1672.HK

Ascletis Pharma Inc.

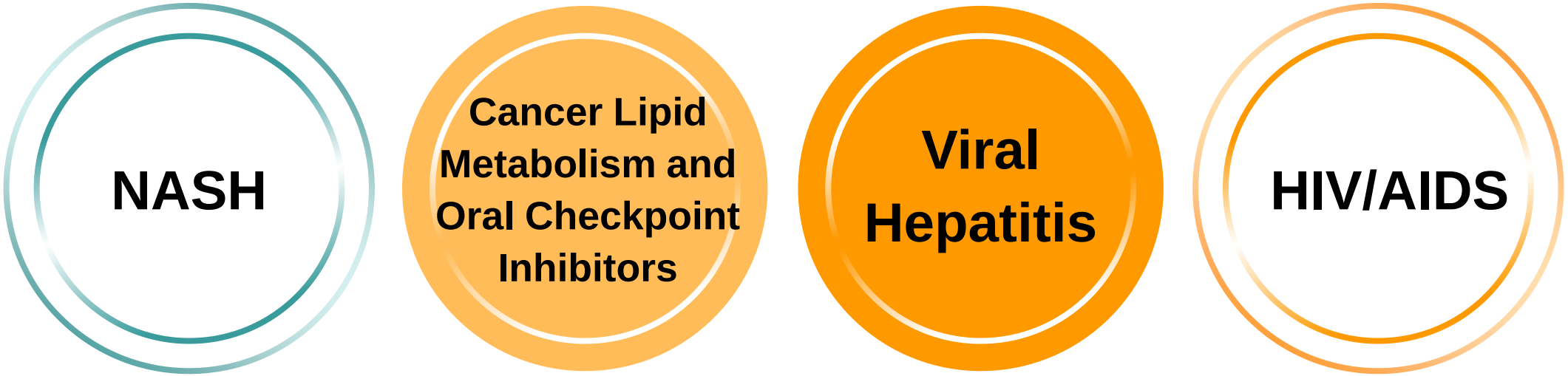
From First-in-China to First Globally

April 2021

歌礼
ascletis

Multi-Disease Platform

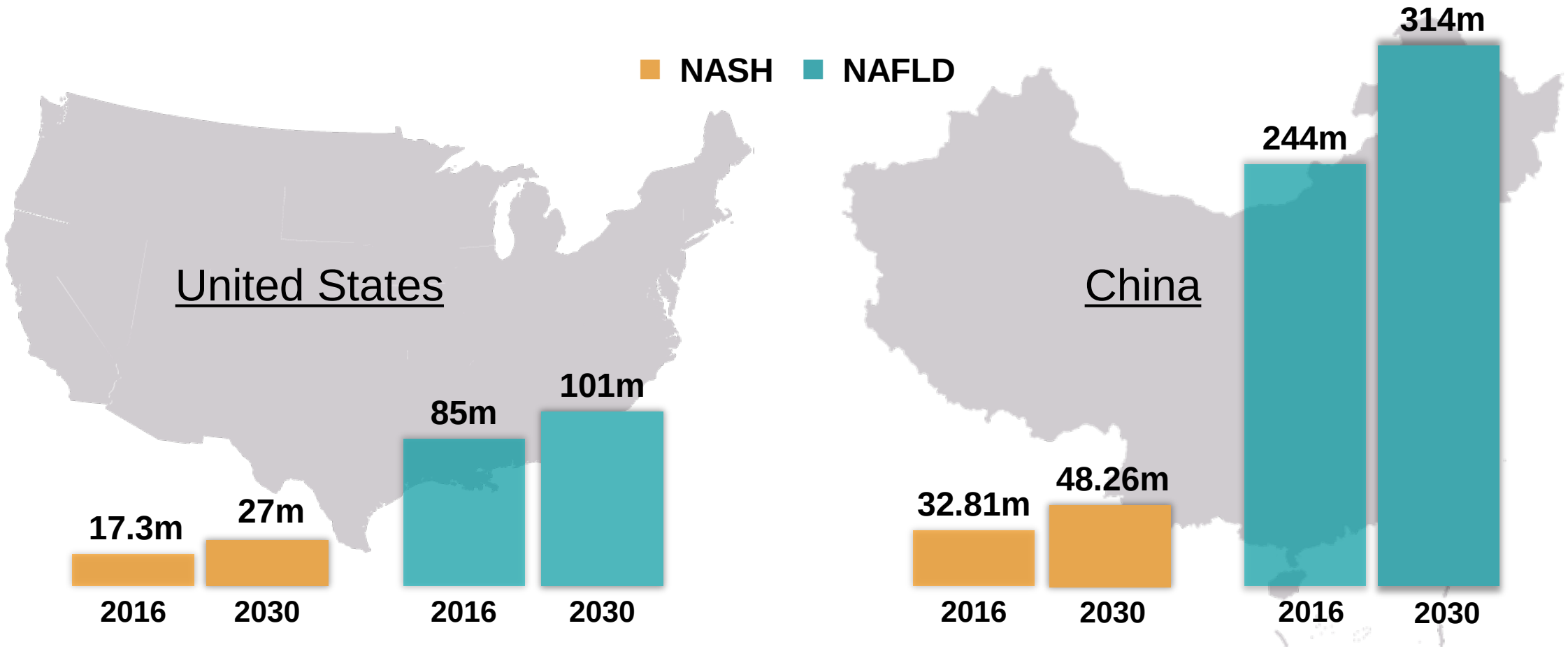
- Since Hong Kong IPO in 2018, Ascletis has developed into a multi-disease platform from a single disease – HCV platform. Ascletis has three marketed products and seventeen R&D pipeline drug candidates (eleven of them developed in-house).



歌礼 ascletis

Non-alcoholic Steatohepatitis (NASH)

NAFLD and NASH Represent a Large and Growing Health Problem



C. Estes et al., J HEP 2018 (69): 896–904

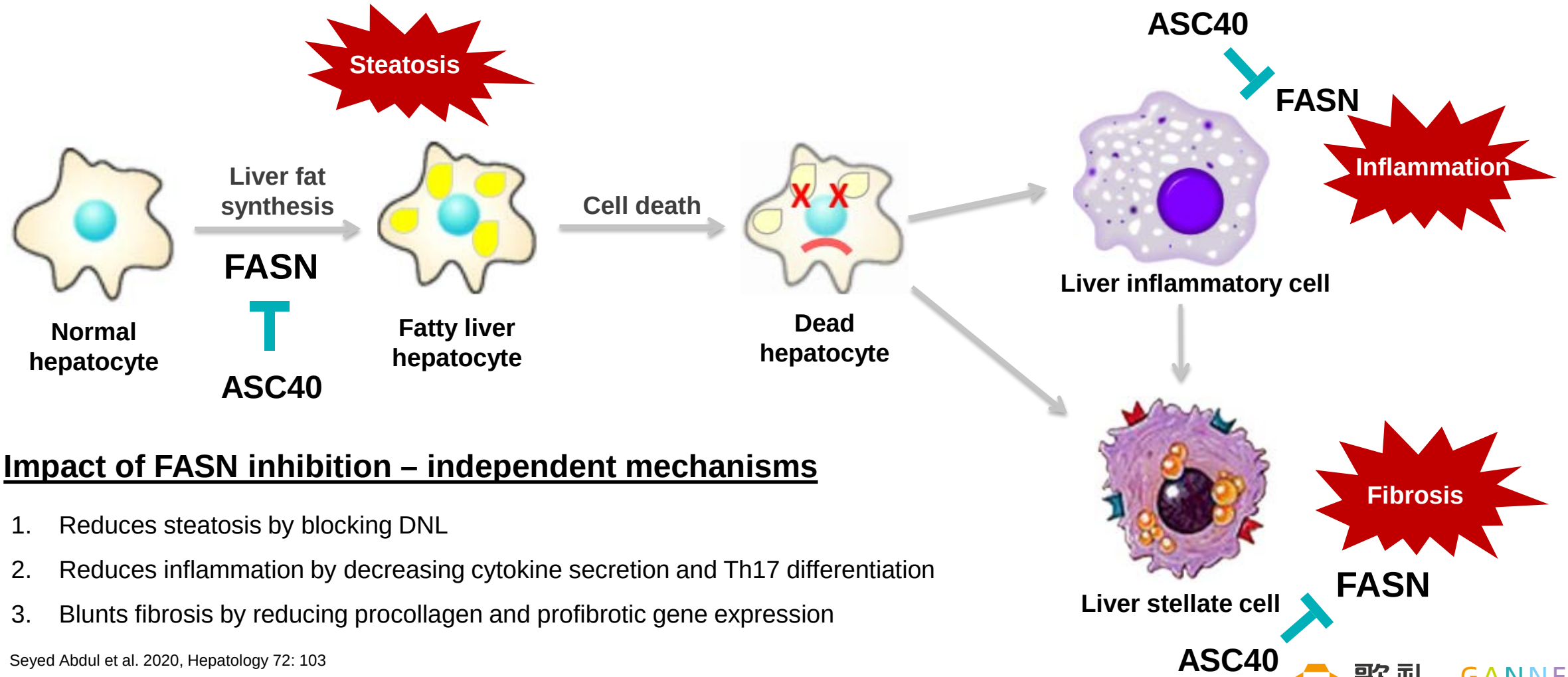
Single Agent and Combo Therapy Pipeline[1]

Target	Product/ Candidate	Commercial Rights	Pre-IND	IND	Phase I	Phase IIa	Phase IIb/III	NDA	Marketed
FASN	ASC40	Greater China[2]	*U.S. FDA Fast Track*						
THR-β	ASC41	Global							
FXR	ASC42	Global	*U.S. FDA Fast Track*						
FASN + FXR	ASC40/ASC42 Combo Therapy	Global[2]							
THR-β + FXR	ASC41/ASC42 Combo Therapy	Global							
FASN + THR-β	ASC40/ASC41 Combo Therapy	Global[2]							

Notes: 1. NASH pipeline is owned by Gannex Pharma Co., Ltd., an independent biotech which is currently wholly-owned by Ascletis Pharma Inc.(1672.HK). 2. ASC40 is licensed from Sagimet Biosciences Inc. (“Sagimet”) (previously known as 3-V Biosciences, Inc.) for the exclusive rights in the Greater China.

ASC40：First-in-Class Oral Fatty Acid Synthase (FASN) Inhibitor

- Proposed mechanism of action of FASN inhibitor ASC40 in NASH related fibrosis



Impact of FASN inhibition – independent mechanisms

1. Reduces steatosis by blocking DNL
2. Reduces inflammation by decreasing cytokine secretion and Th17 differentiation
3. Blunts fibrosis by reducing procollagen and profibrotic gene expression

Seyed Abdul et al. 2020, Hepatology 72: 103

ASC40: U.S. Cohort of Phase II Trial in NASH Patients

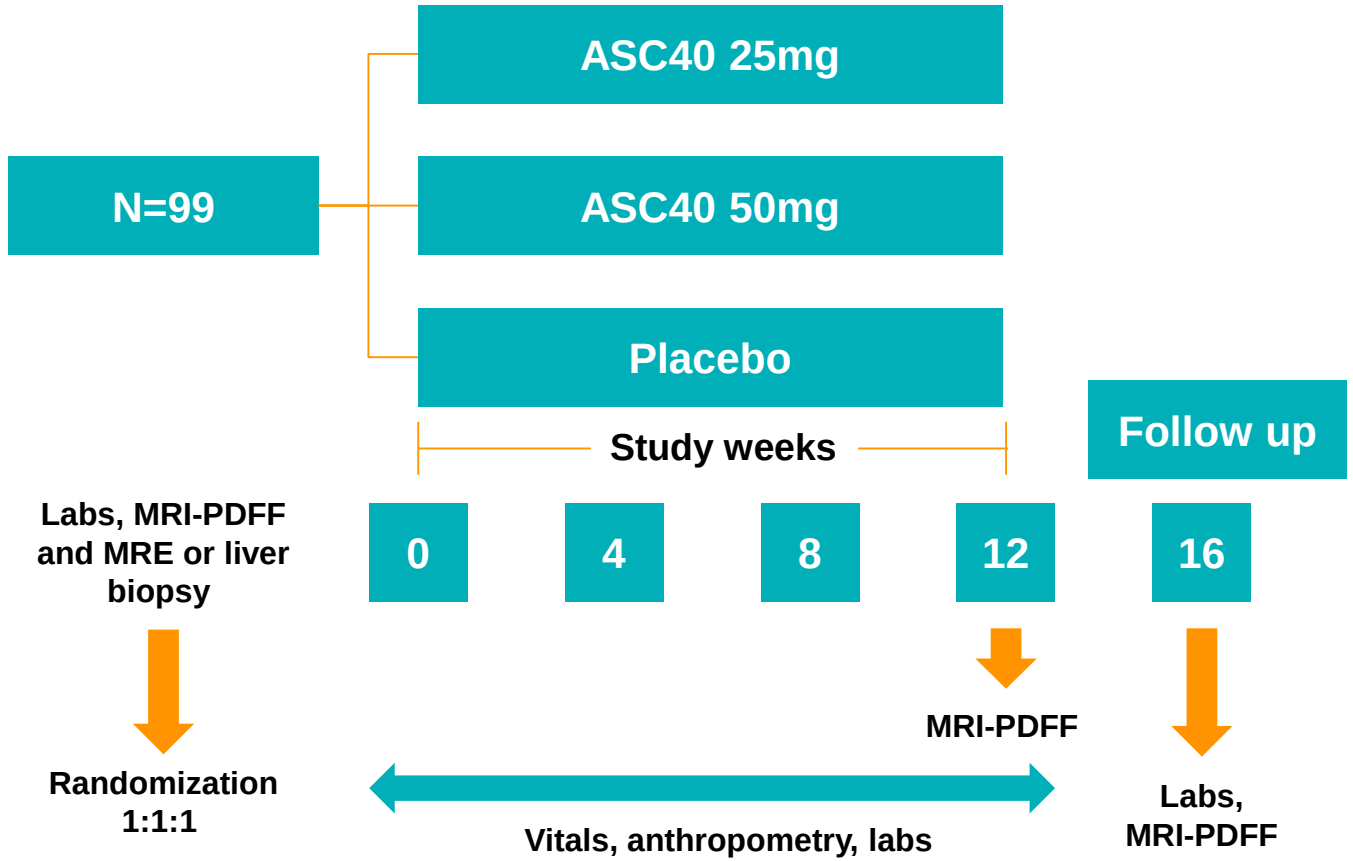
Multicenter, randomized, placebo-controlled trial 1:1:1 25mg:50mg:placebo (N=99)

Criteria

- Inclusion
  - ≥ 8% liver fat
  - MRE ≥ 2.5kPa or recent biopsy
- Exclusion
  - Evidence of cirrhosis
  - Other chronic liver disease

Endpoints

- Primary
  - Liver fat reduction by MRI-PDFF
  - Safety
- Secondary
  - % pts ≥30% reduction of liver fat
  - ALT, AST
  - Biomarkers



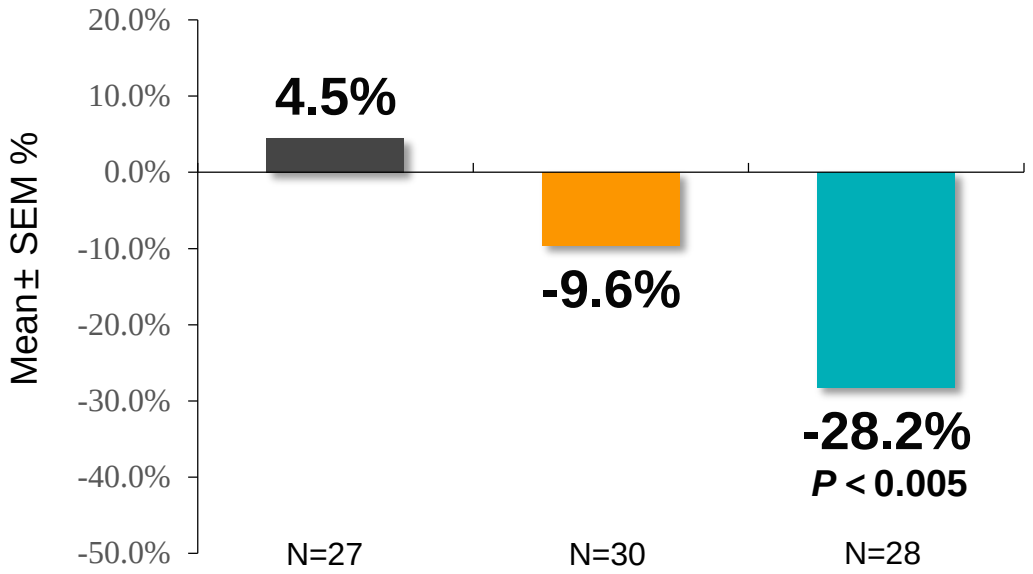
Rohit Loomba et al. 2020, Hepatology 72;103. EASL 2020 Oral Presentation

U.S. Cohort: ASC40 Showed a Dose Dependent and Robust MRI-PDFF Response

MRI-PDFF responders were defined as those with ≥ 30% MRI-PDFF decline relative to baseline

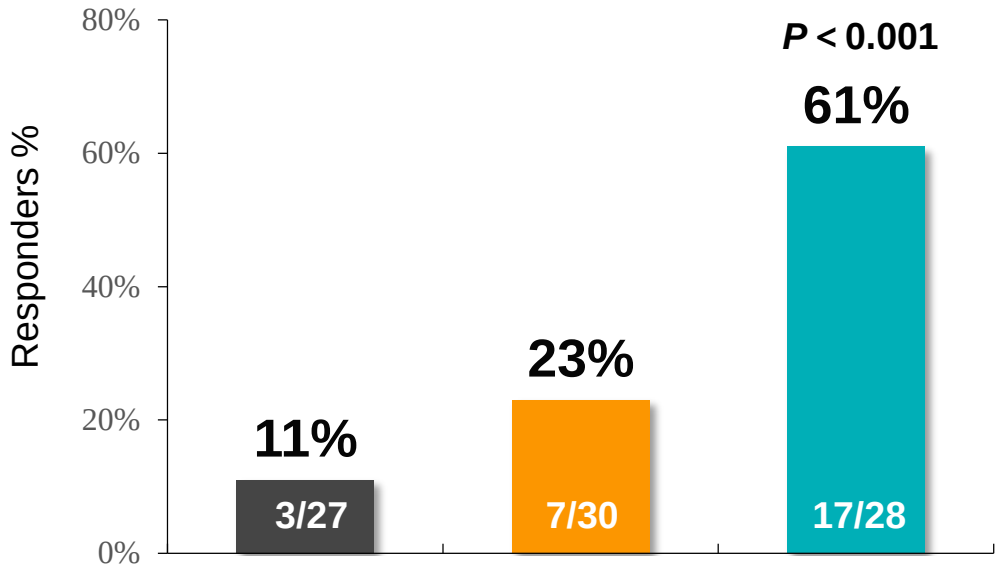
Mean relative liver fat reduction

MRI-PDFF at week 12



Responder frequency

Patients with ≥30% relative reduction

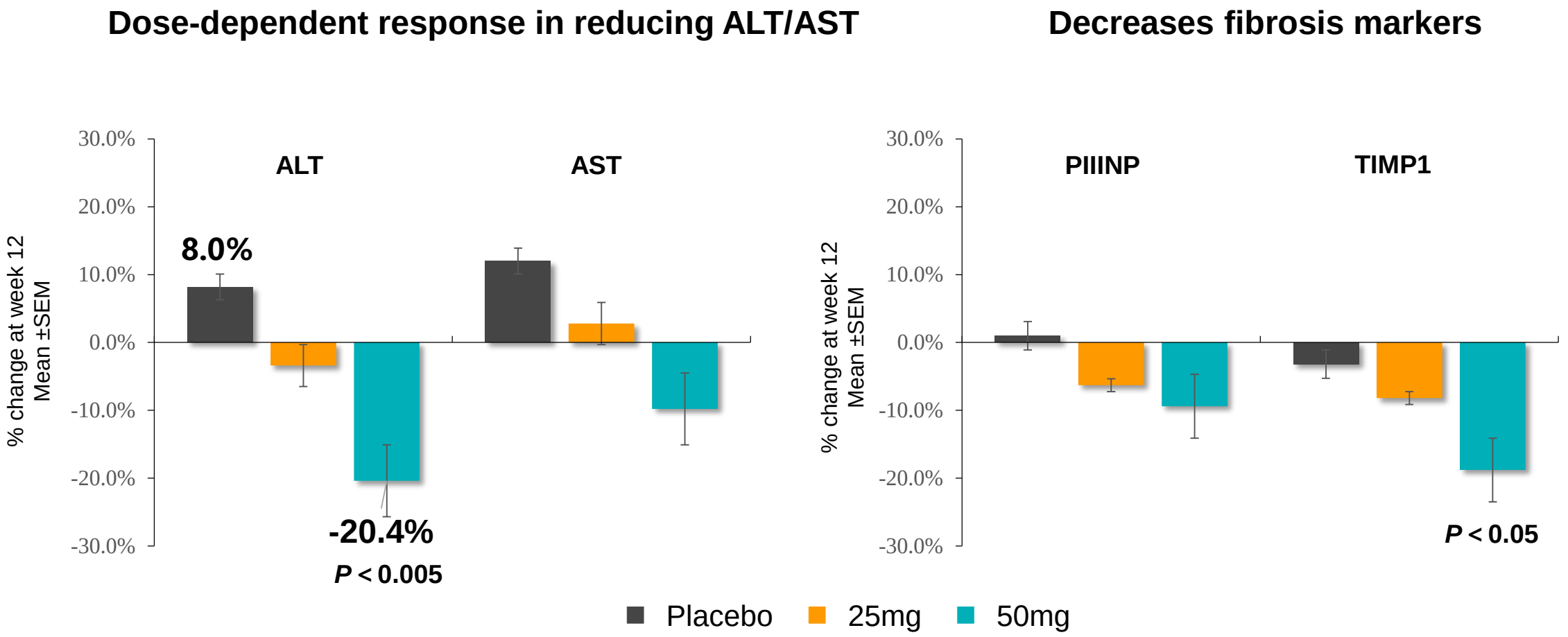


Placebo 25mg 50mg

Rohit Loomba et al. 2020, Hepatology 72;103. EASL 2020 Oral Presentation

歌礼 ascletis GANNEX A Member of the Ascletis Group

U.S. Cohort: ASC40 Showed Dose-dependent Response in Reducing ALT/AST and Fibrosis Markers



Rohit Loomba et al. 2020, Hepatology 72;103. EASL 2020 Oral Presentation

歌礼 ascletis GANNEX A Member of the Ascletis Group

Phase II ASC40 (TVB-2640) Compares Favorably With Other Phase II/III NASH Drugs

Drug Candidate	Company	Target	Dose	Weeks	≥ 30% liver fat reduction responder rate, %		Placebo adjusted ≥ 30% liver fat reduction responder rate, %	Safety
					Drug	Placebo		
ASC40[1] (TVB-2640)	Gannex /Sagimet	FASN	50 mg	12	60.7	11.1	49.6	minimal side effects
Firsocostat[2]	Gilead	ACC	20mg	12	47.8	15.4	32.4	TG ↑
Tropiflexor[3]	Novartis	FXR	200μg	12	64	20	44	LDL-C ↑, pruritus
Resmetirom[4]	Madrigal	THR-β	80mg	36	74.4	29.4	45	diarrhea, nausea

Non-head to head research

1、Rohit Loomba et al. 2020,Hepatology 72;103.EASL 2020 Oral Presentation
2、Eric J Lawitz et al. Clin Gastroenterol Hepatol. 2018 Dec;16(12):1983-1991
3、 Marcos Pedrosa et al. Contemp Clin Trials. 2020 Jan;88:105889.
4、Stephen A Harrison et al. Lancet. 2019 Nov 30;394(10213):2012-2024

歌礼 ascletis GANNEX A Member of the Ascletis Group

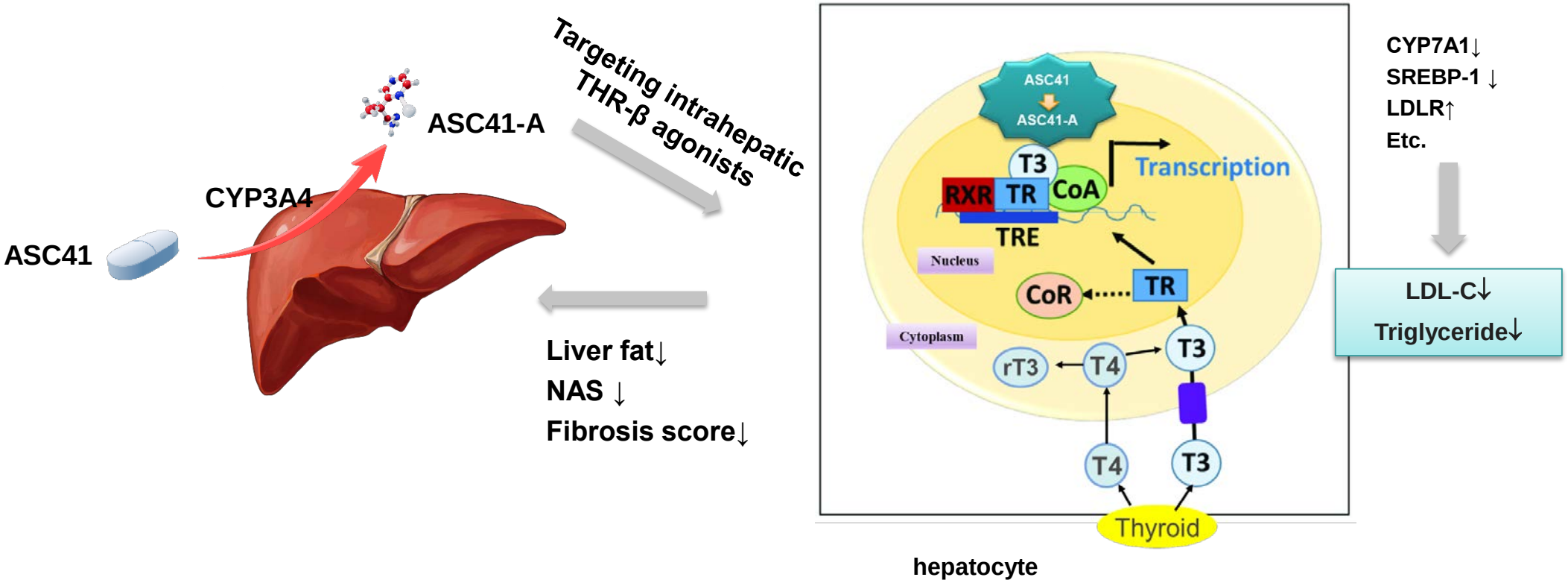
ASC40: China Cohort of Phase II Trial in NASH Patients

Phase II, multicenter, randomized, placebo-controlled trial 2:1 50mg:placebo (N=30)

- ASC40 meaningfully reduced liver fat, the primary efficacy endpoint of this trial, with a 50% responder rate (patients achieving ≥30% reduction)
- ASC40 showed a statistically significant decrease in ALT by 29.8% (*P*=0.0499) (mean decrease of 33 U/L at week 12)
  - Indicates reduction of liver inflammation
- In 63% of patients on ASC40, ALT decreased by17 U/L or greater, which has been shown to correlate with liver biopsy response in NASH patients
- ASC40 was well tolerated with no serious adverse events. All treatment emergent adverse events were grade 1 or 2 and there were no statistically significant changes in serum triglycerides
- Data from the China cohort are consistent with those of the U.S. cohort, previously reported at the AASLD Liver Meeting in November 2020
- Based on the positive Phase II data, doses for the Phase IIb/III NASH trial in China have been selected

ASC41: A Liver Targeting Thyroid Hormone Receptor Beta (THR-β) Agonist

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



Gannex data

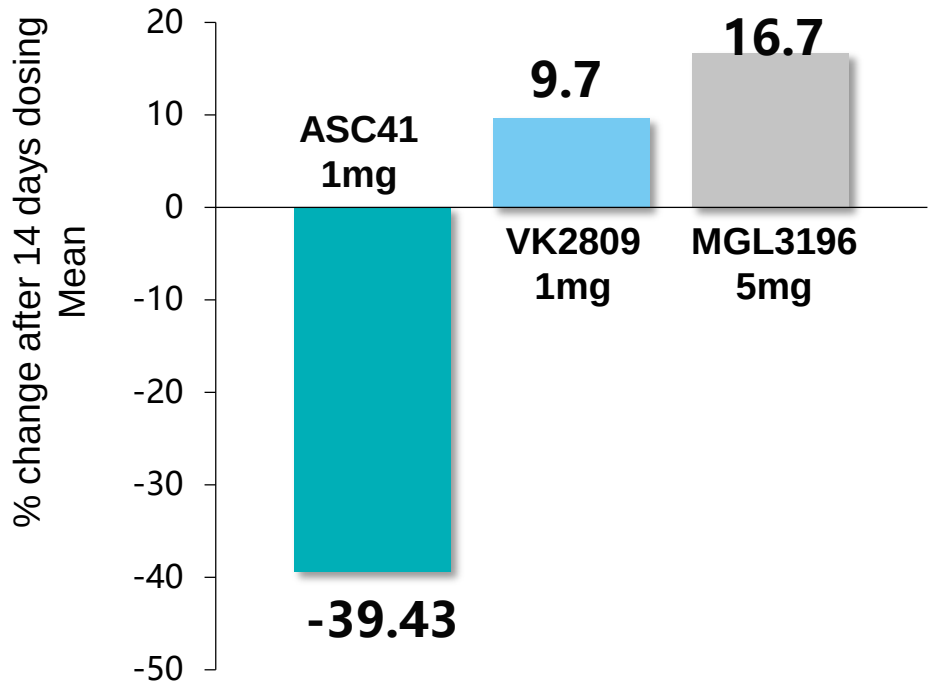
ASC41: Currently a Third-in-class THR-β Agonist in Development

- In two NASH animal models, at 1/10th dose of MGL-3196, ASC41 demonstrated the same improvement in liver steatosis, inflammation and fibrosis.
- Commercially ready oral tablet formulation developed with in-house proprietary technology
- 2 Phase Ⅰ studies completed
  - Single doses (1, 2, 5, 10, 20 mg) and 14 day multiple doses (1, 2, 5 mg) in 65 subjects with elevated LDL-C > 110 mg/dL
  - Food effect in 12 healthy subjects
- U.S. IND approved Feb 2021
- 1 Phase Ⅰb study completed
  - 28 day, 10 mg in 20 overweight and obese subjects with elevated LDL-C > 110 mg/dL
- Based on above studies, doses have been selected for Phase II trials in patients with NASH

THR-β Differentiations: Gannex vs Viking and Madrigal

	Gannex ASC41[1]	Viking VK2809[2]	Madrigal MGL3196[3]
Oral formulation	Tablet, room temp storage, commercially ready	Capsule, refrigerated	Tablet, room temp storage, commercially ready
Dosing frequency	Once a day	Once every two days	Once a day
Human dose needed for > 30% TG reduction	1 mg	2.5 mg	50 mg

Placebo adjusted triglyceride reduction from baseline after 14 day dosing

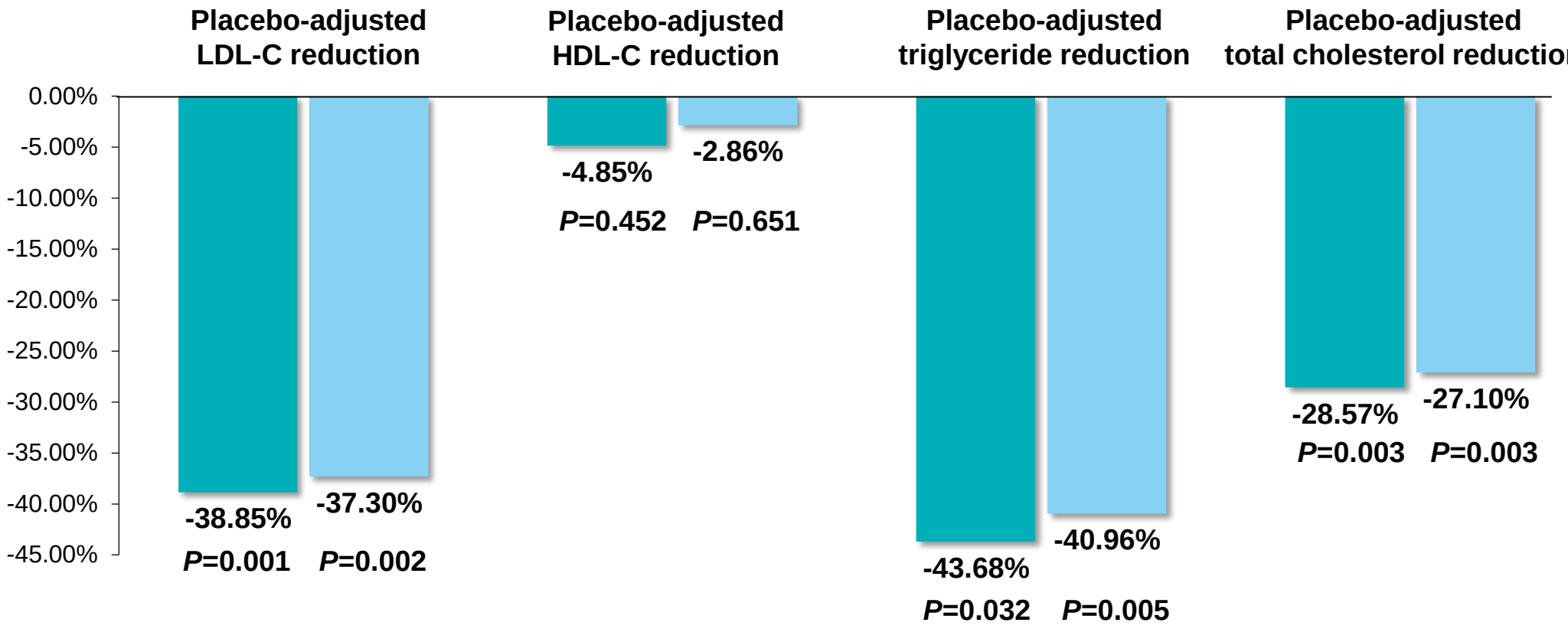


1.Gannex data 2.EASL2020 Abstract No. AS073.
3.Stephen A Harrison et al. Resmetirom (MGL-3196) for the treatment of non-alcoholic steatohepatitis: a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. www.thelancet.com Published online November 11, 2019 https://doi.org/10.1016/S0140-6736(19)32517-6

歌礼 ascletis GANNEX A Member of the Ascletis Group

Positive Clinical Results in Overweight and Obese Subjects

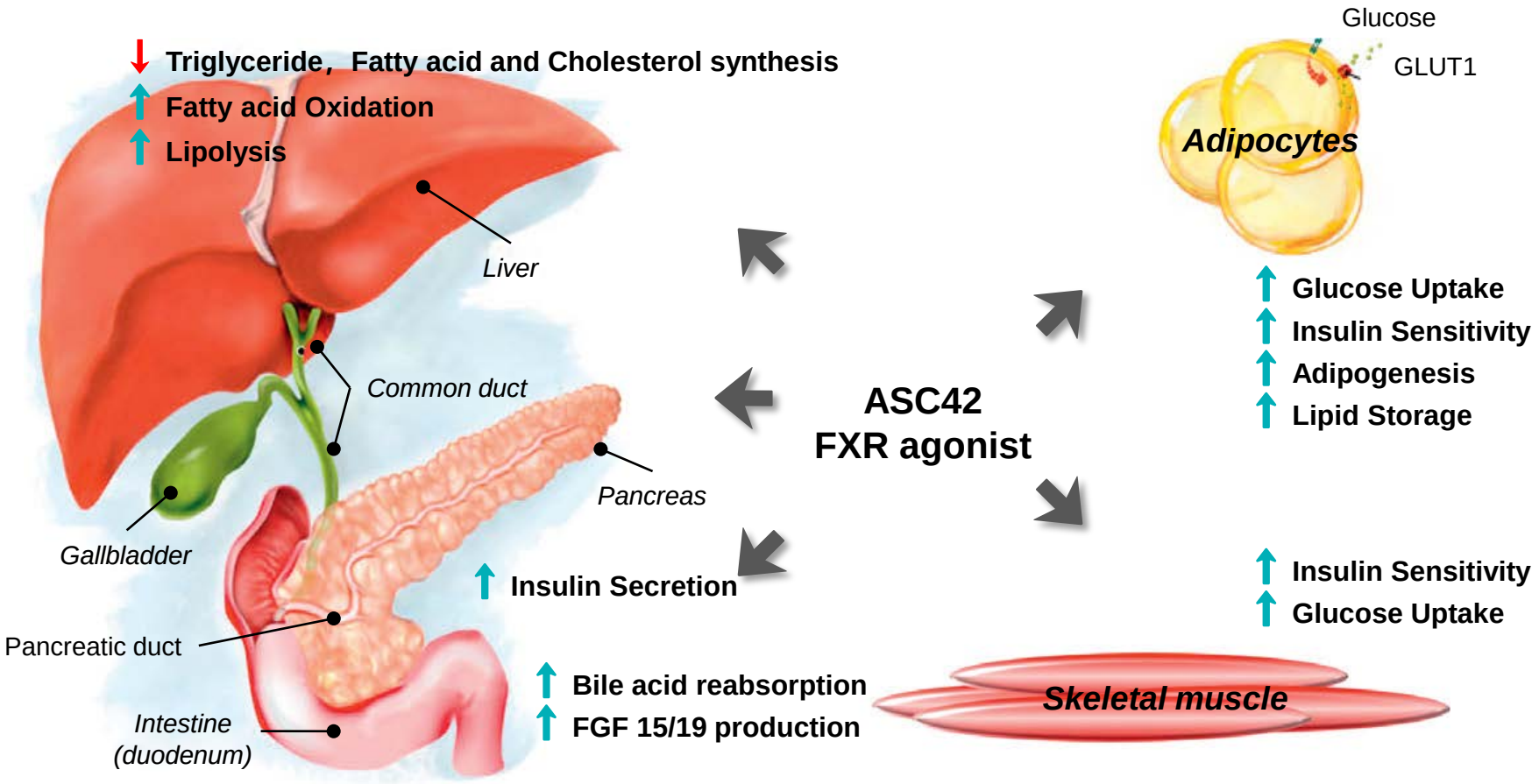
Placebo-adjusted relative change (mean) from baseline after 14 or 28 days of once daily oral dosing of 10 mg ASC41 tablets in overweight and obese subjects



P-value vs placebo

Gannex data

ASC42：A Farnesoid X Receptor (FXR) Agonist



- Increased insulin sensitivity of adipocytes and skeletal muscle cells increases glucose uptake in peripheral tissues and increases energy consumption
- Reduced the synthesis of triglycerides, fatty acids and cholesterol in the liver, promoted liver fat decomposition and fatty acid oxidation

Luciano Adorini et al. Farnesoid X receptor targeting to treat nonalcoholic steatohepatitis. Drug Discovery Today Volume 17, Numbers 17/18 September 2012

ASC 42: A Novel Non-steroidal, Selective, Potent FXR Agonist

- Potentially Best-in-class
- U.S. FDA IND approval in Oct 2020
- U.S. FDA Fast Track Designation in Dec 2020
- In two NASH animal models, demonstrated significant improvement in liver steatosis, inflammation, and fibrosis
- U.S. Phase Ⅰ trials ongoing and good safety profile to date
  - Single ascending doses and multiple ascending doses
  - Food effect
- Oral tablet formulation developed with in-house proprietary technology and stable at room temperature

Combo Therapies: Synergies among ASC40, ASC41 and ASC42

Treatment Goals	Monotherapy			Combo therapy		
	ASC40 FASN	ASC41 THR-β	ASC42 FXR	ASC40/ASC42 FASN+FXR	ASC41/ASC42 THR-β+FXR	ASC40/ASC41 FASN+THR-β
Liver fat reduction	★★★	★★★	★★	★★★	★★★	★★★
Anti-inflammation	★★	★★	★★	★★	★★	★★
Anti-fibrosis	★★	★★	★★★	★★★	★★★	★★
Lowering LDL-C and TG		★★★			★★★	★★★

Cancer Lipid Metabolism

Cancer Molecular Therapies

Category	Mechanism	Examples of Approved drugs
Signal Transduction	Angiogenesis and proliferation inhibitor	Bevacizumab, Imatinib, Erlotinib, Sorafenib, Ibrutinib, Tofacitinib, Palbociclib
Immunotherapy	Checkpoint inhibitor	Keytruda®, Opdivo®, Tecentriq®, Bavencio®, Imfinz®
Metabolism	Control aberrant energy and substance needs, inhibit toxic metabolites	Ivosidenib, Enasidenib

Cancer Metabolism: Long History, Recent Breakthrough

Warburg Effect (~1921)
Increased glucose uptake and fermentation of glucose to lactate even in the presence of completely functioning mitochondria

Enasidenib Approved for AML (2017)

FDA approves first-in-class cancer metabolism drug

The FDA approved Agios' and Celgene's enasidenib for acute myeloid leukaemia (AML), validating metabolism-modulating drugs as a means of killing cancer cells.

Enasidenib (formerly AG-221) is a first-in-class inhibitor of mutated isocitrate dehydrogenase 2 (IDH2). The IDH enzymes normally metabolize isocitrate into α-ketoglutarate. When they are mutated in cancers, they also convert α-ketoglutarate into 2-hydroxyglutarate, an oncometabolite that causes cell differentiation defects by impairing histone demethylation.

In clinical trials of enasidenib, 23% of treated patients had complete responses or complete responses with partial haematologic recovery lasting a median of 8.2 months. The most common side effects were nausea, vomiting, diarrhoea, elevated bilirubin and decreased appetite. The agency approved the drug with a black box warning noting the risk of differentiation syndrome, a potentially fatal complication that is associated with certain forms of AML.

Nature Reviews Drug Discovery, **2017**,*16*, 593

RESEARCH 10.1126/science.aaw5473

REVIEW Science 2020

CANCER

Metabolic reprogramming and cancer progression

BJC 2020 British Journal of Cancer www.nature.com/bjc

EDITORIAL

Cancer Metabolism

Development of cancer metabolism as a therapeutic target: new pathways, patient studies, stratification and combination therapy

Cancer metabolism has undergone a resurgence in the last decade, 70 years after Warburg described aerobic glycolysis as a feature of cancer cells. A wide range of techniques have elucidated the complexity and heterogeneity in preclinical models and clinical studies. What emerges are the large differences between tissues, tumour types and intratumour heterogeneity. However, synergies with inhibition of metabolic pathways have been found for many drugs and therapeutic approaches, and a critical role of window studies and translational trial design is key to success.

British Journal of Cancer (2020) 122:1–3; https://doi.org/10.1038/s41416-019-0666-4

歌礼 ascletis

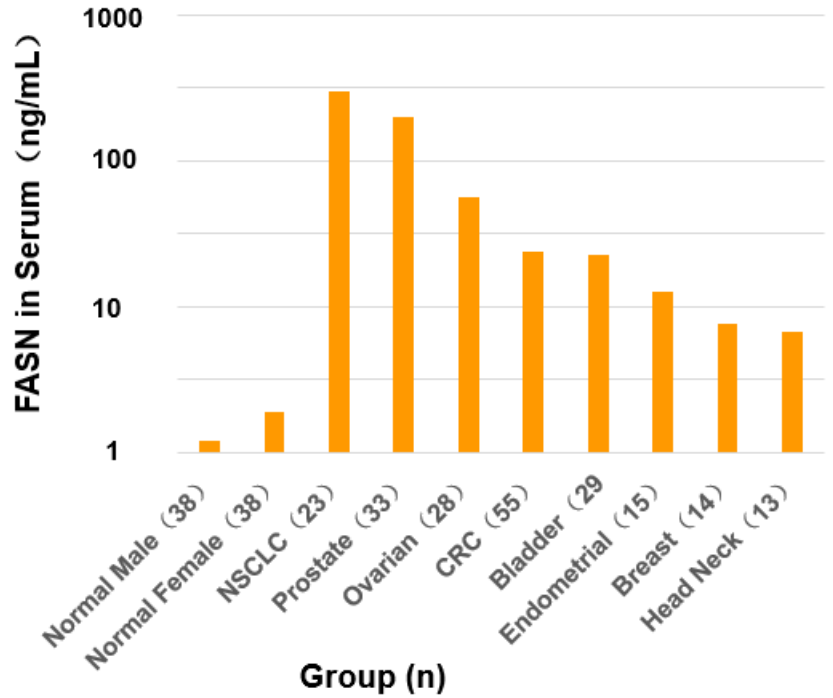
Cancer Metabolism: Approved Drugs and Clinical Stage Candidates

Drug	Target	Indication	Development phase and Company
Ivosidenib (AG-120)	**Mutant IDH1** TCA cycle metabolism	AML with IDH1 Mutation	Approved Agios Pharmaceuticals/Celgene
Enasidenib (AG-221)	**Mutant IDH2** TCA cycle metabolism	AML with IDH2 Mutation	Approved Agios Pharmaceuticals/Celgene
Vorasidenib (AG-881)	**Mutant IDH1/2** TCA cycle metabolism	Low grade glioma	Phase III Agios Pharmaceuticals
Devimistat (CPI-613)	**Pyruvate dehydrogenase/α-ketoglutarate dehydrogenase** TCA cycle metabolism	Lymphoma, Leukemia, Pancreatic cancer	Phase II / Pivotal Rafael Pharmaceuticals
INCB001158	**Arginase inhibitor** Maintains arginine levels	Relapsed or Refractory multiple myeloma	Phase II Incyte Corporation
AZD3965	**Monocarboxylate transporter 1** Lactate metabolism	Advanced cancer	Phase I Cancer Research UK
TVB-2640 (ASC40)	**Fatty acid synthase** Lipid metabolism	GBM, Breast cancer and other solid tumors	Phase II Ascletis (Greater China)/Sagimet Biosciences (outside Greater China)

Fatty Acid Synthase, A Promising Cancer Drug Target

Fatty Acid Synthase (FASN):

- Synthesis palmitic acid from acetyl-CoA and malonyl-CoA
- Discovered as Oncogenic Antigen 519 (OA-519) in 1990's
- Over expressed in many cancer, prognosis marker



Pharmacol Ther, **2017**, 177, 23-31

CellPress

Cell Metabolism
Review

Greasing the Wheels of the Cancer Machine: The Role of Lipid Metabolism in Cancer

Marteinn Thor Snaebjornsson,[1,2,*] Sudha Janaki-Raman,[1,*] and Almut Schulze[1,2,*]
[1]Biochemistry and Molecular Biology, Theodor-Boveri-Institute, Biocenter, Am Hubland, 97074 Würzburg, Germany
[2]Division of Tumor Metabolism and Microenvironment, German Cancer Research Center, Im Neuenheimer Feld 581, 69120 Heidelberg, Germany
*Correspondence: m.snaebjoernsson@dkfz-heidelberg.de (M.T.S.), sudha.janaki_raman@uni-wuerzburg.de (S.J.-R.), almut.schulze@dkfz-heidelberg.de (A.S.)

https://doi.org/10.1016/j.cmet.2019.11.010

Altered lipid metabolism is among the most prominent metabolic alterations in cancer. Enhanced synthesis or uptake of lipids contributes to rapid cancer cell growth and tumor formation. Lipids are a highly complex group of biomolecules that not only constitute the structural basis of biological membranes but also function as signaling molecules and an energy source. Here, we summarize recent evidence implicating altered lipid metabolism in different aspects of the cancer phenotype and discuss potential strategies by which targeting lipid metabolism could provide a therapeutic window for cancer treatment.

FULL PAPER

BJC

British Journal of Cancer (2018) 118, 43–51 | doi: 10.1038/bjc.2017.374

Keywords: acetyl-CoA carboxylase; cancer; metabolism; membrane characteristics; metastasis; soraphen A; proliferation; tumour growth

Targeting *de novo* lipogenesis as a novel approach in anti-cancer therapy

Katharina Stoiber[1,2], Olga Nagło[1], Carla Pernpeintner[2,3], Siwei Zhang[1], Andreas Koeberle[4], Melanie Ulrich[1], Oliver Werz[4], Rolf Müller[5], Stefan Zahler[1], Theobald Lohmüller[2,3], Jochen Feldmann[2,3] and Simone Braig[*,1]

歌礼 ascletis

Cancer Lipid Metabolism: Recent Breakthrough of FASN Inhibitors

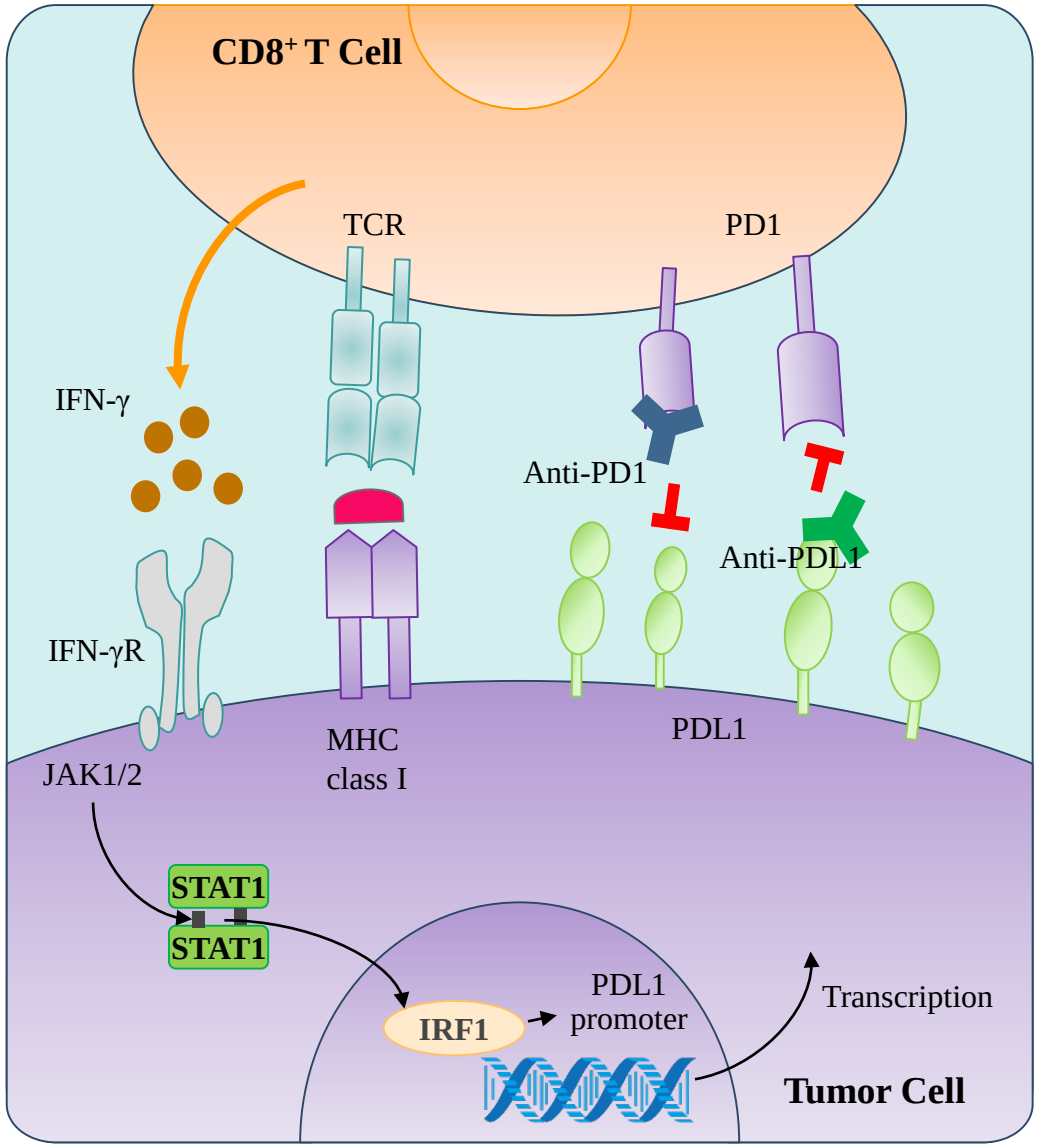
- Investigator sponsored Phase II trial of TVB-2640 with Bevacizumab in Patients with First Relapse of High-Grade Astrocytoma
  - 25 patients enrolled, both grade III and IV astrocytoma
  - All patients received ASC40 (TVB-2640) (100mg/m^2 PO QD) plus bevacizumab (10mg/kg IV D1,15) until treatment-related toxicity or progressive disease
- The overall response rate (ORR) for ASC40 (TVB-2640) plus bevacizumab of 65%
  - Complete response (CR) of 20%
  - Partial response (PR) of 45%
- Progression-free survival at six months (PFS6) for ASC40 (TVB-2640) plus bevacizumab was 47%
  - Representing a statistically significant improvement in PFS6 over historical bevacizumab monotherapy (BELOB 16%, *P*=0.01)
- ASC40 (TVB-2640) in combination with bevacizumab was safe and well tolerated in such patient population
- Presented at European Society for Medical Oncology 2020

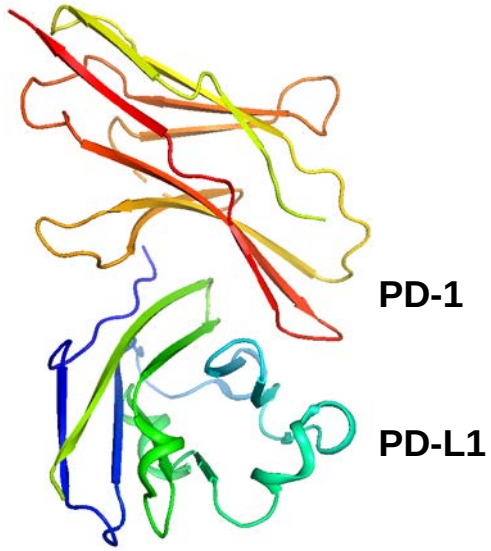
Oral Checkpoint Inhibitors

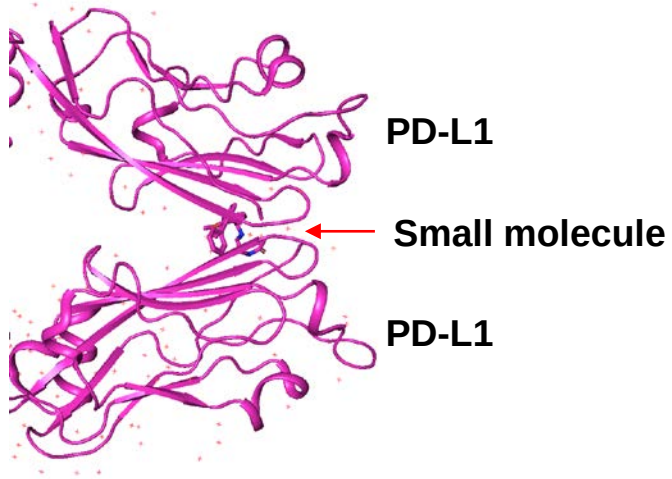
Immunotherapies: Great Success for mAb, It is Time for Oral Drugs

- BMS is the first company working on oral PD-L1 inhibitors
  - Filed patents for oral PD-L1 small molecule inhibitors in 2013
  - BMS stopped working PD-L1 inhibitors later due to drugability issues etc
- Gilead is one of leaders in oral PD-L1 inhibitors
  - A few years ago, Gilead announced its oral PD-L1 inhibitors for HBV
  - At JP Morgan virtual conference in 2021, Gilead announced its oral PD-L1 inhibitor GS-4224 was in Phase I for NSCLC
- Incyte is another leader in oral PD-L1 inhibitors
  - At SITC 2020, Incyte announced its oral PD-L1 inhibitor INCB86550 was in Phase I for solid tumors

PD-L1 Small Molecule Inhibitors: Challenges and Opportunities





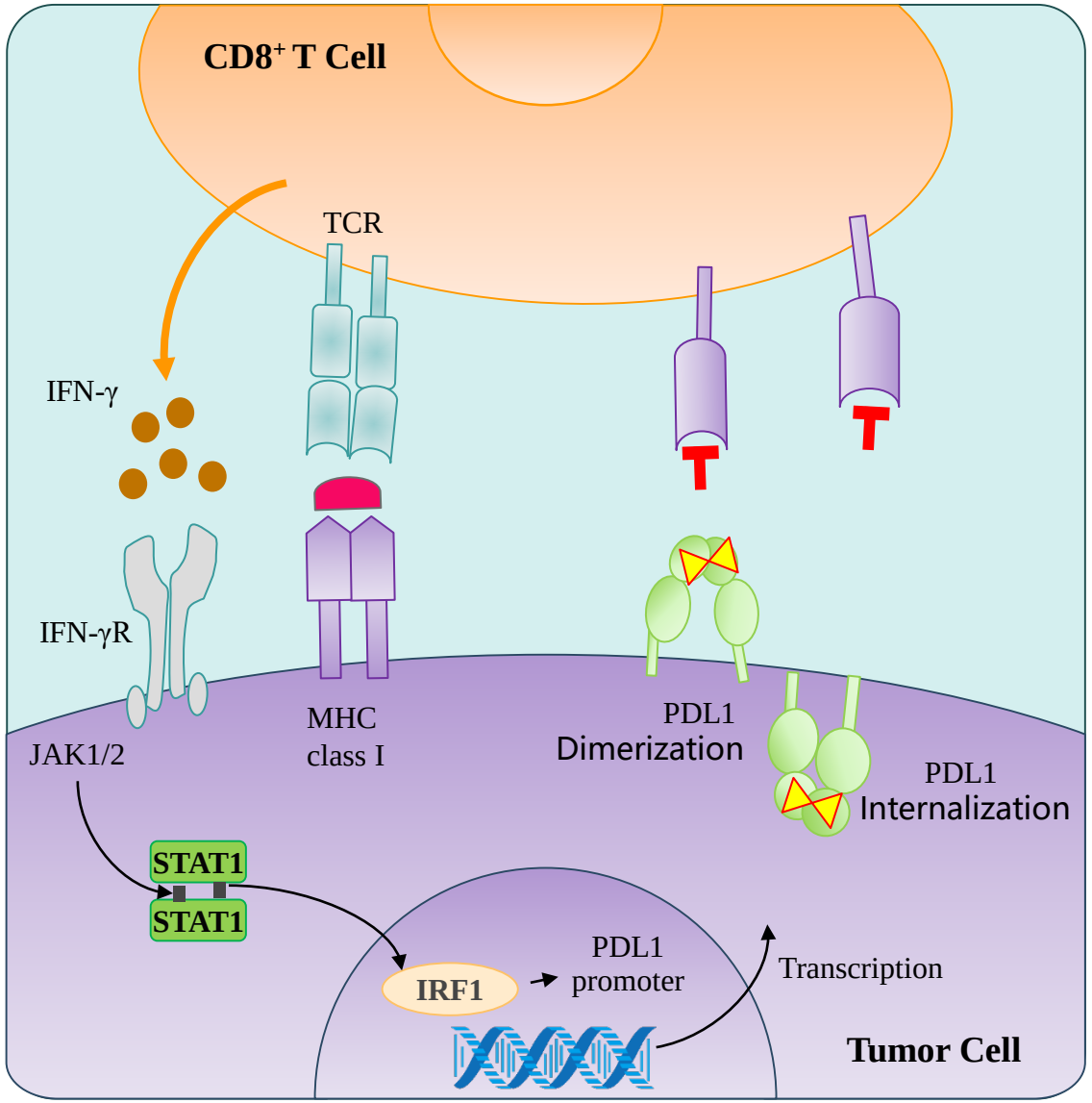


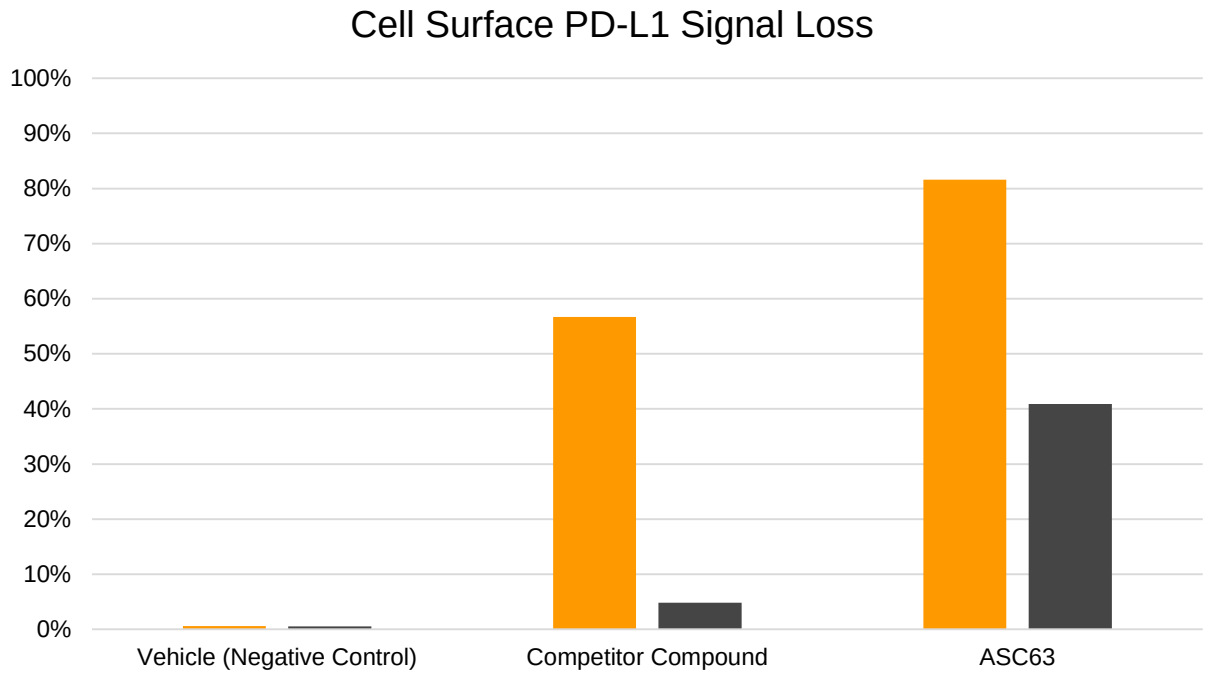
- Antibodies block PD-1/PD-L1 interface
- Traditional small molecules not good at inhibiting protein-protein interaction

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

歌礼 ascletis

ASC63: Induce PD-L1 Dimerization and Sustained Internalization



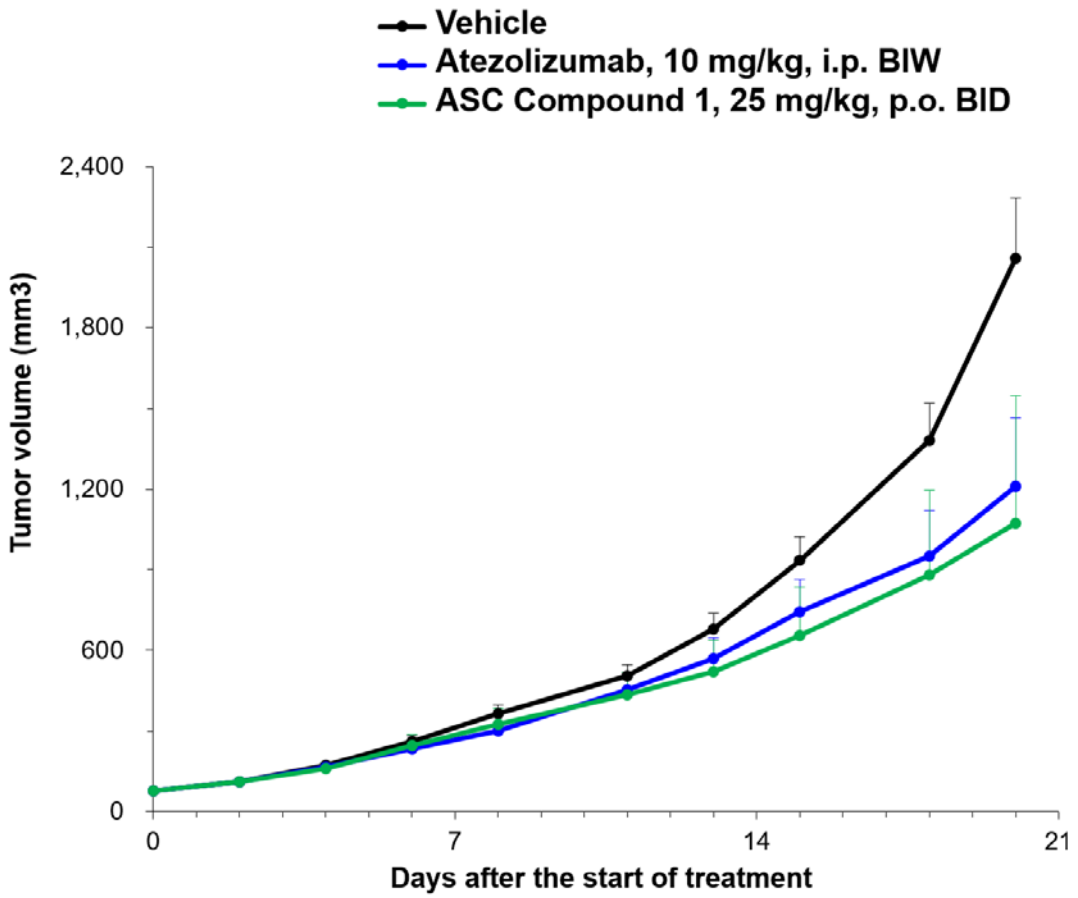


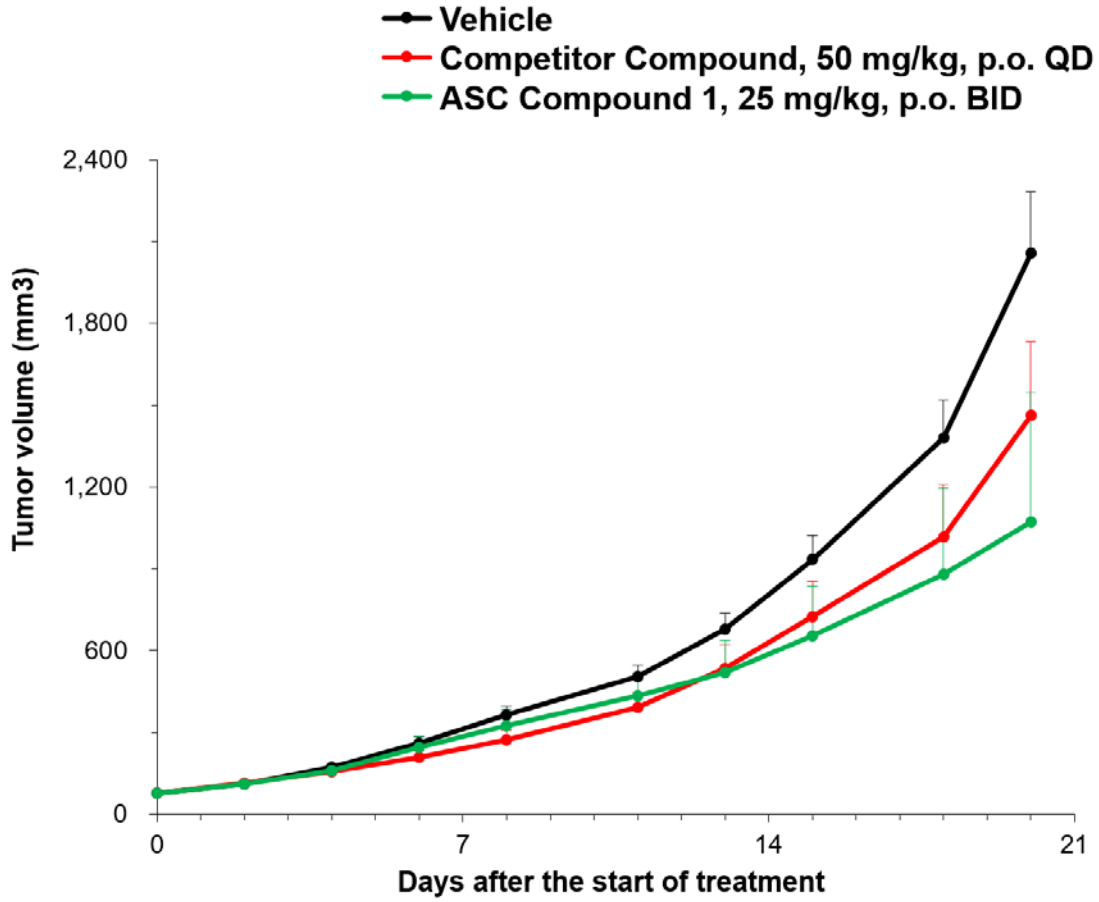
Ascletis' ASC63

- 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)

歌礼 ascletis

Ascletis' Oral PD-L1 Inhibitor: Anti-Tumor Activity in Syngeneic Mouse Model





歌礼 ascletis

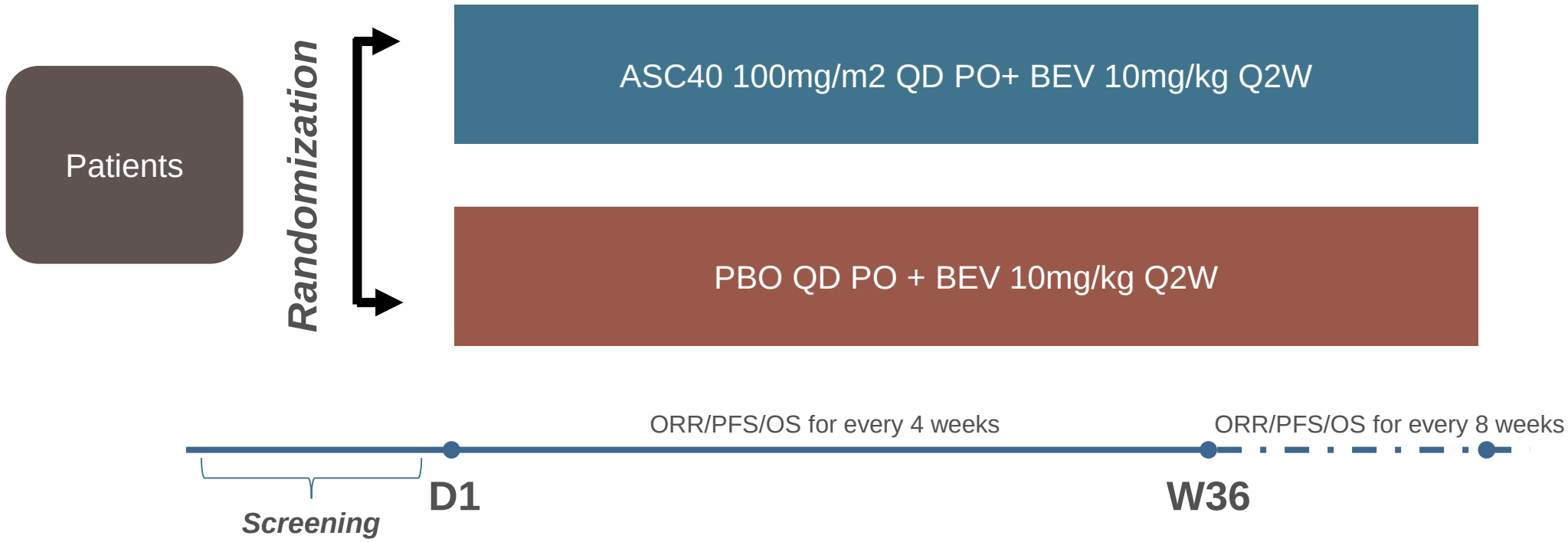
Cancer Lipid Metabolism and Oral Checkpoint Inhibitors

Target	Product/ Candidate	Indication	Commercial Rights	Pre-IND	IND	Phase I	POC	Pivotal	NDA	Marketed
FASN+VEGF	ASC40（Oral） +Bevacizumab	Glioblastoma	Greater China[1]			*IST Phase II Completed*				
FASN	ASC40 (Oral)	Multiple Solid Tumors	Greater China[1]							
FASN	ASC60 (Oral)	Multiple Solid Tumors	Greater China[1]							
PD-L1	ASC61 (Oral)	Multiple Tumors	Global							
PD-L1	ASC63 (Oral)	Multiple Tumors	Global							

Notes: 1. ASC40 and ASC60 are licensed from Sagimet for the exclusive rights in the Greater China.

Future Plan:

A Pivotal Randomized, Double Blind, Placebo Controlled Phase II Trial of ASC40 in Combination with Bevacizumab in Chinese Patients with First Relapse of High-grade Astrocytoma



Milestones for the next 12 months

- Initiate a Pivotal Phase II Trial of ASC40 in Combination with Bevacizumab in Chinese Patients with First Relapse of High-grade Astrocytoma
- Explore ASC40 in combination with chemotherapies for high-grade astrocytoma immediately following the surgery and radiation therapy
- Explore ASC40 in combination with other therapies for various solid tumors
- Advance ASC60, as a next generation oral FASN small molecule inhibitor, in combination with other therapies for various solid tumors
- Advance oral PD-L1 small molecule inhibitors as next generation checkpoint inhibitors into clinical studies

Viral Hepatitis

Viral hepatitis

HBV

Target	Product/ Candidate	Commercial Rights	Pre-IND	IND	Phase I	Phase IIa	Phase IIb/III	NDA	Marketed
Interferon receptor	Pegasys® (Peginterferon alfa-2a)	Mainland China[1]							
PD-L1	ASC22	Greater China[2]							
Undisclosed	Candidate identified	Global							
FXR	ASC42	Global							

Notes: 1. Pegasys® is licensed from Shanghai Roche Pharmaceuticals Ltd. for the exclusive rights in the Mainland China. 2. ASC22 is licensed from Suzhou Alphamab Co.,Ltd. (“Alphamab”) for the exclusive rights in the Greater China.

HCV

Target	Product/ Candidate	Commercial Rights	Pre-IND	IND	Phase I	Phase IIa	Phase IIb/III	NDA	Marketed
NS3/4A	GANOVO® (Danoprevir)	Greater China[1]							
NS5A	ASCLEVIR® (Ravidasvir)	Greater China[2]							
Dual Targeted FDC	ASC18	Greater China							

Notes: 1. GANOVO® is licensed from Roche (F. Hoffmann-La Roche AG) for the exclusive rights in the Greater China. 2. ASCLEVIR® is licensed from Presidio Pharmaceuticals, Inc. for the exclusive rights in the Greater China.

歌礼 ascletis

Building HBV Franchise Leading to Clinical Cure

- Cornerstones: Marketed Pegasys® and subcutaneously injected PD-L1 antibody - ASC22
- Pegasys® in combination with in-house developed drug candidates against novel targets such as FXR
- PD-L1 antibody ASC22 in combination with in-house developed drug candidates against novel targets such as FXR
- Pegasys® or PD-L1 antibody ASC22 - Partner with drug candidates of industrial leaders
  - siRNA
  - HBV Entry inhibitors
  - Therapeutic Vaccine

MOA of PD-L1 Antibody Against Chronic Hepatitis B

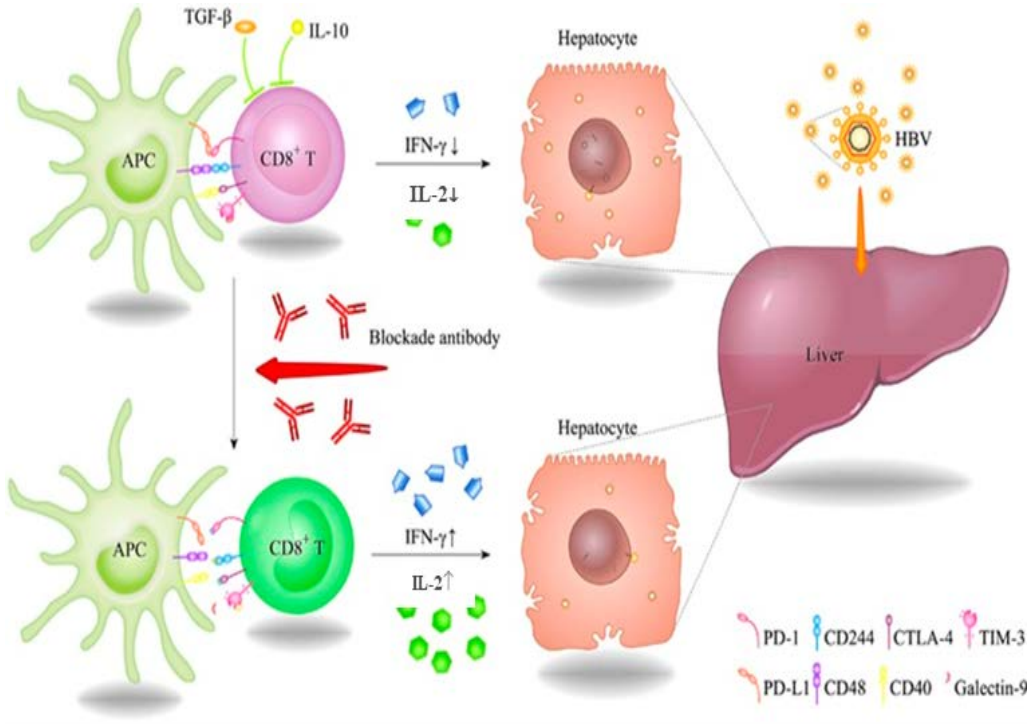
- ASC22 (KN035) can block the PD-1/PD-L1 pathway to restore T Cell immune function and eliminate HBV.

PD-1/PD-L1 interaction leads to T cell exhaustion

—— **Persistent HBV infection**

Blockade of PD-1/PD-L1 pathway restores T cell function

—— **Elimination of HBV**



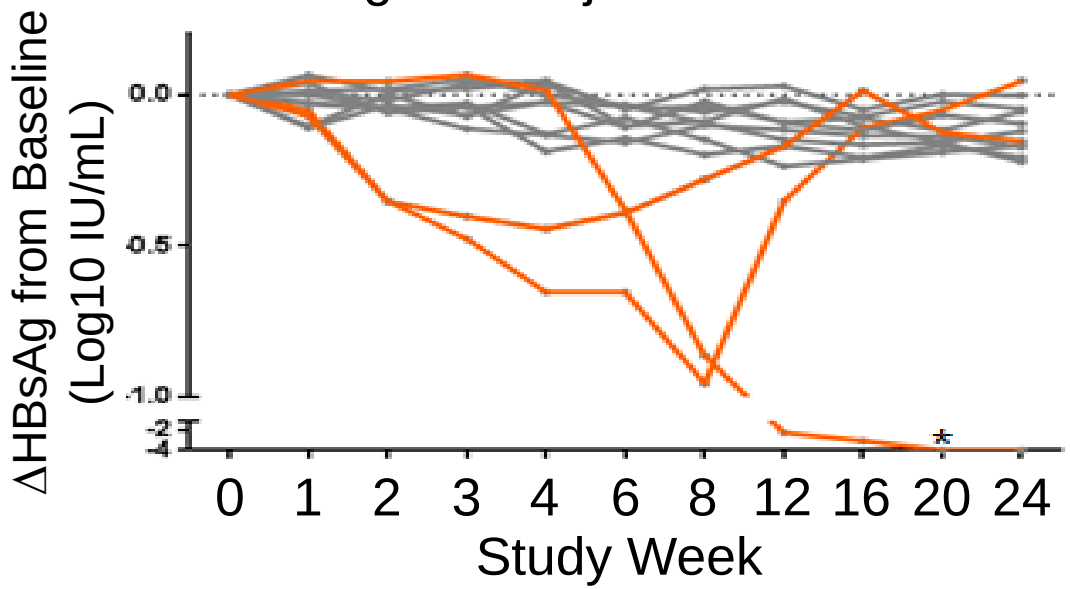
1. Peng G, et al. PD-1 upregulation is associated with HBV-specific T cell dysfunction in chronic hepatitis B patients. Mol Immunol. 2008;45(4):963-70.
2. B Ye, et al. T-cell exhaustion in chronic hepatitis B infection: current knowledge and clinical significance. Cell Death Dis. 2015 Mar 19;6:e1694.

歌礼 ascletis

HBV Clinical Cure: PD-1 Antibody - Opdivo (Nivolumab)

Nivolumab: Monoclonal antibody against PD-1 Approved for solid organ tumors and lymphomas

Phase 1 Nivolumab 0.3 mg/kg, single i.v. injection at week 0



- 1/10 patient Achieved HBsAg loss at week 16 and maintained negative during follow-up
- 1/10 patient experienced 1 log HBsAg decline at week 8 but rebounded afterwards
- 1/10 patient had moderate HBsAg decline

Human Proof of Concept study demonstrated HBsAg loss and its sustainability by single i.v. injection of PD-1 antibody.

Gane, EASL 2017

歌礼 ascletis

Cure for HBV: First-in-class Subcutaneously Injected PD-L1 Ab

ASC22, **Global First-in-class** PD-L1 antibody immunotherapy, which may lead to a significant breakthrough towards a clinical cure for chronic Hepatitis B.

Global First-in-class

Blockade of PD-1/PD-L1 pathway to restore specific T-cell function

Best immunotherapy for HBV

Only subcutaneously administered PD-1/PD-L1 antibody entered into late-stage clinical development

Demonstrated good safety profile

- Phase IIa data showed ASC22 is safe and well tolerated in chronic hepatitis B (CHB) patients and Phase IIb clinical trial has been initiated
- In addition to CHB patients, 1000+ cancer patients exposed in multiple clinical trials in US, China and Japan, Including two pivotal trials in China

Differentiated Profile

- Subcutaneous route of administration
- Good stability at room temperature

歌礼 ascletis

HBV Clinical Cure: s.c. PD-L1 Ab ASC22 vs i.v. PD-L1 Abs

Company	Roche	MSD	AstraZeneca	Ascletis
Product	Atezolizumab	Avelumab	Durvalumab	ASC22（KN035）
Target	PD-L1	PD-L1	PD-L1	PD-L1
Dose	1200 mg/3 weeks	800mg/2 weeks	10mg/kg/2 weeks	1-2.5mg/kg/2 week
Administration	I.V	I.V	I.V	S.C
Indication	Late stage or metastasized Urothelial Carcinoma; Unresectable late stage NSCLC	Adult or Adolescent metastasized Merkel Cell Carcinoma； Late stage or metastasized Urothelial Carcinoma	Late stage or metastasized Urothelial Carcinoma; Unresectable late stage NSCLC	Hepatitis B

1. ASC22 (KN035) has lower dose, with advantage in administration route and storage condition.
2. ASC22 is the first PD-1/PD-L1 antibody with subcutaneous injection entering into late phase clinical trial.
3. Phase IIa data showed ASC22 is safe and well tolerated in chronic hepatitis B (CHB) patients and Phase IIb clinical trial has been initiated.
4. ASC22 has been investigated in several studies conducted in China, USA, and Japan involving greater than 1000 subjects in oncology with proven safety.

Data from ASC22 Phase II Study

- The data from Phase IIa study indicated that ASC22 (KN035) is safe and well tolerated in the CHB patients receiving nucleos(t)ides as the background therapy. All adverse effects were grade 1 and no grade 2 or above adverse effects were observed

Sustainable HCV Franchise to Cure 10 million Patients in China

- All oral regimen (RDV/DNV Regimen) : NDA has been approved for marketing in July, 2020 by China's National Medical Products Administration (NMPA)
- ASC18: one-pill once-a-day oral regimen
  - First fixed-dose combination (FDC) as a complete HCV therapy developed by a Chinese biotech
  - Phase III data, with 2 separate pills, indicated pan-genotypic and >95% cure rate (SVR12)

DNV: GANOVO® (Danoprevir)
RDV: ASCLEVIR® (Ravidasvir)

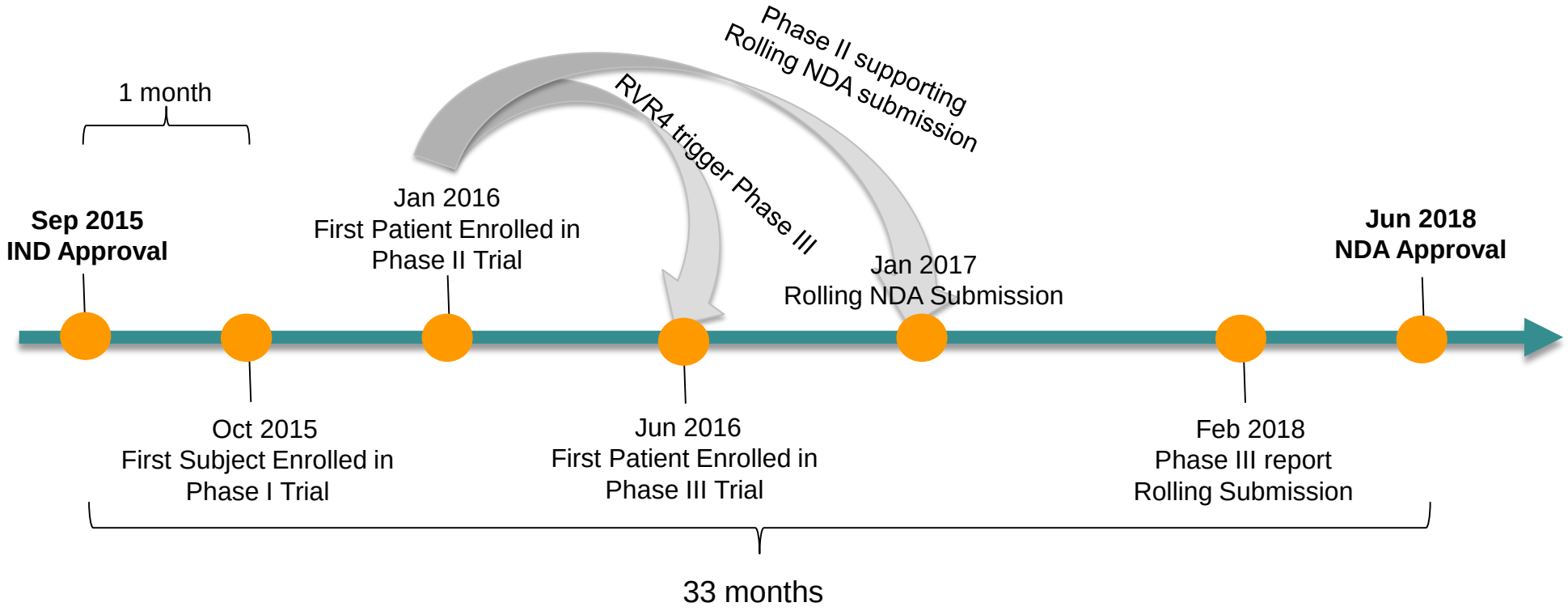
歌礼 ascletis

HIV/AIDS

Expand our portfolio

- Functional cure with immunotherapies
- Treatment
- Prevention

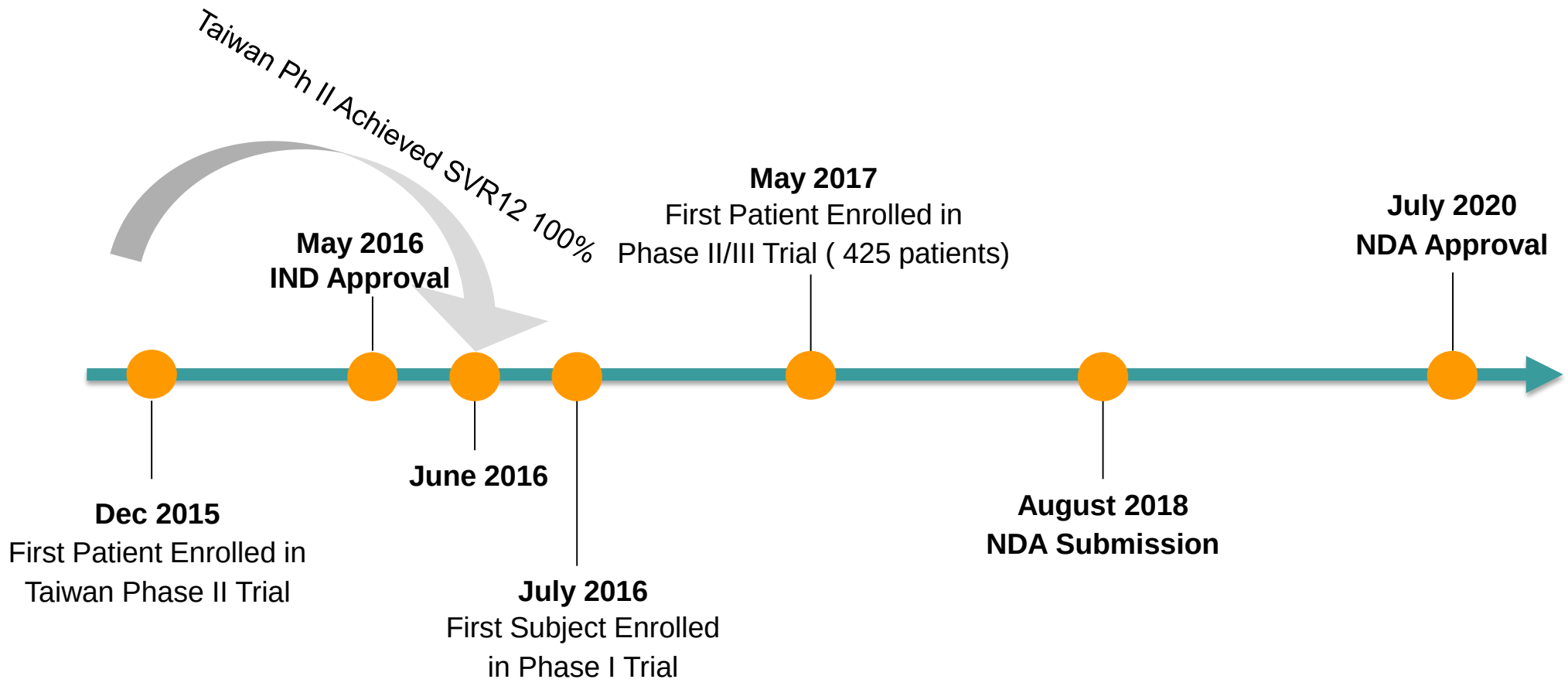
R&D Efficiency : GANOVO® from IND to NDA Approval: 33 months



Company (Target)	IND Approval	NDA Approval	IND approval to NDA approval (months)
Ascletis (HCV NS3/4A)	Sept 2015	June 2018	33
BMS (HCV NS3/4A and 5A)	June 2013	June 2017	48

歌礼 ascletis

R&D Efficiency: ASCLEVIR ® from IND to NDA Approval: 50 months



歌礼 ascletis

Experienced and Extensive Sales Network

Experienced Team

Roche · Bristol-Myers Squibb · GILEAD · gsk GlaxoSmithKline · NOVARTIS · MERCK

√ **5** major units including medical affairs, sales, marketing strategy, market access, and channel / distribution

√ Directors and above management have 10+ years experience of HCV and HBV at the above representative companies

Network Coverage

- **~1,000** Hospitals located in regions where hepatitis B&C is most prevalent in China
- **~5,400** specialists and key opinion leaders covered in the hepatitis field
- **22** distribution agreements with major distributors, enabling nationwide coverage and timely delivery of products.

Strategy

- Branding Activities and Market Research
- Patients Research and Analysis
- HCV/HBV Awareness Raising

GANOVO®

19 Days

2018

NDA Approved	GMP Certified	Inaugural Sales
June 8	**June 14**	**June 27**

歌礼 ascletis

GMP Manufacturing Facilities

中华人民共和国

药品GMP证书

CERTIFICATE OF GOOD MANUFACTURING PRACTICES FOR PHARMACEUTICAL PRODUCTS

PEOPLE'S REPUBLIC OF CHINA

证书编号：ZJ20180068

Certificate No.

企业名称：歌礼药业（浙江）有限公司

Manufacturer：Ascletis Pharmaceuticals Co., Ltd.

地　址：绍兴滨海新城沥海镇云海路1号

Address：No.1, Yunhai Road, Linhai District, Binhai New Town, Shaoxing City

认证范围：片剂

Scope of Inspection：Tablets

经审查，符合中华人民共和国《药品生产质量管理规范》要求。

特发此证。

This is to certify that the above-mentioned manufacturer complies with the requirements of Chinese Good Manufacturing Practices for Pharmaceutical Products.

有效期至 2023 年 06 月 13 日

This certificate remains valid until 06/13/2023

发证机关：

Issued By

Date for Issuing 06/14/2018 2018 年 06 月 14 日

国家食品药品监督管理总局制

CHINA FOOD AND DRUG ADMINISTRATION

GMP Certified	Quality Assurance	International Standards	Supply ensured
▪ Quality-by-design approach implemented ▪ Complied with cGMP	▪ State-of-art equipment with cutting-edge technology capabilities	▪ Experienced manufacturing employees from MNCs	▪ Production capacity of 130 million tablets

歌礼 ascletis

Global Cooperation

Roche

janssen | PHARMACEUTICAL COMPANIES OF Johnson & Johnson

PRESIDIO®

康宁杰瑞 ALPHAMAB

SAGIMET BIOSCIENCES

Galmed Pharmaceuticals

歌礼 ascletis

Summary

- Ascletis focuses on NASH, cancer lipid metabolism and oral checkpoint inhibitors, viral hepatitis and HIV/AIDS
  - NASH: global development of novel drug candidates against three different targets – FASN, THR-β and FXR, and three combination therapies
  - Cancer lipid metabolism and oral checkpoint inhibitors: 1)Pivotal Phase II trial of ASC40 in combination with Bevacizumab in Chinese patients with first relapse of high-grade astrocytoma; 2) ASC40 in combination with chemotherapies for high-grade astrocytoma immediately followed the surgery and radiation therapy; 3) ASC40 in combination with other therapies for various solid tumors; 4) Advance ASC60, as a next generation oral FASN small molecule inhibitor, in combined with other therapies for various solid tumors; 5) Advance oral PD-L1 small molecule inhibitors as next generation checkpoint inhibitors into clinical studies
  - Viral hepatitis: 1) commercializing Pegasys® for HBV clinical cure; 2) developing breakthrough therapies for HBV clinical cure； 3) commercializing all oral HCV regimen
  - HIV/AIDS: expanding current portfolio for treatment, prevention and functional cure
- Ascletis will accelerate investments in NASH, cancer lipid metabolism and oral checkpoint inhibitors and HBV clinical cure, and look for opportunities to expand into new disease areas
  - Current cash reserve of approximately US$416M and upcoming product sales revenue support such aggressive goals

Disclaimer

- The documents, opinions and materials presented and distributed in the presentation (collectively, the "Document"), which were prepared by Ascletis Pharma Inc. (the "Company") together with its subsidiaries and affiliates (collectively, the "Group"), are provided to you solely for your exclusive use and information in connection with a proposed investment and are not for public dissemination. The Document is not prepared by Morgan Stanley Asia Limited, Goldman Sachs (Asia) L.L.C. and China Merchants Securities (HK) Co., Limited (collectively, the "Joint Sponsors"), nor any of their respective affiliates, controlling persons, directors, officers, partners, employees, agents, advisors or representatives. You fully understand that the Document is being made available on a confidential basis and subject to the following provisions, to a limited number of recipients for the sole purpose of providing information to assist them in deciding whether they wish to proceed with a further investigation of the Company. The contents of this Document have not been reviewed by any regulatory authority in any jurisdiction. The distribution of this Document in certain jurisdictions may be restricted by law, and the recipients into whose possession this Document comes should inform themselves about, and observe such restrictions. By accessing this Document, you are agreeing (i) that you have read and agree to comply with the contents of this notice and disclaimer and (ii) to maintain absolute confidentiality regarding the information disclosed in this Document.
- This Document has not been independently verified and is not intended to form the basis of any investment decision. It does not constitute an offer or invitation to sell, or any solicitation of any offer to subscribe for or purchase any securities in any jurisdiction in which the making of such offer, solicitation or sale would be unlawful prior to registration or qualification under the securities laws of such jurisdiction or would not otherwise be in compliance with the laws and regulations of such jurisdiction, and nothing contained herein shall form the basis of any investment decision, contract or commitment whatsoever. Any decision to purchase securities of the Company in any public or private offering should be made solely on the basis of the prospectus and/or international offering circular to be prepared by the Company in relation to any such contemplated offering together with any supplementary pricing information. This Document contains no information or material which may result in it being deemed (1) to be a prospectus within the meaning of section 2(1) Companies (Winding Up and Miscellaneous Provisions) Ordinance (Chapter 32 of the Laws of Hong Kong) (the "Companies Ordinance"), or an advertisement in relation to a prospectus or proposed prospectus or extract from or abridged version of a prospectus within the meaning of section 38B of the Companies Ordinance or an advertisement, invitation or document containing an advertisement or invitation falling within the meaning of section 103 of the Securities and Futures Ordinance (Chapter 571 of the Laws of Hong Kong) (the "Securities and Futures Ordinance") or (2) in Hong Kong to have effected an offer to the public without compliance with the laws of Hong Kong or being able to invoke any exemption available under the laws of Hong Kong, and is subject to material change without notice.
- The securities of the Company have not been and will not be registered under the U.S. Securities Act 1933, as amended (the "U.S. Securities Act"), or under the laws of any state of the United States. This Document does not constitute or form a part of any offer or solicitation to purchase or subscribe for securities in the United States and is not for distribution and may not be distributed, directly or indirectly, in or into the United States (including its territories and possessions, any state of the United States and the District of Columbia). The securities of the Company will not be offered or sold in the United States except pursuant to an exemption from, or in a transaction not subject to the registration requirements of the U.S. Securities Act. There will be no public offer of the Company's securities in the United States.
- This Document and the information contained herein as well as information presented orally or otherwise are strictly confidential and must be treated as such. No part of this Document or its contents may be copied or reproduced, or redistributed or passed on, directly or indirectly, to any other person in any manner or published, in whole or in part, for any other purpose. By accessing this Document, you are deemed to represent to the Company and the Joint Sponsors and their respective affiliates, controlling persons, directors, offices, partners, employees, agents, advisors or representatives that you are, and any customers you represent are either (i) a "qualified institutional buyer" within the meaning of Rule 144A of the U.S. Securities Act, or (ii) outside the United States. You also represent that you are, and any customers you represent are "professional investors" described in Part I of Schedule 1 to the Securities and Futures Ordinance and any subsidiary legislation thereunder (including but not limited to the Securities and Futures (Professional Investor) Rules (Chapter 571D of the Laws of Hong Kong)).To the extent you purchase the securities of the Company, you will be doing so pursuant to either Rule 144A or Regulation S or another exemption from registration under the U.S. Securities Act. Neither this Document nor any copy of it may be taken or transmitted into or distributed, directly or indirectly, in the United States. Neither this Document nor any copy of it may be taken or transmitted into Canada or distributed or redistributed in Japan or to any resident thereof. Upon request, the recipient will promptly return this Document and all information made available in connection with the proposed investment, without retaining any copies.
- The information in this Document has been provided by the Company. This Document does not purport to be comprehensive or to contain all the information that a recipient may need in order to evaluate the Group. No representation, warranty or undertaking, express or implied, is given and, so far as is permitted by law, no responsibility or liability is accepted by any person (for the avoidance of doubt, including but not limited to, the Company and the Joint Sponsors and their respective affiliates, controlling persons, directors, officers, partners, employees, agents, advisors or representatives of any of the foregoing), with respect to the accuracy, reliability, correctness, fairness or completeness of this Document or its contents or any oral or written communication in connection with the proposed investment. In particular, but without limitation, no representation or warranty is given as to the achievement or reasonableness of, and no reliance should be placed on, any assumptions, projections, targets, estimates, forecasts or any forward-looking statements contained in this Document. Each of the Company and the Joint Sponsors and their respective affiliates, controlling persons, directors, officers, partners, employees, agents, advisors or representatives of any of the foregoing assumes no obligation to update or otherwise revise these forward-looking statements for new information, events or circumstances that occur subsequent to such dates. None of the Company and the Joint Sponsors and any of their respective affiliates, controlling persons, directors, officers, partners, employees, agents, advisors or representatives of any of the foregoing shall have any liability (in negligence or otherwise) in respect of the use of, or reliance upon, the information contained herein by you or any person to whom the information herein is disclosed.
- In furnishing this Document, the Company and the Joint Sponsors and their respective affiliates undertake no obligation to provide any additional information or to update this Document or any additional information or to correct any inaccuracies which may become apparent. This Document does not create an obligation on the Company or the Joint Sponsors or any of their respective affiliates to consider any offer. The provision of the information contained herein shall not be or be taken as any form of commitment on the Company, the Joint Sponsors, any of their respective affiliates or on you to proceed with the proposed placing or offering of securities in the Company.
- The Company reserves the right to negotiate with one or more prospective investors at any time and to enter into a definitive agreement for the sale for the financing of this transaction without prior notice to the other prospective investors. The Company, the Joint Sponsors and their respective affiliates each also reserves the right, without advance notice, to change the procedure or to terminate negotiations at any time prior to the entry into of any binding contract for the proposed investment.
- The Joint Sponsors or their affiliates are acting for the Company and not the recipient of this Document and the receipt of this Document by any recipient is not to be taken as constituting the giving of investment advice by the Joint Sponsors or their affiliates to that recipient, nor to constitute a customer or client relationship between the recipient and the Joint Sponsors or any of their affiliates. Accordingly, the Joint Sponsors or any of their affiliates will not be responsible to the recipient for providing protections afforded to their customers or clients or advising the recipient in relation to the proposed investment.
- You acknowledge and represent to the Company and the Joint Sponsors and their respective affiliates, controlling persons, directors, officers, partners, employees, agents, advisors or representatives that you are a professional investor, that you have the knowledge, experience and capability to conduct your own assessment of the Company and its securities and that you have conducted and will conduct your own investigation with respect to the Company and its securities and have obtained or will obtain your own independent advice relating to any investment in the securities of the Company.
- All enquiries or requests for additional information in connection with this Document should be submitted or directed to the Joint Sponsors. Management of the Company should not be contacted directly under any circumstances in connection with this Document and any unauthorized contact may result in termination of negotiations in relation to the proposed investment.

歌礼 ascletis