[6] Liver damage^[6]
- **Topical medications** Light sensitive 30% to 40% of patients do not adhere to their topical treatments ^[7]

References:

- Allied Market Research
- Frost & Sullivan Report
- Li D, Chen Q, Liu Y, et al. BMJ Open. 2017 Apr;7(4):e015354. DOI: 10.1136/bmjopen-2016-015354.
- Shen Y, Wang T, Zhou C, et al. Acta Derm Venereol. 2012;92(1):40-44. doi:10.2340/00015555-1164
- Guideline for Diagnosis and Treatment of Acne (The 2019 Revised Edition)
- Brzezinski P, Borowska K, Chiriac A, Smigielski J. Dermatol Ther. 2017;30(4):10.1111/dth.12483. doi:10.1111/dth.12483
- Purvis CG, Balogh EA, Feldman SR. Ann Pharmacother. 2021;55(10):1297-1299.

ASC40 (FASN) for Acne: Phase III Enrollment to Be Completed in 2024Q4

ASC40: Innovative Mechanism for Acne Treatment



ASC40 Acne Phase III Trial

- Phase III trial of ASC40 initiated in Q4, 2023
- Plan to enroll 480 pts in China



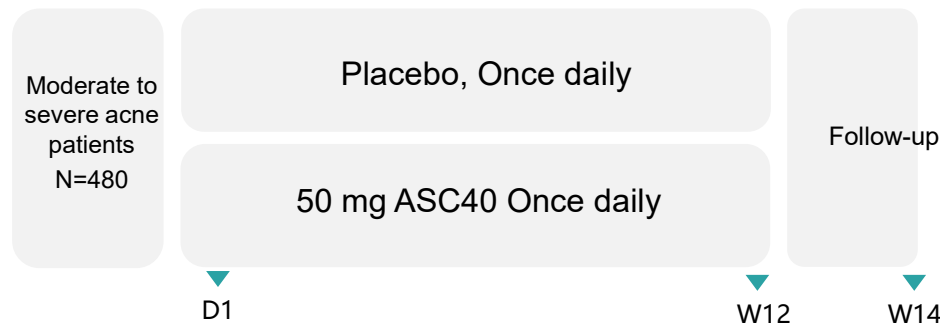
China's top dermatology clinical center –Huashan Hospital, Fudan University– leads the study

1.Guideline for Diagnosis and Treatment of Acne (The 2019 Revised Edition)

Inclusion Criteria

- ◆ 18-40 years old (including 18 and 40); baseline IGA score of 3-4
- ◆ Subjects should have facial lesions counted as follows:
Inflammatory lesions 30~75 (30 ~ 75 papules, pustules, and nodules, among which no more than 2 nodules)
- ◆ Non-inflammatory lesions 30 ~ 100 (30 ~ 100 open and closed pimples)

Phase III Clinical Trial Design





Primary Endpoints


- ◆ % change in total lesion count from baseline at week 12 of the treatment
- ◆ % change in inflammatory lesion count from baseline at week 12 of the treatment
- ◆ % of patients with a decrease of ≥ 2 points from baseline in the investigator's overall static score (IGA) and reached 0 or 1 point at week 12 of the treatment

Placebo Adjusted Efficacy of 50 mg ASC40, Oral, Once daily is Superior to Placebo Adjusted Efficacy of Winlevi® (not head-to-head comparison)

Endpoints	50 mg ASC40, oral, once daily (n=44), placebo adjusted	1% Clascoterone cream twice daily for 12 weeks, placebo adjusted	
	Phase II	Phase II	Phase III
% change from baseline in total lesion count at week 12 [§] <i>(primary endpoint)</i>	-27.1	NA	-11.9
% change from baseline in inflammatory lesion count at week 12 [§] <i>(key secondary endpoint)</i>	-33.6	-13.4	-12.8
Absolute change from baseline in inflammatory lesion count at week 12 <i>(key secondary endpoint)</i>	-13	-3.2	-5.6
% Treatment success at week 12	14.3	7.5	11.6

 **Efficacy:** Compared to placebo, all ASC40 groups (25, 50 and 75 mg) showed statistically significant benefits to acne patients in % change from baseline in total (primary) and inflammatory (key secondary) lesion counts at week 12

 **Safety:** At all doses, oral ASC40 with once-daily, 12-week treatment was safe and well tolerated

 **In Comparison with Winlevi® :** 1%, twice daily, placebo adjusted efficacy of 50 mg ASC40, oral, once daily is superior to Winlevi® in terms of % change from baseline in total and inflammatory lesion counts at week 12 as well as % treatment success at week 12

§ Data are medians

Safety Data Analysis: ASC40 (FASN) for Acne is Safe and Well Tolerated

Category	25mg dose group (n=45)		50mg dose group (n=44)		75 mg dose group (n=45)		Placebo group (n=45)	
	Number	Incidence(%)	Number	Incidence(%)	Number	Incidence(%)	Number	Incidence(%)
Drug-related TEAE	22	48.89%	21	47.73%	28	62.22%	22	48.89%
Drug-related TEAE of severity Grade 3 or higher	0	0.00%	0	0.00%	0	0.00%	0	0.00%
Drug-related severe adverse event (SAE)	0	0.00%	0	0.00%	0	0.00%	0	0.00%
Drug-related TEAE leading to discontinuation of the study drug	1	2.22%	1	2.27%	3	6.67%	0	0.00%
Drug-related TEAE leading to subject withdrawal from the study	1	2.22%	0	0.00%	3	6.67%	0	0.00%
Drug-related TEAE leading to death	0	0.00%	0	0.00%	0	0.00%	0	0.00%

TEAE: treatment-emergent adverse event.

Sarecycline Phase II vs ASC40 Phase II in ILC & NILC

Parameters	Sarecycline (1.5mg/kg)	ASC40 (50mg)	
	Phase 2, LSM[1]	Phase 2, Median[2]	Phase 2, Mean[2]
Patient number	70	44	44
change from baseline in percentage ILC: vs PBO, %	52.7 vs 38.3	65.0 vs 31.4	56.7 vs 36.5
p	0.02	0.003	0.003
change from baseline in absolute ILC: ILC vs PBO	16.9 vs 12.5	26 vs 13	24.9 vs 15.3
p	0.03	0.003	0.003
change from baseline in percentage NILC: vs PBO, %	37.5 vs 35.2	58.0 vs 42.9	46.6 vs 35.0
p	0.68	0.113	0.113
change from baseline in absolute NILC: ILC vs PBO	19.4 vs 17.9	28.5 vs 24.0	28.5 vs 22.1
p	0.63	0.196	0.196

Sarecycline is an oral, tetracycline derivatives antibiotic acne drug developed by Almirall. It was launched in the US in October 2018 and is mainly used to treat patients aged 9 years and older with moderate to severe acne vulgaris

ILC: Inflammatory Lesion Counts; NILC: Non-Inflammatory Lesion Counts; LSM: least squared mean; NA: not available; CSR: clinical study report; PR: from press release.

[1]. Leyden, J. J., et al.[J] J Drugs Dermatol, (2018); [2] Data from CSR;

Sarecycline Phase III vs ASC40 Phase II in ILC & NILC

Parameters	Sarecycline (1.5mg/kg)		ASC40 (50mg)	
	SC1401 Phase3, Mean[1]	SC1402 Phase3, Mean[1]	Phase 2, Median[2]	Phase 2, Mean[2]
Patient number	483	519	44	44
change from baseline in percentage ILC: vs PBO, %	52.2 vs 35.2	50.8 vs 36.4	65.0 vs 31.4	56.7 vs 36.5
p	<0.001	<0.001	0.003	0.003
change from baseline in absolute ILC: ILC vs PBO	15.3 vs 10.2	15.5 vs 11.1	26 vs 13	24.9 vs 15.3
p	<0.001	<0.001	0.003	0.003
change from baseline in percentage NILC: vs PBO, %	25.1 vs 22.2	28.5 vs 22.5	58.0 vs 42.9	46.6 vs 35.0
p	0.579	NA	0.113	0.113
change from baseline in absolute NILC: ILC vs PBO	14.7 vs 11.2	16.6 vs 14.7	28.5 vs 24.0	28.5 vs 22.1
p	0.001	NA	0.196	0.196

ILC: Inflammatory Lesion Counts; NILC: Non-Inflammatory Lesion Counts; LSM: least squared mean; NA: not available; CSR: clinical study report; PR: from press release.

[1]. Sarecycline review file 209521Orig1s000

[2]. Data from CSR;



Pipeline Highlights--rGBM

rGBM: Huge Unmet Medical Needs Globally

GBM: One of the Most Malignant

- 48%**
GBM as 48% of total CNS cancer
- 15k^[1]**
Incidence in US
- 40~64k^[2]**
Incidence in China
- ~100%^[2]**
Recurrent rate
- 5.8%^[3]**
5yr survival rate
- 12~14 months^[3]**
Median OS
- WHO IV**
High malignant grade
- No SoC**
For rGBM patients

SoC: standard of care

MoA of FASN: Lipid Metabolism^[4]

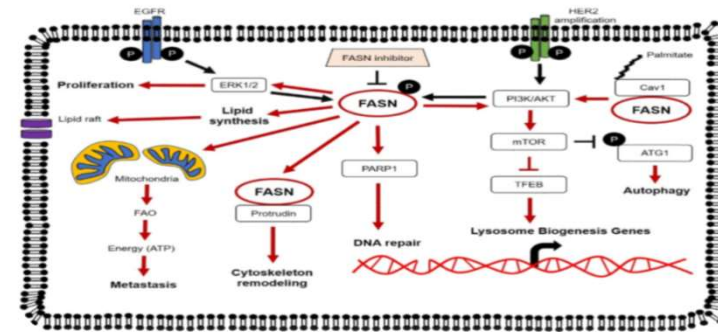
- Tumor cells rely on de novo synthesis of fatty acids for growth
- FASN plays a crucial role in maintaining energy metabolism and cell membrane structural homeostasis in tumor cells
- FASN is the only enzyme in the human body that can convert glucose metabolites to palmitate
- Palmitate saturated fatty acids are important components of the growth chain, polyunsaturated fatty acids, and essential components of cell signaling
- FASN is highly expressed in a variety of tumors, supports tumor cell growth and proliferation, and is associated with tumor invasion

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- 中国卫健委, 脑胶质瘤诊疗指南 (2022年版本)
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- Fhu CW, Ali A.):3935. doi:10.3390/molecules25173935
- Stupp R, Wong ET, Kanner AA, et al. NovoTTF-100A versus physician's choice chFatty Acid Synthase: An Emerging Target in Cancer. Molecules. 2020;25(17)emotherapy in recurrent glioblastoma: a randomised phase III trial of a novel treatment modality. Eur J Cancer. 2012;48(14):2192-2202

rGBM Treatments are Limited

- Surgical resection** : *lack of high-level evidence-based medical evidence for the benefit of surgical treatment of recurrent glioma*
- Radiation therapy**: *radiation may cause severe brain damage*
- chemotherapy**: *no standard chemotherapy for rGBM patients*
- TTF**: *no OS improvement compared with chemotherapy^[6], low affordability*

FASN Plays A Key Role in Cancer^[5]



(Molecules. 2020 Sep; 25(17): 3935.)

ASC40(FASN) for rGBM: Phase III Interim Analysis Expected in 2H 2024

ASC40(TVB-2640)+BEV Phase II Study^{[1]*}

Objective Response Rate 56%
Complete Response 17%
Partial Response 39%^[1]

- 25 patients enrolled
- All treated with ASC40 (TVB-2640) (100 mg/m² PO QD) plus BEV (10 mg/kg IV D1, 15) until disease progression or toxicity was intolerable

Phase II Results: mPFS=4.6, mOS=8.9

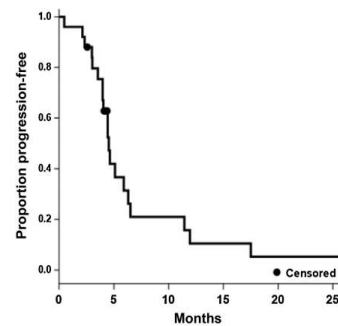


Figure 1. Kaplan-Meier estimate of progression (all patients, N=25; median = 4.5; 95% CI, 4.0-6.3).

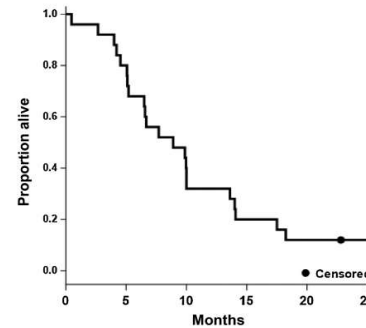


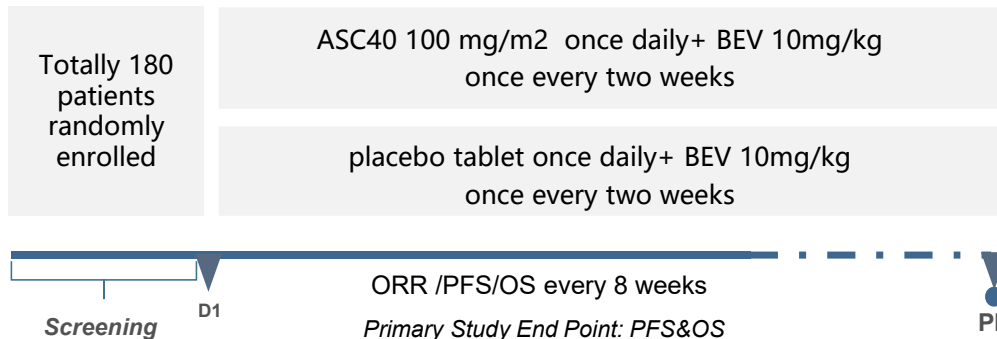
Figure 2. Kaplan-Meier estimate of OS (all patients, N = 25; median = 8.9; 95% CI, 5.2-13.6).

PFS6 Improvement & Safety

- **PFS6=31.4%**, representing a statistically significant improvement in PFS over the historical Bevacizumab monotherapy PFS of 16% (BELOB Trial) (P=0.008)
- **Safe and tolerated:** ASC40 (TVB-2640) in combination with BEV was safe and well tolerated for the treatment of rGBM pts
- Results have been published on **CLINICAL CANCER RESEARCH**

Clinical Phase III Trial of ASC40 + BEV to Treat rGBM

Study Design



China's prestigious brain cancer center--Beijing Tiantan Hospital--leads the study. Other 28 top-tier hospitals participated in clinical research



120 patients enrollment --the basis for pre-planned interim analysis (93 PFS events)-- completed as of Q3,2023



If Phase III interim results shows PFS is significant improved, ASC40 for rGBM may obtain the conditional approval

1. Kelly, William et al. "Phase II Investigation of TVB-2640 (denifanstat) with Bevacizumab in Patients with First Relapse High-Grade Astrocytoma." *Clinical cancer research: an official journal of the American Association for Cancer Research*, CCR-22-2807.



Summary & Outlook

Focus on Unmet Medical Needs

Target Patients	Therapeutic Area	Current Situation	Ascletis Highlights	Updates
480mm CN+US	Obesity	<ul style="list-style-type: none"> x GLP-1 capacity shortage remains x More long-acting, low-cost GLP-1 agonists needed 	<ul style="list-style-type: none"> • ASC30 is the first and only small molecule GLP-1 receptor (GLP-1R) agonist that can be dosed once-monthly subcutaneously and once-daily orally to treat obesity 	<ul style="list-style-type: none"> • Topline data from ongoing U.S. Phase I clinical trials of ASC30 once-monthly subcutaneous injection and once-daily oral tablet to treat obesity expected first quarter 2025
120mm CN	Acne	<ul style="list-style-type: none"> x Moderate and severe acne patients account for 23-35% x Isotretinoin and antibiotics have many side effects 	<ul style="list-style-type: none"> • Innovative mechanism inhibits sebum secretion • Excellent phase II clinical trial data, good safety profile; oral once daily, convenient for administration 	<ul style="list-style-type: none"> • Phase III trial of ASC40 initiated in Q4, 2023 • China's top dermatology clinical center -Huashan Hospital, Fudan University- leads the study
86mm CN	HBV	<ul style="list-style-type: none"> x NAs: high relapse rate once off treatment x Interferon: various side effects 	<ul style="list-style-type: none"> • ASC22 is the world's fastest-progressing immunotherapy for the treatment of hepatitis B through PD-1/PD-L1 mechanism 	<ul style="list-style-type: none"> • Interim data of ASC22 IIb expansion cohort: 21.6% pts with baseline HBsAg\leq100 reached HBsAg loss with 24 wk treatment
48mm CN	MASH	<ul style="list-style-type: none"> x Large patient population x limited MASH drug approved 	<ul style="list-style-type: none"> • THR-β: ASC41 First-in-China/ Third-in-Global • FASN: ASC40 First-in-class in the world 	<ul style="list-style-type: none"> • ASC41: positive interim data of Phase II potentially BIC THR-β agonist globally • ASC40: Phase IIb biopsy data met two primary endpoints
40~60k CN	GBM	<ul style="list-style-type: none"> x 5-year survival rate is extremely low(5.8%) for GBM x High relapse rate after surgery, limited effective treatments 	<ul style="list-style-type: none"> • Novel lipid metabolism mechanisms for the treatment of solid tumors • Phase II clinical data : PFS6=31.4% 	<ul style="list-style-type: none"> • Over 120 patients enrolled in Phase III (180 totally) • May have enough events for interim analysis of PFS

133+mm HK\$ Buyback* Significantly Improved Shareholders' Return

Substantial Buyback to Boost Market Confidence

- Approved 200mm HK\$ for buyback in 2024.7
- 80+mm shares repurchased to date*
- The largest buyback among 18A biotechs

Clinical Progress Increases Intrinsic Value

- ASC40-MASH-PhIIb biopsy results: met two primary endpoints
- ASC41-MASH-PhII interim results: potential BIC THRβ
- ASC40-Acne-PhIII: to complete enrollment in Q4







Listen to and Value Our Investors

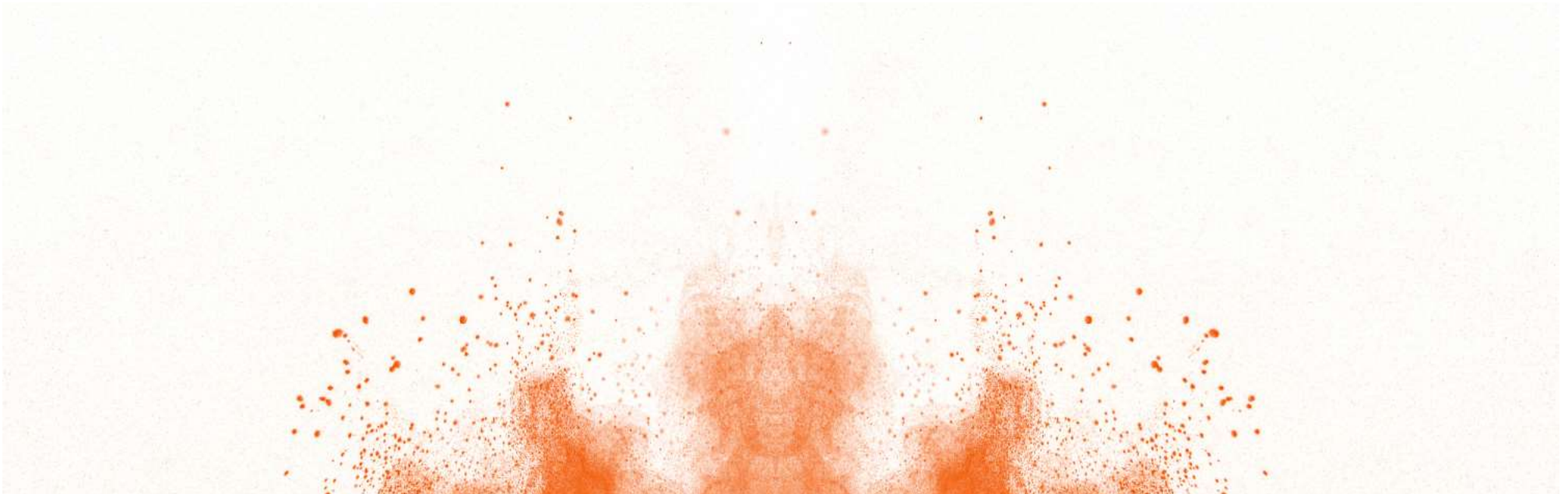
- Expand channels to enhance investor understanding
- Timely, sincere, and transparent
- Take opinions and feedback seriously



*2023.6.15-2024.8.30

Expected Milestones

Indications	Catalysts	Status
MASH	ASC41(THR-β)MASH—Complete Phase II enrollment	
MASH	ASC40(FASN)MASH-Submit the Phase IIb data from US and initiate discussion with China NMPA for Phase III trial of NASH	
Acne	ASC40(FASN)acne—Complete Phase III enrollment	
rGBM	ASC40(FASN)rGBM--Complete Phase III trial	
Oncology	ASC61(PD-L1)solid tumors—Complete the Phase I multiple ascending dose clinical trial of ASC61 in the U.S	
Obesity	Topline data from ongoing U.S. Phase I clinical trials of ASC30 to treat obesity expected first quarter 2025	



Thanks

Innovative cures liberate life to the fullest

