1672.HK

Ascletis Pharma Inc.

From First-in-China to First Globally

November 2020

歌礼
ascletis

Multi-Disease Platform

Since Hong Kong IPO in 2018, Ascletis has developed into multi-disease platform from a single disease – HCV platform. Ascletis has three marketed products and eleven R&D pipeline drug candidates (7 of them developed in house).

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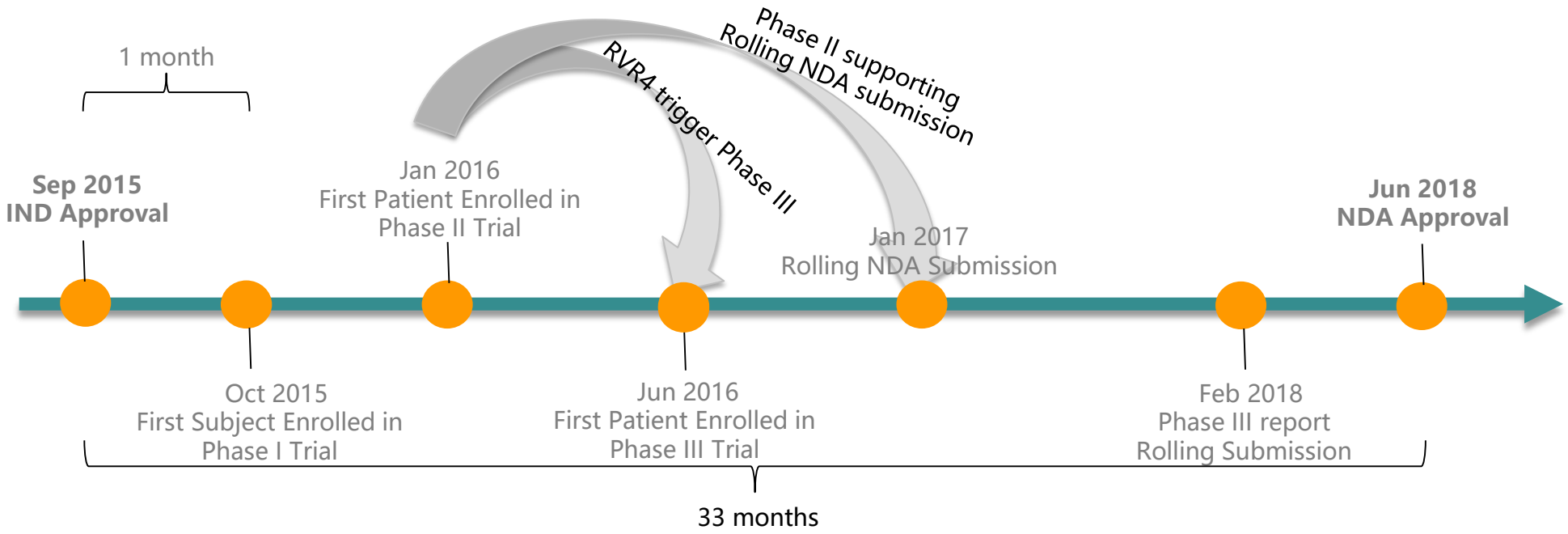
R&D Efficiency : Ganovo® from IND to NDA Approval: 33 months



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

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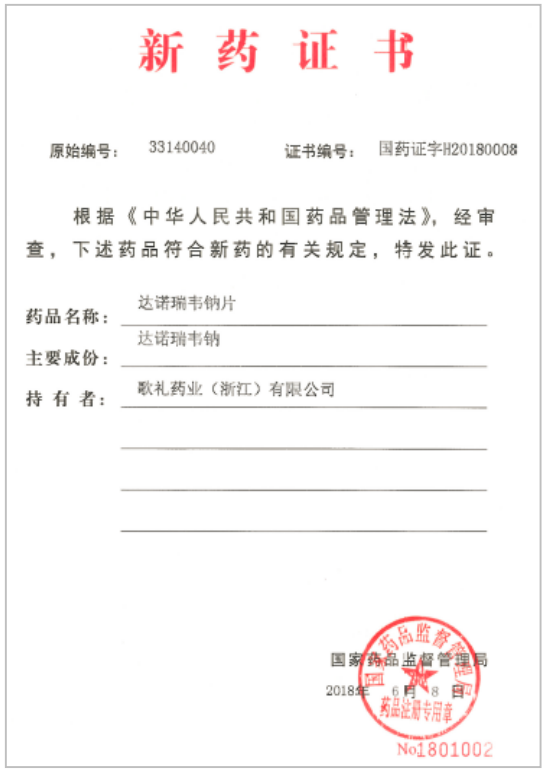
Ganovo® is the First Approved Innovative HCV DAA Developed by a China Biotech

The first category 1 targeted hepatitis C innovative drug developed by Chinese local enterprises.



新 药 证 书

原始编号： 33140040　　证书编号： 国药证字H20180008

根据《中华人民共和国药品管理法》，经审查，下述药品符合新药的有关规定，特发此证。

药品名称： 达诺瑞韦钠片

主要成份： 达诺瑞韦钠

持 有 者： 歌礼药业（浙江）有限公司

国家药品监督管理局

2018年 6月 8日

No1801002

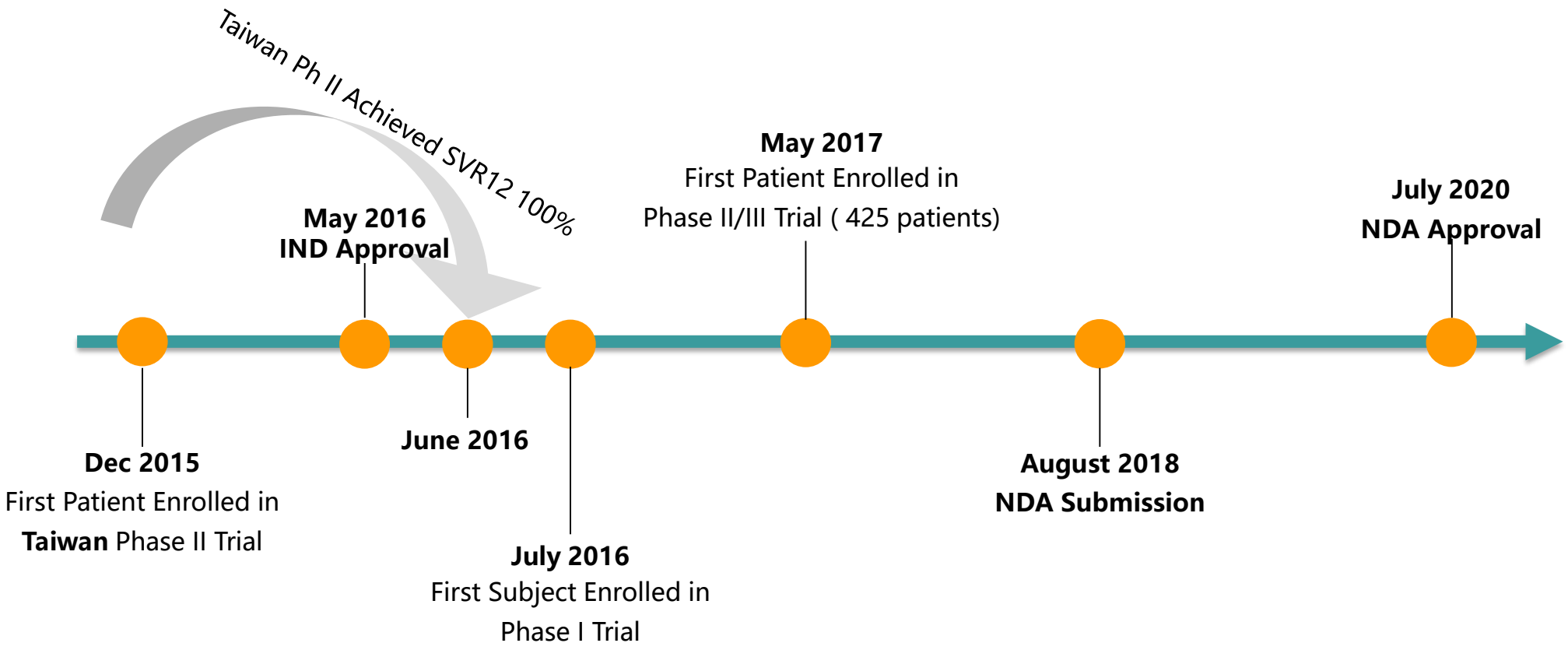
33 Months From IND approval to NDA approval

97% Cure rate (SVR12) with 12 week treatment

3000+ Patients enrolled in clinical trials

歌礼 ascletis

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



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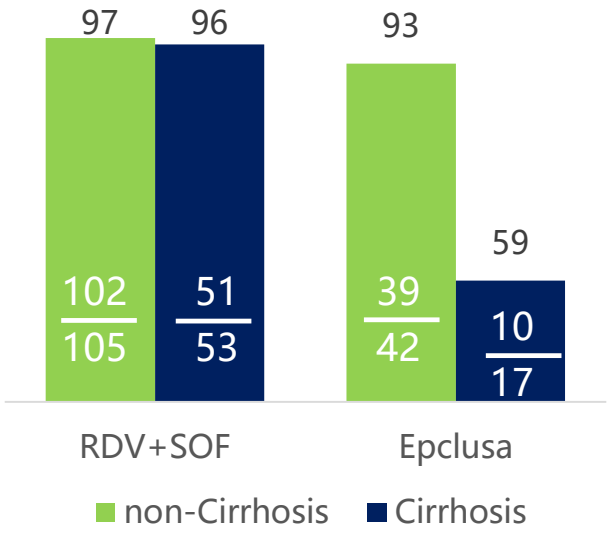
First All-oral, Interferon-free, HCV Regimen Developed by a Domestic Company in China

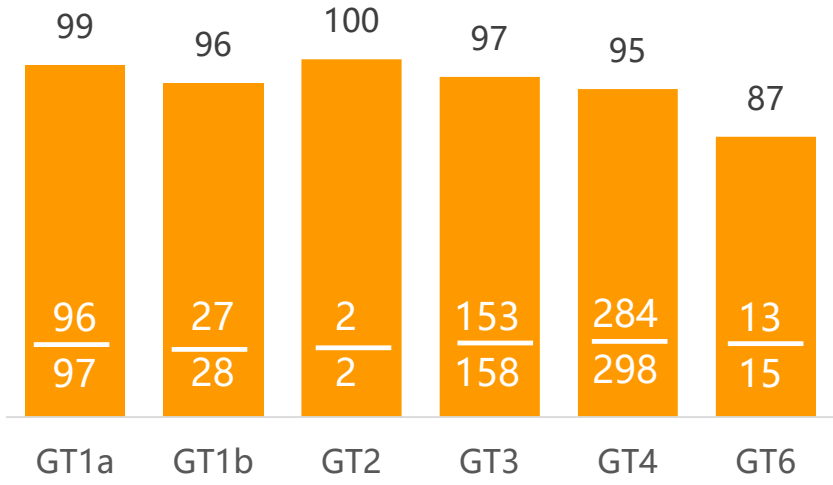
Asclevir ® is a pan-genotypic best-in-class HCV NS5A inhibitor, has been approved for marketing by China’ s NMPA in July, 2020. Phase II/III clinical trial has shown that RDV/DNV Regimen demonstrated a cure rate of **99 %** (SVR12) with a short treatment duration of 12 weeks in genotype 1 patients.

GT3:SVR12(%)



RDV+SOF treatment is an effective pan-genotypic HCV treatment

SVR12 (%)



Data from (1) DNV/RDV China Phase II/III clinical trial;
(2) RDV/SOF Malaysia and Thailand Phase II/III clinical trial;
(3) SOF/VEL (Epclusa) China phase III clinical trial.

DNV: Ganovo ® (Danoprevir)
RDV: Asclevir ® (Ravidasvir)
SOF: Sofosbuvir

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Viral hepatitis

HBV

Target	Products/Drug Candidate	Pre-IND	IND Approval	Phase I	Phase II	Phase III	NDA Filed	Marketed	Licensed From/ In-house	Commercial Rights
Interferon receptor	Pegasys® (Peginterferon alfa-2a)								Roche	Mainland China
PD-L1	ASC22								康宁杰瑞 ALPHAMAB	Greater China
Undisclosed	Candidate identified								In-house	Global
FXR	ASC42								In-house	Global

HCV

Target	Products/Drug Candidate	Pre-IND	IND Approval	Phase I	Phase II	Phase III	NDA Filed	Marketed	Licensed From/ In-house	Commercial Rights
NS3/4A	Ganovo® (Danoprevir)								Roche	Greater China
NS5A	Asclevir® (Ravidasvir)								PRESIDIO	Greater China
Dual Targeted FDC	ASC18								In-house	Greater China

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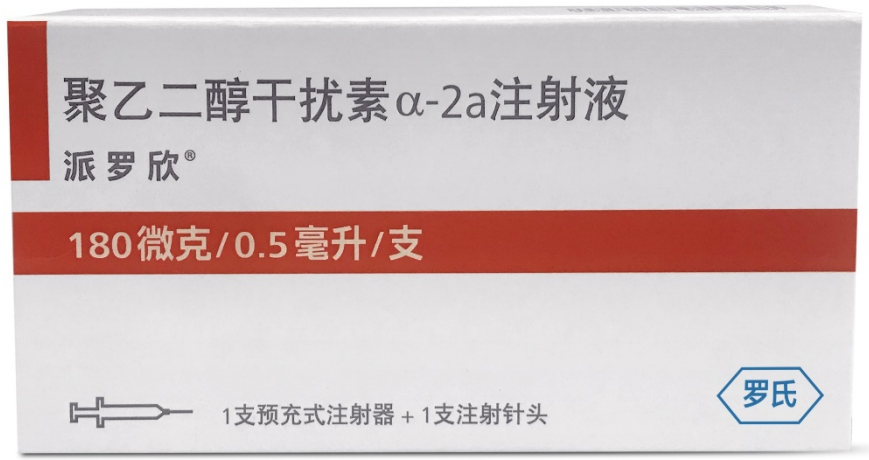
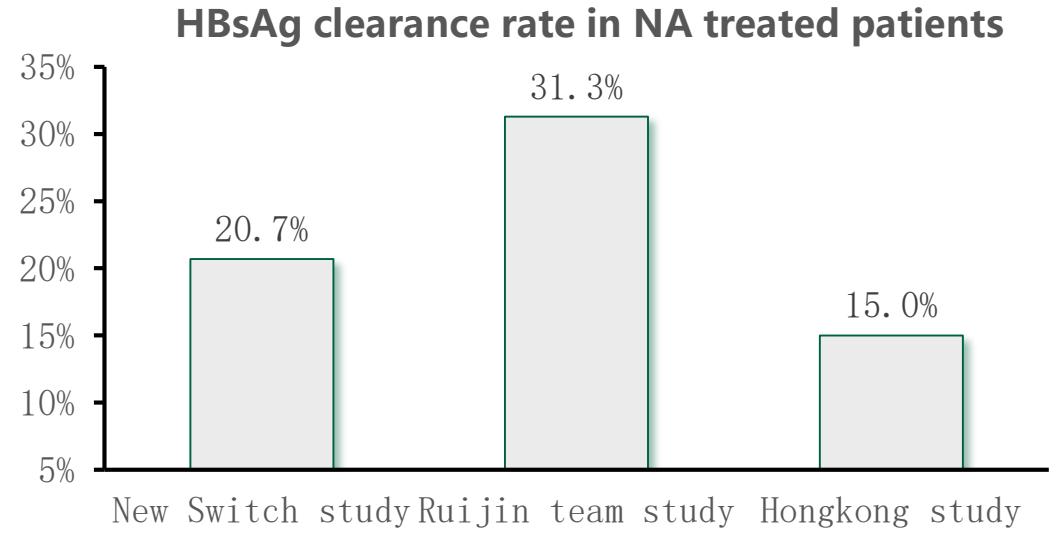
Building HBV Franchise Leading to Clinical Cure

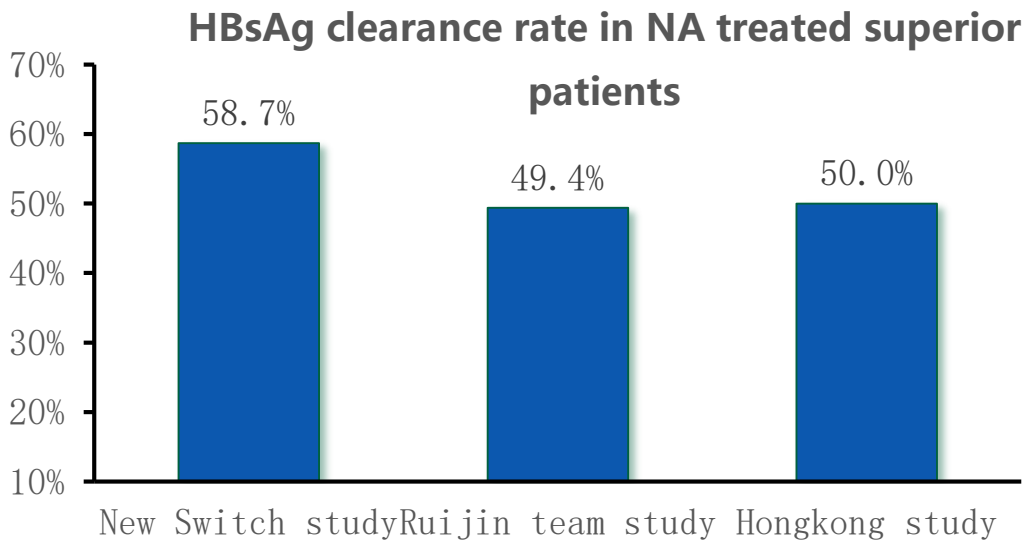
- Cornerstones: Marketed Pegasys® and subcutaneously injected PD-L1 antibody - ASC22
- Pegasys® in combination with in-house developed drug candidates against novel targets
- PD-L1 antibody ASC22 in combination with in-house developed drug candidates against novel targets
- Pegasys® or PD-L1 antibody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

Pegasys®： An Important Treatment For Chronic Hepatitis B Patients Seeking Clinical Cure

Pegasys®(pegylated interferon α - 2A injection) was approved in 2002 for the treatment of chronic hepatitis B and hepatitis C in adults. Over 115 countries and regions have been approved to use it for 18 years, benefiting 2.5 million patients with viral hepatitis, and 3986 related literatures have been published.







1、New switch study：Hu P, et al. J Clin Transl Hepatol. 2018;6:25-34.
2、Ruijin team study：Ren PP, et al. Hepatology, 2019, AASLD2019(Abstracts (poster 466)).
3、Hongkong study：Chan HLY, et al. J Viral Hepat, 2019, 26(1): 126-135.

歌礼 ascletis

MOA of PD-L1 Antibody Against Chronic Hepatitis B

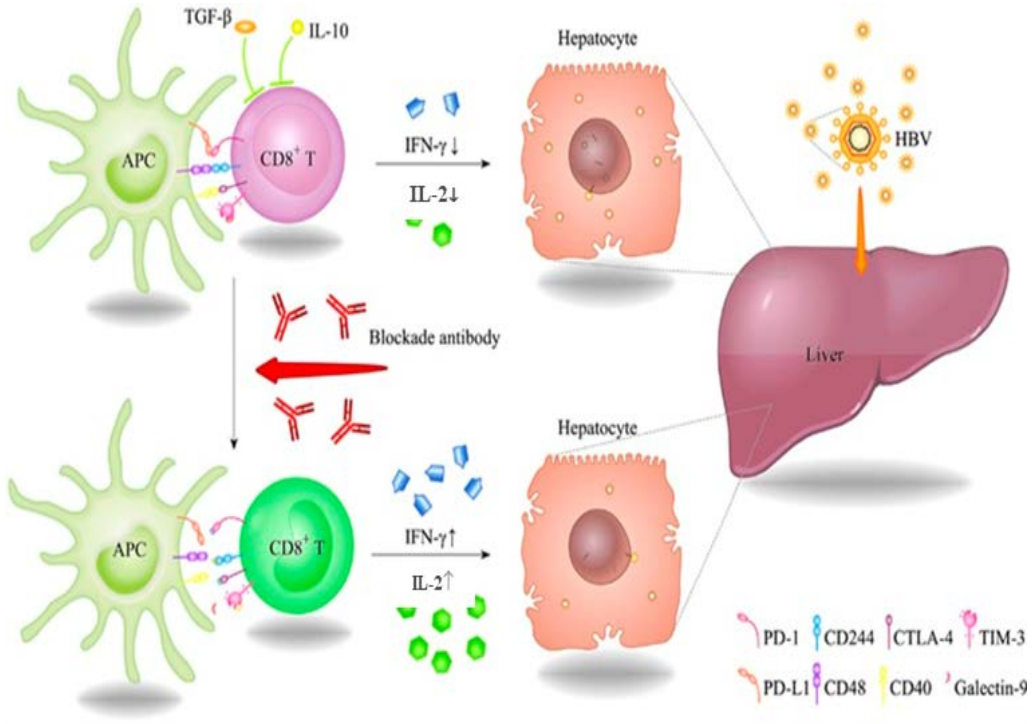
- ASC22 (KN035) can block the PD-1/PD-L1 pathway to restore T Cell immune function and eliminate HBV.

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.

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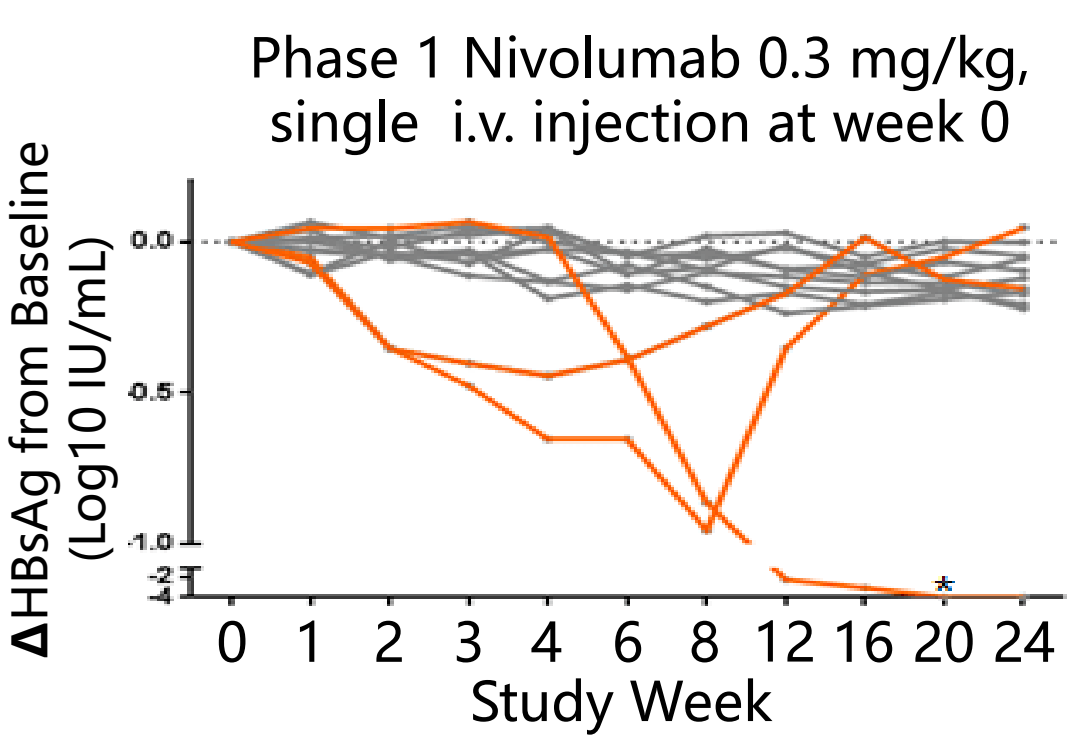
HBV Clinical Cure: PD-1 Antibody - Opdivo (Nivolumab)

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



- 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

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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

1000+ cancer patients exposed in multiple clinical trials in US, China and Japan, Including Two pivotal trials in China

Differentiated Profile

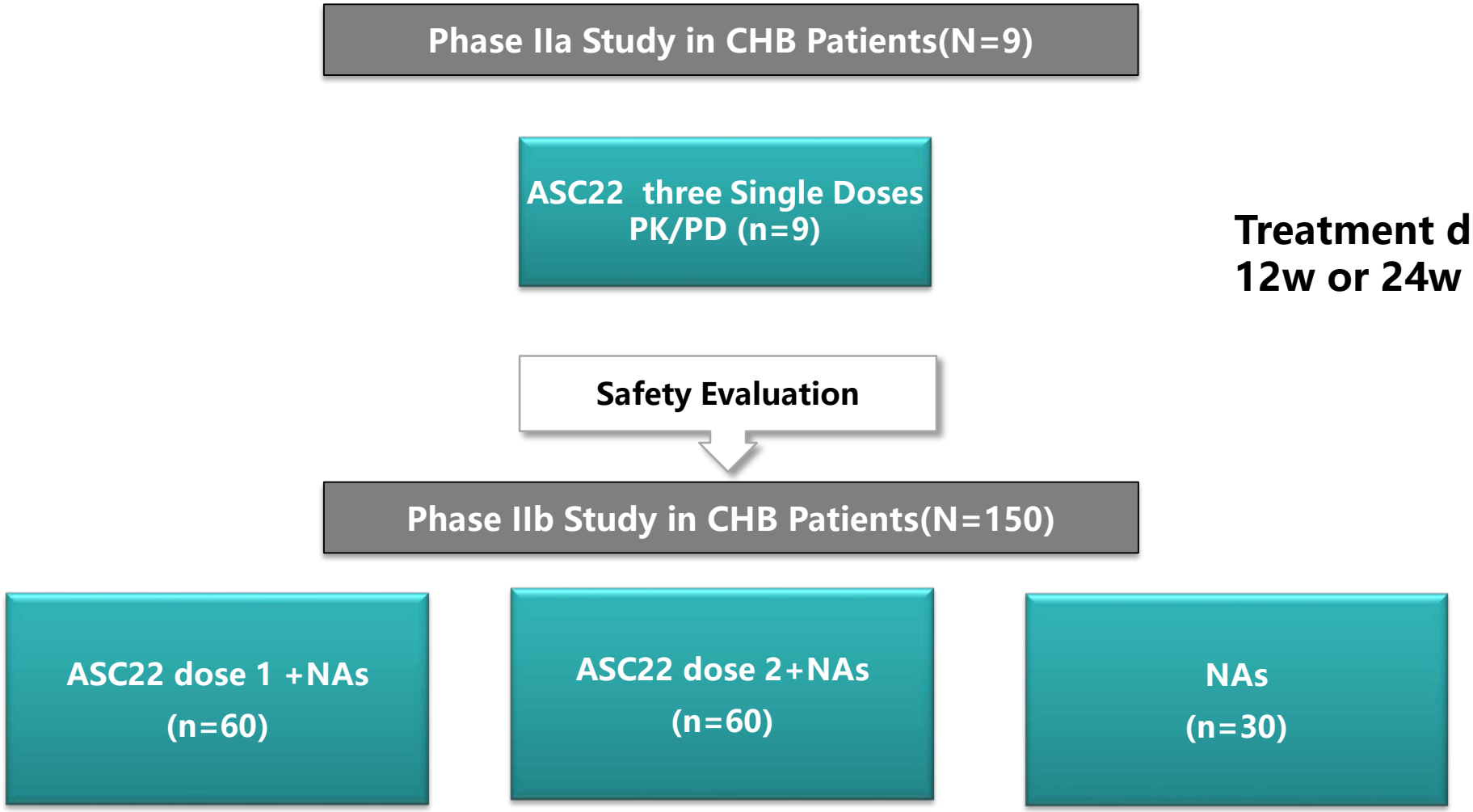
- Subcutaneous route of administration
- Good stability at room temperature

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/1 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. ASC22 has been investigated in several studies conducted in China, USA, and Japan involving greater than 1000 subjects in oncology with proven safety.

ASC22 Phase II Chronic HBV Cure Study Design



Treatment duration: 12w or 24w

CHB=chronic HBV infection, PK=Pharmacokinetic, PD=Pharmacodynamics

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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)

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NASH

Target	Products/Drug Candidate	Pre-IND	IND Approval	Phase Ⅰ	Phase Ⅱ	Phase Ⅲ	NDA Filed	Marketed	Licensed From/ In-house	Commercial Rights
FASN	ASC40								SAGIMET BIOSCIENCES	Greater China
THR-β	ASC41								In-house	Global
FXR	ASC42								In-house	Global
FASN + FXR	ASC40/ASC42 Combo Therapy								In-house	Global
THR-β + FXR	ASC41/ASC42 Combo Therapy								In-house	Global
FASN + THR-β	ASC40/ASC41 Combo Therapy								In-house	Global

2016

NAFLD：85m
NASH：17.3m

NAFLD：244m
NASH：32.81m

2030

NAFLD：101m
NASH：27m

NAFLD：314m
NASH：48.26m

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

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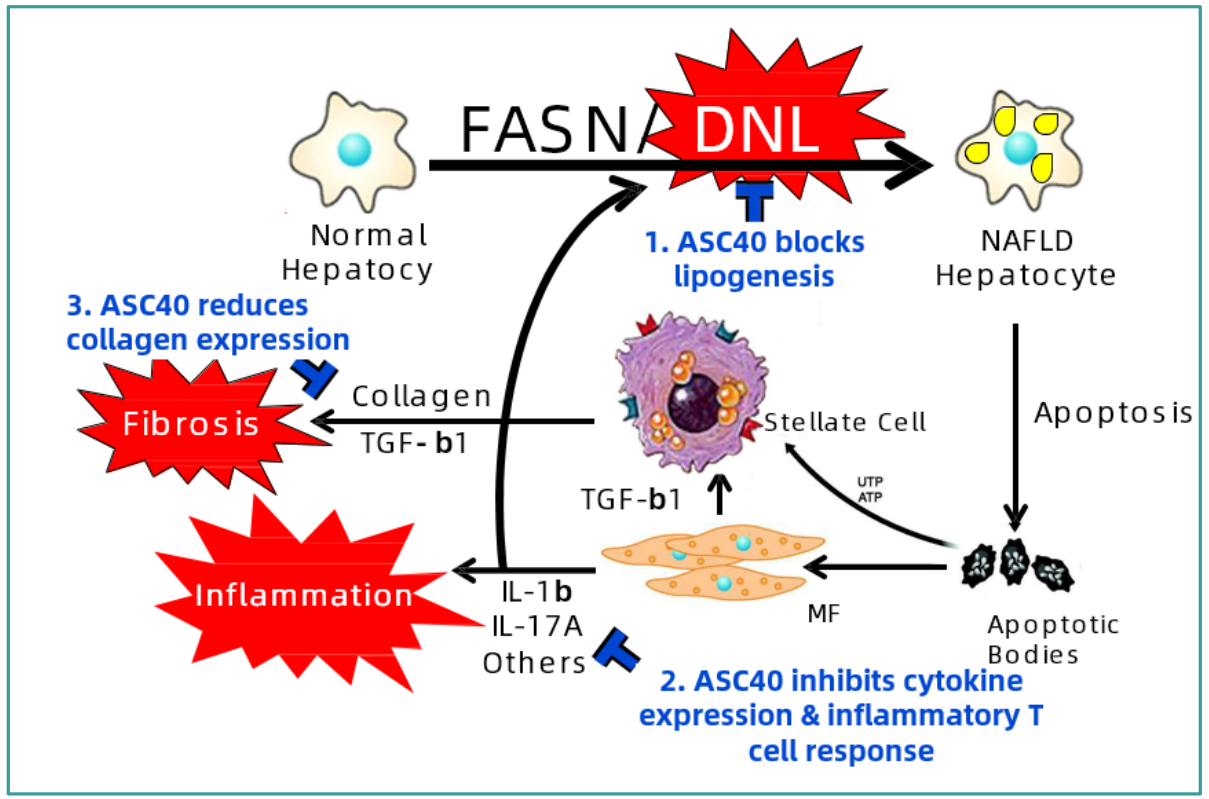
ASC40, a Global First-in-class, Oral FASN Inhibitor for NASH

NASH: multi-billion dollar market potential with no treatments approved



- Inhibition of liver fat synthesis
- Anti-fibrosis
- Anti-inflammatory

Clinical proof-of-mechanism

reduction in fat synthesis and overall liver fat

- Dose-dependent reduction of 24%-73% in liver fat synthesis
- Positive impact on metabolic biomarkers

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

FASN: fatty acid synthase NASH: non-alcoholic steatohepatitis
NAFLD: non-alcoholic fatty liver disease

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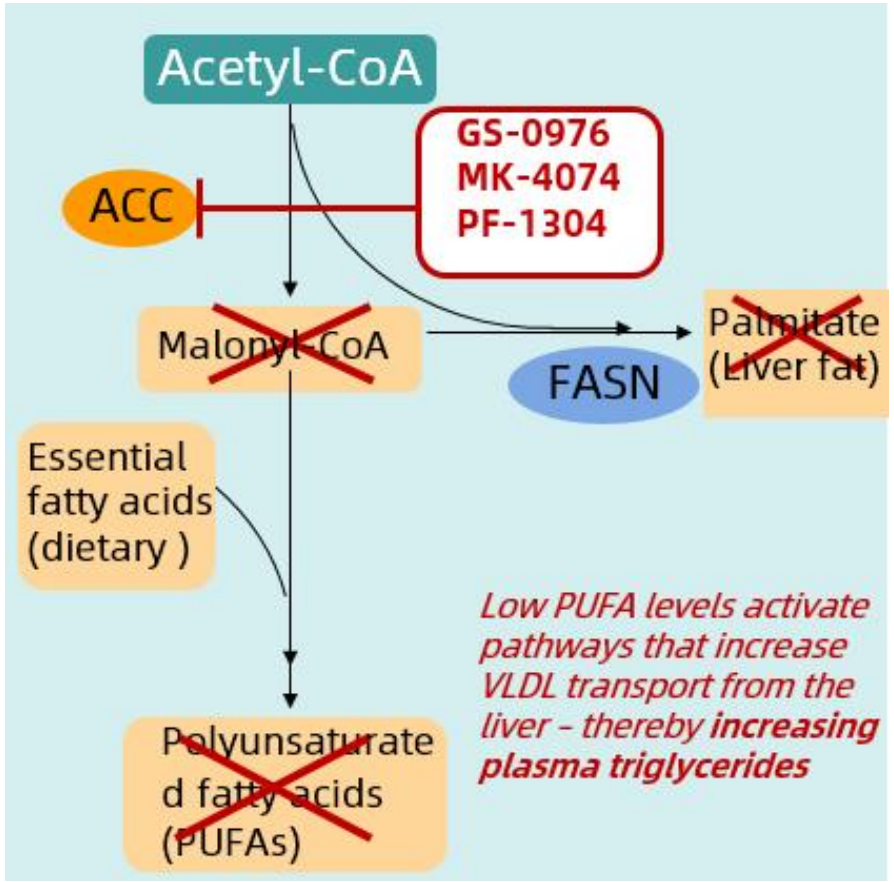
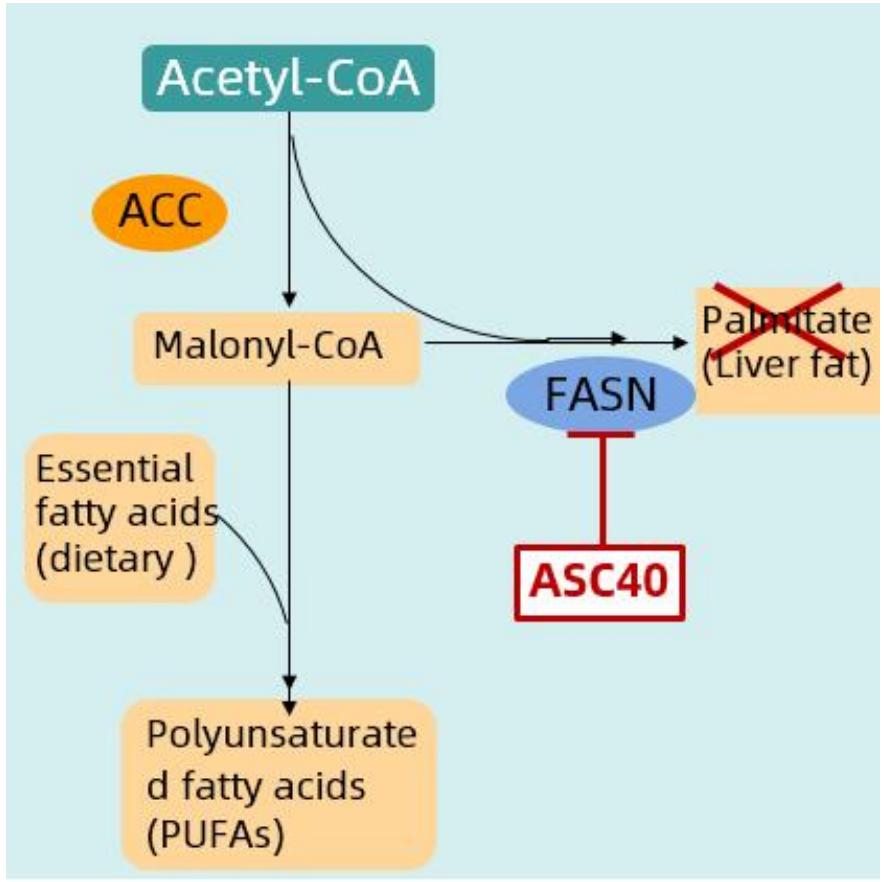
Unlike ACC Inhibition, FASN Inhibition Does not Increase Plasma Triglycerides

ACC Inhibition



FASN Inhibition



ACC inhibition leads to a reduction of malonyl-CoA and PUFAs, **BUT** PUFAs reduction leads to <u>increased plasma TG</u>

FASN inhibition only blocks Palmitate synthesis. Therefore it <u>does not results in increased plasma TGs</u>

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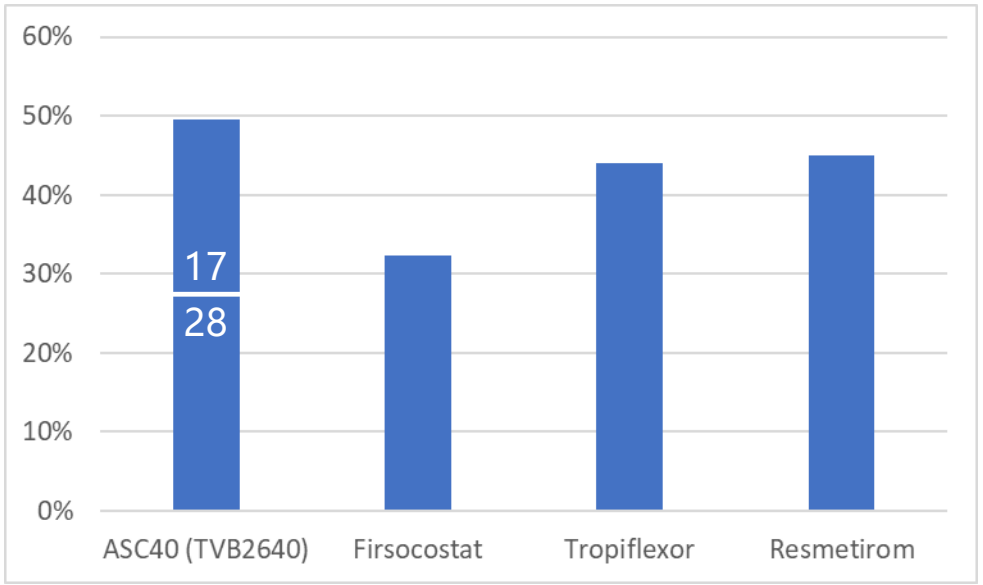
Phase II ASC40 (TVB2640) Compares Favorably With Other Phase II/III NASH Drugs

Drug Candidate	Company	Target	Dose	Weeks	≥ 30% liver fat reduction responder rate, %		Placebo adjusted ≥ 30% liver fat reduction responder rate, %	Safety
					drug	Placebo		
ASC40 (TVB2640)	Sagimet/Ascletis	FASN	50 mg	12	60.7	11.1	49.6	minimal side effects
Firsocostat	Gilead	ACC	20 mg	12	47.8	15.4	32.4	TG↑
Tropiflexor	Novartis	FXR	200 ug	12	64	20	44	LDL-C↑, pruritus
Resmetirom	Madrigal	THRβ	80 mg	36	74.4	29.4	45	diarrhea,nausea

Phase II placebo adjusted ≥ 30% liver fat reduction responder rate



The Phase II (FASCINATE-1) clinical trial enrolled 99 patients in USA, the preliminary data showed that ASC40 (TVB-2640) significantly reduced liver fat, the primary efficacy endpoint of this trial, with a **61%** (17/28) responder rate in the 50 mg group.

Rohit Loomba et al. Gastroenterology. 2018 Nov;155(5):1463-1473.e6; Lucas, KJ et al. 2019. Late-breaking Abstracts at AASLD. Boston, Massachusetts;
Harrison SA et al. Lancet. 2019;394(10213):2012-2024. doi:10.1016/S0140-6736(19)32517-6

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ASC41

- Liver-targeted prodrug (ASC41) and active moiety (ASC41-A) is selective for THR-β
- In two NASH animal models, at 1/10 dose of MGL-3196, ASC41 demonstrated the same improvement in liver steatosis, inflammation and fibrosis
- A highly potent and selective THR-β agonist with anticipated human efficacious dose <10 mg QD
- Proprietary oral tablet formulation stable at room temperature and whose exposure is same as solution formulation in dogs
- Topline data of Phase I safety, PK and preliminary efficacy (LDL-C) in healthy volunteers with LDL-C > 110 mg/dL is expected to be available by the end of 2020
- Combination opportunities with ASC42 (FXR) and ASC40 (FASN)

ASC42

- A novel non-steroidal, selective, potent FXR agonist
- U.S. IND approved in October 2020
- In two NASH animal models, ASC42 demonstrated the significant improvement in liver steatosis, inflammation, and fibrosis
- An oral tablet formulation developed with proprietary therapy, stable at room temperature
- Combination opportunities with ASC41 (THR-β) and ASC40 (FASN)

HIV/AIDS

Expand our portfolio

- Functional cure with immunotherapies
- Treatment
- Prevention

Experienced and Extensive Sales Network

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

√ **135** members and **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

Experienced Team

Network Coverage

- **~1,000** Hospitals located in regions where hepatitis B&C is most prevalent in China
- **~6,000** specialists and key opinion leaders covered in the hepatitis field
- **19** distribution agreements with major distributors, enabling nationwide coverage and timely delivery of Ganovo.

Strategy

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

Ganovo®

19 Days

2018

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

3 months

Ganovo® was enrolled in Basic Medical Insurance of Tianjin after 3 months from Ganovo® approval. To date, Ganovo® has been enrolled in the Basic Medical Insurance of Chengdu and Zhejiang.

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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-by-design approach implemented
- Complied with cGMP

Quality Assurance

- State-of-art equipment with cutting-edge technology capabilities

International Standards

- Experienced manufacturing employees from MNCs

Supply ensured

- Production capacity of 130 million tablets

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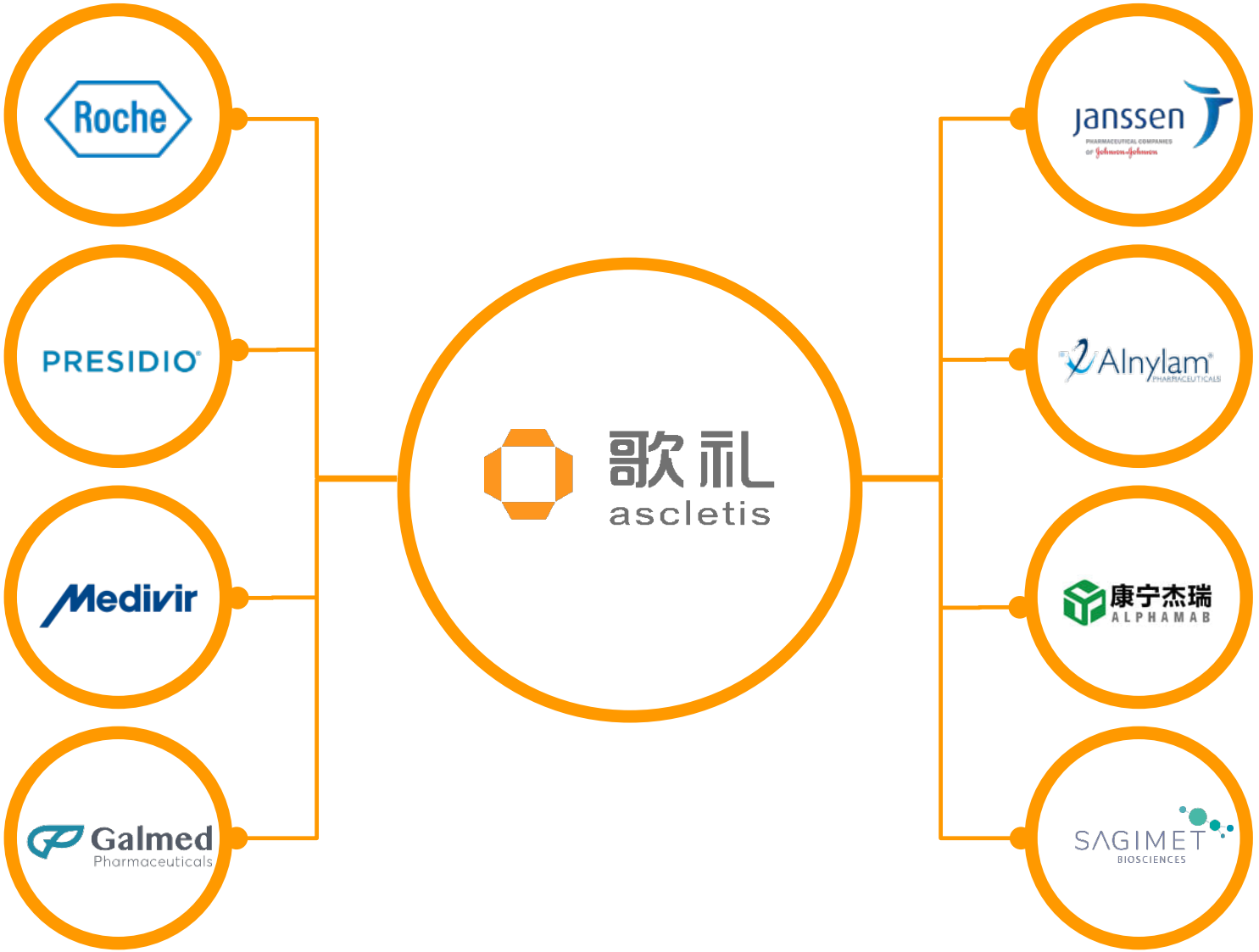
Global Cooperation



Summary

- Over the last two years, Ascletis has developed from a single disease HCV platform into a multi-disease platform
  - Viral hepatitis: 1) commercializing all oral HCV regimen; 2) commercializing Pegasys® for HBV clinical cure; 3) developing breakthrough therapies for HBV clinical cure
  - NASH: global development of novel drug candidates against three different targets – FASN, THR-β and FXR, and three combination therapies.
  - HIV/AIDS: expanding current portfolio for treatment, prevention and functional cure
- Over the next two years, Ascletis will accelerate investments in viral hepatitis, NASH and HIV/ADIS and look for opportunities to expand into new disease areas
  - Current cash reserve of approximately US$420M and upcoming product sales revenue support such aggressive goals

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