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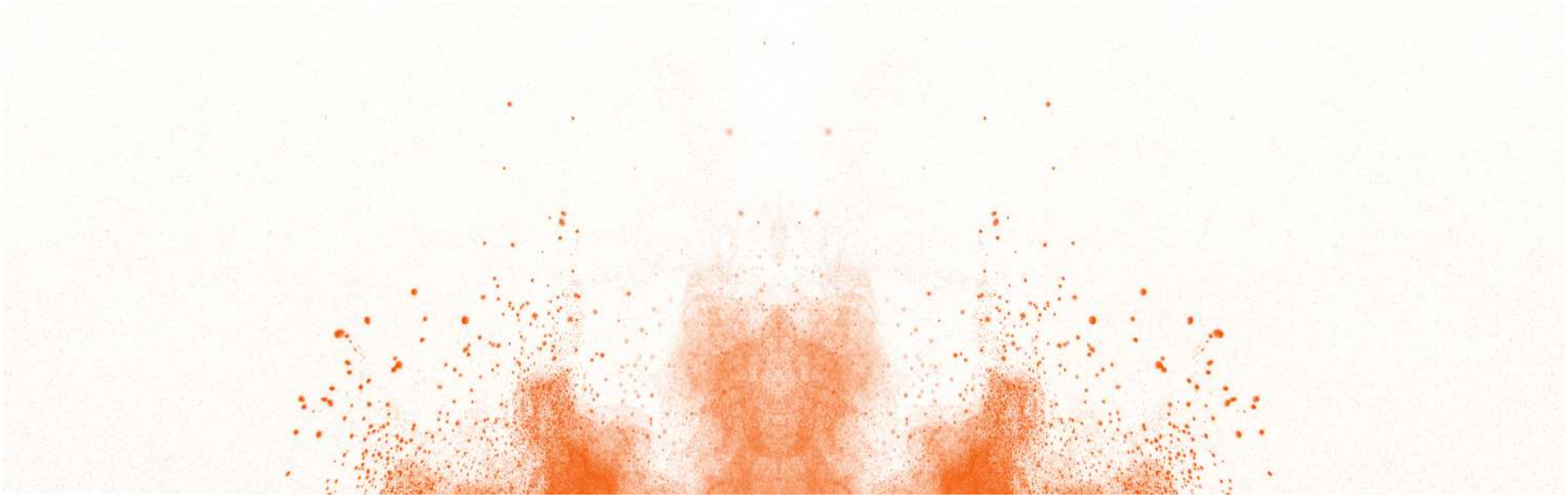
Ascletis Pharma (1672.HK)

Investor Day

Jan 4, 2024, Shanghai



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Overview

R&D Pipeline

Therapeutical Area	Product (Modality)	Target	Indication	Commercial Rights	Pre-IND	IND	Phase I	Phase II	Phase III
Viral Diseases	ASC22 (Subcutaneous mAb)	PD-L1	CHB functional cure	Global[1]					
NASH	ASC40 (Oral small molecule)	FASN	NASH	Greater China[2]					
	ASC41 (Oral small molecule)	THRβ	NASH	Global					
	ASC43F FDC (Oral small molecule)	THRβ + FXR	NASH	Global					
Oncology	ASC40 (Oral small molecule) +Bevacizumab	FASN+ VEGF	Recurrent glioblastoma	Greater China[2]					
	ASC61 (Oral small molecule)	PD-L1	Advanced solid tumor	Global					
Acne	ASC40 (Oral small molecule)	FASN	ACNE	Greater China[2]					

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

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Focus on Unmet Medical Needs

China Patients	Therapeutic Area	Current Situation	Highlights	Ascletis Updates
120mm	Acne	x Moderate and severe acne patients account for 23-35% x Isotretinoin and antibiotics have many side effects	• Innovative mechanism inhibits sebum secretion • Excellent phase II clinical trial data, good safety profile; oral once daily, convenient for administration	• Phase III trial of ASC40 initiated in Q4, 2023 • China's top dermatology clinical center –Huashan Hospital, Fudan University– leads the study
86mm	HBV	x NAs: high relapse rate once off treatment x Interferon: various side effects	• ASC22 is the world's fastest-progressing immunotherapy for the treatment of hepatitis B through PD-1/PD-L1 mechanism	• Interim data of ASC22 IIb expansion cohort: 21.6% pts with baseline HBsAg≤100 reached HBsAg loss with 24 wk treatment
48mm	NASH	x No NASH drug approved by FDA,EMA,NMPA yet x GLP-1 has no improvements for liver fibrosis	• THR-β: ASC41 First-in-China/ Third-in-Global • FASN: ASC40 First-in-class in the world	• ASC41: positive interim data of Phase II potentially BIC THR-β agonist globally • ASC40: Phase II liver biopsy data to release soon
40~60k	GBM	x 5-year survival rate is extremely low(5.8%) for GBM x High relapse rate after surgery, limited effective treatments	• Novel lipid metabolism mechanisms for the treatment of solid tumors • Phase II clinical data : PFS6=31.4%	• Over 120 patients enrolled in Phase III (180 totally) • May have enough events for interim analysis of PFS

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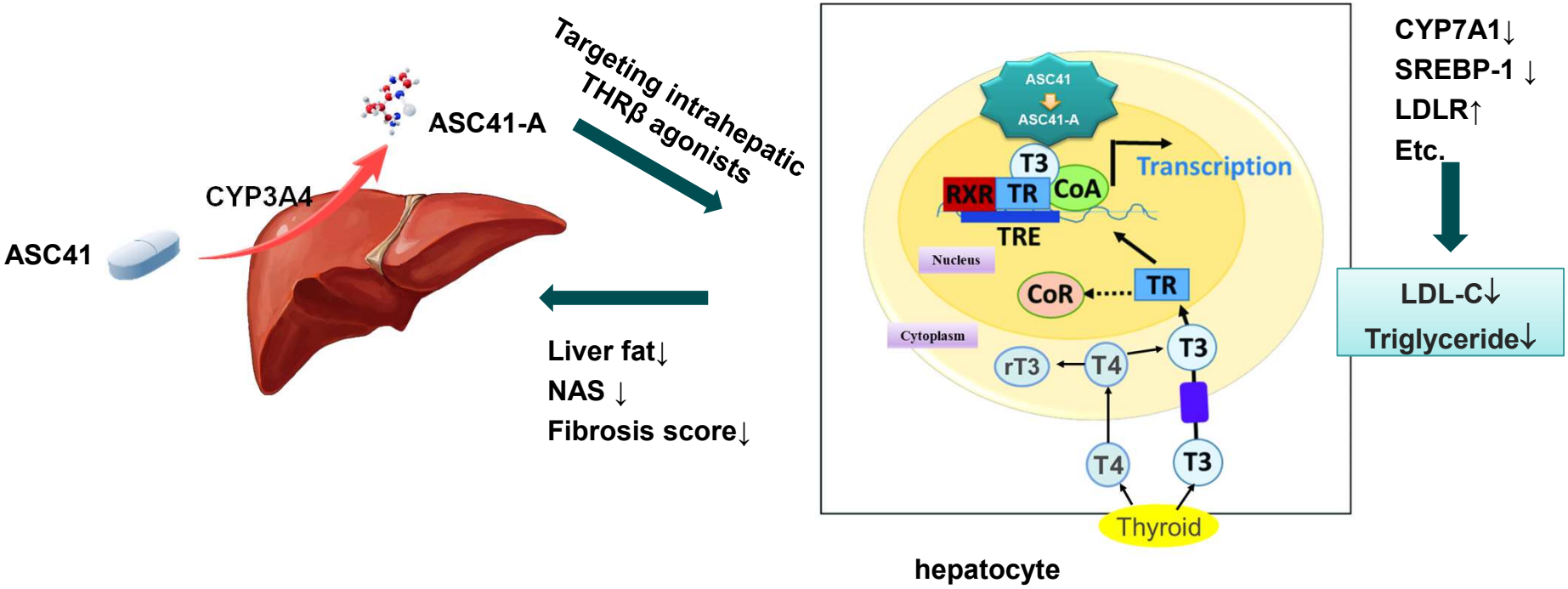
Pipeline Updates

ASC41 NASH

ASC41: A Liver Targeting Thyroid Hormone Receptor Beta (THRβ) Agonist

- ASC41 is a liver targeted small molecule which is converted to its active metabolite ASC41-A - a potent and selective THRβ agonist



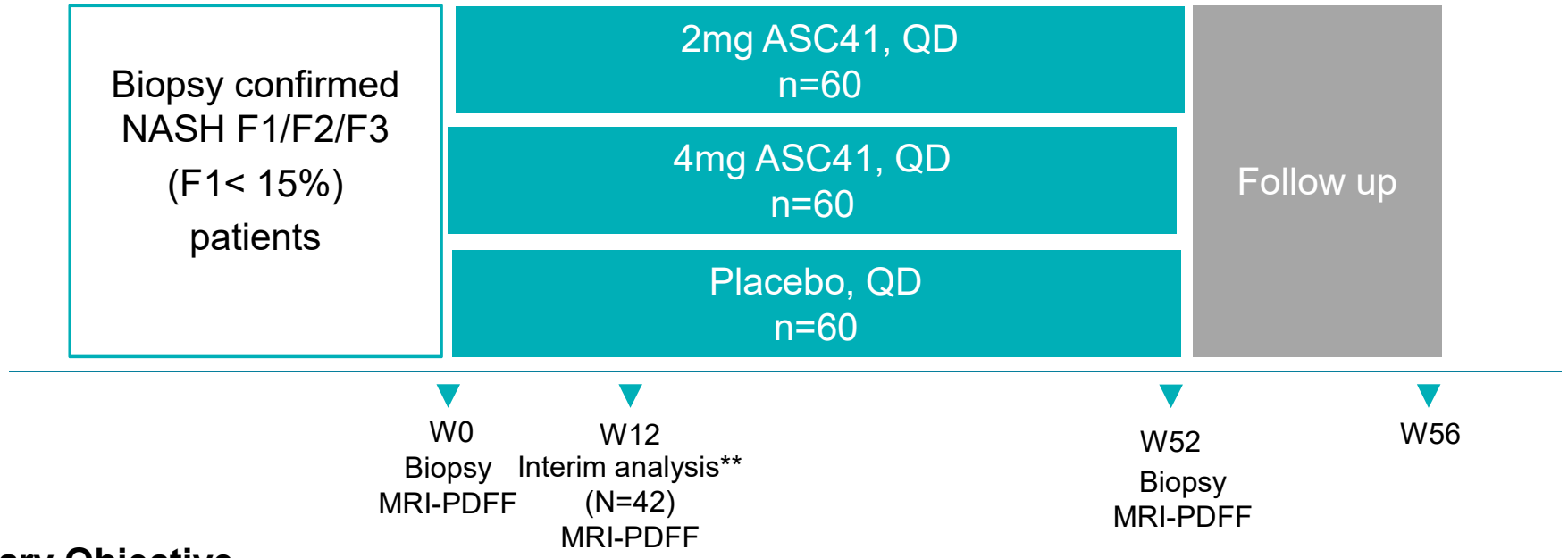
Source: Gannex data

ASC41: A Potential best-in-class THRβ Agonist

- ASC41 is a liver-targeted prodrug, and its active metabolite is a highly selective THRβ agonist.
- In two NASH animal models, at 1/10 dose of resmetirom (MGL-3196), ASC41 demonstrated the same improvement of liver steatosis, inflammation and fibrosis.
- Commercially ready oral tablet formulation developed with in-house proprietary technology
- 2 China Phase I studies completed
  - Statistically significant and clinical meaning reductions in lipids such as LDL-C starting from 2 mg QD
- 2 US bridging studies completed
  - No significant difference in drug exposure among Chinese and Americans; no significant drug-drug interactions
- 1 China Phase Ib study completed
  - 28 day, 10 mg QD in 20 overweight and obese subjects with elevated LDL-C > 110 mg/dL; statistically significant reduction in lipids such as LDL-C.
- Based on above studies, 2 mg and 4 mg once-daily doses have been selected for a 52-week Phase II trial in biopsy-confirmed NASH patients
  - Pre-specified interim analysis at Week 12 demonstrated ASC41 as a potential best-in-class THRβ agonist versus other THRβ agonists currently at clinical or registration stages

Source: 1. Jinzi J. Wu et al, AASLD 2021 abstract 1851; 2. Jinzi J. Wu et al, EASL 2021 abstract PO-1851;

ASC41: 52-week Phase II Study in Biopsy-confirmed NASH 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 Week12 Data from 52-Week ASC41 Tablet Study

- Up to 68.2% mean liver fat reduction from baseline in biopsy-confirmed non-alcoholic steatohepatitis (NASH) patients receiving 12-week treatment of ASC41 tablet
- Up to 93.3% patients achieved at least a 30% relative reduction in liver fat after 12-week treatment
- At Week 12, placebo-adjusted mean reductions in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) from baseline were up to 37.8% and 41.5%, respectively
- At Week 12, placebo-adjusted mean reductions in low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC) and triglyceride (TG) from baseline were up to 27.7%, 23.4% and 46.5%, respectively
- Adverse events (AEs), including gastrointestinal (GI)-related AEs, were similar among the cohorts receiving ASC41 tablet treatment versus the placebo

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)

Reduction in Liver Inflammatory Biomarkers from Baseline at Week 12

- Mean ALT and AST at baseline ranged from 65.9 to 84.8 U/L and 44.2 to 53.8 U/L, respectively, across ASC41 tablet and placebo cohorts.
- At Week 12, placebo-adjusted mean absolute reductions in ALT and AST from baseline were up to 34.2 U/L and 21.4 U/L, respectively.
- At Week 12, placebo-adjusted mean relative reductions in ALT and AST from baseline were up to 37.8% and 41.5%, respectively.
- Placebo-adjusted percentage of patients achieving mean ALT decrease > 17 U/L was up to 51.9%.
- Statistically significant and clinical meaningful reductions in ALT and AST in patients receiving ASC41 tablet treatment notably differentiate ASC41 from other THRβ agonists currently at clinical or registration stages.
  - ➢ Decline in serum ALT in NASH patients is associated with improvement in liver histology.

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.

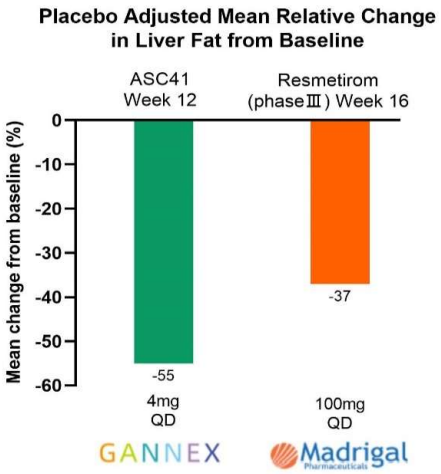
Safety and Tolerability

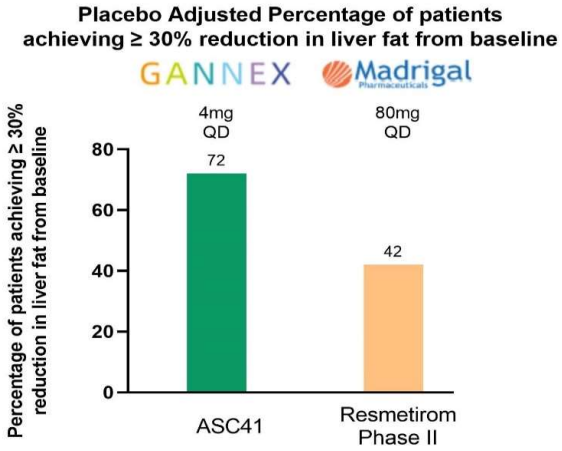
- Levels of thyroid axis hormones, including thyroid stimulating hormone (TSH), free triiodothyronine (fT3) and free thyroxine (fT4) were relatively unchanged from baseline among the cohorts receiving ASC41 tablet treatment versus the placebo.
- Changes in vital signs and electrocardiogram (ECG) were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

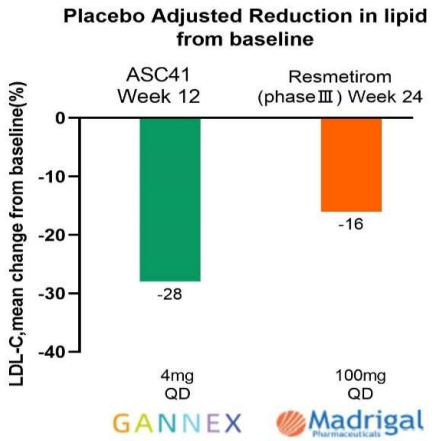
	Placebo (n = 14)	ASC41 Tablet	
		2 mg, QD (n = 13)	4 mg, QD (n = 15)
TEAEs [1] Number of subjects (%)	13(92.9%)	13(100%)	15(100%)
Drug-related TEAEs [2]	6(42.9%)	7(53.9%)	7(46.7%)
Grade 1	6(42.9%)	7(53.9%)	7(46.7%)
Drug-related GI AEs	2(14.3%)	3(23.1%)	1(6.7%)
Nausea	0(0.0%)	0(0.0%)	0(0.0%)
Vomiting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

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

THRβ Agonists: ASC41 vs Resmetirom







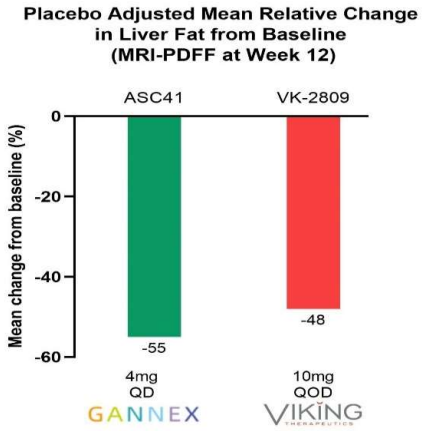
Placebo-adjusted mean reductions in liver inflammatory biomarkers from baseline at Week 12	ASC41 tablet, stable at room temperature	Resmetirom tablet[1], stable at room temperature
ALT	**Up to 37.8%** (Statistically significant difference vs placebo)	No statistically significant difference vs placebo
AST	**Up to 41.5%** (Statistically significant difference vs placebo)	No statistically significant difference vs placebo

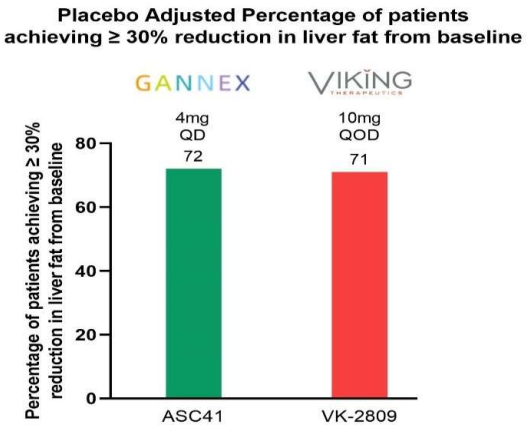
	ASC41 tablet		Resmetirom tablet Phase III	
	Placebo (n = 14)	2mg/4mg QD (n=28)	Placebo (n = 321)	100mg QD (n=323)
TEAEs Number of subjects(%)	13(92.9%)	28(100%)	269 (92.2%)	296 (91.6%)
Drug-related TEAEs	6(42.9%)	14(50%)	86 (26.8%)	134 (41.5%)
Drug-related TEAEs leading to study discontinuation	0(0.0%)	1(3.6%)	8 (2.5%)	22 (6.8%)
Drug-related GI AEs	2(14.3%)	4(14.3%)	NA	NA
Nausea	0(0.0%)	0(0.0%)	40 (12.5%)	62 (19.2%)
Diarrhea	1(7.1%)	4(14.3%)	50 (15.6%)	109 (33.7%)
Vomiting	0(0.0%)	0(0.0%)	17 (5.3%)	35 (10.8%)
Abdominal distension	1(7.1%)	0(0.0%)	NA	NA

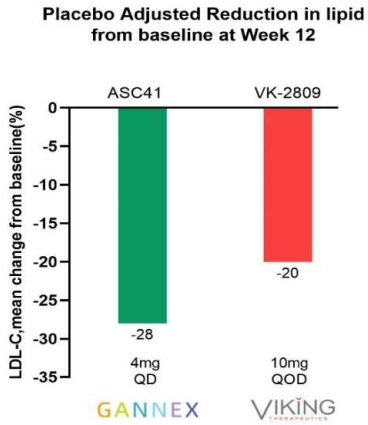
[1] 36-week phase 2 and 52-week phase 3
[2] NA:Not avaliable

Resmetirom: Stephen A. Harrison, et al. EASL 2023 abstract number GS-001; Harrison, S. A., et al.[J] Lancet, (2019).DOI: 10.1016/s0140-6736(19)32517-6

THRβ Agonists: ASC41 vs VK-2809







Placebo-adjusted mean reductions in liver inflammatory biomarkers from baseline at Week 12	ASC41 tablet, stable at room temperature	VK2809 Capsule[1], stable only under refrigeration
ALT	**Up to 37.8%** (Statistically significant difference vs placebo)	Similar to placebo
AST	**Up to 41.5%** (Statistically significant difference vs placebo)	Similar to placebo

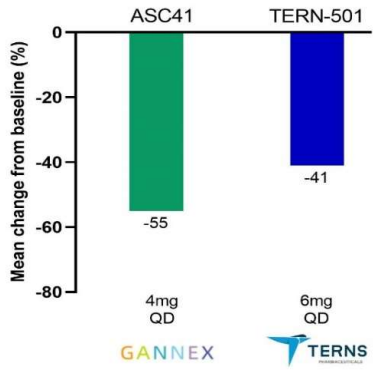
	ASC41 tablet		VK2809 Capsule	
	Placebo (n = 14)	2mg/4mg QD (n=28)	Placebo (n = 65)	10mg QOD (n=61)
TEAEs Number of subjects(%)	13(92.9%)	28(100%)	47(72.3%)	54(88.5%)
Drug-related TEAEs	6(42.9%)	14(50%)	22(33.8%)	23(37.7%)
Drug-related TEAEs leading to study discontinuation	0(0.0%)	1(3.6%)	5(7.7%)	5(8.2%)
Drug-related GI AEs	2(14.3%)	4(14.3%)	12(18.5%)	7(11.5%)
Nausea	0(0.0%)	0(0.0%)	5(7.7%)	3(4.9%)
Diarrhea	1(7.1%)	4(14.3%)	2(3.1%)	3(4.9%)
Vomiting	0(0.0%)	0(0.0%)	NA	NA
Abdominal distension	1(7.1%)	0(0.0%)	NA	NA

[1]Viking press release, May 2023
[2]NA:Not avaliable

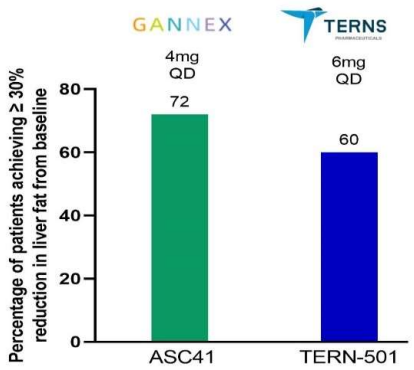
VK-2809: Rohit Loomba, et al. AASLD 2023 abstract number 5016-C;https://ir.vikingtherapeutics.com/2023-11-13-Viking-Therapeutics-Presents-New-Data-from-Phase-2b-VOYAGE-Study-of-VK2809-in-Patients-with-Biopsy-Confirmed-Non-Alcoholic-Steatohepatitis-NASH-at-The-Liver-Meeting-R-2023; https://ir.vikingtherapeutics.com/corporatepresentation, November 2023

THRβ Agonists: ASC41 vs TERN-501

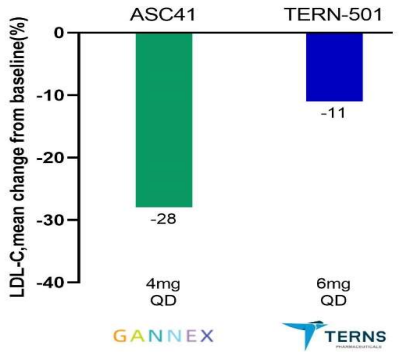
Placebo Adjusted Mean Relative Change in Liver Fat from Baseline(MRI-PDFF at Week 12)



Placebo Adjusted Percentage of patients achieving ≥ 30% reduction in liver fat from baseline



Placebo Adjusted Reduction in lipid from baseline at Week 12

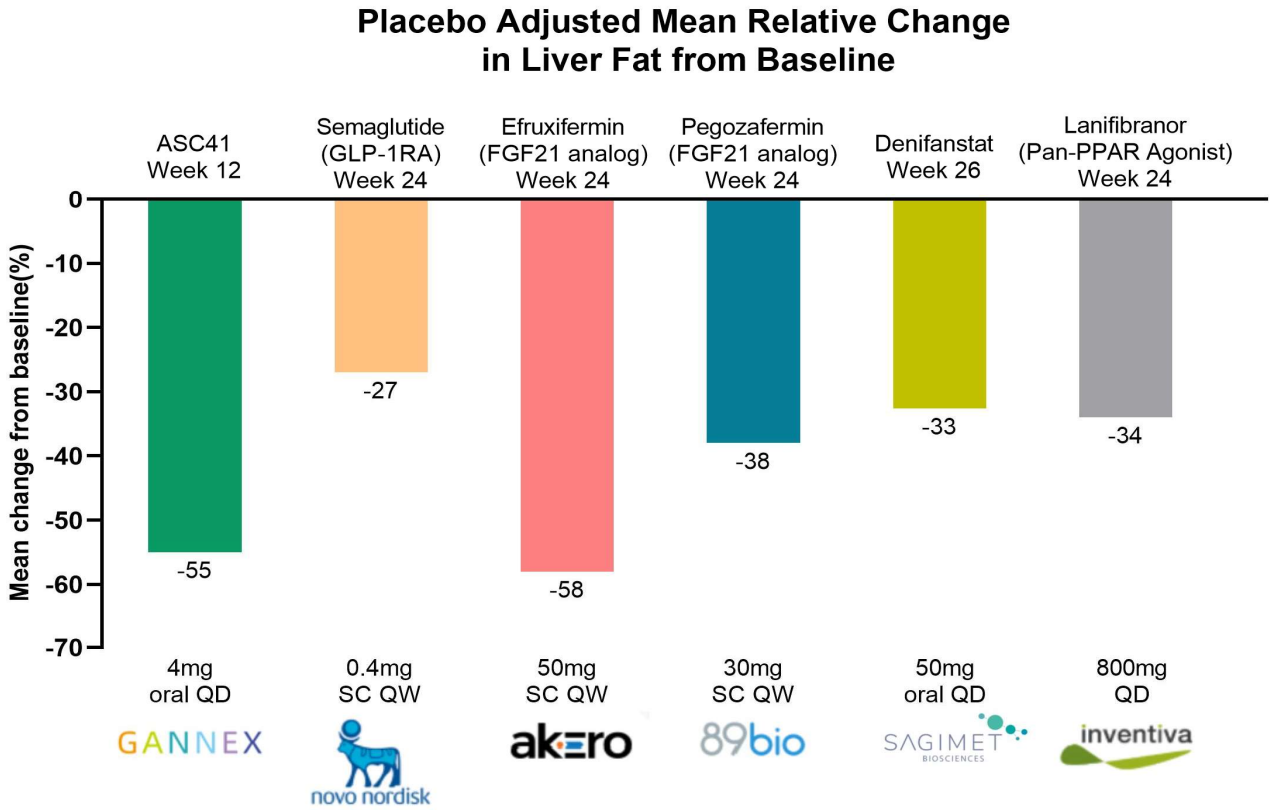


Placebo-adjusted mean reductions in liver inflammatory biomarkers from baseline at Week 12	ASC41 tablet, stable at room temperature	Tern-501[1],formualtion and storage condition unknown
ALT	**Up to 37.8%** (Statistically significant difference vs placebo)	Similar to placebo
AST	**Up to 41.5%** (Statistically significant difference vs placebo)	Similar to placebo

	ASC41 tablet		Tern-501	
	Placebo (n = 14)	2mg/4mg QD (n=28)	Placebo (n =24)	6mg QD (n=22)
TEAEs Number of subjects(%)	13(92.9%)	28(100%)	NA	NA
Drug-related TEAEs	6(42.9%)	14(50%)	NA	NA
Drug-related TEAEs leading to study discontinuation	0(0.0%)	1(3.6%)	1(4.2%)	1(4.5%)
Drug-related GI AEs	2(14.3%)	4(14.3%)	2(8.3%)	2(9.1%)
Nausea	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Diarrhea	1(7.1%)	4(14.3%)	1(4.2%)	1(4.5%)
Vomiting	0(0.0%)	0(0.0%)	1(4.2%)	0(0.0%)
Abdominal distension	1(7.1%)	0(0.0%)	0(0.0%)	0(0.0%)

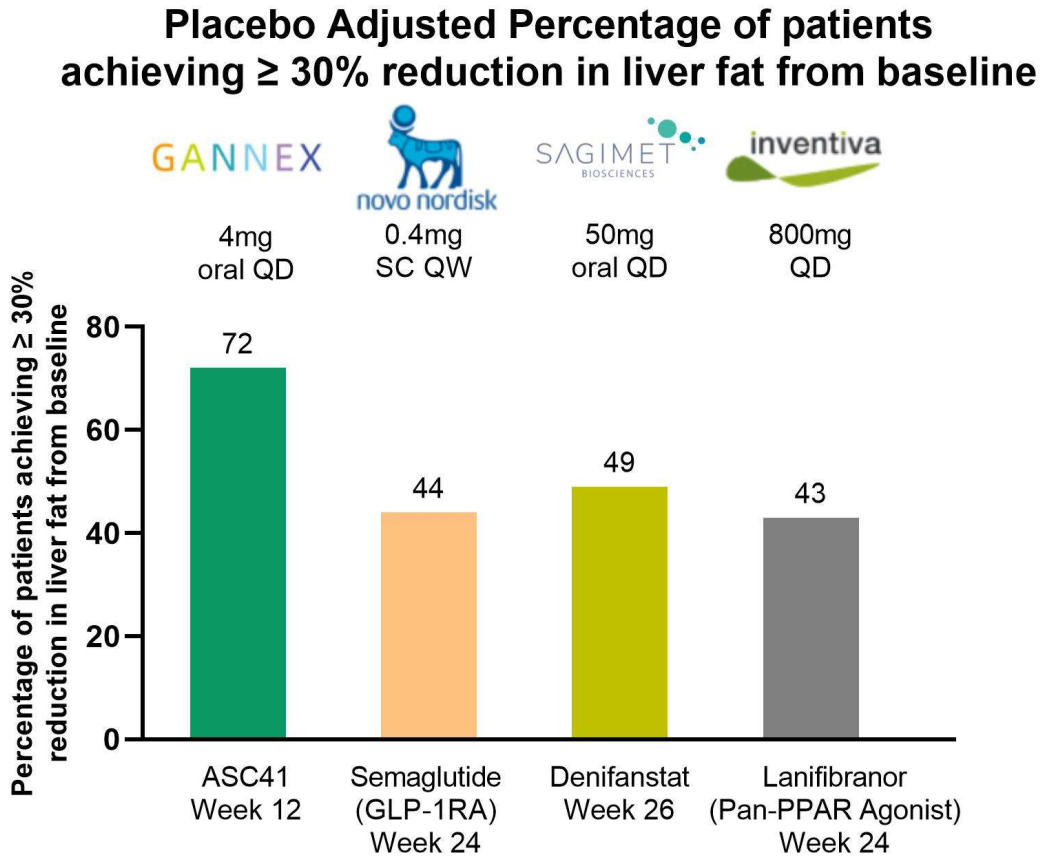
[1] Terns press release, August 2023
TERN-501: https://ir.ternspharma.com/events/event-details/terns-duet-top-line-results

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



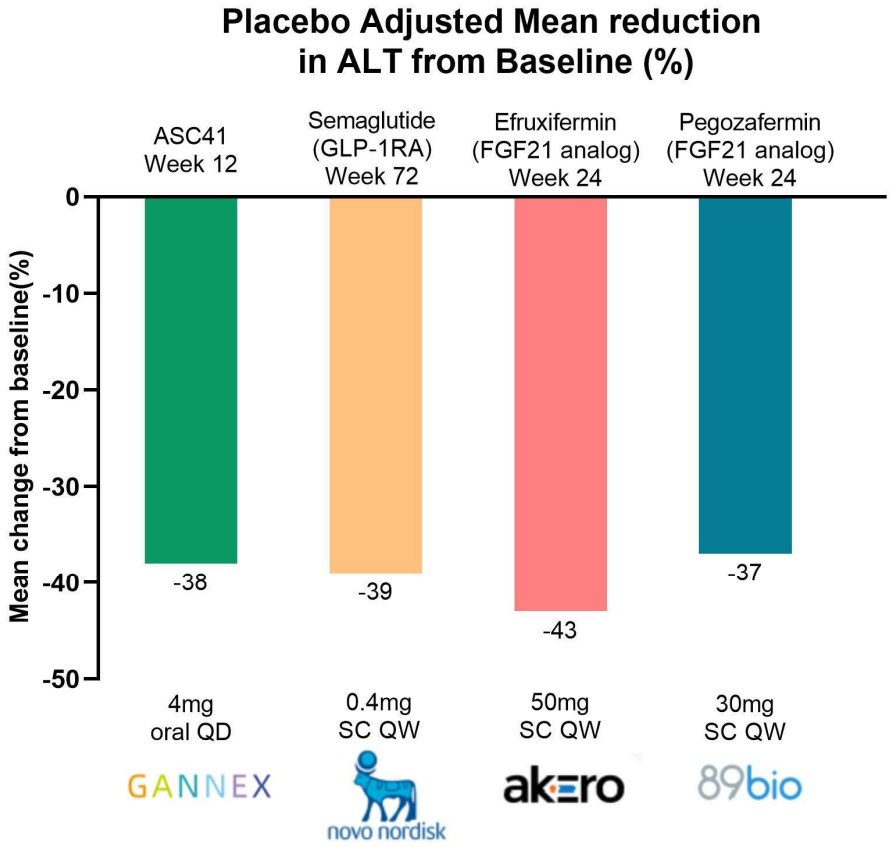
1. Semaglutide: Flint, A., et al.[J] Aliment Pharmacol Ther, (2021).DOI: 10.1111/apt.16608;
2. Efruxifermin: Stephen A. Harrison., et al. AASLD 2022 Abstract #39094;
3. Pegozafermin: https://ir.89bio.com/news-releases/news-release-details/89bios-phase-2b-enliven-trial-pegozafermin-nonalcoholic;
4. Denifanstat: 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: ≥30% Liver Fat Reduction



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-nonalcoholic;

Conclusions of ASC41 Interim Data

- Interim data in liver fat and lipids at Week 12 demonstrated ASC41 as a potential best-in-class THRβ Agonist vs other THRβ agonists currently at clinical or registration stages
- Statistically significant and clinical meaningful reductions in ALT and AST in patients receiving ASC41 tablet treatment notably differentiate ASC41 from other THRβ agonists
- ASC41 tablet showed excellent safety and tolerability profile, including GI.

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)	Globally	\	\

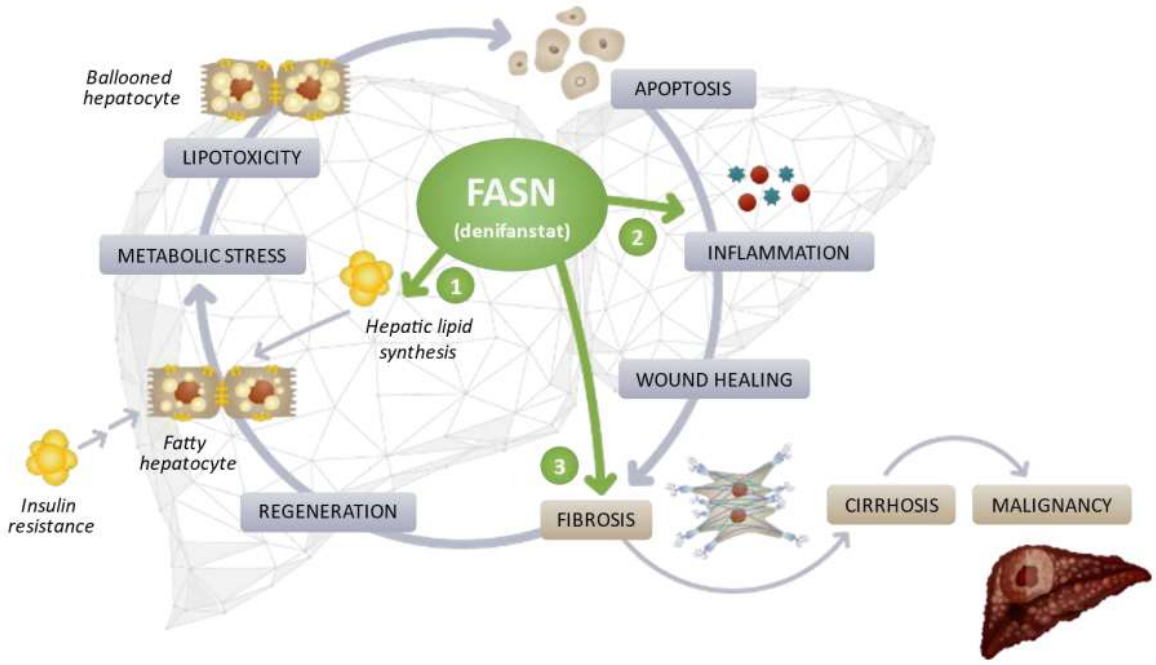
1. Patents and patent applications information released as of Aug 20, 2023

ASC40 NASH

ASC40(FASN): Novel Mechanism for NASH

MoA of ASC40 for NASH Treatment

1. Block **steatosis** via inhibiting de novo lipogenesis in hepatocytes
2. Reduce **inflammation** via preventing immune cell activation
3. Blunt **fibrosis** via inhibiting stellate cell activation



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ASC40-IIb Interim Analysis Cohort Represents Target Patient Population

Mean(SD)	Placebo (n=22)	ASC40-Denifanstat 50mg (n=30)	Combined
Age (years)	56.8 (9.4)	56.1 (12.4)	56.4 (11.1)
Female/Male (%)	14 (63.6%) / 8 (36.4%)	17 (56.7%) / 13 (43.3%)	31 (59.6%) / 21 (40.4%)
Not Hispanic or Latino	16 (72.7%)	24 (80.0%)	40 (76.9%)
Weight (kg)	97.8 (21.9)	100.9 (21.2)	99.6 (21.4)
Diabetes (% T2DM)	13 (59.1%)	21 (70.0%)	34 (65.4%)
F2/F3 (%)	12 (54.5%) / 10 (45.5%)	12 (40.0%) / 18 (60.0%)	24 (46.2%) / 28 (53.8%)
MRI-PDFF (%)	21.78 (5.46)	17.46 (6.36)	19.29 (6.32)
Fibroscan (kPa)	10.67 (4.07)	12.29 (7.33)	11.56 (6.04)
ALT (U/L)	69.77 (42.50)	57.14 (27.55)	62.70 (35.11)
AST (U/L)	51.00 (29.87)	44.43 (22.65)	47.32 (26.00)
LDL (mg/dL)	111.37 (40.6)	96.29 (50.27)	102.86 (46.4)
ELF	9.70 (0.76)	9.73 (0.76)	9.72 (0.75)
PRO-C3 cobas® (ng/mL)	35.72 (15.71)	32.54 (11.19)	33.91 (13.28)

Patients enrolled:

•Typical F2/F3 NASH population • Middle-aged	• High % of diabetes • High liver fat by MRI-PDFF	•Elevated liver enzymes: inflammation • Non-invasive markers of fibrosis consistent with F2/F3

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Interim Data from ASC40 Phase IIb Clinical Trial: 67% of Patients Reduced Liver Fat by More Than 30%

	ASC40 50 mg (n=30)	Placebo (n=22)	P-value vs placebo
Relative reduction in liver fat	*-34.1%*	*- 1.5%*	*p<0.001*
≥30% reduction of liver fat (responder rate)	*67%*	*18%*	*p<0.01*
ALT (U/L)	*- 16.5*	*- 4.0*	*p<0.05*
Dual liver fat & ALT responder >30% + >17U/L decrease	*37.0%*	*9.0%*	*p<0.05*
PRO-C3	*– 8.2%*	*-1.5%*	*p<0.05*
Enhanced liver fibrosis (ELF) score*	*- 0.34*	*- 0.02*	*p<0.05*
LDL cholesterol (mg/dL)	*-12.4*	*0.0*	*p<0.05*
FGF21	*+73.1%*	*+ 0.9%*	*p<0.01*

**approximately half of denifanstat responders decreased liver fat by ≥50%*

https://sagimet.com/sagimet-biosciences-announces-positive-interim-phase-2b-clinical-trial-data-with-denifanstat-tvb-2640-a-first-in-class-fatty-acid-synthase-inhibitor-in-moderate-to-severe-non-alcoholic-steatohepa/

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ASC40(FASN) NASH IIb Safety Profile

FASCINATE-2 IIb - Blinded data set

TEAE	Grade 1: 115 (68.5%) Grade 2: 69 (41.1%) Grade 3: 10 (6.0%) Grade 4: 1 (0.6%)	All randomized subjects: blinded data set including active and placebo • Majority of AEs to date were Grade 1 or 2; no Grade ≥3 drug-related AEs • A planned safety review of unblinded data from all 168 patients conducted by Independent Data Monitoring Committee – no concerns
TEAE leading to drug/placebo discontinuation	21	
Treatment Emergent Serious Adverse Event (SAE)	11 (all unrelated to study treatment)	• Expect to use Phase 2b results including AI pathology scores to design and power Phase 3 • Startup activities expected 2024
Drug/placebo-related TEAE	Grade 1: 52 (30.1%) Grade 2: 25 (14.9%)	Phase IIb biopsy results of ASC40 for NASH expected in 1Q 2024

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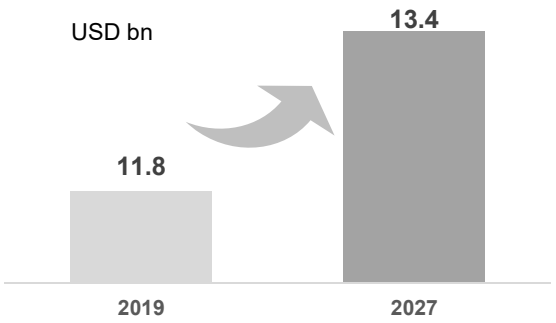
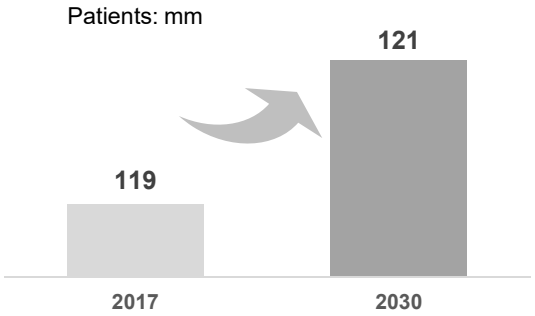
ASC40 Acne

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

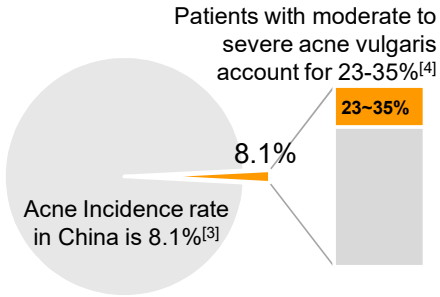
Global Acne Market Forecast[1]



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

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ASC40 (FASN) for Acne: Phase III Clinical Trial Initiated in Dec 2023

ASC40: Innovative Mechanism for Acne Treatment

Human sebum production requires DNL

ASC40 is an oral, selective, FASN small molecule inhibitor

FASN is a key enzyme which regulates de novo lipogenesis (DNL)

Human sebum production requires DNL, which is increased in acne and can be suppressed by ASC40

ASC40 Acne Phase III Trial

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

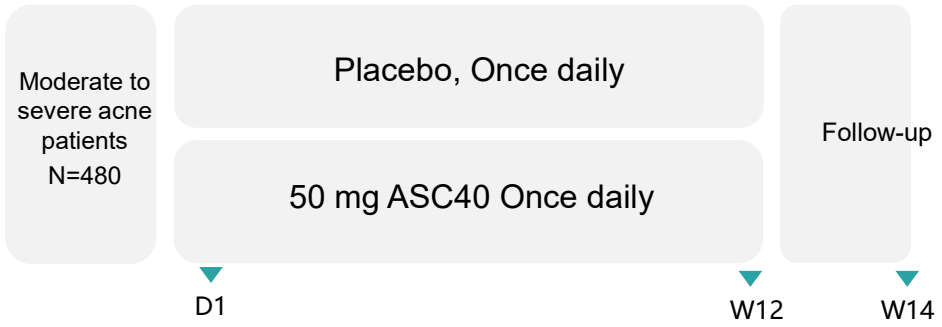
China’s top dermatology clinical center –Huashan Hospital, Fudan University– leads the study

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§ ***(primary endpoint)***	***-27.1***	*NA*	*-11.9*
% change from baseline in inflammatory lesion count at week 12§ ***(key secondary endpoint)***	***-33.6***	*-13.4*	*-12.8*
Absolute change from baseline in inflammatory lesion count at week 12 ***(key secondary endpoint)***	***-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

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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.

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ASC40 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

12~14months[3]
Median OS

WHO IV
High malignant grade

No SoC
For rGBM patients

SoC: standard of care

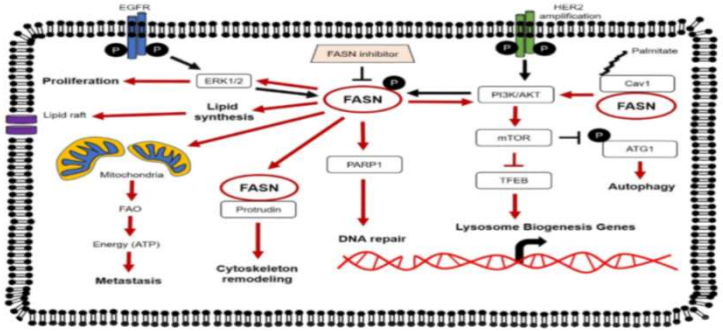
MoA of FASN: Lipid Metabolism[4]

- 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

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]



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2.中国卫健委，脑胶质瘤诊疗指南（2022年版本）
3. Stupp R, Mason W P, van den Bent M J, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma [J]. Kelly, William et al.
4.Tan A C, Ashley D M, Lopez G Y, et al. Management of glioblastoma: State of the art and future directions [J]
5.Fhu CW, Ali A.):3935. doi:10.3390/molecules25173935
6.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(17emotherapy in recurrent glioblastoma: a randomised phase III trial of a novel treatment modality. Eur J Cancer. 2012;48(14):2192-2202

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ASC40(FASN) for rGBM: Phase III Enrolled 120 Patients as of Sept 2023

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

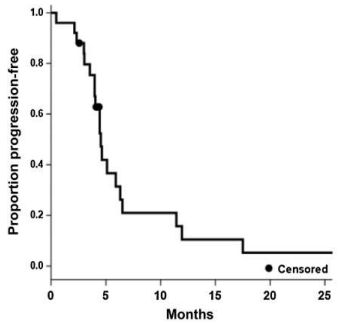

Figure 1.
Kaplan–Meier estimate of progression (all patients, $N = 25$; median = 4.5; 95% CI, 4.0–6.3).

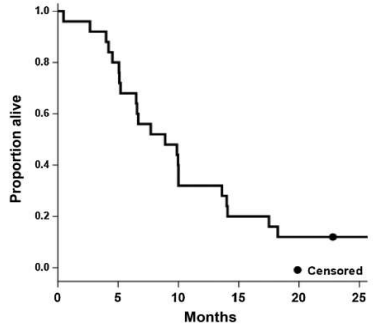

Figure 2.
Kaplan–Meier estimate of OS (all patients, $N = 25$; median = 8.9; 95% CI, 5.2–13.6).

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

Totally 180 patients randomly enrolled

- ASC40 100 mg/m2 once daily+ BEV 10mg/kg once every two weeks
- placebo tablet once daily+ BEV 10mg/kg once every two weeks

Screening — D1 — ORR /PFS/OS every 8 weeks — PD

Primary Study End Point: PFS&OS

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.

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ASC22 HBV

ASC22(PD-L1) for Chronic Hepatitis B Functional Cure

86 MM
People living with HBV in China

1 MM
New incidence in China

7 MM
Infected with HBV in the US, EU and Japan

Current standard therapy (NAs) can only suppress the virus

but can not achieve functional cure

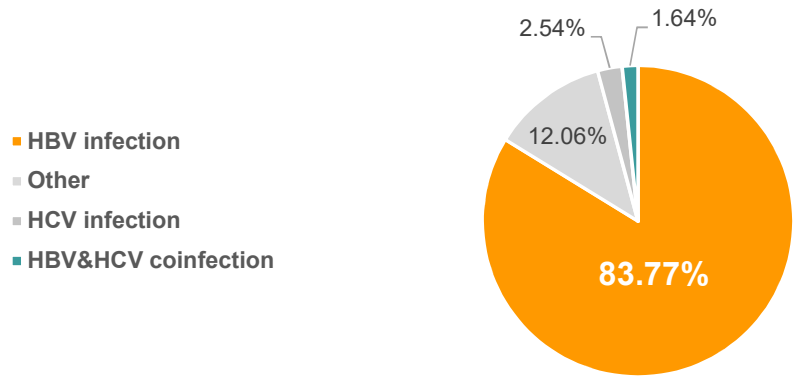
CHB Functional Cure

6 months after treatment

Normal liver function
Negative serum HBV DNA (<20 IU/ml)
Negative serum HBsAg (<0.05 IU/ml)

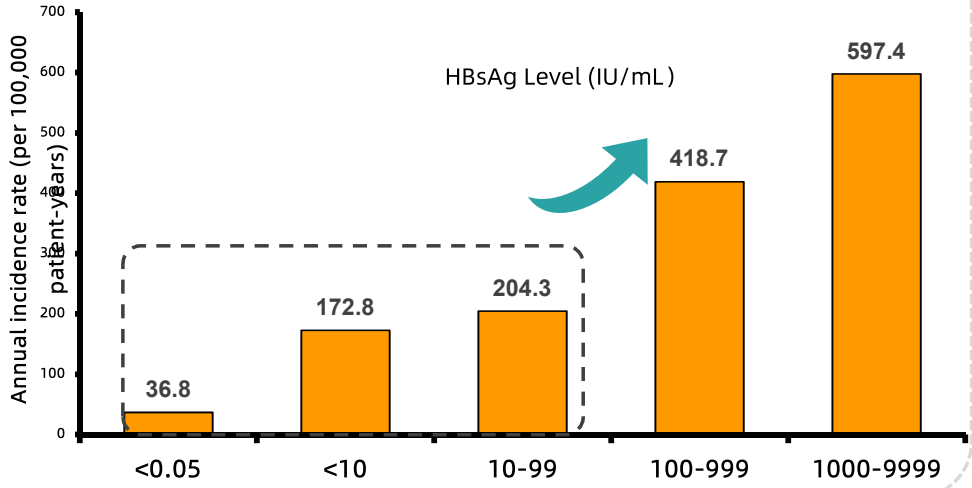
There is a huge unmet medical needs from HBV patients

HBV Infection is the Leading Cause of liver cancer



- The relative risk of HCC in patients with chronic HBV is **14~223** times higher than in the normal population[1]
- The lifetime HCC prevalence in HBV carriers ranges from 10% to 25%[2]
- Over 80%[3] HCC patients in China are caused by HBV infection

Patients with low HBsAg levels remain at high risk of hepatocellular carcinoma (HCC)



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2.McGlynn KA. Clin Liver Dis. 2015 May ; 19(2): 223–238.
3.秦叔逵，中国原发性肝癌临床登记调查（CLCS）的中期报告，2020CSCO

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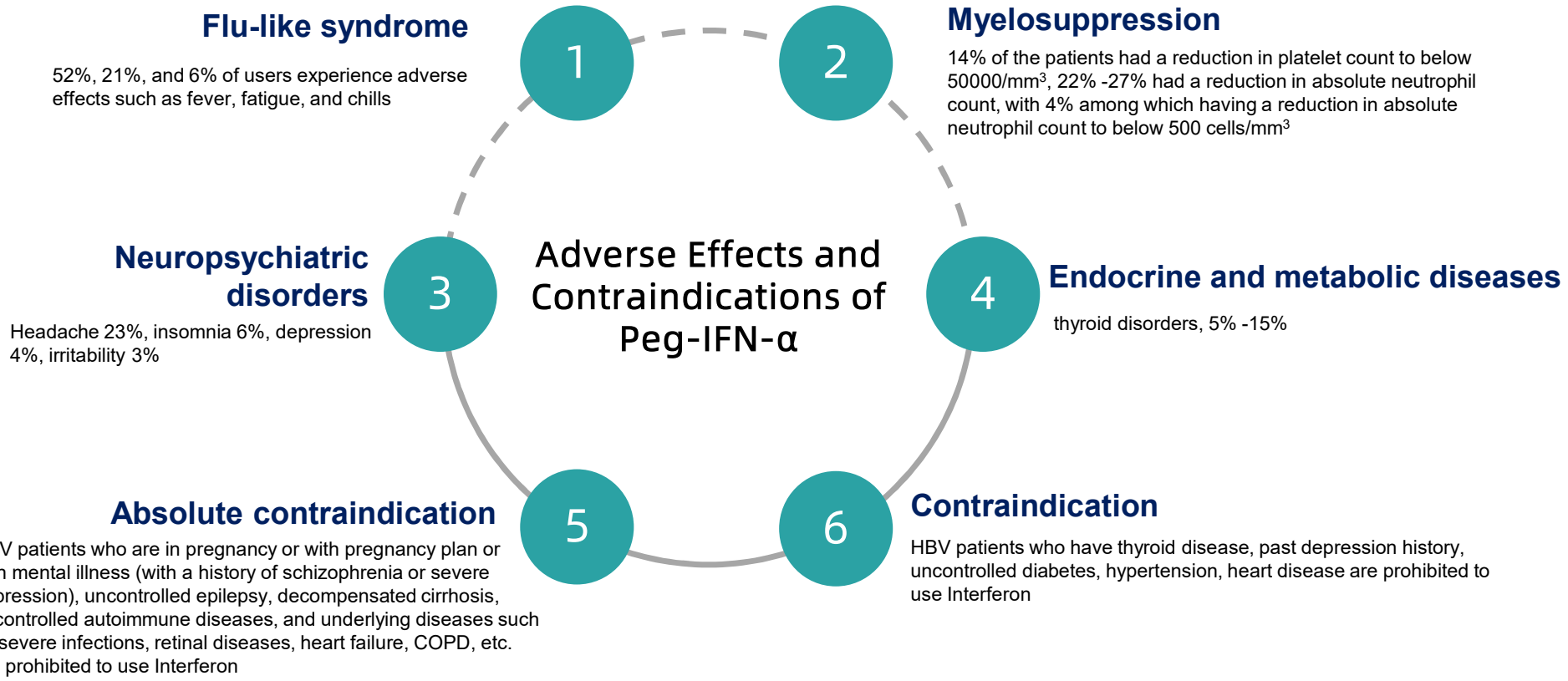
Interferon: Various Adverse Effects and Contraindications When Used for HBV



1. Chinese Journal of Infectious Diseases, 2023,41(1) : 3-28.
2. From the specification of Peginterferon α-2a
3. Expert Committee on Clinical Management of Adverse Reactions of Interferon-α Therapy for Chronic Viral Hepatitis [J] Chinese Journal of Experimental and Clinical Infectious Diseases (Electronic Edition), (2014).

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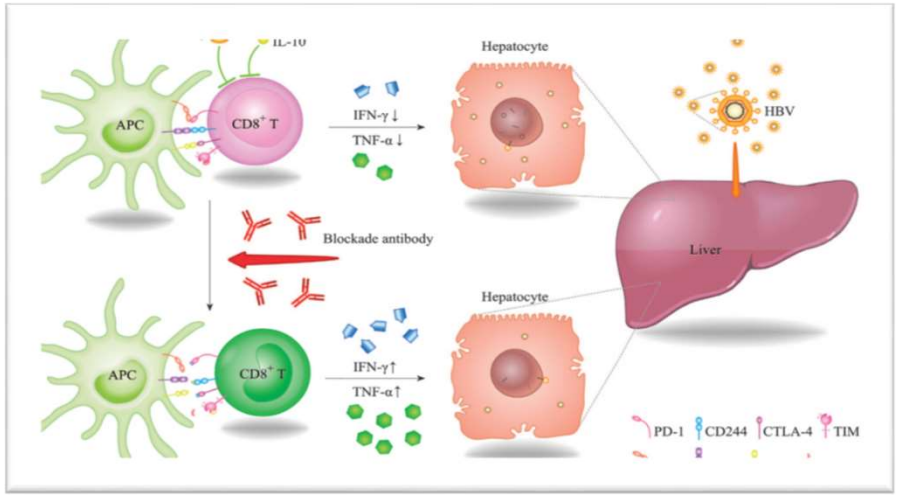
21.6% Patients (Baseline HBsAg≤100) Achieved HBsAg Loss at End of 24-Wk Treatment

Mechanism of PD-1/PD-L1 Pathway for Treatment of CHB



ASC22 is the Leading Candidate of PD-1/PD-L1 for CHB Treatment

Pipeline	Company	Target	Clinical stage	Clinical trial No.
ASC22	Ascletis	PD-L1	Phase IIb	NCT04465890
RG6084 (RO7191863)	Roche	CpAM/TLR7/siRNA/PEG-IFN/PD-L1	Phase II	NCT0422571
GS4224	Gilead	PD-L1	Phase I	ACTRN12618001957280
AB-101	Arbutus	PD-L1	Phase I	NCT05960240
ARB-272572	Arbutus	PD-1	Pre-IND	NA
ALG-093453	Aligos	PD-L1	Pre-IND	NA
ALG-093702	Aligos	PD-L1	Pre-IND	NA

ASC22 Phase IIb Expansion Cohort: enrolled 49 patients with baseline HBsAg≤100 IU/mL

1.0mg/kg ASC22 Q2W+NAs (n=40)	Follow-Up	
Placebo Q2W+NAs (n=9)	Follow-Up	

D0 W24 W48

Interim results from Phase IIb expansion cohort of ASC22

	Rate of HBsAg loss after 24-week treatment	HBsAg loss after 24-week follow-up	Safety profile
ASC22+NAs	ASC22 Cohort: **21% (4/19)** Placebo Cohort: 0 (0/6)	In follow-up, unknown	Generally safe and well tolerated. Most of drug related AE were Grade 1 or 2.

*Interim analysis was conducted when approximately 50% of enrolled patients completed 24-week treatment of ASC22 or placebo

1. Peng G, et al. PD-1 upregulation is associated with HBV-specific T cell dysfunction in chronic hepatitis B patients. Mol Immunol. 2008;45(4):963-70.
2. B Ye, et al. T-cell exhaustion in chronic hepatitis B infection: current knowledge and clinical significance. Cell Death Dis. 2015 Mar 19;6:e1694.

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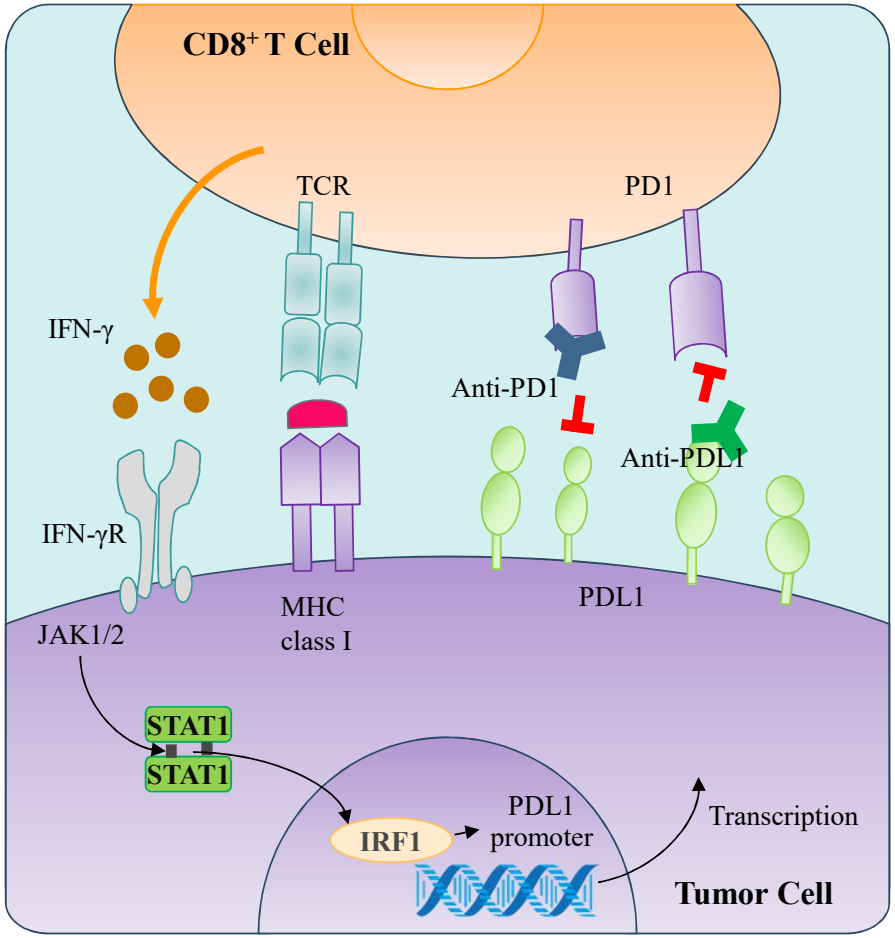
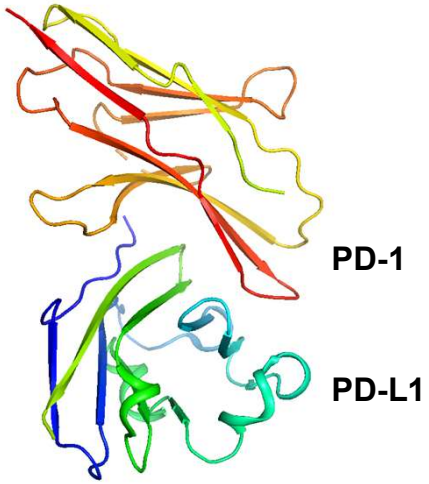
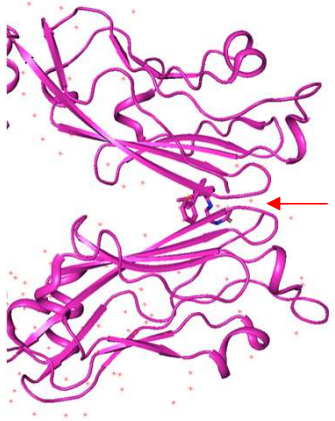
ASC61 Solid Tumors

PD-L1 Small Molecule Inhibitors: Challenges and Opportunities





- Antibodies block PD-1/PD-L1 interface
- Traditional small molecules not good at inhibiting protein-protein interaction



- PD-L1 small molecule inhibitors induce PD-L1 dimerization and internalization, preventing PD-1/PD-L1 interaction

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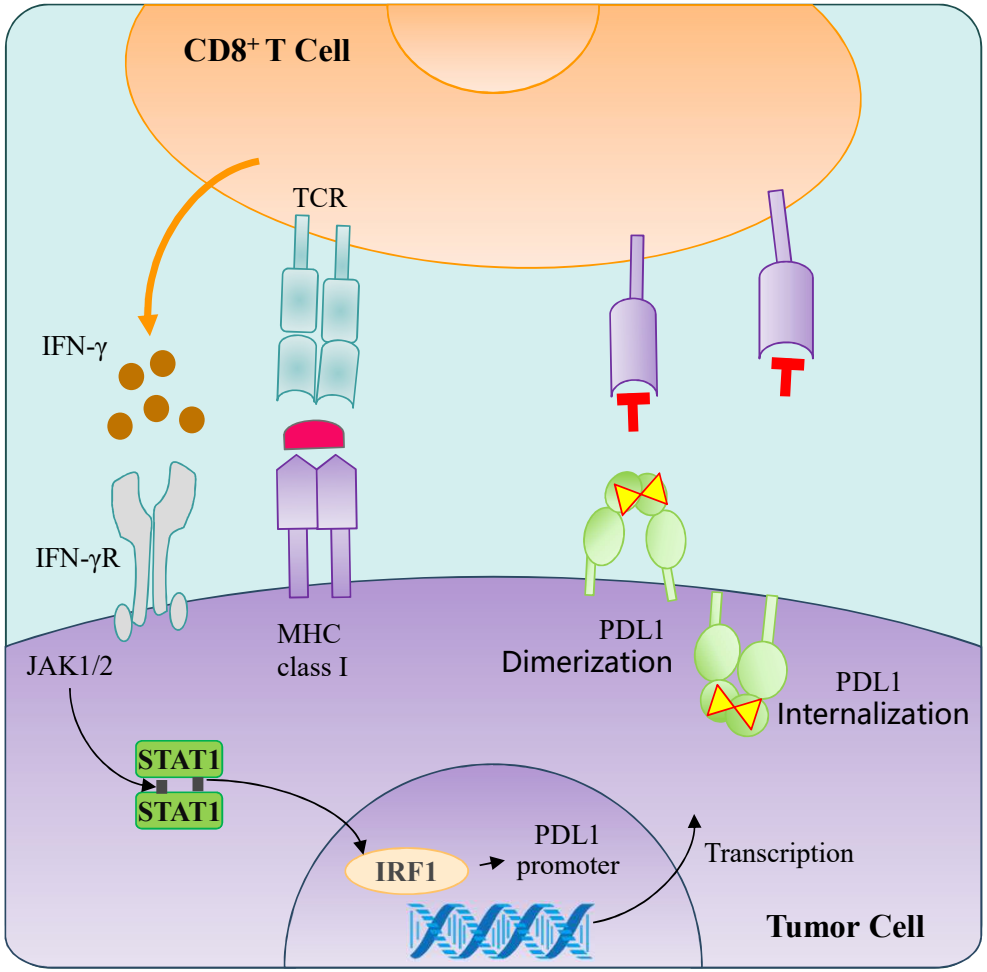
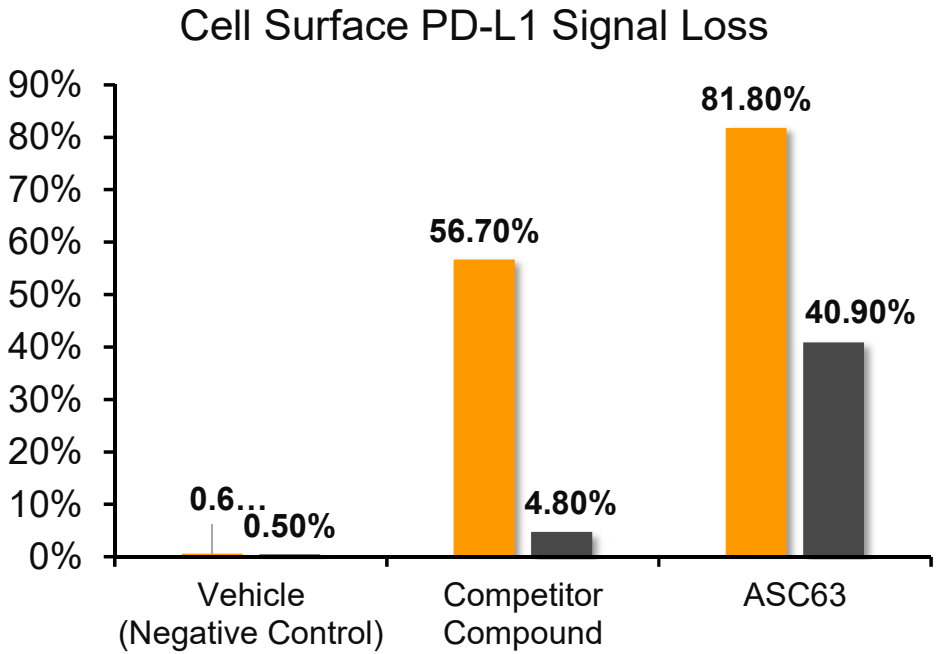
ASC61: Induce PD-L1 Dimerization and Sustained Internalization





ASC61

- Potently induce PD-L1 dimerization and internalization (orange)
- Induce long-lasting PD-L1 signal loss from cell surface (after compound removed from medium for 16 hours, still resulted in 40% PD-L1 signal loss) (black)

Source: Ascletis data

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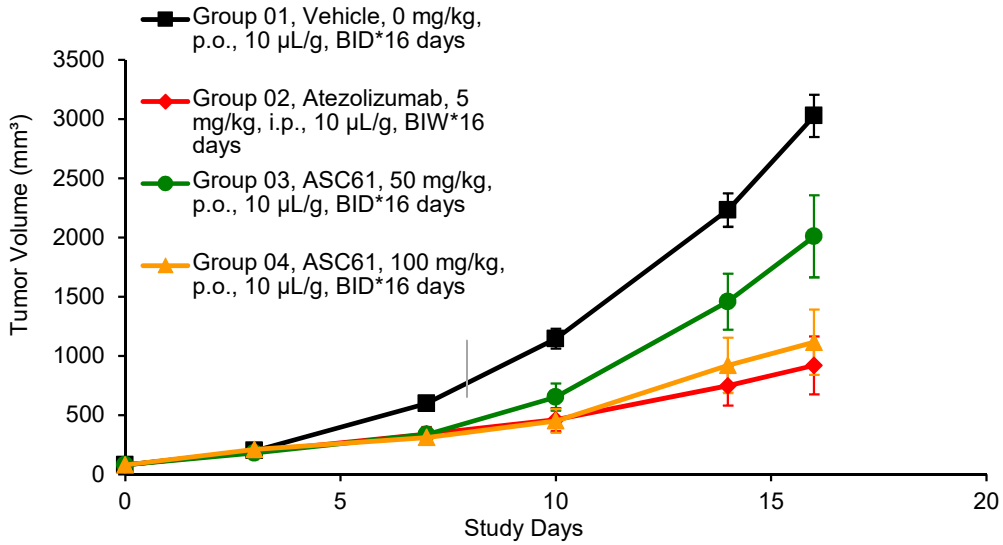
ASC61 showed comparable antitumor activities as the FDA- approved PD-L1 antibody, Atezolizumab, in mouse tumor models



Note: PD-1/PD-L1 dKI HuGEMM mice with human PD-1 and PD-L1 gene double knock-in are an ideal model for testing human-specific PD-1/PD-L1 immune checkpoint inhibitor drugs.

Description	Tumor Size (mm^3) [a] on day 16	T/C (%) on day 16 [b]	TGI (%) on day 16	p value compare with G1[c]	p value compare with G2[d]
Vehicle, p.o., 10 μL/g, p.o., BID*3 weeks	3027.54±179.16	-	-	-	-
Atezolizumab, 5 mg/kg, i.p., BIW*3 weeks	919.73±244.00	30.38	69.62	<0.001	-
ASC61, 50 mg/kg, p.o., BID*3 weeks	2009.72±346.48	66.38	33.62	0.0954	0.0362
ASC61, 100 mg/kg, p.o., BID*3 weeks	1115.61±275.17	36.85	63.15	<0.001	0.954

Note: a. Mean ± SEM; b. tumor volume treatment/control; c. compared with group 1 tumor volume on day 16 using Tukey's HSD test; d. compared with group 2 tumor volume on day 16 using Tukey's HSD test.

■ Oral administration of ASC61 resulted in significant tumor growth inhibitions in mouse tumor models. Antitumor activity of ASC61 was shown to be dose-dependent.

■ No significant difference of body weight was observed among all groups during studies, indicating that ASC61 was generally well-tolerated in mice.

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Summary

Corporate Strategy--Focus on Differentiation

Pipeline Prioritizing

- ✓ Completed existing pipeline review and assessment
- ✓ Made a strategic optimization of resources on 12 clinical stage assets
- ✓ focuses on the pipeline which has global FIC or BIC potential

Commercialization Repositioning

- ✓ Sales team for HCV dismissed in H1 2023 due to market shrinkage
- ✓ Now the majority staff is for discovery and clinical development
- ✓ Co-commercialization with partners in the future

FIC/BIC as Core Competiveness

- ✓ Allocate increasing resources to early discovery and clinical development
- ✓ More global FIC/BIC candidates with edges in the world or in China

Value Creating Oriented

- ✓ Ascletis has a proven track record of BD capabilities
- ✓ Seek out-license partnership to maximize the value of the pipeline

Focus on Advantages + Unmet Needs + Core Pipeline » Differentiation

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Repurchased Over 45 million Shares *

Communications

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

Market Confidence

- Grant 200mm HK$ for buyback
- 45+mm shares repurchased to date*
- 85+mm HK$ used*

Intrinsic Value

- early discovery & clinical development well progressing
- ASC40 acne Phase III initiation
  ASC41 positive IIb interim data
- More catalysts scheduled

Ascletis Pharma Inc.
歌禮製藥有限公司

自願性公告
建議根據購回授權進行股份購回

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*As of Dec.22, 2023

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Strong Execution--Key Milestones

	Indication	Catalysts	Progress
2023Q2	acne	Topline Phase II clinical results of ASC40 (FASN) for treatment of acne	
2023Q3	rGBM	Complete the enrollment of ~120 rGBM patients in Phase III clinical of ASC40(FASN), which is needed for the planned interim analysis with 93 PFS events.	
2023Q3	HBV	Topline interim results from Phase IIb expansion cohort of ASC22 (PD-L1) for functional cure of CHB in patients with the baseline HBsAg≤ 100	
2023Q4	acne	Initiation of Phase III clinical trial of ASC40 (FASN) for treatment of acne	
2024Q1	NASH	Topline interim results from Phase II clinical trial of ASC41(THR-β) of liver fat reduction, LDL-C reduction, liver enzymes and biomarkers of approximately 40 NASH patients after 12-week treatment	
2024Q1	NASH	Phase IIb topline clinical results from 168 biospy-proven NASH patients of Phase II clinical trial of ASC40(FASN) after 52 weeks of treatment	

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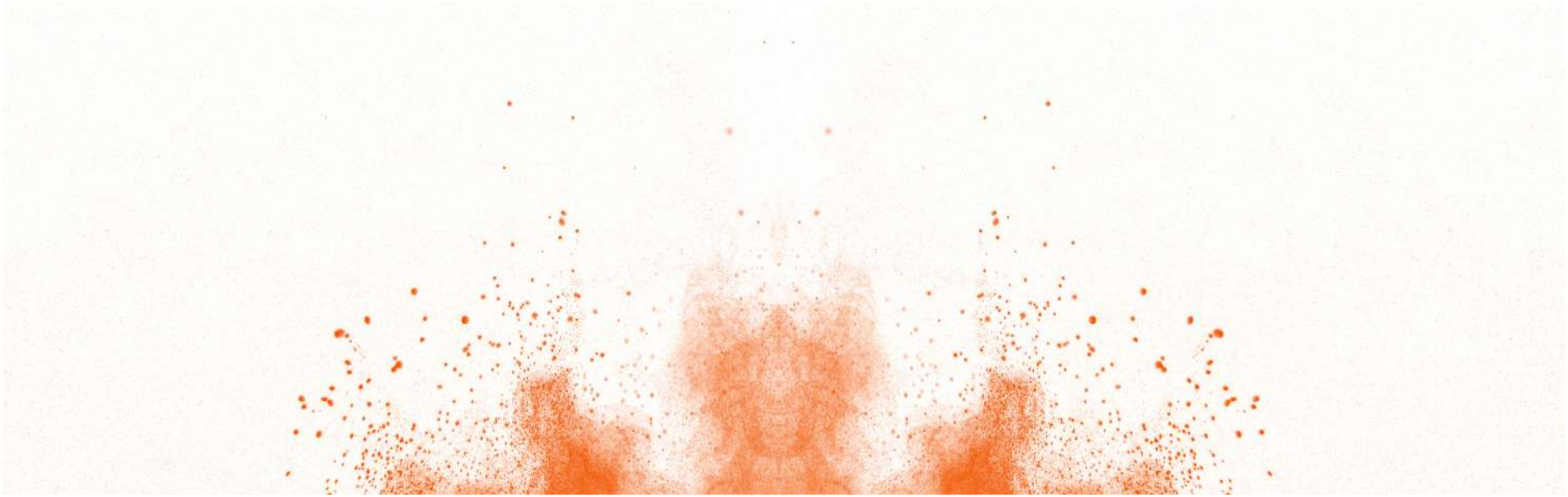

Thanks

Innovative cures liberate life to the fullest