Introduction of
JD BIOSCIENCE

JD BIOSCIENCE

July 2023

Summary of JD Bioscience Inc

JD BIOSCIENCE

01. 대사질환

Biopharma company established in **2017** focused on developing small molecules for **metabolic diseases** (NASH, fibrosis, inflammation, and cancer)

02. 의약/화학

Team of **~30** employees, ~20 of those with extensive expertise in **medicinal chemistry**

03. 혁신신약

Developing **first-in-class drug candidates** such as the lead candidate **GM-60106** for NASH, currently in Phase 1

04. 파트너쉽

다수의 external research **collaboration partners** and expanding research capabilities in **ADC**

NASH: Non-Alcoholic Steatohepatitis; PROTAC: Proteolysis targeting chimera; ADC: Antibody Drug Conjugate

JD Bioscience Team

JD BIOSCIENCE

Co-founders

Jin Hee Ahn, Ph.D

CEO & Founder

Doo Seop Kim, Ph.D.

Executive Advisor

Januvia (sitagliptin) 25mg, 50mg, 100mg tablets

Hail Kim M.D., Ph.D.

Target discovery, mechanism of action, and efficacy tests

KAIST

In-Kyu Lee M.D., Ph.D.

Target discovery, mechanism of action, and efficacy tests

KNUH 경북대학교병원

Seongrim Byeon, Ph.D

Chemistry Director

Sungmin Song, Ph.D

BD Director

Peter Goughnour, Ph.D

Director of Innovative Research

SAB

UC San Diego

Rohit Loomba, M.D, MSHc

Professor at UCSD

Berkeley UNIVERSITY OF CALIFORNIA

Marc Hellerstein, M.D., Ph.D.

Professor at UC Berkeley

연세대학교 의과대학 YONSEI UNIVERSITY COLLEGE OF MEDICINE

Joon Yong Park, M.D, Ph.D

Professor at Yonsei University College of Medicine

연세대학교 의과대학 YONSEI UNIVERSITY COLLEGE OF MEDICINE

Jung Il Lee, M.D, Ph.D

Professor at Yonsei University College of Medicine

Company History

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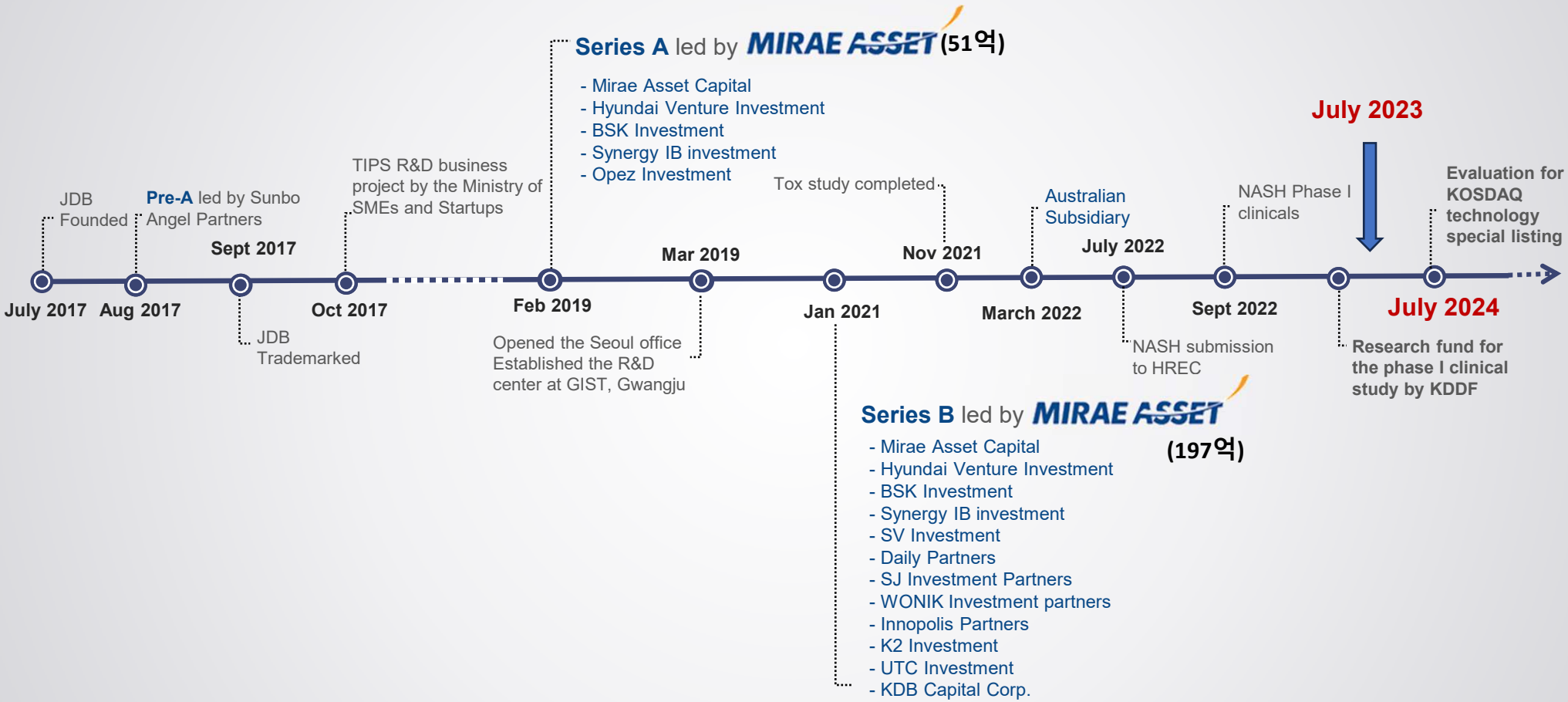
Date of establishment	31 July 2017	Locations	Gwangju, South Korea (headquarters, research institute) Seoul, South Korea (business development, regulatory affair units)



Pipeline Overview

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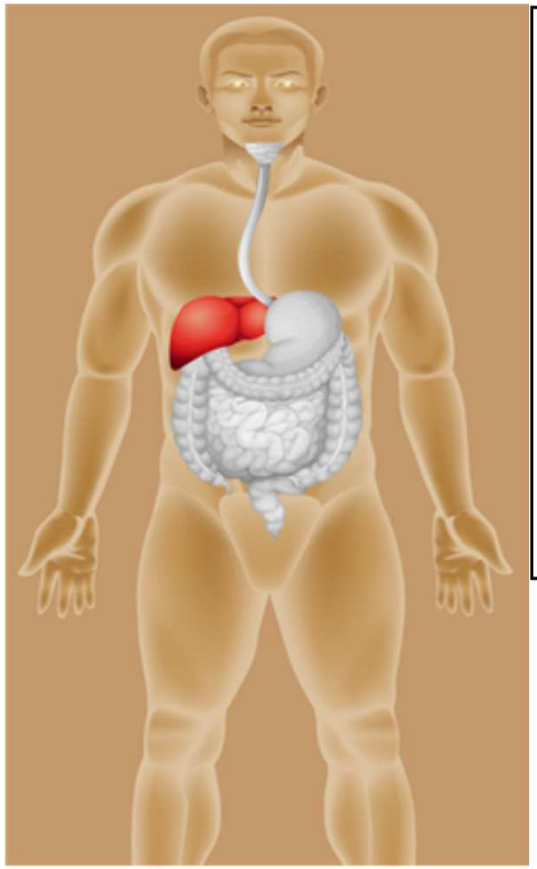
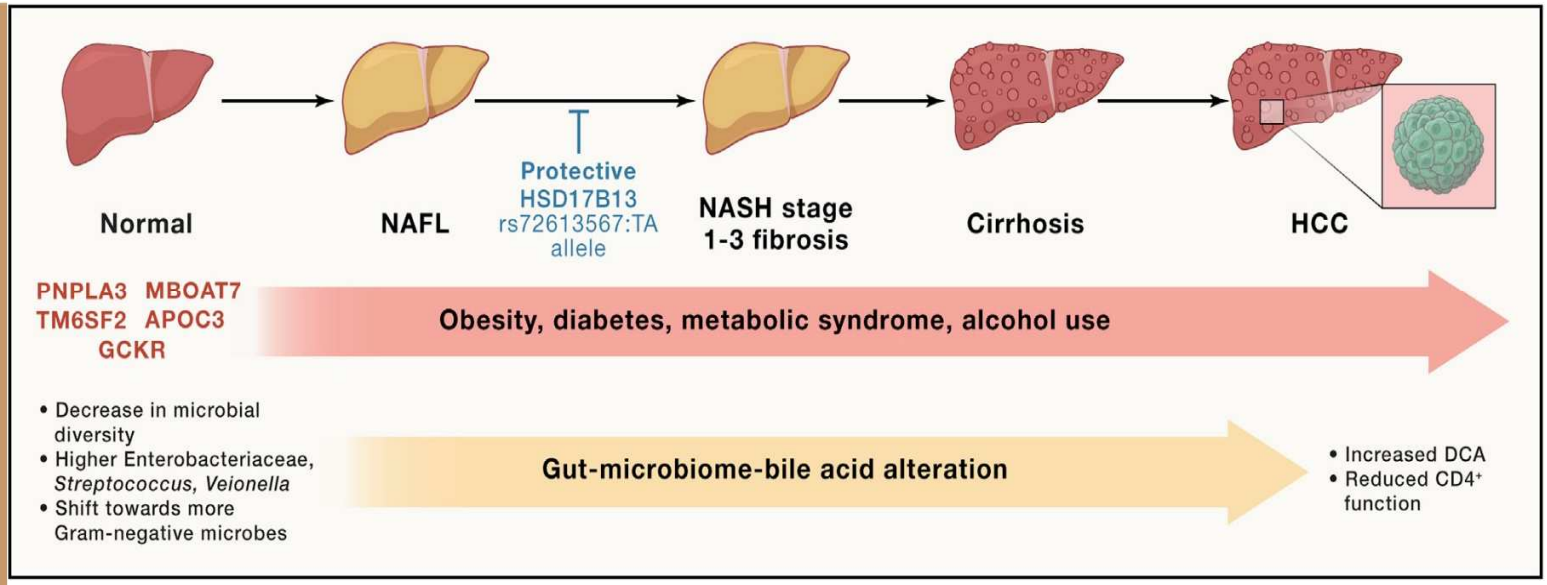
- **GM60106 is the lead candidate for NASH, currently at Phase 1a/b clinical development**

Candidate	Indication	Target	Discovery	Pre-clinical	Phase 1	Phase 2	Plans for BD
GM-60106	NASH/Fibrosis	HTR					L/O Collaborators
GM-60387	Cancer	HTR					L/O Collaborators
GM-10395	Inflammatory Diseases*/Cancer	PDK					L/O Collaborators
GM-10134	Pancreatitis/ Sepsis	PDK					L/O Collaborators
GM-90861	Cancer	Confidential					Searching Collaborators
GM-ADC	Cancer	Confidential					Searching Collaborators
GM-PROTAC	Cancer	Confidential					Searching Collaborators

Lead Candidate Back-up Candidate

◎ NASH(비알콜성지방간염)은 NAFL(지방간)으로부터 유래되어 간섬유화, 간경변, 간암으로 진행됨





Loomba and Shulman, Cell, 2021, 184, 2537

출처:https://www.sriramakrishnahospital.com/blog/liver-transplant/what-are-the-early- signs-and-treatment-of-liver-disease/

Target Patient Population & Unmet Medical Needs

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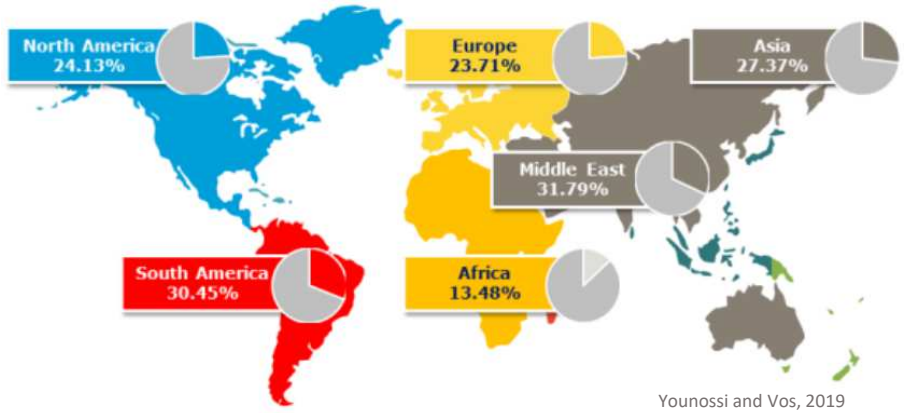
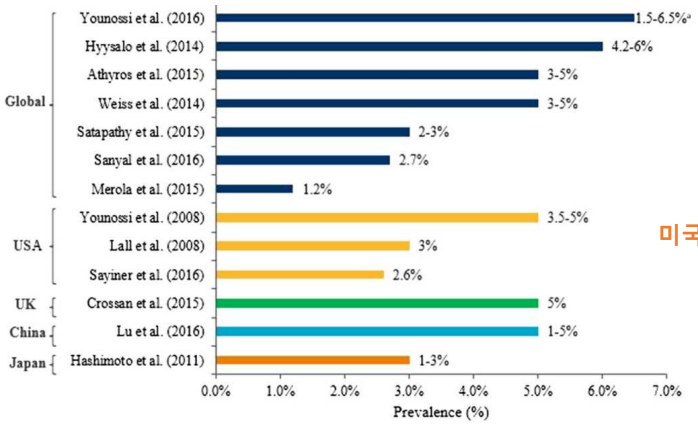
NAFLD 환자 분포도 & NASH 환자 유병율

NASH Prevalence (<5%)



Younossi and Vos, 2019

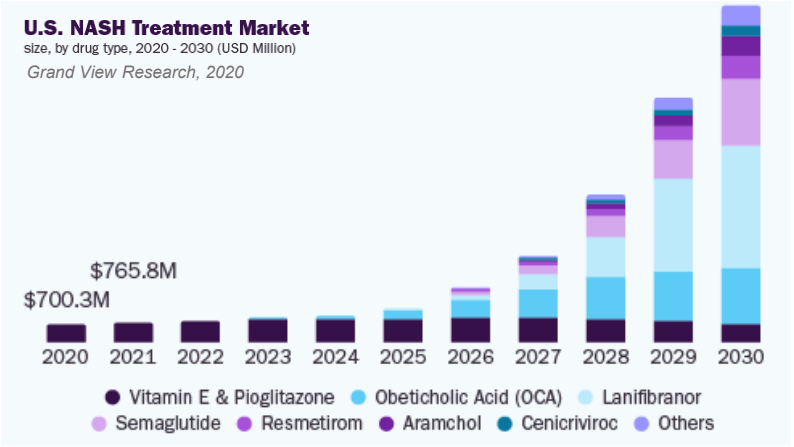
NAFLD Population (25%)



Povsic and Bottomley, 2019

미국 내 NASH 환자 수:
약 3,000만명

잠재시장 규모 & 기술거래 현황



년도	기술이전기업	기술도입기업	유효물질	개발단계	기술료/M&A
2020. 08.	Thera Biosciences	LG Chem	**VAP-1 antagonist**	전임상	**$3.5억**
2020. 08.	Hanmi Pharma	Merck & Co.	GLP-1/GCG dual agonist	임상2상	**$8.7억 (upfront: $10M)**
2020. 11.	Enleofen	B.I.	IL-11 AB	전임상	**$10억**
2020. 12.	Aligos Therapeutcis	Merck & Co.	Oligo nucleotide	임상1상	**$4.58억**
2021.11	Arrowhead Pharmaceutical	GSK	**GalNAc-RNAi**	임상1/2상	**$10.3억 (upfront : $120M)**
2022.09	Dong-A ST	NeuroBo	**GPR119 agonist**	임상1b	**$3.3억 (upfront : $ 2.2K)**
2022.09			**Oxyntomodulin analogue**	전임상	

거대한 환자군을 보유하고 있는 NASH 치료제의 잠재적 시장 규모는 수 십조원으로 추정됨
따라서, 매 년 기술거래 빅딜이 보고되고 있으나 아직 NASH 치료제로 허가 받은 약물은 전무함

Target Selection and Validation

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nature COMMUNICATIONS

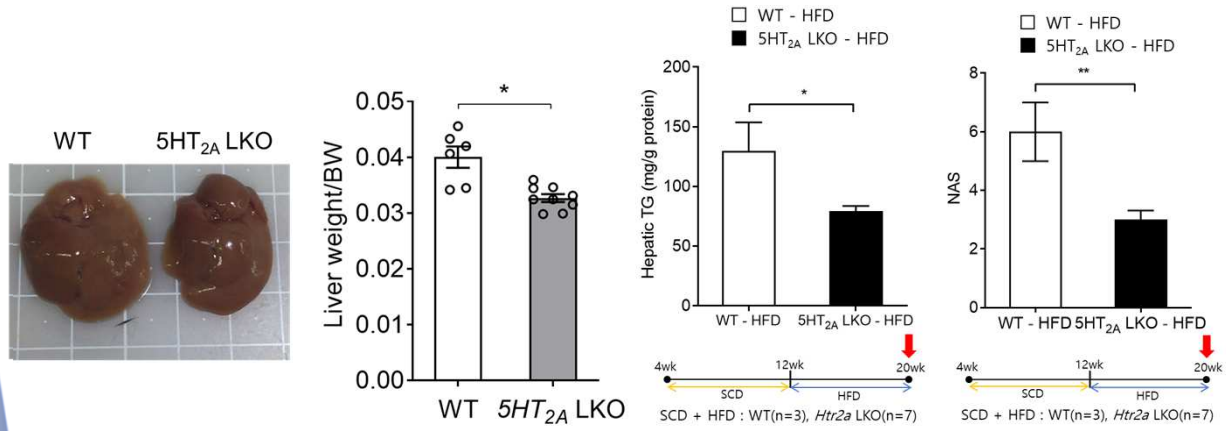
Hail Kim et al.,
Nat. Commun. 2018, 9, 4824

Prof. Hail Kim (MD. Ph.D)
Co-Founder
KAIST

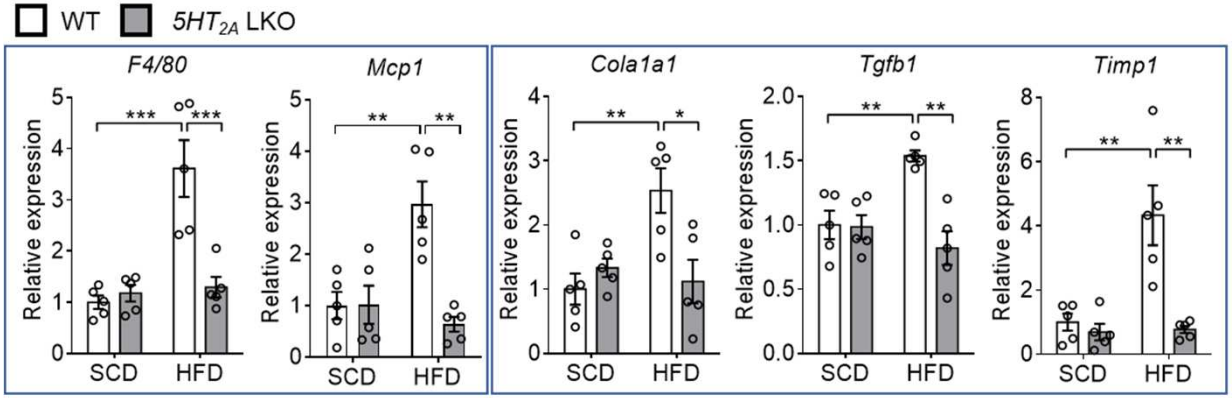
지방간염 환자 또는 동물모델에서 타겟 발현양상

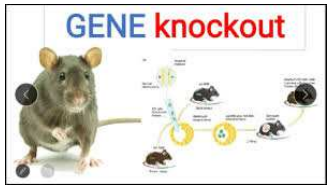
- NASH 환자에서 HTR2A 발현 증가
- 간 성상세포 활성화 시 HTR2A 발현 증가
- 비만유도 쥐에서 HTR2A 발현 증가

HTR2A Liver-specific KO 마우스에서 간 무게, 간지방, NAS 수치



HTR2A Liver-specific KO 마우스에서 염증, 섬유화 관련 마커의 발현 양상





Chemical Profile of GM-60106

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Code	*In vitro* (cellular assay)	Solubility/PPB/ CLogP	Chemical stability	Hepatocyte stability (3 hrs)	Plasma stability
GM-60106	**14 nM**	1.3 mg/mL pH = 6.8/ 97.5 % (m) 96.7 % (r) 97.1 % (h) /3.16	99.8 % (25 °C, 3 weeks) 99.6 % (60 °C, 3 weeks) No form change	94 % (human) 88.5 % (dog) 84.6 % (monkey) 68.9 % (rat) 75.0 % (mouse)	>99.9 % (m) >99.9 %(r) >98.6 ± 11.7 %(h) (% remaining after 4 hrs)
Cytotoxicity (IC_{50})	**AMES**	**Acute Toxicity**	**CYP inhibition (at 10 μM)**	***In vivo* PK (rat)**	**In vivo PK (dog)**
VERO > 100 μM HFL-1 > 100 μM L929 > 100 μM NIH3T3 > 100 μM CHO-K1 > 100μM	Negative	LD_{50} > 1000 mpk	1A2: < 1 % 2C9: 3.17 % 2C19: 6.83 % 2D6: 26.3 % 3A4: 17.6 %	IV (5mpk) Oral (10mpk) T1/2: 4.14 h AUC: 2.88 ug.h/ml CL: 2.82 L/h/kg V: 8.86 L/kg **BA 61 %**	IV (5mpk) Oral (5mpk) T1/2: 8.6h AUC: 19.11 ug.h/ml CL: 0.42 L/h/kg V: 4.36 L/kg **BA 73 %**
***In vivo* efficacy in normal with high fat**	***In vivo* efficacy in DIO mice**	**NASH in MCD diet in db/db mice**	**STAM mice**	**Dog telemetry**	**BBB permeability**
Body weight gain reduction, Reduced fat accumulation 5, 10 mpk	Body weight gain reduction, Reduced fat accumulation in liver 5,10 mpk	Reduced inflammation, fibrosis and fat accumulation in liver 5 mpk	Reduced inflammation and fibrosis in liver 5, 10 mpk	Cardiovascular Radiotelemetry Assessment in Conscious Dogs 50,100, 200 mpk (No change)	BQL (below lower limit) in Brain based on tissue distribution of [14C]-GM-60106

Safety and MOA of GM-601060

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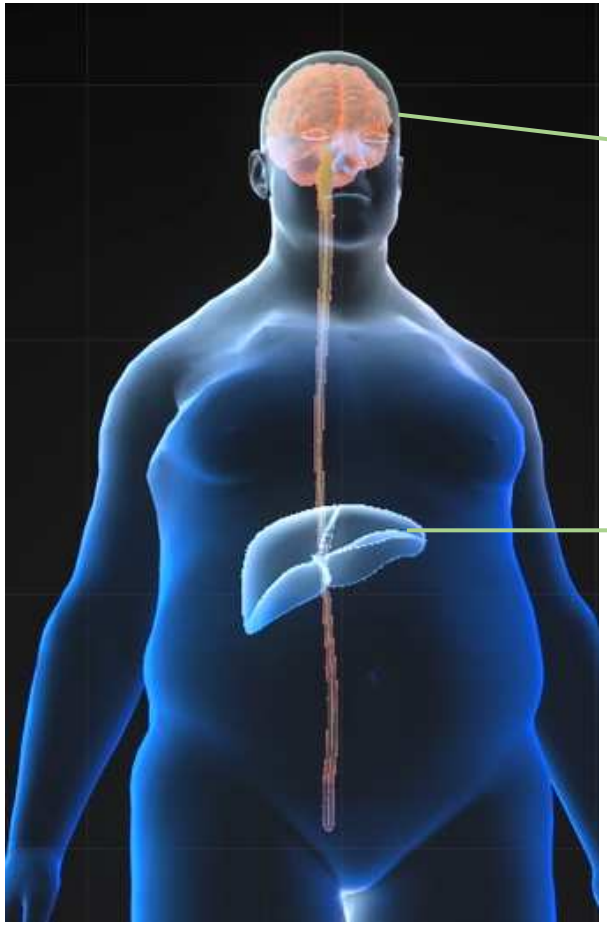
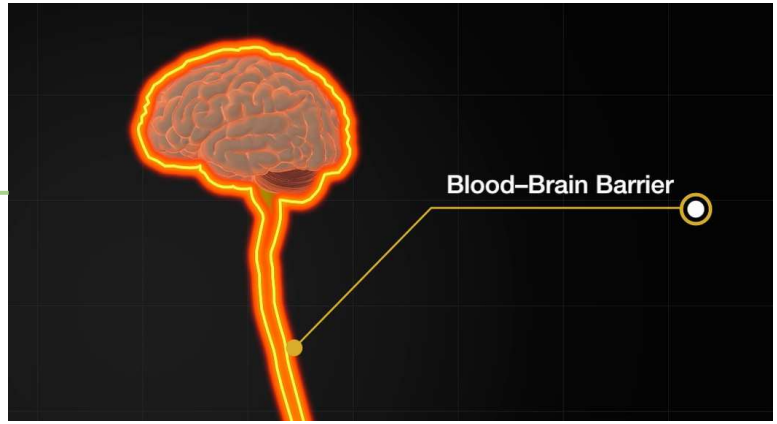
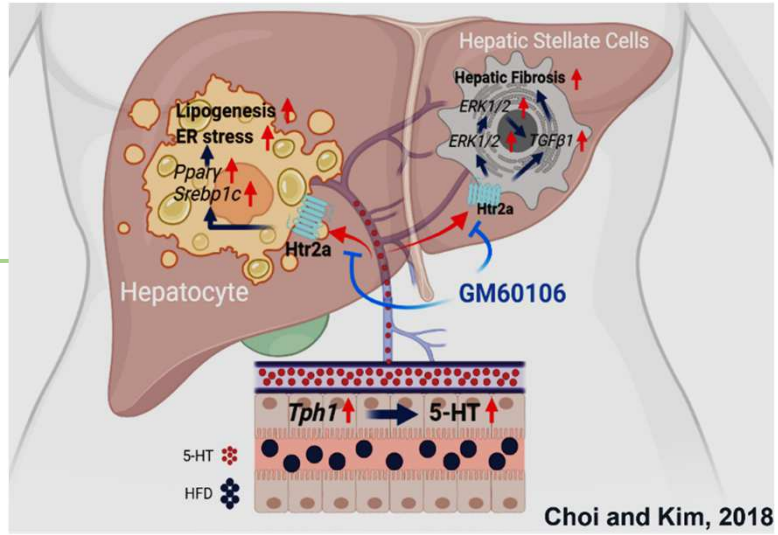


Safety Aspect of GM-60106



Efficacy Aspect of GM-60106



Safety: GM-60106 화합물은 혈뇌장벽(Blood-Brain Barrier, BBB)을 투과하지 않아 CNS 부작용이 최소화된 안전한 약물임

MOA: 간세포에서 지방생성(Lipogenesis)을 억제하는 동시에 간 성상세포에서는 섬유화를 억제하는 이중 작용기전을 가짐

Phase I Clinical Trial for Safety and Tolerability (임상 1상, 호주)

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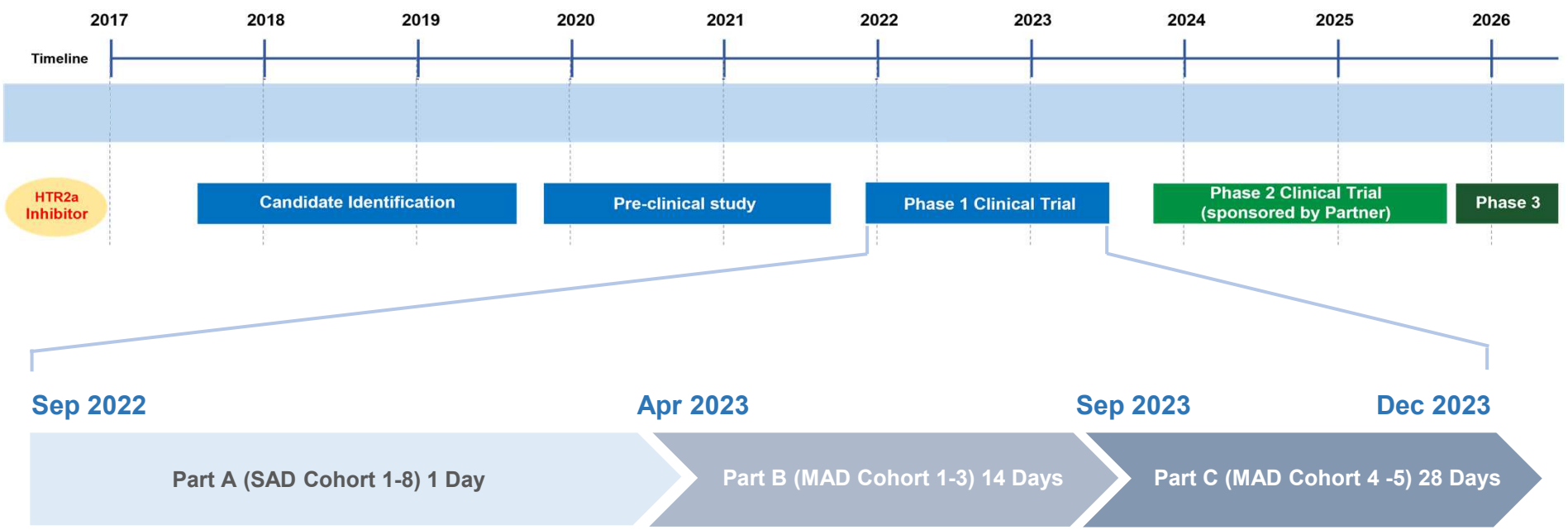

SAD: Single Administration Dosing, MAD; Multiple Administration Dosing

Clinicaltrials.gov 등록 (2022.08.26.)

NCT05517564

ENROLLING BY INVITATION

First-in-Human Study of GM-60106 in Healthy Adults and Otherwise Healthy Adults With an Increased Body Mass Index and Markers of Non-Alcoholic Fatty Liver Disease

CONDITIONS

Non-alcoholic Steatohepatitis

임상 CRO 및 협력기관 (Vendors)

CRO, Clinical Site , CMO, and Chemical Lab

NOVOTECH The Asia Pacific CRO

Nucleus Network

STA 合全药业

药明康德 WuXi AppTec

360biolabs a BioAgilytix company

Phase I Clinical Trial for Safety and Tolerability

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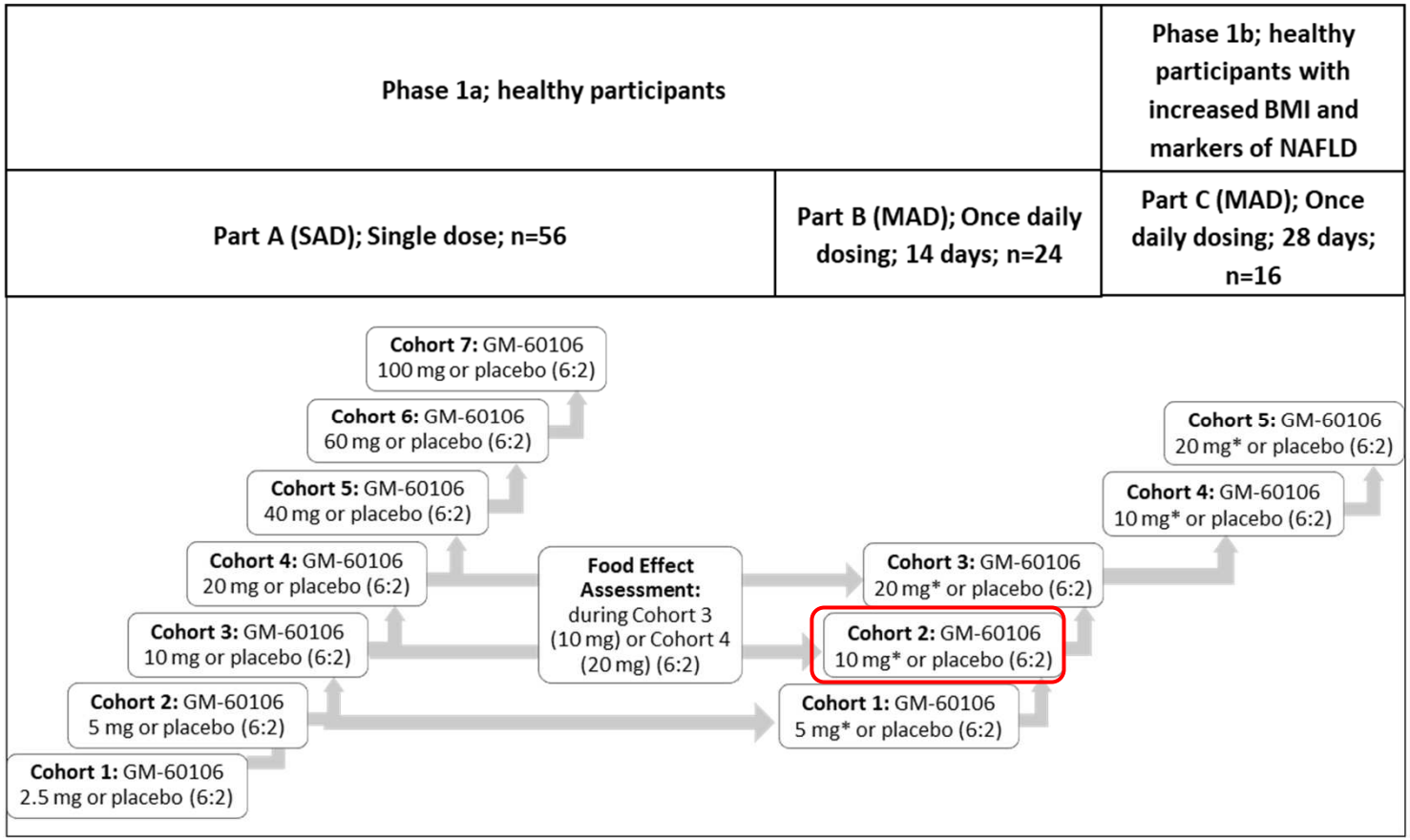
Schematic Plan for Phase I study (코드명: JDB-106001)

Rohit Loomba, M.D, MSHc

Professor at UCSD

UC San Diego



Part A, B는 정상인을 대상으로 안전성, 내약성, 물성(PK)를 테스트 중이며, Part C는 NASH 보유자를 대상으로 효능을 검증할 계획임

2023년 7월 기준, MAD Cohort 2 (40 mg)까지 단 회 투여를 마쳤으며, **현재까지 약물과 연관된 SAE (심각한 부작용)은 없음**

** SAE: Serious Adverse Event, 중대한 부작용*

KDDF 국가신약개발사업단 Korea Drug Development Fund

2023년도 국가신약개발사업 선정
임상개발비용 총 35억원 지원

GM-60106 Indication Expansion

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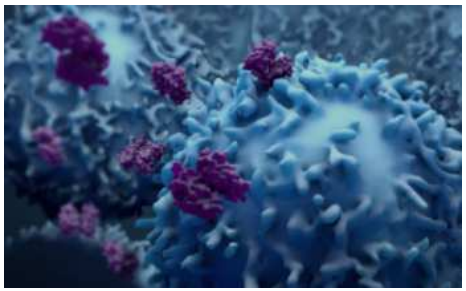
- 조직 섬유화로 인해 유발되는 타 질환(폐섬유증, 신장섬유증 등)으로 적응증 확장

GM-60106

IPF (Idiopathic pulmonary fibrosis)

CKD (Chronic Kidney Disease)



Inflammation/Cancer

Pipeline Overview

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- **GM-10395 is a candidate for Inflammatory Bowel Disease, currently at preclinical stage**

Candidate	Indication	Target	Discovery	Pre-clinical	Phase 1	Phase 2	Plans for BD
GM-60106	NASH/Fibrosis	HTR					L/O Collaborators
GM-60387	Cancer	HTR					L/O Collaborators
GM-10395	Inflammatory Diseases*/Cancer	PDK					L/O Collaborators
GM-10134	Pancreatitis/ Sepsis	PDK					L/O Collaborators
GM-90861	Cancer	Confidential					Searching Collaborators
GM-ADC	Cancer	Confidential					Searching Collaborators
GM-PROTAC	Cancer	Confidential					Searching Collaborators

Lead Candidate Back-up Candidate

Main MOA of GM-10395

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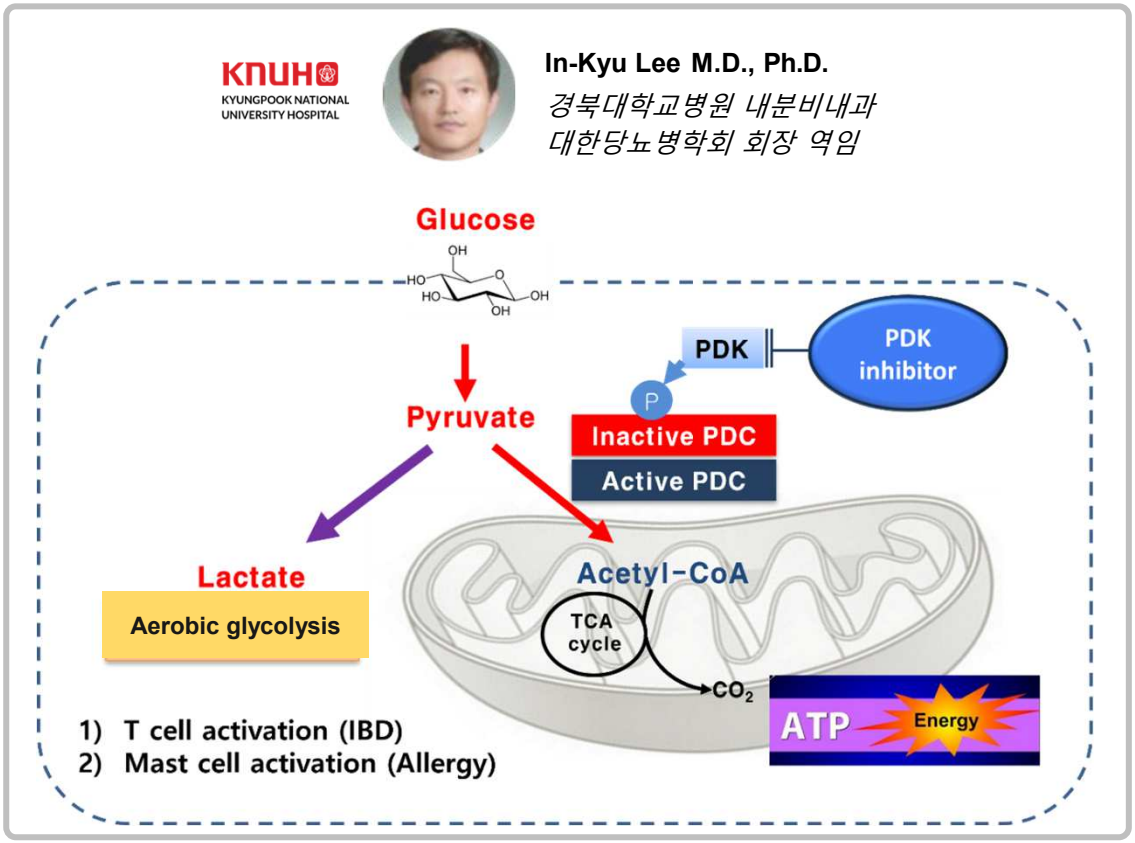
Novel drug candidates for IBD and chronic kidney disease



염증성 질환 환자의 미토콘드리아 내 Pyruvate dehydrogenase kinase (PDK)양이 증가됨을 확인

→ 이 경우 Aerobic glycolysis가 비정상적으로 증가됨으로써 미토콘드리아 기능이 약화됨

Target Selection and Validation

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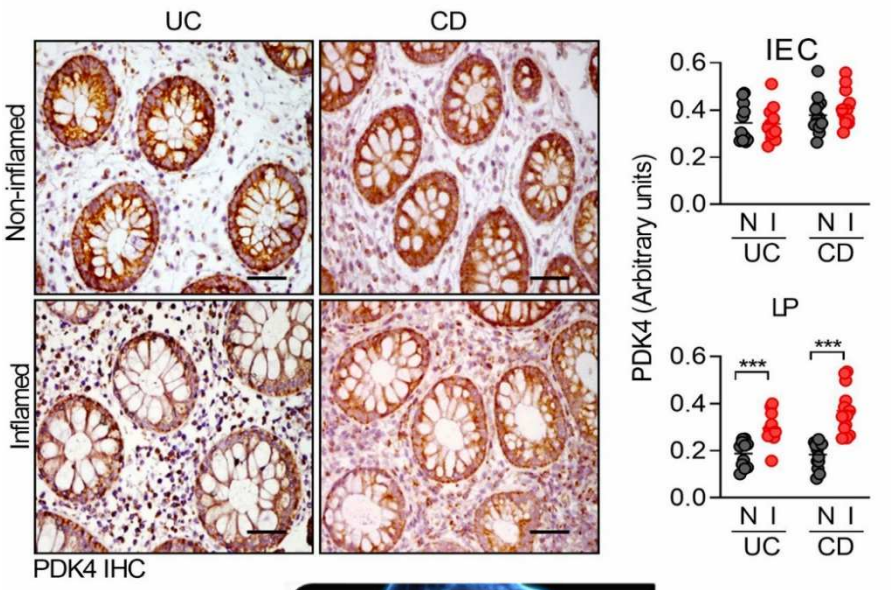
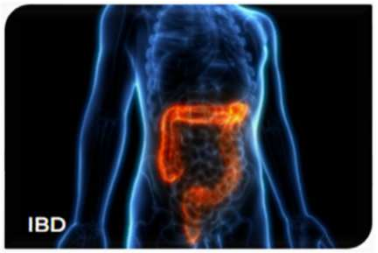
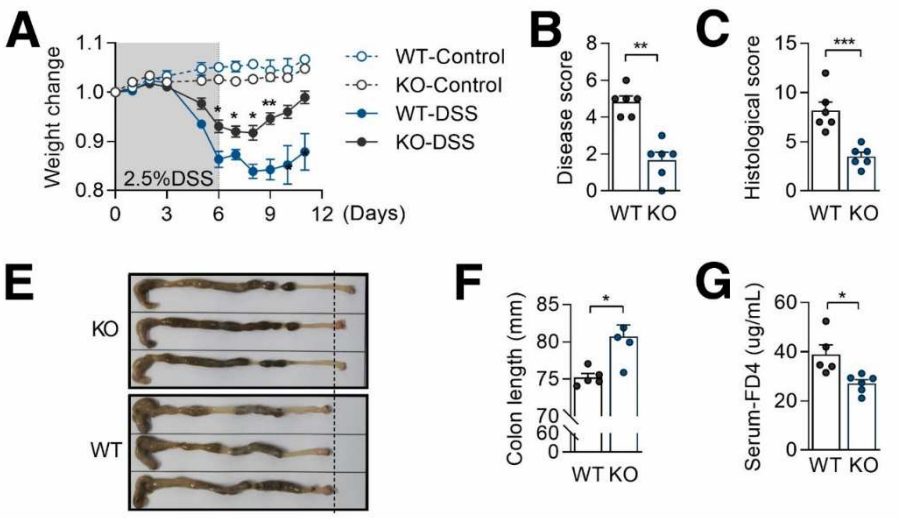
- 염증성 장질환(IBD) 환자샘플 분석과 동물시험을 통해 최적의 타겟(PDK4)을 확정

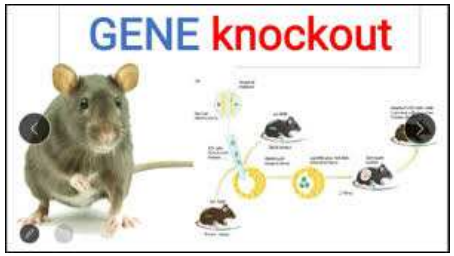
PDK4 발현양상 확인 (IBD 환자)





PDK4 K/O 마우스에서 IBD 질환마커 감소 확인





염증성 장질환 환자와 동물모델(DSS-induced colitis model)에서 PDK4 발현이 증가됨을 확인

PDK4가 결핍된 동물모델에 IBD를 유발해본 결과 조직학 점수, 대장 길이, 장 투과도가 모두 현저히 개선됨

Chemical Profile of GM-10395

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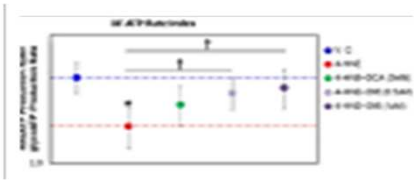
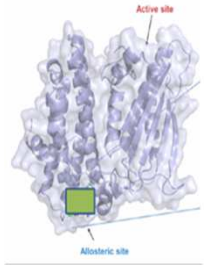
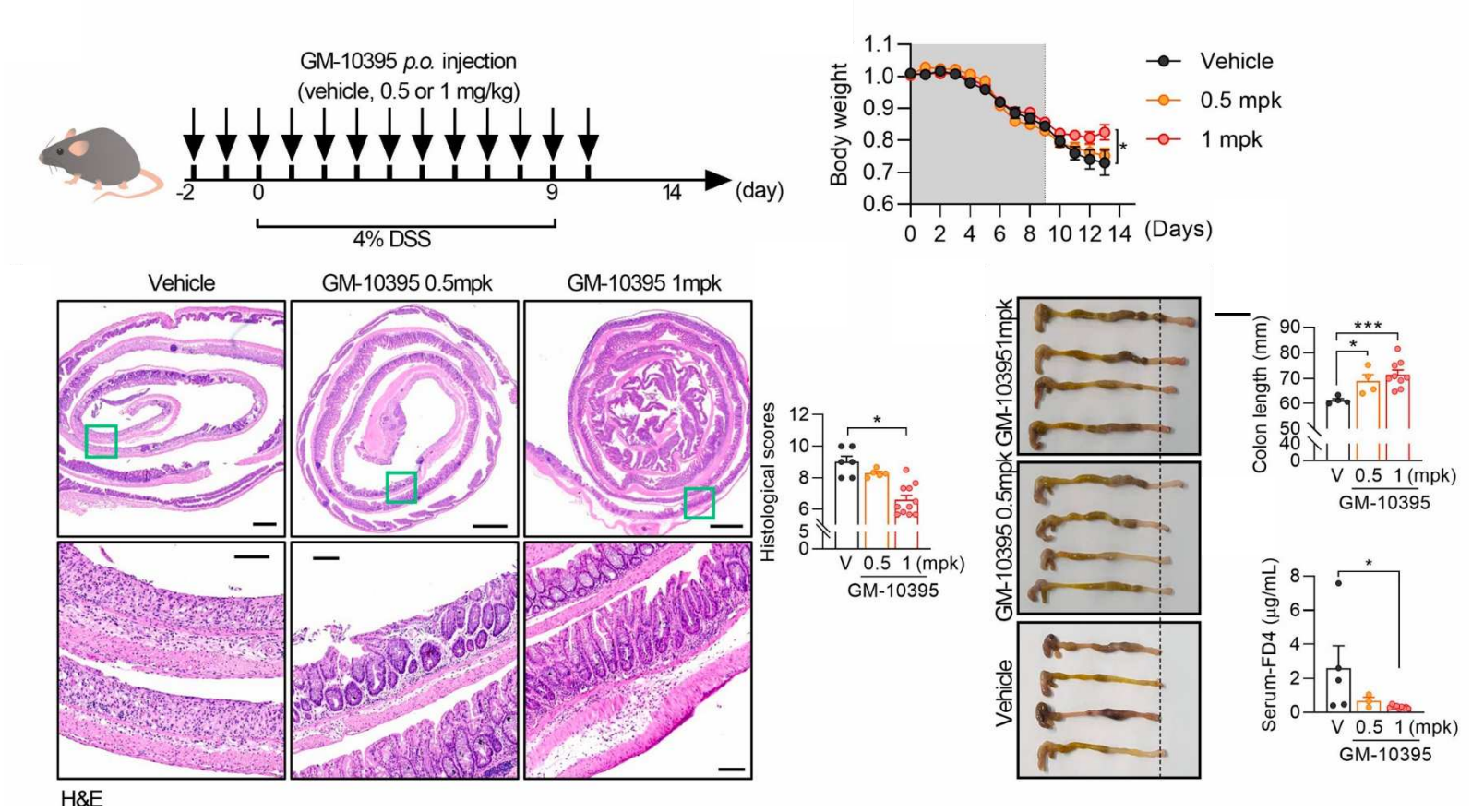
Code	Inhibitor Class	In vitro (cellular Assay)	Recovery of mitochondria function		
GM-10395	Allosteric inhibitor	IC_{50} 44 nM Inhibition of PDHE1α Phosphorylation 159nM(IC_{50})	 GM10395 recovered Mitochondria function with Dose dependent manner		
CYP inhibition (IC_{50} μM)	**HERG inhibition**	**PPB**	**Plasma stability (4hr incubation)**	**AMES test**	**Acute toxicity**
IA2: 33.69 2C9: 12.64 2C19: 12.18 2D6: 7.94 3A4: 7.72	32.8% at 10μM	99.3%(m) 99.5%(m)	Human 89%	Negative	LD50> 1000mpk
In vivo PK	**In vivo IBD study**	**In vivo Anti-cancer efficacy**	**In vivo efficacy (anti-diabetes)**	**Co-crystal Structure (진행중)**	
IV(5mpk) Ora (10mpk) T1/2: 5.15h AUC:1.76 μg/ml(IV) BA: 48%	Improved histological Score colon length In vivo at 1mpk	Reduced tumor Volume In xenograft mice At 1 mpk dose	Glucose AUC reduction (OGTT) Oral administration		

◎ 동물시험을 통해 GM-10395의 염증성장질환 개선 효능을 확인



IBD 동물모델에 2주간 GM-10395 투여 시 조직학 점수, 대장 길이, 장 투과도, 염증 마커가 모두 현저히 개선됨

→ GM-10395는 First-in-class 염증성장질환 치료제 후보물질임을 증명완료

GM-10395 Indication Expansion

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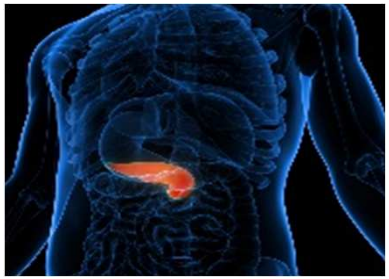
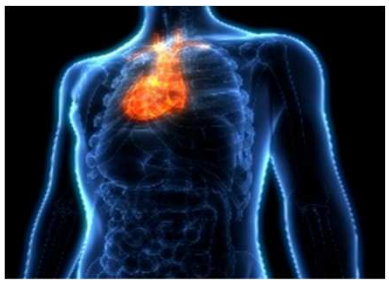
- 염증으로 인해 유발되는 타 질환(급성 췌장염, 심장근육병증 등)으로 적응증 확장

GM-10395

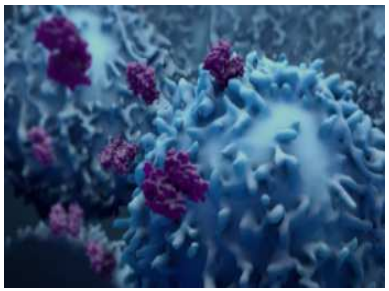


Acute Pancreatitis



Heart Disease

CKD (Chronic Kidney Disease)



Inflammation/Cancer

Pipeline Overview

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GM-ADC is a New Innovative Drug Modality that JDB is Actively Developing

Candidate	Indication	Target	Discovery	Pre-clinical	Phase 1	Phase 2	Plans for BD
GM-60106	NASH/Fibrosis	HTR					L/O Collaborators
GM-60387	Cancer	HTR					L/O Collaborators
GM-10395	Inflammatory Diseases*/Cancer	PDK					L/O Collaborators
GM-10134	Pancreatitis/ Sepsis	PDK					L/O Collaborators
GM-90861	Cancer	Confidential					Searching Collaborators
JD-X	Dravet Syndrome	SCN1A					
GM-ADC	Cancer	Confidential					Searching Collaborators
GM-PROTAC	Cancer	Confidential					Searching Collaborators

Lead Candidate Back-up Candidate

ADC for collaboration (Payload)

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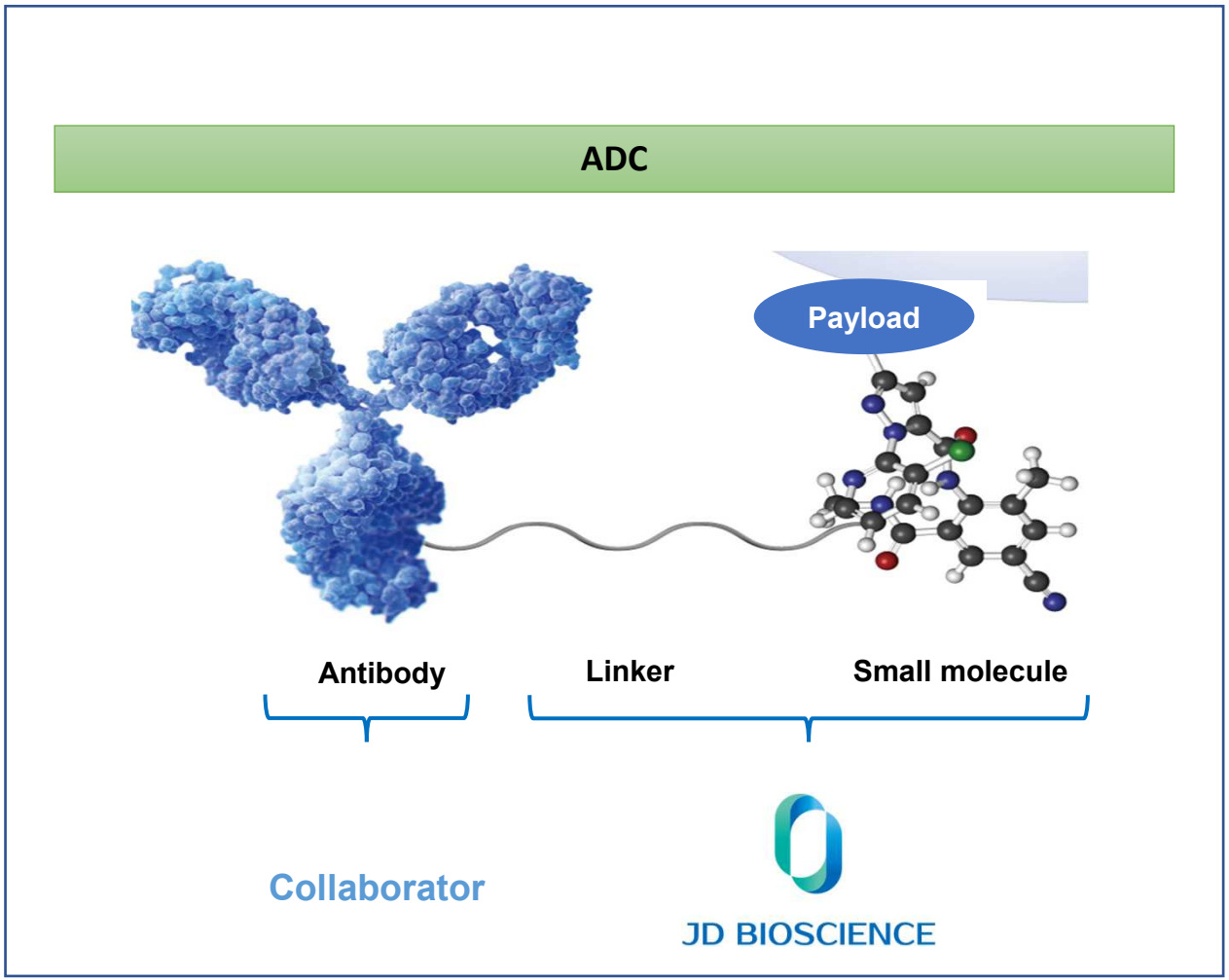
- 항체치료제 전문기업과 함께 협업을 통해 최적의 ADC 치료제 개발이 목표임



ADC-based New Drug Development

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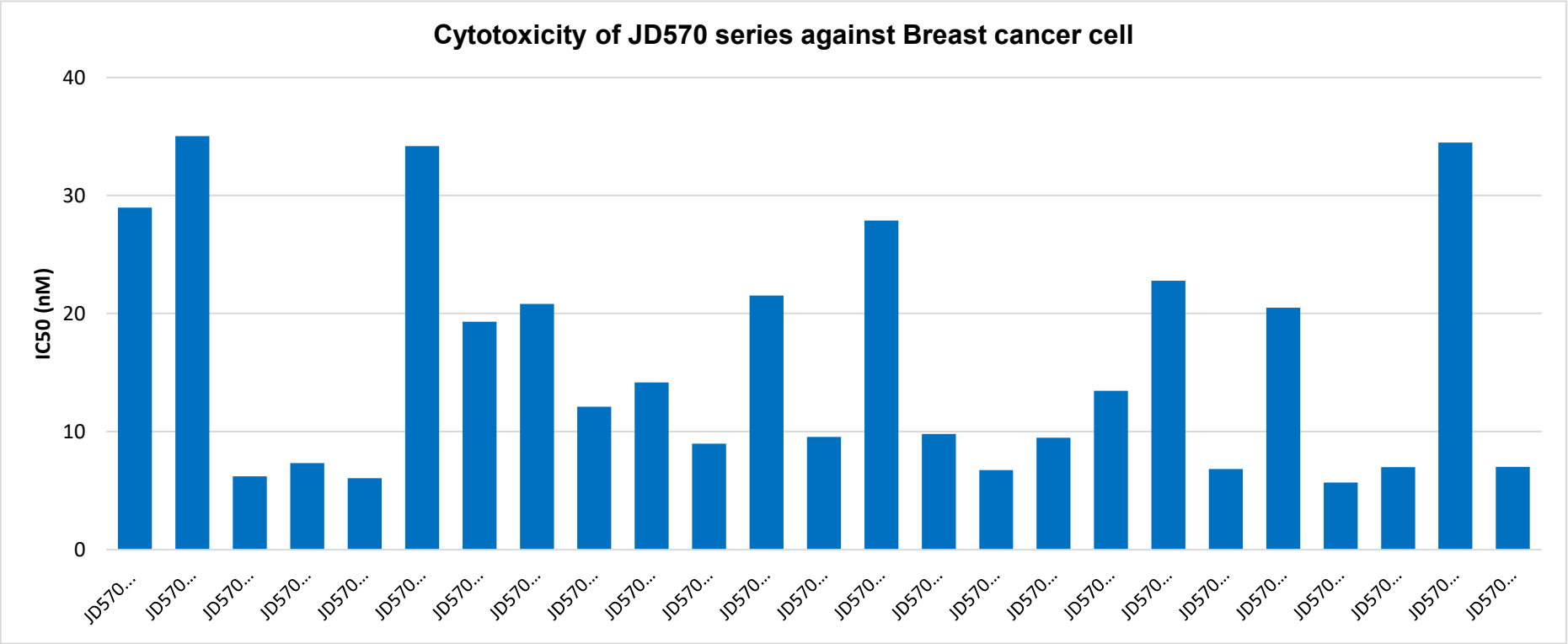
- 최적의 항암 살상력을 보이는 신규 Payload를 기반으로 기존약물 보다 향상된 ADC 약물을 개발 중임



Cytotoxicity 결과를 토대로 최적의 Payload 선정 → ADC 제작 → 우수한 효능 및 물성확인

Partnerships for collaborative research

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- 폐사의 의약화학 노하우가 접목된 신약후보물질을 함께 개발할 수 있는 파트너社를 지속적으로 탐색 중

Medicinal Chemistry
(Design, Synthesis, SAR, Optimization)

Industry Partners

LysoTech

CELLTRION

AVENTI BIOTECHNOLOGY

KBlueBio

INNOVO THERAPEUTICS

HUENCHEM Human Endocrinology Chemistry

GENOME OPINION

REDNVIA Real-world Evidence in Drug Development

COWELL BIODIGM

Future Plans

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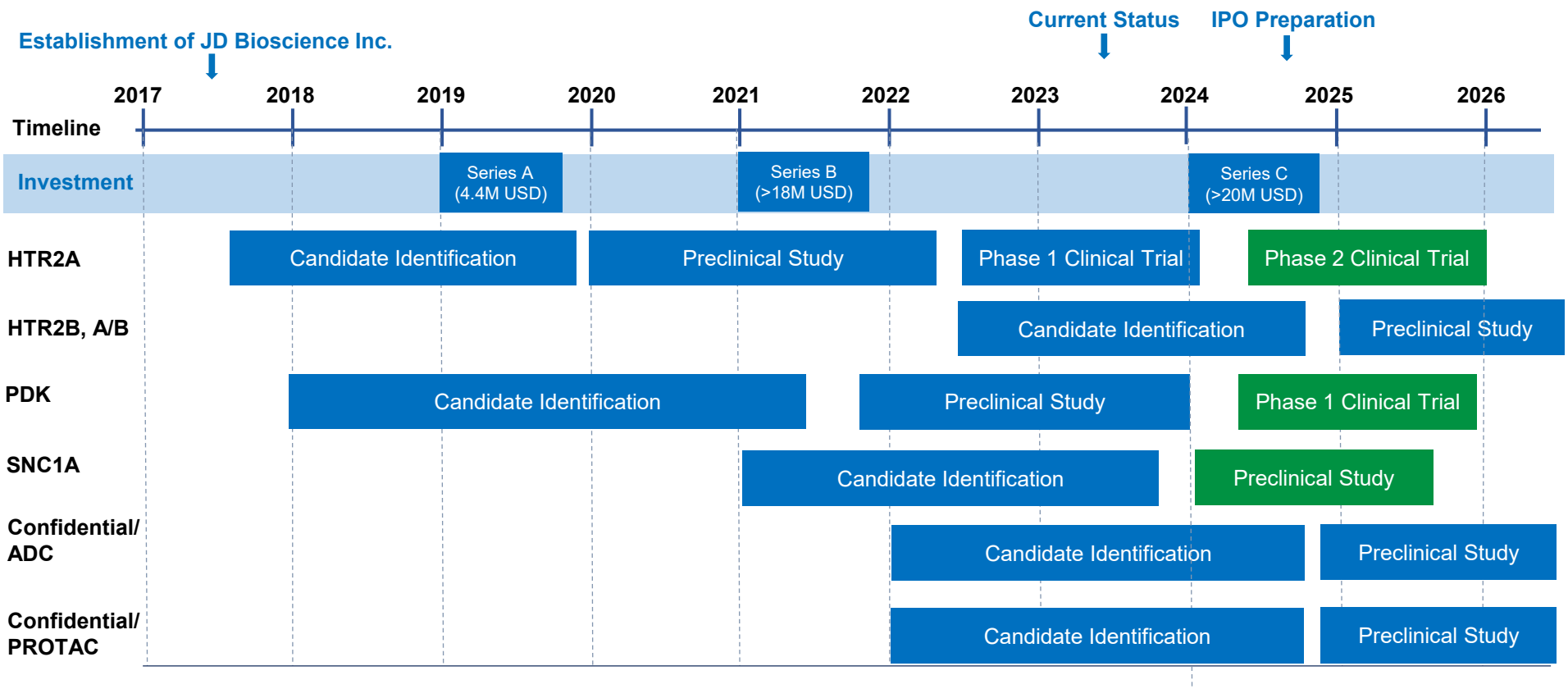

JD Bioscience

Sponsor/Collaboration

"To discover novel therapeutics for metabolic disease with unmet medical needs that help people live longer and healthier"

감사합니다

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