Introduction of
JD BIOSCIENCE

JD BIOSCIENCE

November 2021

Disclaimer

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JD BIOSCIENCE

1. Overview

- Overview
- Members and organization
- Vision, mission and goals
- History
- Business model

1. Overview

JD BIOSCIENCE

Name	**JD Bioscience Inc.**	**Pipelines**	• Modality: small molecule-based novel drug candidates • Indications: metabolic diseases (NASH, IBD, heart disease etc.)
CEO	**Ahn, Jin Hee**	**Business model**	• Commercialization of first-in-class drug candidates • Collaborative research with pharmaceutical companies
Date of establishment	**31 July 2017**	**Number of employees**	24 members (> 20 researchers)
Web page	**www.jdbiosci.com**	**Locations**	• Gwangju, South Korea (headquarters, research institute) • Seoul, South Korea (business development, regulatory affair units)

Medicinal chemistry

Ahn, Jin Hee Ph.D.

Chief executive officer

Medicinal chemistry

Kim, Doo Seop Ph.D.

Executive advisor

Medicinal chemistry

Target discovery

Kim, Hail M.D., Ph.D.

Target discovery, mechanism of action, and efficacy tests

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

Target discovery, mechanism of action, and efficacy tests

Stability testing of API

Myung Ae Bae Ph.D.

Pharmacokinetics and druggability

Scientific Advisory Board

1. Overview

JD BIOSCIENCE

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

Ahn, Jin hee

- **2017~present Founder & CEO, JD Bioscience**
- 2016~present Professor, GIST
- 2000~2016 Principal researcher, KRICT
- 1998~2000 Postdoc, Chemistry, UC Berkeley
- 1993~1997 Ph.D., Chemistry Sogang Univ.

Kim, Doo seop

- **2019~present Chief Director, JD Bioscience**
- 2009~2018 Vice president & CTO, Kainos Medicine
- 1990~2009 Chief investigator, Merck & Co.
- 1988~1990 Postdoc, Bioorganic Chemistry, Columbia Univ.
- 1984~1988 Ph.D., Organic Chemistry, Univ. of Pittsburg

Bae, Myung Ae

Kim, Hail

PDK

HTR

TPH ★ L/O

Lee, In-kyu

Lee, Don Haeng

GPCR ★ L/O

2014 2016

TAZ modulator

2013 2016

DGAT-1

2010 2013

Hwang, Eun-Sook

Kim, Doo Seop

11β-HSD1 ★ L/O

2007 2010

DPP-IV ★ L/O

2004 2008

PPARγ

2001 2005

PTP-1B

2000 2004

2000 Present

1. Overview

JD BIOSCIENCE

Key members

Song, Sungmin

- **2021~present BD director, JD Bioscience**
- 2015~2021 Technology licensing manager, GIST
- 2013~2014 Researcher, KRIBB
- 2008~2013 Ph.D./post-doc, Biology, Freiburg University

Lee, Hee jong

- **2019~ present Senior researcher, JD Bioscience**
- 2017~2019 Researcher, Bioqure IMS
- 2013~2017 Researcher, Chodang Pharm. Co.
- 2000~2012 Researcher, SJ Biomed
- 2002~2011 Ph.D., Biochemistry, Hanyang Univ.

Pagire, Haushabhau

- **2019~ present Senior researcher, JD Bioscience**
- 2016~2019 Postdoc, GIST
- 2011~2016 Ph.D., Medicinal chemistry , UST
- 2006~2011 Researcher, APDC

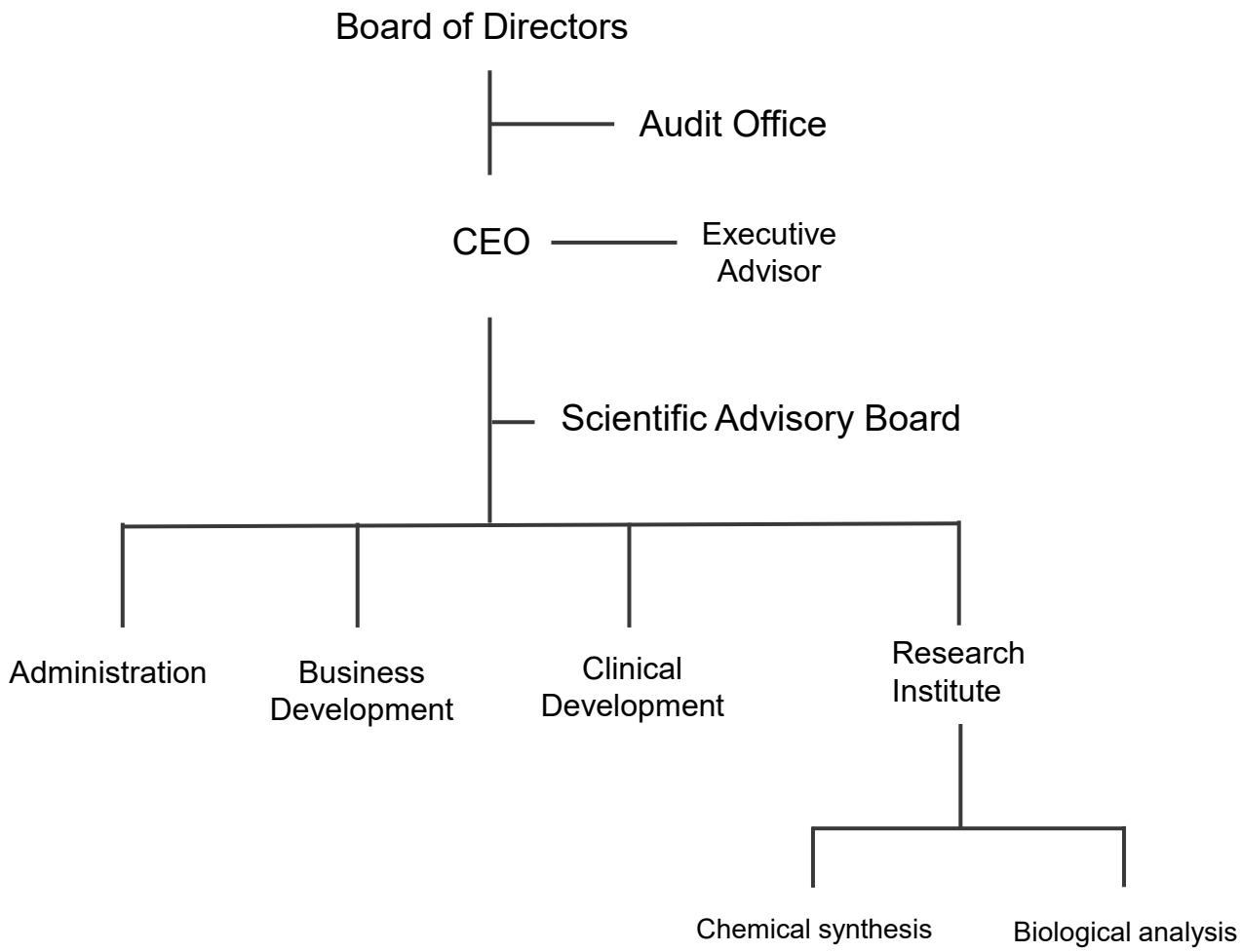
Lee, Eun young

- **2019~ present Senior researcher, JD Bioscience**
- 2013~2019 Postdoc, GIST
- 2003~2009 Ph.D., Biochemistry, SUNY SB
- 2000~2003 Researcher, Biochemistry, Yonsei Univ.

Han, Mi jung

- **2017~Present Senior manager, JD Bioscience**
- 2015~2019 M.S. Completion, Chungnam National Univ.
- 2009~2011 Researcher, LG Life Sciences Ltd.,
- 2001~2009 Researcher, KRICT KCB

Organization Chart



1. Overview

JD BIOSCIENCE

Vision

To be the world's top pharmaceutical company in the field of metabolic disease

Our Mission

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

Our Goal

Since 2020
Expanding drug pipeline and making global licensing deals

- Surveying unmet medical needs
- Searching for novel biomarkers that meet unmet medical needs
- Initiating first-in-class drug development using novel biomarkers
- Making technology licensing deal

Since 2019
Initiating collaborative research with bio ventures

- Providing medicinal chemistry services to partners
- Accumulating knowhow and experience for novel drug development
- Creating a stable sales revenue

Since 2017
Developing drug candidates for Metabolic diseases

- NAFLD/NASH
- Inflammatory bowel disease
- Heart disease and other diseases

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■ Company History

2019

10
- Entered the pre-clinical trial for the main pipeline (a novel drug candidates for NASH)

07
- Signed collaborative research contracts with 3 bio ventures

ENHANCEDBIO INC / SoVarGen Somatic Variations Genomics / RaND Bioscience

03
- Opened the Seoul office
- Established the R&D center at GIST, Gwangju

02
- Raised $4.4 million in Series A funding from investors
  - Mirae Asset Capital
  - Hyundai Venture Investment
  - BSK Investment
  - Synergy IB investment
  - Opez Investment

2017

10
- Selected for the TIPS R&D business project by the Ministry of SMEs and Startups (Oct. 2017 ~ Sep. 2019)

08
- Raised a seed capital through Sunbo Angel Partners

07
- **Established JD BIOSCIENCE Inc.**

2021

04-08
- Signed collaborative research contracts with 3 ventures

주식회사 휴엔켐 / cellus / COWELL BIODIGM

01-03
- Raised $18 million in Series B funding from investors
  - Mirae Asset Capital
  - Hyundai Venture Investment
  - BSK Investment
  - Synergy IB investment
  - SV Investment
  - Daily Partners
  - SJ Investment Partners
  - WONIK Investment partners
  - Innopolis Partners
  - K2 Investment
  - UTC Investment

01-03
- Signed collaborative research contracts with 2 pharma companies

KBlueBio / CELLTRION

2020

06
- Selected for a biomedical technology development business project by the ministry of Science and ICT ('20.06~'24.12)
- Selected for a Post-TIPS R&D business project by the Ministry of SMEs and Startups ('20.06~'22.05)

05
- Selected for the development of the energy safety technology program by the Ministry of Trade, Industry and Energy ('20.05~'23.12)

04
- Signed a collaborative research contract with Innovo Therapeutics

INNOVO THERAPEUTICS

01
- Selected for a Development of hospitals into the innovation hubs of the research ecosystem by the Ministry of Health and Welfare('20.01~'22.12)
- Signed collaborative research contract with 3 ventures

가천의대길병원 Gachon University Gil Hospital / 연세대학교 의과대학 YONSEI UNIVERSITY COLLEGE OF MEDICINE / AVENTI BIOTECHNOLOGY / (주)라이조테크

1. Overview

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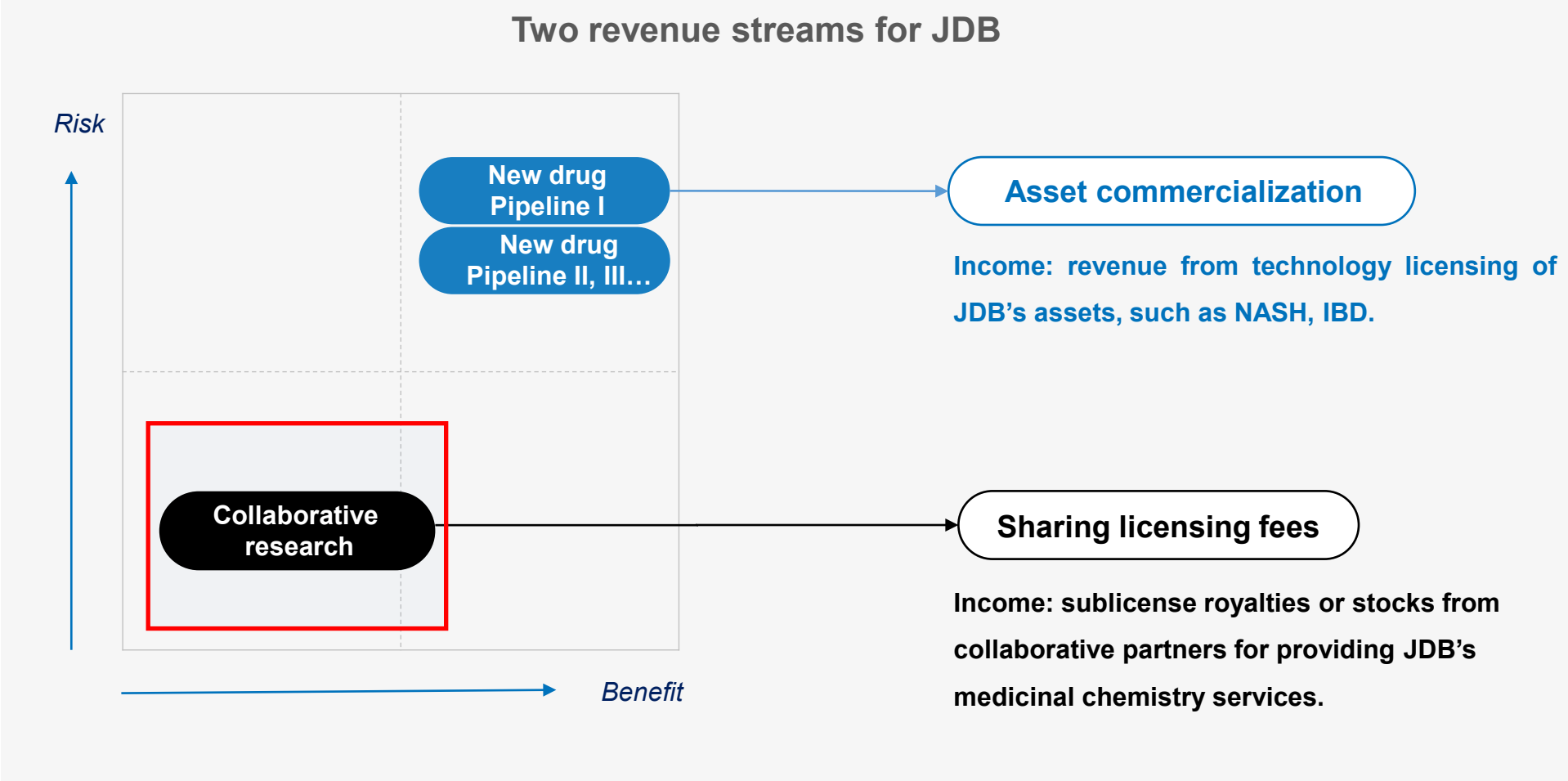
Business Strategies

- **Development of first-in-class drug candidates for metabolic diseases.**
- **Collaborative drug development with partners (JDB providing medicinal chemistry services).**



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2. Drug Pipelines

2-1 NASH

2-2 IBD

2-3 Heart disease

2-4 Acute pancreatitis

2. Drug pipeline

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Pipeline	Code	Indication	Target	Discovery	Pre-clinic	Phase 1	Phase 2	Plans for BD
1	**GM60106**	NASH	HTR	→	→			**L/O for USA or China at P1 clinical stage**
	GM60186	NASH	HTR	→				**Backup of GM60106**
2	**GM-X3**	Inflammation / Cancer	PDK	→				**L/O for USA or China at preclinical stage**
	GM-X2	Pancreatitis/ Heart disease	PDK	→				
3	**GM-X4**	NASH / TNBC	confidential	→				**L/O for USA or China at P2 clinical stage**
4	-	Sepsis/ Septic shock	confidential				→	**Commercialize in USA and Korea market**
5	-	NASH	confidential				→	**Commercialize in Korea market**

2-1. Non-alcoholic steatohepatitis (NASH)

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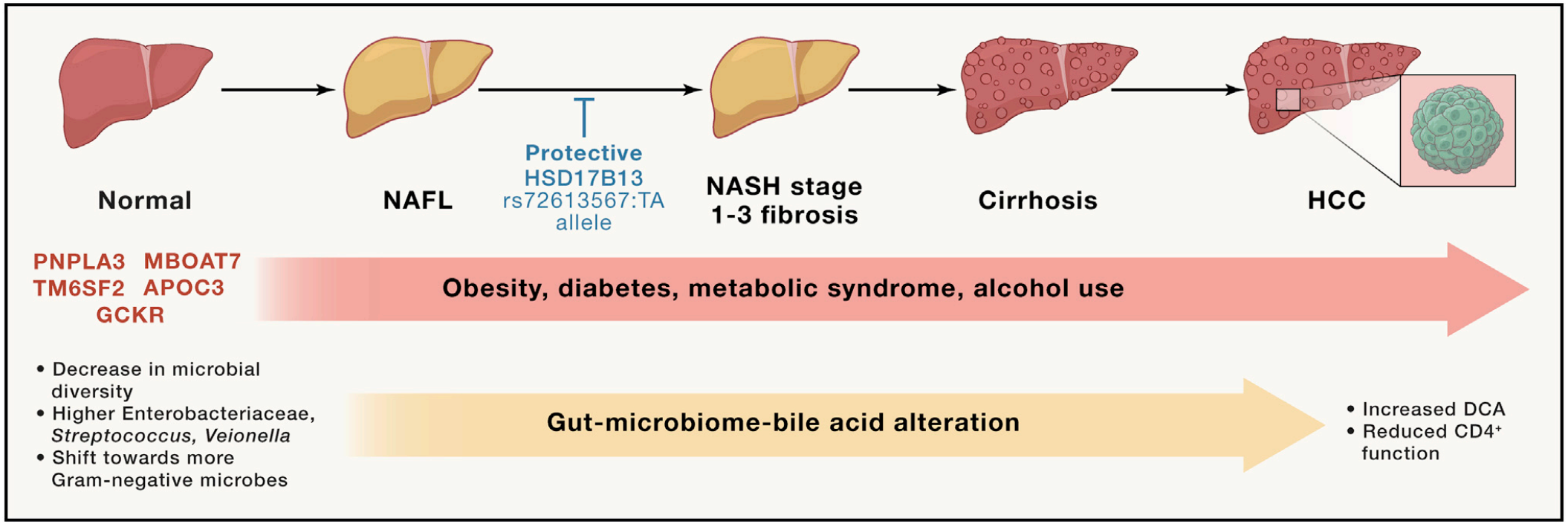
Risk factors and progression of NASH

- NASH, an advanced form of non-alcoholic fatty liver disease (NAFLD), can progress to liver fibrosis, cirrhosis, and hepatocellular carcinoma
- Genetic factors, environmental factors, and microbiome alterations are mainly involved in disease progression



Loomba and Shulman, 2021

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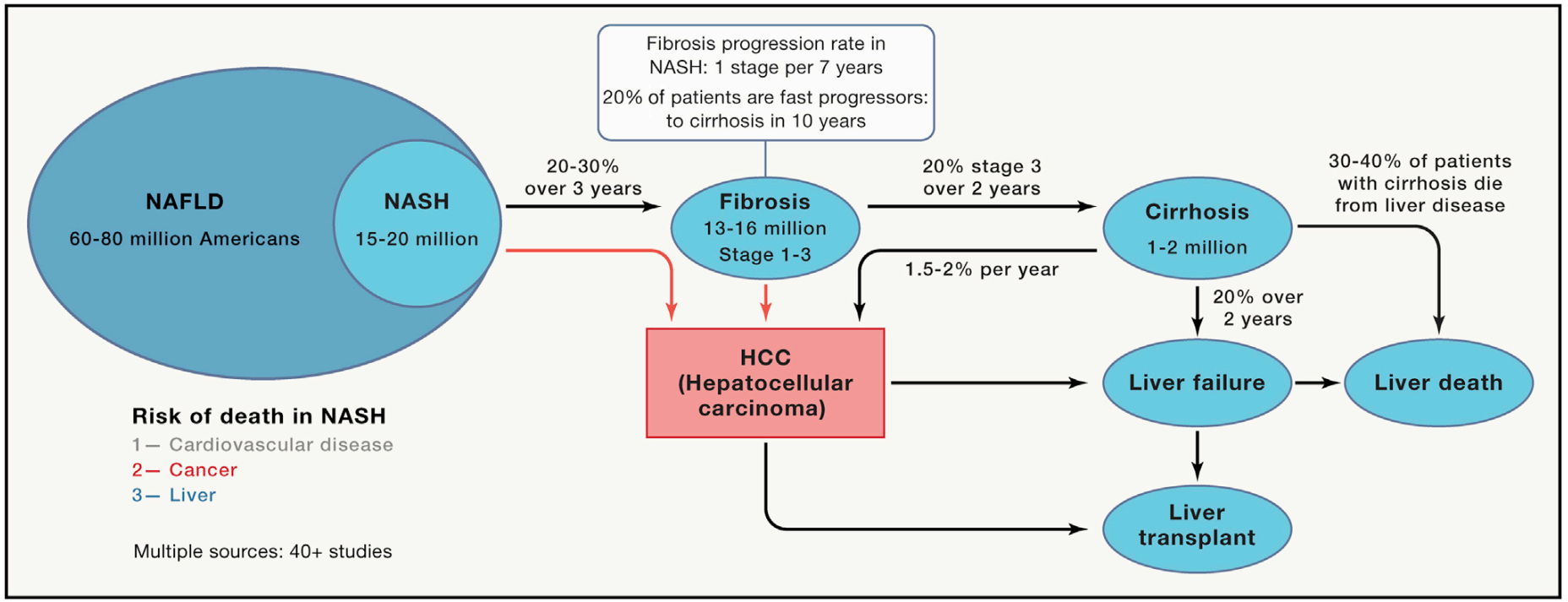
Drug market of NASH

- Experts estimated that 24% of U.S. adults have NAFLD and more than 6.5% of them have NASH (NIH report, 2021). 20~ 30% of patients with NASH progress to liver fibrosis in 7 years, and 20% of them progress to cirrhosis in two years.
- However, since no drugs for NASH are commercially available, off-label drug use is only available treatment option



Loomba and Shulman, 2021

2-1. Non-alcoholic Steatohepatitis (NASH)

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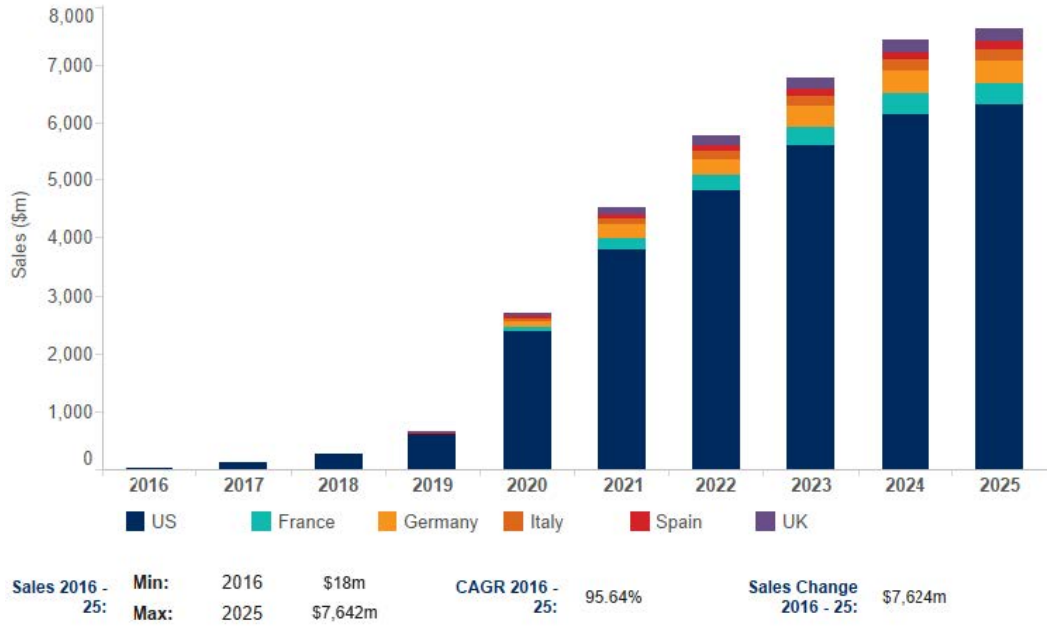
NASH market overview

- The current market size of NASH treatment is less than $1 billion due to a lack of drug options. The sale volume of NASH drugs is expected to grow rapidly, however, after the first drug for NASH is approved by FDA, initiating sales in the market.
- The number of large licensing deals for NASH assets (> $100 million) has increased recently, and majority of these assets are small molecules.

2016 to 2025 NASH drug sales in the seven countries



DATAMONITOR Healthcare Jan. 2017

Licensing deals of NASH assets from 2014 to 2020

Year	Licensor	Licensee	Active ingredient	Stage	Licensing fees
2014. 12.	Phenex	Gilead	**FXR agonist**	P2	**$470M**
2015. 05.	Pharmaxis	B.I.	**SSAO/VAP-1**	P1	**$600M (upfront: $31M)**
2016. 09.	Akarna Therapeutics	Allergan	**FXR agonist**	P.C.	**Unknown (upfront: $50M)**
2016. 09.	Tobira Therapeutics	Allergan	**CCR2/5 antagonist**	P2	**$1.7B**
2019. 01.	Yuhan Corp.	Gilead	**Small molecules (undisclosed)**	P.C.	**$785M (upfront: $15M)**
2019. 07.	Yuhan Corp.	B.I.	GLP-1/FGF21 dual agonist	P.C.	**$870M (upfront: $40M**
2019.12.	Pliant Therapeutics	Novartis	**αVβ1 integrin agonist**	P.C.	**Undisclosed (upfront: $80M)**
2020. 08.	Thera Biosciences	LG Chem	**VAP-1 antagonist**	P.C.	**$350M**
2020. 08.	Hanmi Pharma	Merck & Co.	GLP-1/GCG dual agonist	P2	**$870M (upfront: $10M)**
2020. 11.	Enleofen	B.I.	IL-11 AB	P.C.	**$1B**
2020. 12.	Aligos Therapeutcis	Merck & Co.	Oligo nucleotide	P1	**$458M**

2-1. Non-alcoholic Steatohepatitis (NASH)

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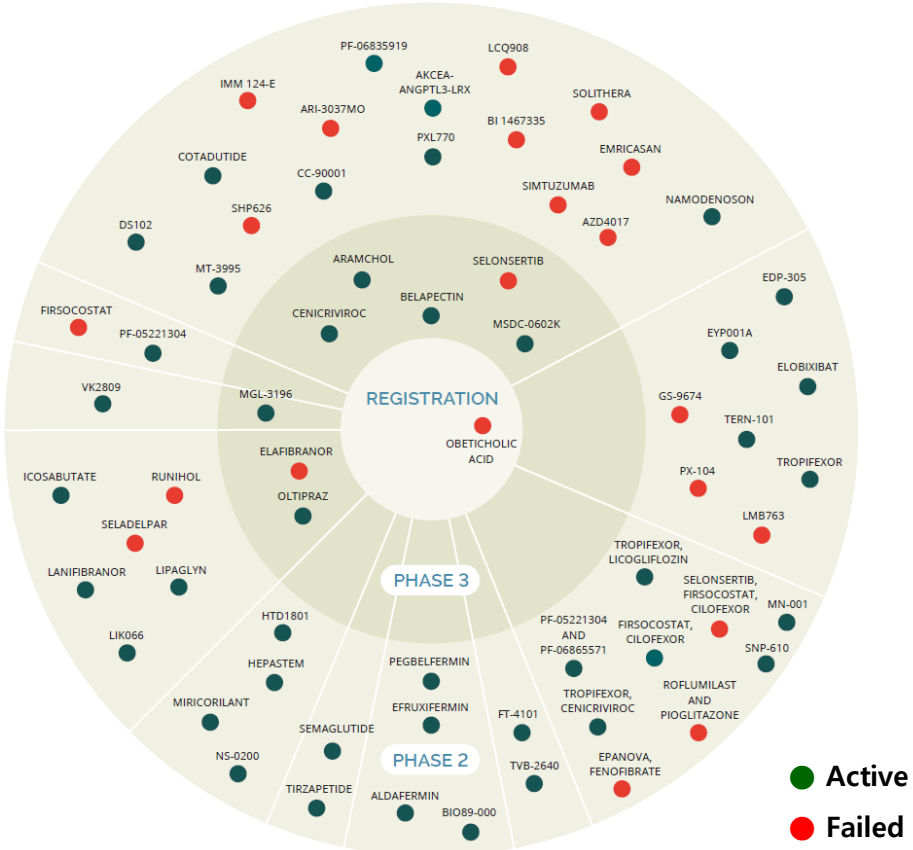
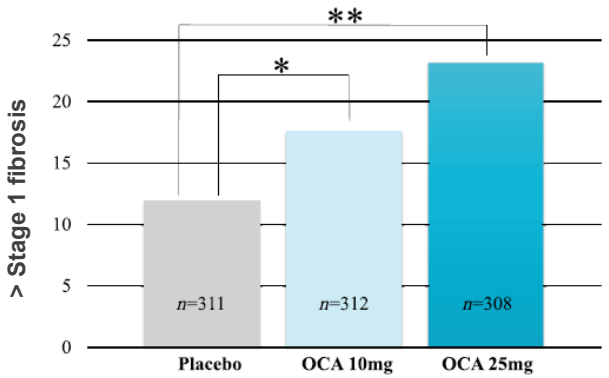
Major drug candidates for NASH

- More than 100 drug candidates are currently in clinical trials, but no drugs have been approved yet.
- Ocaliva significantly improves hepatic fibrosis and hepatic steatosis, but these therapeutic effects did not outweigh its risk of significant side effects in clinical trials, and selonsertib failed to show significantly improved hepatic fibrosis in a phase III clinical trial.



Back Bay Life Science Advisors Dec. 2020

REGENERATE STUDY (Obeticholic acid)



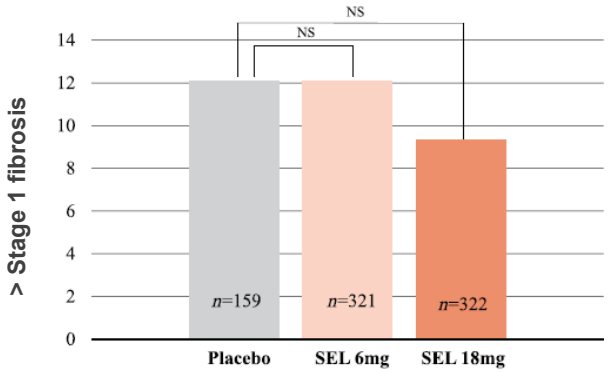
SCIENCE NEWS

FDA Delays Approval of Ocaliva for Fatty Liver Disease

The regulatory agency requested further data to show whether its benefits outweigh its risks.

July 10, 2020 · By Liz Highleyman

STELLAR-4 TRIAL (Selonsertib)



COMPANY NEWS

Gilead's selonsertib fails in second Phase III trial for NASH

26 Apr 2019

Gilead Sciences has reported that selonsertib failed to meet the primary endpoint in the Phase III STELLAR-3 clinical trial performed in patients with bridging fibrosis (F3) caused by nonalcoholic steatohepatitis (NASH).

Sumida and Nakajima, 2019

2-1. Non-alcoholic Steatohepatitis (NASH)

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Combination therapy for NASH

- Since NASH is a multifaceted disease caused by various cellular and signaling events, combination therapies that can target multiple cellular signaling pathways might be crucial for developing effective drugs for NASH.
- Hence, diverse combination studies are at the clinical stage, and we are also seeking opportunities to develop additional combination therapies with drug candidates that can strongly suppressing lipogenesis.

"We expect that treatment response can be enhanced by strategically combining multiple agents targeting distinct metabolic pathways to not only achieve resolution of NASH and improvement in fibrosis but also a reduction in cardiovascular disease risk and future risk of cancer."

Loomba and Shulman, 2021

1. **Obeticholic acid (FXR agonist, Intercept) + Bezafibrate (pan-PPAR agonist, Prior art compound)**
   - The combinatorial efficacy will be studied.

2. **Cenicriviroc (CCR2/5 receptor inhibitor, Allergan) + Tropifexor (FXR agonist, Novartis)**
   - Phase II study is ongoing *combines CVC's anti-inflammatory effects with Tropifexor's anti-lipogenesis profile.

3. **Semaglutide (GLP-1 agonist, Novo Nordisk) + Cilofexor(FXR agonist, Gilead) + Firsocostat(ACC inhibitor, Gilead)**
   - The Phase IIa study was completed and Phase IIb patients will be recruited at the end of 2021.

4. **Licogliflozin (SGLT1/2 inhibitor, Novartis) + Tropifexor (FXR agonist, Novartis)**
   - Patients currently recruited for the Phase II study.

5. **PF-05221304 (ACC1/2 inhibitor, Pfizer) + PF-06865571 (DGAT2 inhibitor, Pfizer)**
   - Phase II recruitment completed.

2-1. Non-alcoholic Steatohepatitis (NASH)

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Mechanism of Action (MOA)

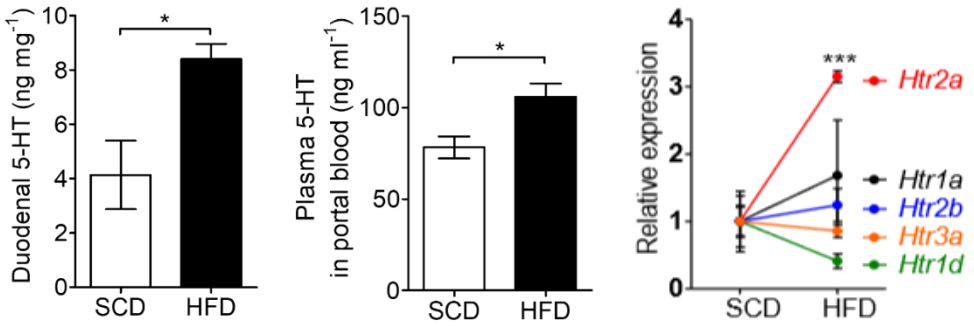
- In a mouse model, a high-fat diet (HFD) increases both serotonin (5-hydroxytryptophan, 5-HT) levels in the plasma levels (portal blood) and serotonin receptor 2a (5-HT receptor 2a, Htr2a) expressions in the liver.
- Activation of the serotonin receptor induces lipogenic gene expression, which in turn enhances lipid storage in hepatocytes.

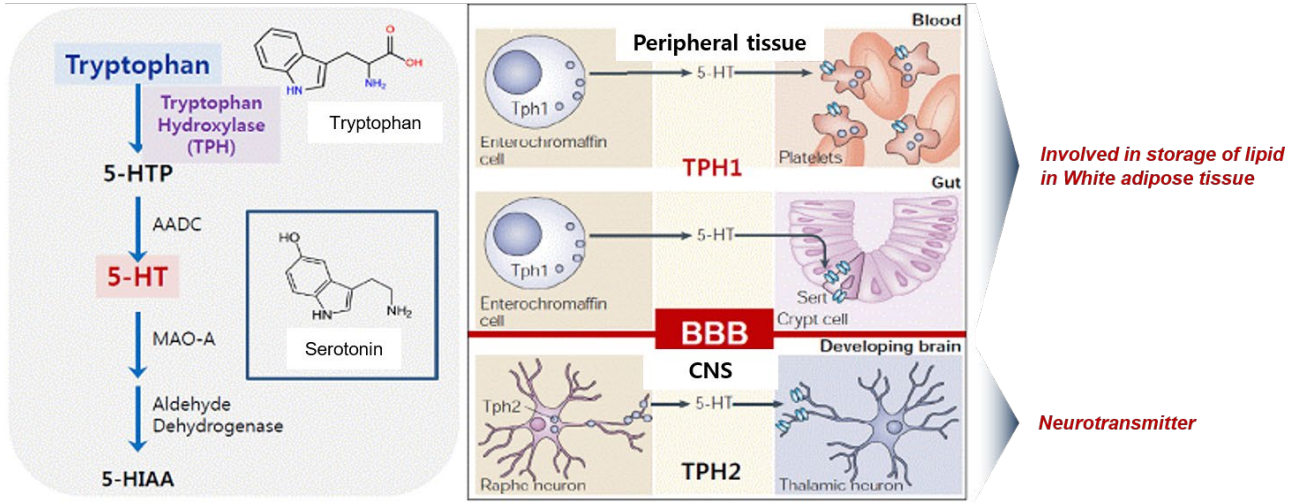
Article | Open Access | Published: 16 November 2018

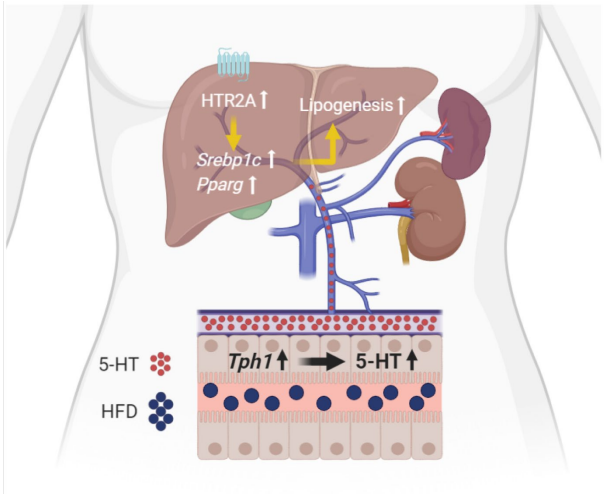
Serotonin signals through a gut-liver axis to regulate hepatic steatosis

Wonsuk Choi, Jun Namkung, Inseon Hwang, Hyeongseok Kim, Ajin Lim, Hye Jung Park, Hye Won Lee, Kwang-Hyub Han, Seongyeol Park, Ji-Seon Jeong, Geul Bang, Young Hwan Kim, Vijay K. Yadav, Gerard Karsenty, Young Seok Ju, Chan Choi, Jae Myoung Suh, Jun Yong Park ✉, Sangkyu Park ✉ & Hail Kim ✉

Nature Communications **9**, Article number: 4824 (2018) | Cite this article







2-1. Non-alcoholic Steatohepatitis (NASH)

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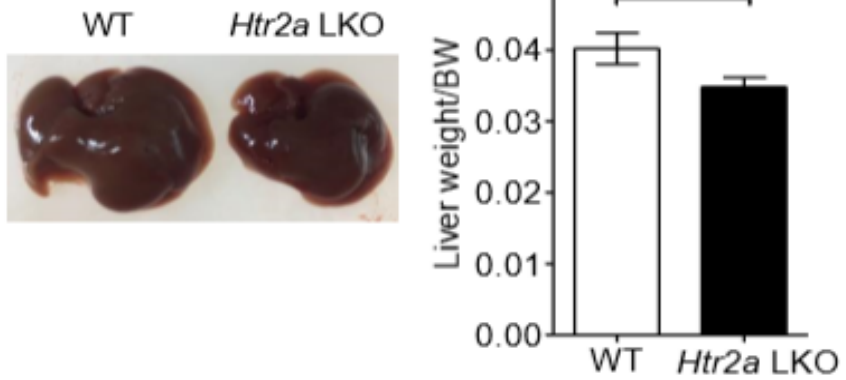
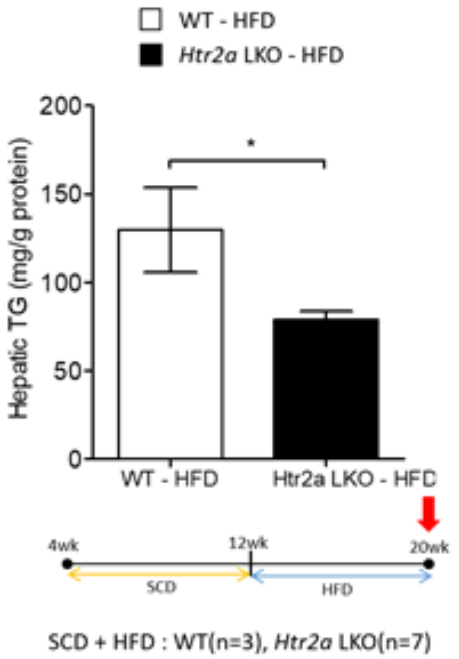
Mechanism of Action

- In liver-specific *Htr2a* knockout mice, suppression of HTR2a significantly reduced hepatic steatosis and the NAFLD activity score. This result clearly indicates that HTR2a is important for hepatic steatosis.

Liver Weight

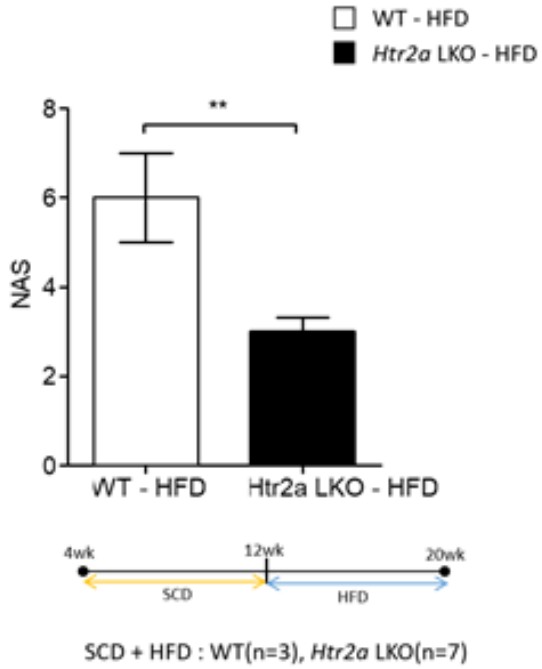


Hepatic TG



SCD + HFD : WT(n=3), *Htr2a* LKO(n=7)

NAFLD activity score



SCD + HFD : WT(n=3), *Htr2a* LKO(n=7)

Choi and Kim, 2018

2-1. Non-alcoholic Steatohepatitis (NASH)

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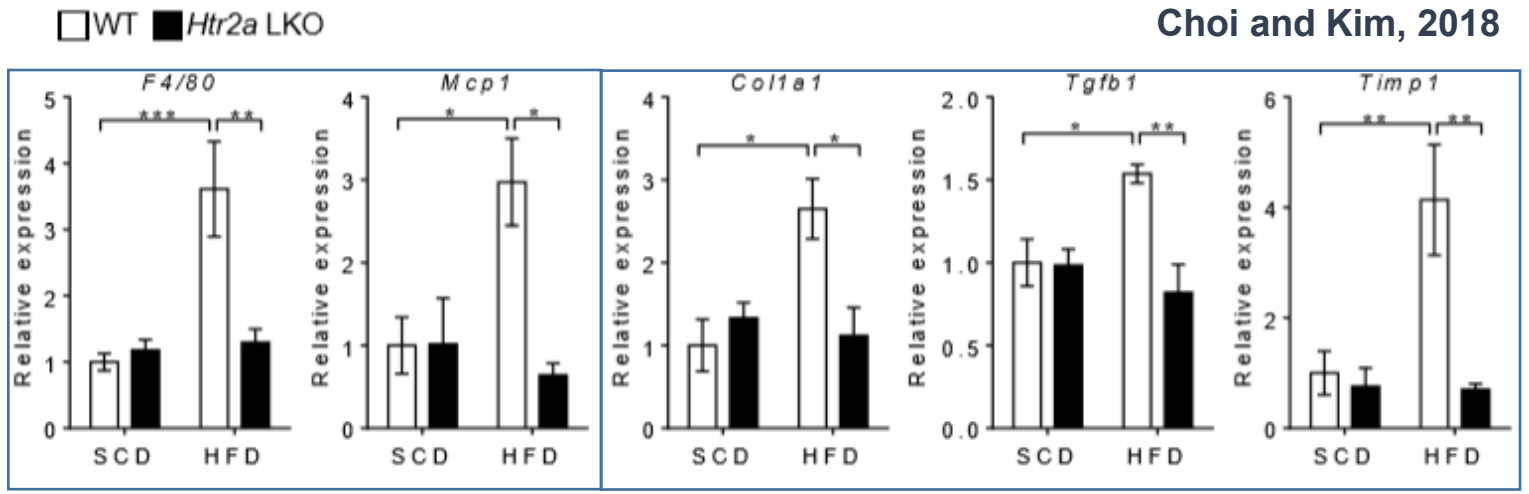
Mechanism of Action

- In liver-specific *Htr2a* knockout mice, suppression of *Htr2a* reduces inflammation and fibrosis-related gene expression in the liver transcriptome, indicating that 5-HT signaling is important for inflammation and fibrosis in the liver.



Inflammation marker genes

Fibrosis marker genes

The synthesis of an Htr2a antagonist might provide a potent drug candidate for NASH and liver fibrosis

2-1. Non-alcoholic Steatohepatitis (NASH)

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Synthesis of GM60106

- We synthesized a novel compound (GM60106) that can effectively reduce lipogenesis, inflammation, and fibrosis in the liver, while minimizing blood-brain barrier (BBB) permeability, so that it would not induce any BBB-mediated side effects.

Journal of Medicinal Chemistry

pubs.acs.org/jmc Article

Design, Synthesis, and Biological Evaluation of New Peripheral $5HT_{2A}$ Antagonists for Nonalcoholic Fatty Liver Disease

Minhee Kim,[‡] Inseon Hwang,[‡] Haushabhau S. Pagire, Suvarna H. Pagire, Wonsuk Choi, Won Gun Choi, Jihyeon Yoon, Won Mi Lee, Jin Sook Song, Eun Kyung Yoo, Seung Mi Lee, Mi-jin Kim, Myung Ae Bae, Dooseop Kim, Heejong Lee, Eun-Young Lee, Jae-Han Jeon, In-Kyu Lee, Hail Kim,* and Jin Hee Ahn*

Cite This: *J. Med. Chem.* 2020, 63, 4171−4182 Read Online

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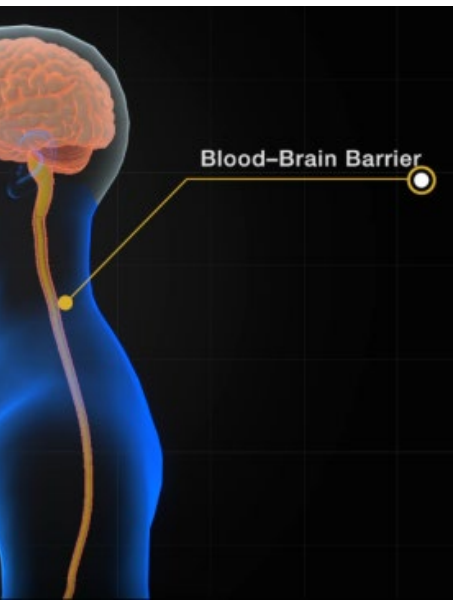
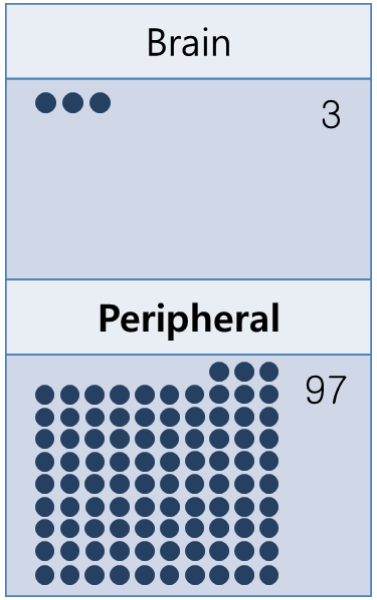
ABSTRACT: Nonalcoholic fatty liver disease (NAFLD) is increasingly prevalent worldwide, causing serious liver complications, including non-alcoholic steatohepatitis. Recent findings suggest that peripheral serotonin (5-hydroxytryptamine, 5HT) regulates energy homeostasis, including hepatic lipid metabolism. More specifically, liver-specific $5HT_{2A}$ knockout mice exhibit alleviated hepatic lipid accumulation and hepatic steatosis. Here, structural modifications of pimavanserin (CNS drug), a $5HT_{2A}$ antagonist approved for Parkinson's disease, led us to synthesize new peripherally acting $5HT_{2A}$ antagonists. Among the synthesized compounds, compound 14a showed good in vitro activity, good liver microsomal stability, 5HT subtype selectivity, and no significant inhibition of CYP and hERG. The in vitro and in vivo blood−brain barrier permeability study proved that 14a acts peripherally. Compound 14a decreased the liver weight and hepatic lipid accumulation in high-fat-diet-induced obesity mice. Our study suggests new therapeutic possibilities for peripheral $5HT_{2A}$ antagonists in NAFLD.





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Chemical profile of GM60106

- Chemical stability, in vivo safety, in vivo efficacy of GM60106 were analyzed before proceeding to pre-clinical study.

Code	*In vitro* (cellular assay)	Chemical stability	Hepatocyte stability (3 hrs)	Plasma stability	CYP inhibition (at 10 μM)
GM-60106	14 nM	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)	1A2: < 1 % 2C9: 3.17 % 2C19: 6.83 % 2D6: 26.3 % 3A4: 17.6 %
Cytotoxicity (IC_{50})	**Solubility**	**Permeability (PAMPA)**	**PPB/CLogP**	***In vivo* PK (rat) with crystalline form**	**BBB permeability**
VERO > 100 μM HFL-1 > 100 μM L929 > 100 μM NIH3T3 > 100 μM CHO-K1 > 100 μM	1.3 mg/mL pH = 6.8 Crystalline Free form	-4.03 ± 0.042 (grade: High)	97.5 % (m) 96.7 % (r) 97.1 % (h) /3.16	IV (5mpk) Oral (10mpk) T1/2: 4.14 h AUC: 1.59 ug.h/ml CL: 2.59 L/h/kg V: 4.68 L/kg **BA 41 %**	**0.02±0.09 (DIO mice)** C_{brain}/C_{plasma}, B/P ratio after 2 hr oral injection
***In vivo* efficacy in normal with high fat**	***In vivo* efficacy in DIO mice**	**NASH in MCD diet in db/db mice**	**STAM mice**	**CDA HFD**	**AMES/ Acute Toxicity**
Body weight gain reduction, Reduced fat accumulation	Body weight gain reduction, Reduced fat accumulation in liver	Reduced inflammation, fibrosis and fat accumulation in liver	Reduced inflammation, fibrosis, and hepatic steatosis	Reduced percentage of fibrotic area and expression levels of fibrosis marker genes	Negative / LD_{50} > 1000 mpk

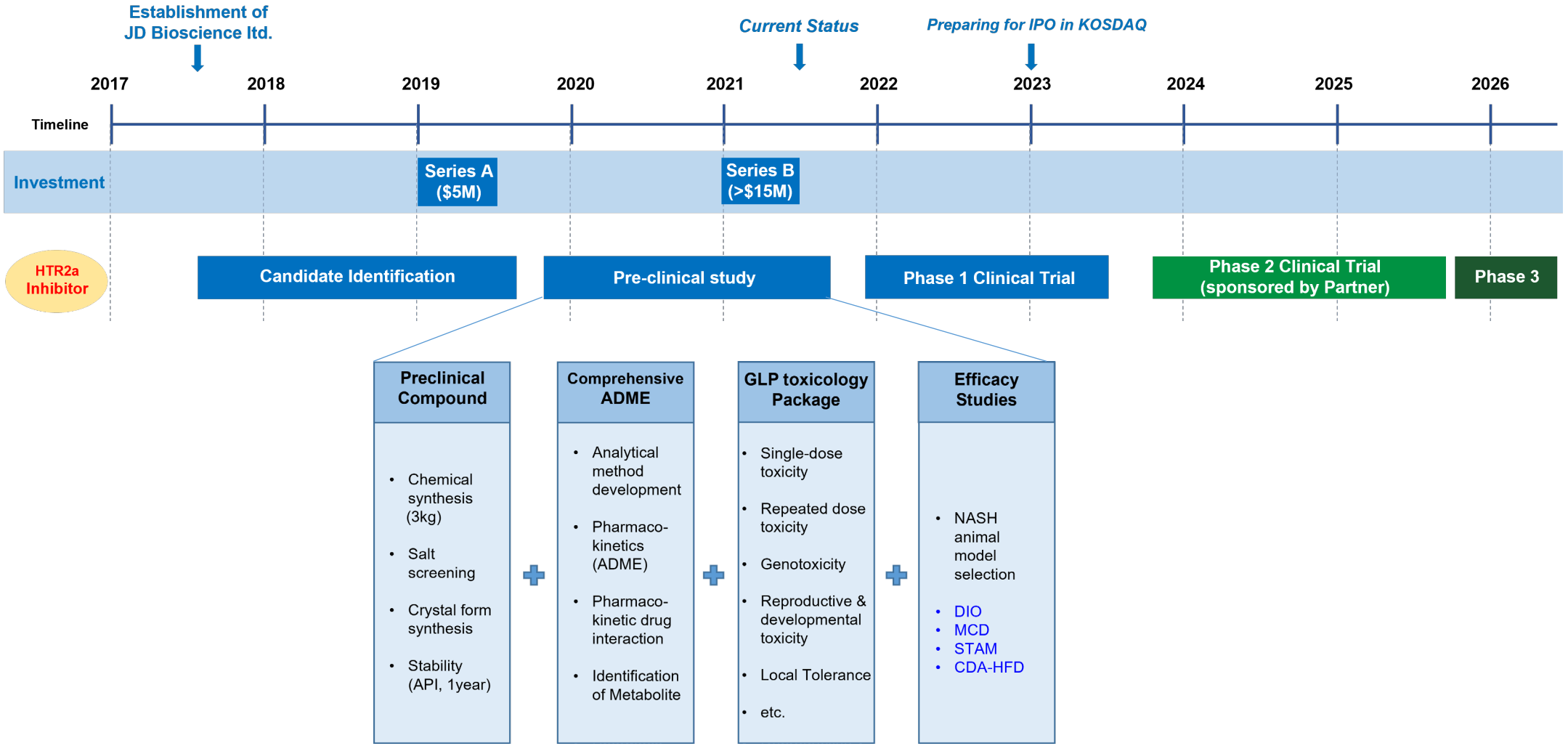
Pre-clinical Study

Parameter	IV, 5mpk	PO, 10mpk
T_{max} (h)	NA	1.83 ± 1.89
C_{max} (μg/mL)	NA	0.18 ± 0.06
$T_{1/2}$ (h)	1.44 ± 0.09	4.14 ± 0.48
AUC_{last} (μg·h/mL)	1.91 ± 0.20	1.30 ± 0.27
AUC_{∞} (μg·h/mL)	1.95 ± 0.21	1.59 ± 0.19
CL (L/h/kg)	2.59 ± 0.29	NA
V_{ss} (L/kg)	4.68 ± 0.16	NA
F_{∞} (%)	NA	40.80

JD BIOSCIENCE

Plan for pre-clinical and clinical studies

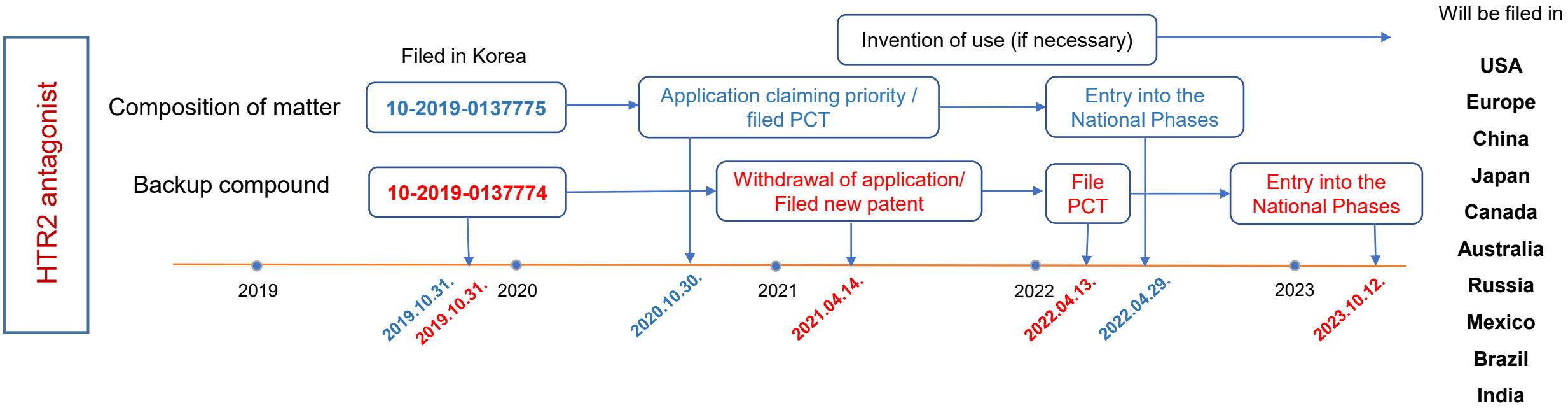
- We completed a pre-clinical study of GM60106 in August 2021 and are preparing an IND application to the FDA for a Phase I clinical study



JD BIOSCIENCE

Intellectual property management plan

- A patent for a composition of matter was filed in 2019 and will enter national phases in 2022.
- A backup compound GM60106 was also prepared, and the patent was filed in 2021.



Summary of our NASH pipeline

- We found unknown roles for Htr receptor-mediated serotonin signaling in liver, which are related to the progression of NASH and liver fibrosis.
- Based on these findings, we synthesized a chemical compound (GM60106) that can directly inhibit Htr2a receptors on liver cells.
- The in vivo efficacy of GM60106 was validated in four different NASH mouse models: DIO, STAM, MCD, and CDA-HFD.
- A pre-clinical study of GM60106 was completed, and proprietary compounds are protected with patent applications.
- Currently, we are preparing an application to the US FDA for a first-in-class human trial of GM60106.

2-2. Inflammatory Bowel Disease (IBD)

JD BIOSCIENCE

Risk factor and causes of IBD

- IBD, including ulcerative colitis (UC) and crohn's disease (CD) can be caused by genetic and environmental factors and can induces uncontrolled activation of intestinal immune cells.
- Pro-inflammatory cytokines, such as TNF, IL-6, produced by the activated immune cells are suggested to drive the perpetuation of inflammation and tissue damage.

Genetics

Susceptibility, Inheritance

Environmental Factors

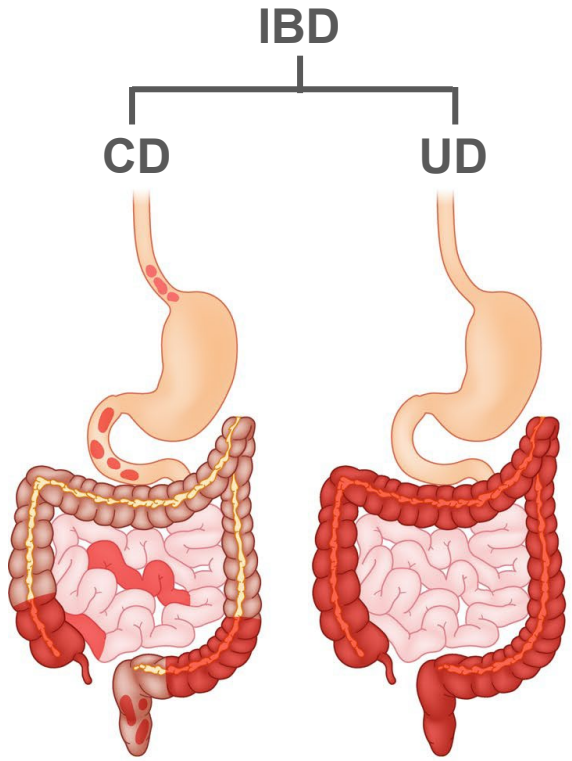
Microbial & dietary toxins, infection, drugs

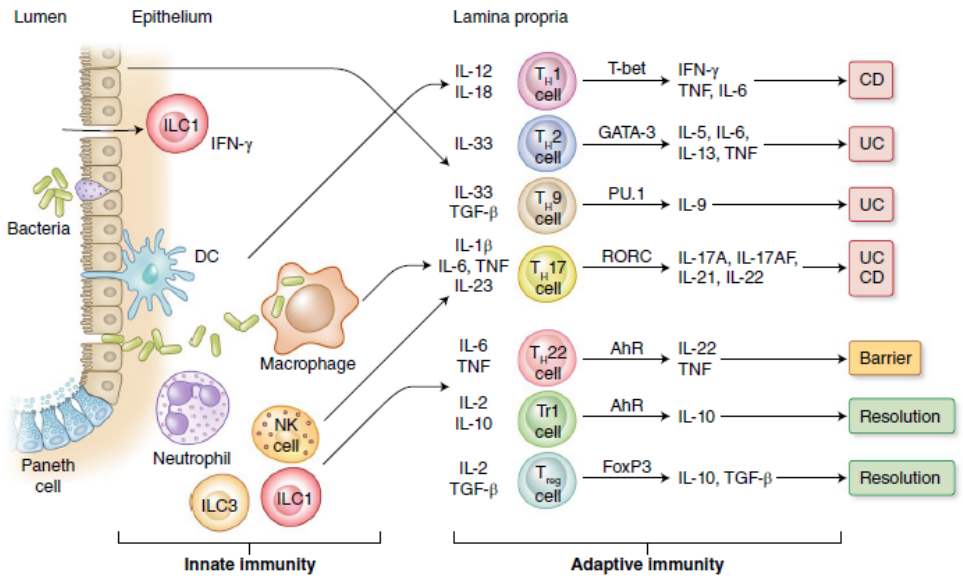
Intestinal Barrier

Permeability, autophagy, goblet cells

Immune Response

Innate response, cytokine expression





Neurath 2019, Nat. Immunol.

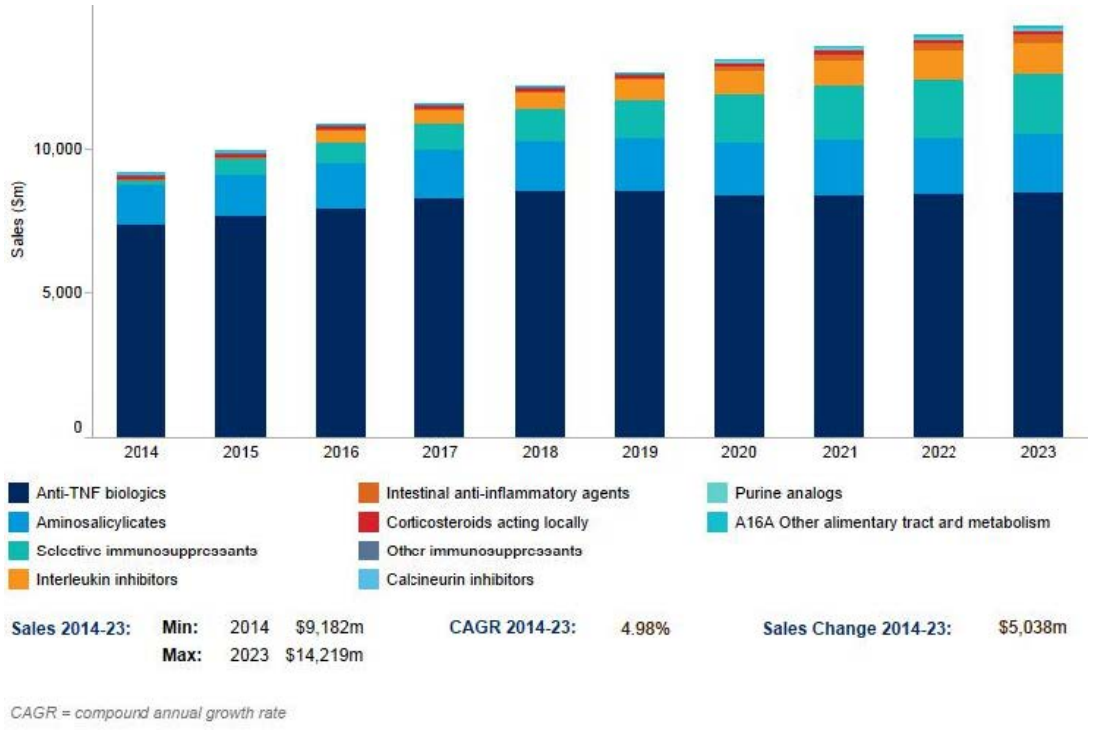
2-2. Inflammatory Bowel Disease (IBD)

JD BIOSCIENCE

Drug market for IBD

- IBD is a global disorder with a high incidence in developed countries (prevalence rate > 0.3%) and accelerating incidence in industrialized countries. Currently anti-TNF antibodies hold the largest market share in the IBD therapeutics market, while the market share of interleukin inhibitors is growing rapidly.

2014 to 2023 IBD drug sales in the seven countries



DATAMONITOR Healthcare Jan. 2016

Licensing deals of IBD assets from 2016 to 2020

Year	Licensor	Licensee	Active ingredient	Stage	Licensing fees
2016 10.	AstraZeneca	Allergan	**IL-23 AB**	P2	**$1.27B (upfront: $250M)**
2017. 04.	Finch Therapeutics	Takeda	**FIN-524 microbiomes**	P.C.	**Undisclosed (upfront: $10M)**
2017. 05.	Protagonist	J&J	**IL-23 inhibitor (oral peptide)**	P.C.	**$0.99B (upfront: $50M)**
2017. 09.	Janssen	Provention Bio	**CSF-1R antagonist, TLR3 AB**	P1/P.C.	**Undisclosed**
2018. 12.	Bridge Bio	Daewoong Pharma	**Pelliono-1 Antagonist**	P1	**$40M**
2019. 04.	IFM therapeutics	Novartis	NLRP3 Antagonist portfolio	P.C.~P1	**$310M ~ $16B**
2019. 07.	Alfasigma	Innovation Pharma	Brilacidin (non-corticosteroid)	P2	**$24M + upfront**
2019. 09.	Prometheus Biosciences	Takeda	(>200,000) Patient samples	Discovery	**$420**
2020. 05.	Gossamer Bio	Aerpio Pharma	HIF-1a stabilizer	P.C.	**$90M (upfront: $15M)**

2-2. Inflammatory Bowel Disease (IBD)

JD BIOSCIENCE

Major drug candidates for IBD

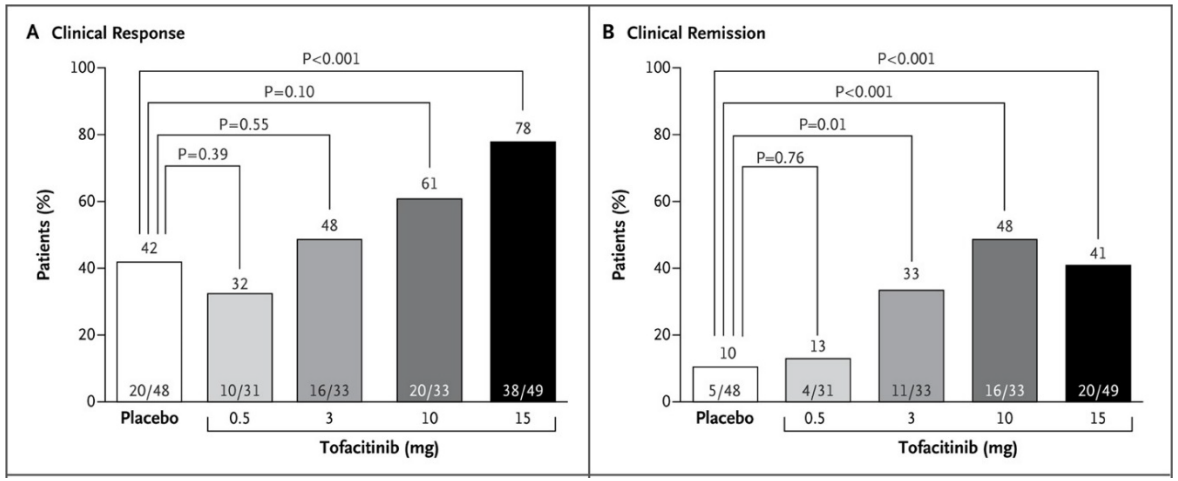
- Although antibody-based immunosuppressants have been widely used to treat IBD, the response rate of antibody treatment is rapidly falling due to alternative signaling mechanisms that contribute to resistance to antibody therapy. This offers added value to multi-cytokine blockers such as tofacitinib (Jak1 and Jak3 inhibitors) for the effective suppression of gut inflammation.

Challenges for Immunosuppressant

- **Unresponsive to biologics** (anti-TNFα, anti-integrin, IL12/IL23): approximately 30% of patients
- **Losing response among previous responders: up to 10%/year**
- Significant **infectious and neoplastic side effects** with current IBD medications

"The Jak1 and Jak3 inhibitor tofacitinib is effective in suppressing mucosal inflammation in UC but not in CD and has been approved for UC therapy"

Sandborn and Wojciech, 2012



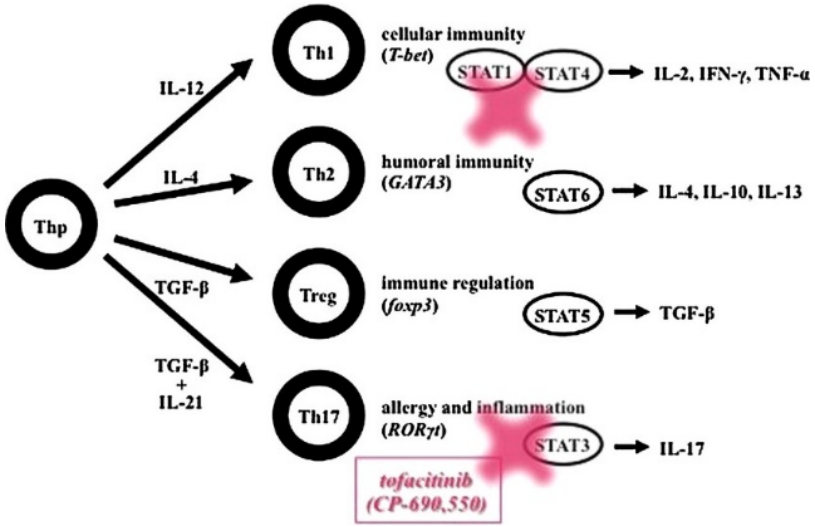
2-2. Inflammatory Bowel Disease (IBD)

JD BIOSCIENCE

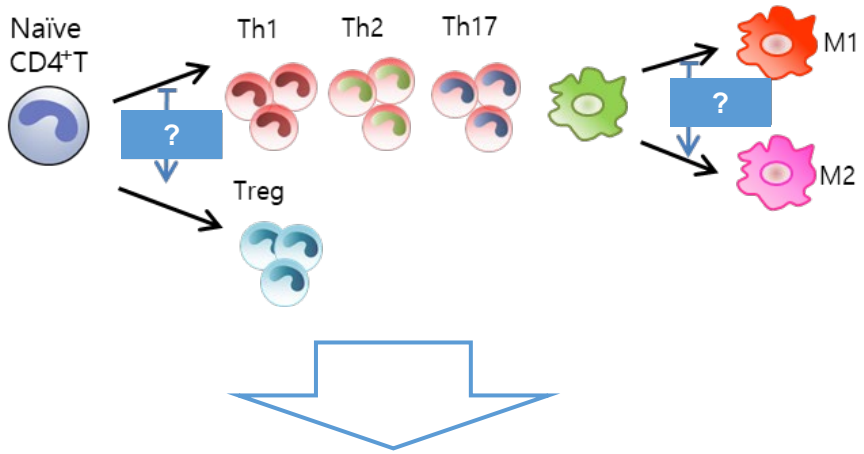
Unmet medical needs of current IBD drugs

- A commercialized multi-cytokine blocker, tofacitinib has had limited therapeutic effects because it can only suppress a limited number of helper T cells. Thus, we decided to discover novel targets that are involved in regulating the behaviors of a diverse range of cytokines.

Jak inhibitor Tofacitinib



A novel target



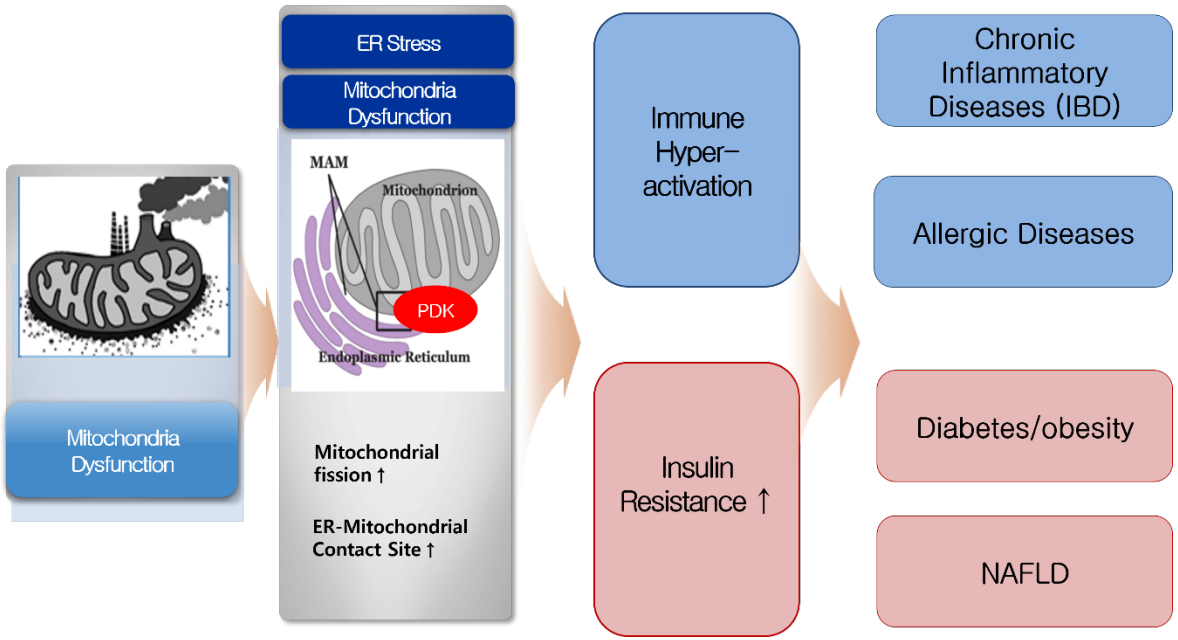
Discover a novel target or targets that are important for multi-cytokine modulation

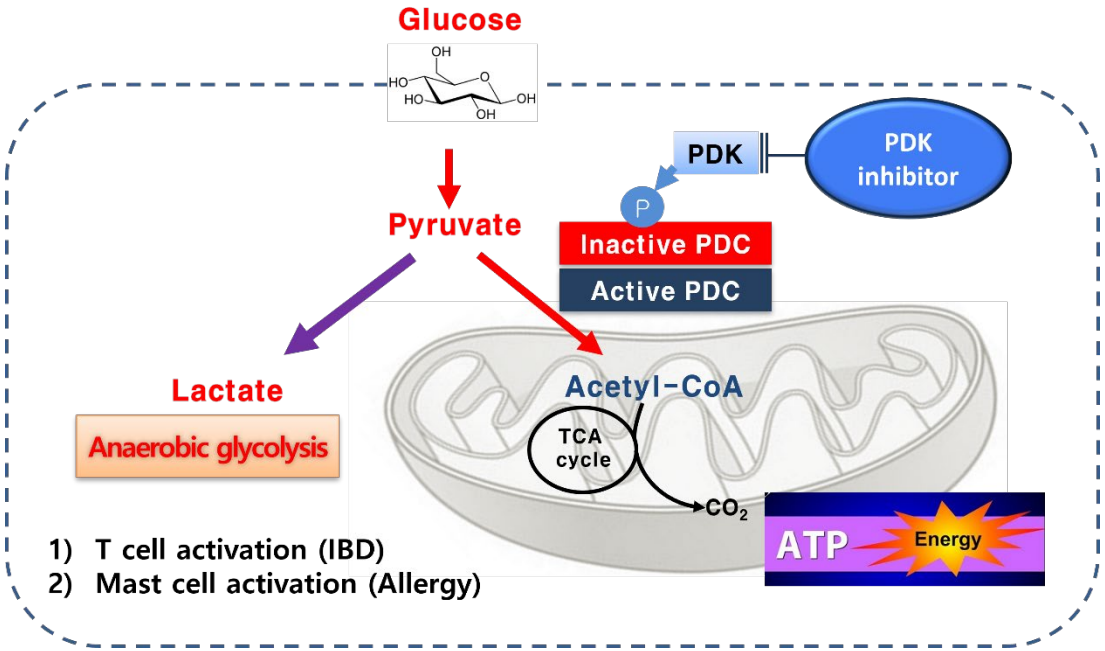
2-2. Inflammatory Bowel Disease (IBD)

JD BIOSCIENCE

Mechanism of Action

• According to our preliminary research, pyruvate dehydrogenase kinase (PDK) can suppress the mitochondrial function of intestinal immune cells, and this leads to the induction of an uncontrolled activation of these cells. Since immune cell hyperactivation is one of the main causes of IBD progression, it is important to suppress PDK to provide an effective cure for IBD.

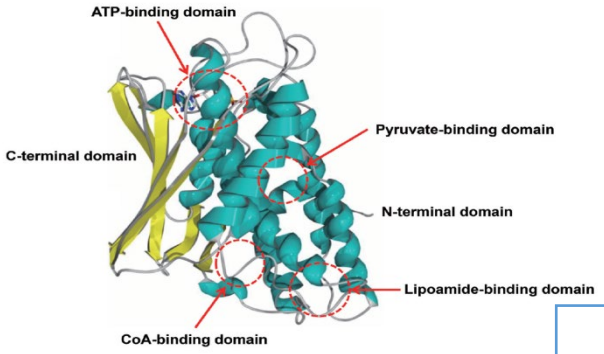




JD BIOSCIENCE

Synthesis of PDK inhibitors

- Our findings indicate that PDK4 inhibitors could provide a new therapeutic approach to IBD. Therefore, we synthesized both competitive and allosteric PDK4 inhibitors.



2-2. Inflammatory Bowel Disease (IBD)

CONFIDENTIAL

Chemical profile of GM-X3

- Chemical stability, in vivo safety, and in vivo efficacy of GM-X3 were analyzed before proceeding to a pre-clinical study.

Code	Inhibitor class	In vitro activity	In vitro (cellular assay)	Mitochondrial function
GM-X3	Allosteric inhibitor	159 nM (IC_{50}) Phosphorylation inhibition	Inhibition of PDHE1a phosphorylation	
CYP inhibition (IC_{50} mM)	hERG inhibition	PPB	Plasma stability (4hr incubation)	In vivo PK
1A2: 33.69 2C9: 12.64 2C19: 12.18 2D6: 7.94 3A4: 7.72	23.0 % at 10 μM	99.3 % (m) 99.5 % (m)	Mouse 50.5 % Human: 89 %	IV (5 mpk) Oral (10 mpk) T1/2: 5.15 h AUC: 1.76 ug.h/ml (IV) AUC: 1.7 ug.h/ml (oral) BA: 48 %
In vivo anti-diabetic efficacy	In vivo anti-cancer efficacy	In vivo IBD study	Acute toxicity	
Glucose AUC reduction (OGTT), oral administration	Reduced tumor volume in xenograft mice at 10 mpk dose	Improved histological score and colon length in vivo at 1 mpk	LD50 > 1000 mpk	

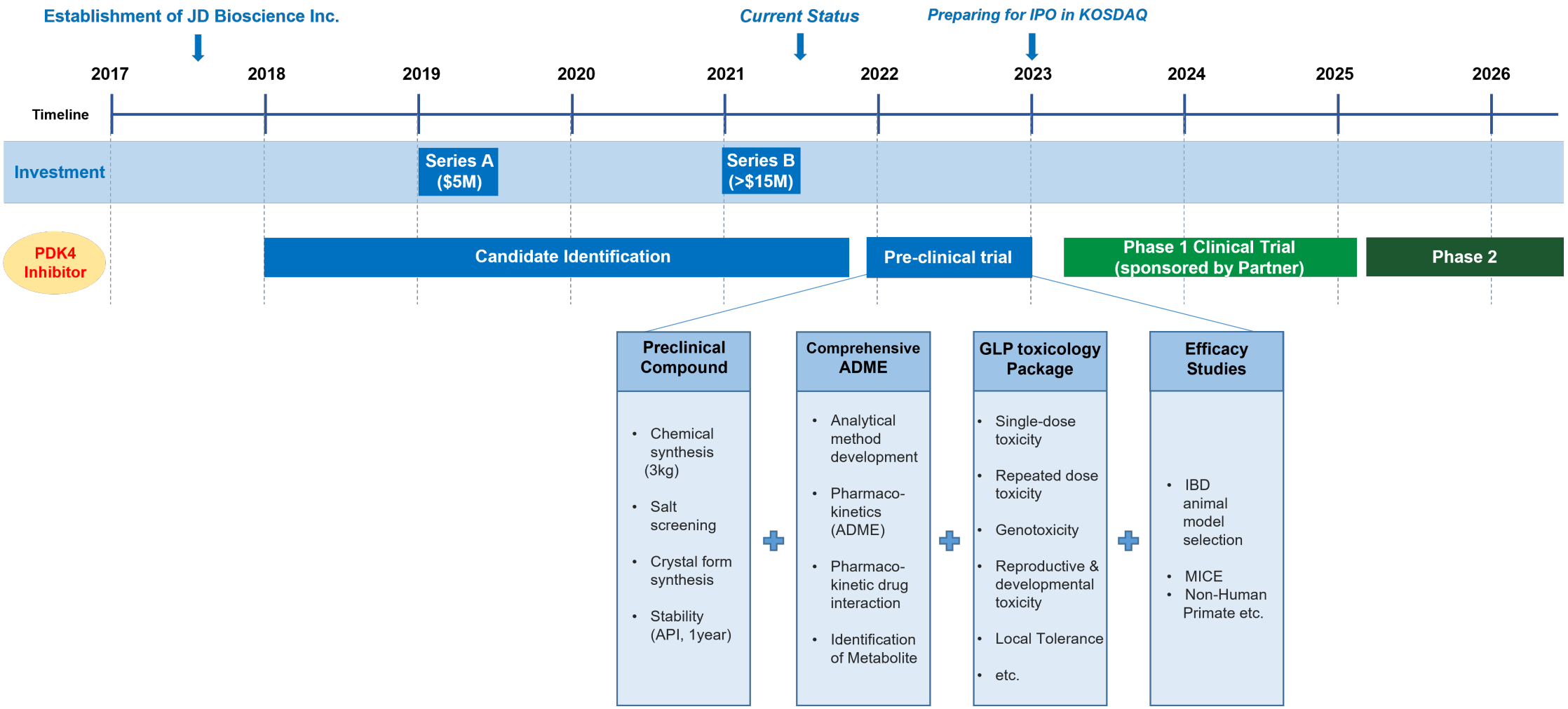
Preclinical Study

2-2. Inflammatory Bowel Disease (IBD)

JD BIOSCIENCE

Plan for pre-clinical and clinical study

- We plan to initiate a pre-clinical trial after completing a non-GLP toxicology study.



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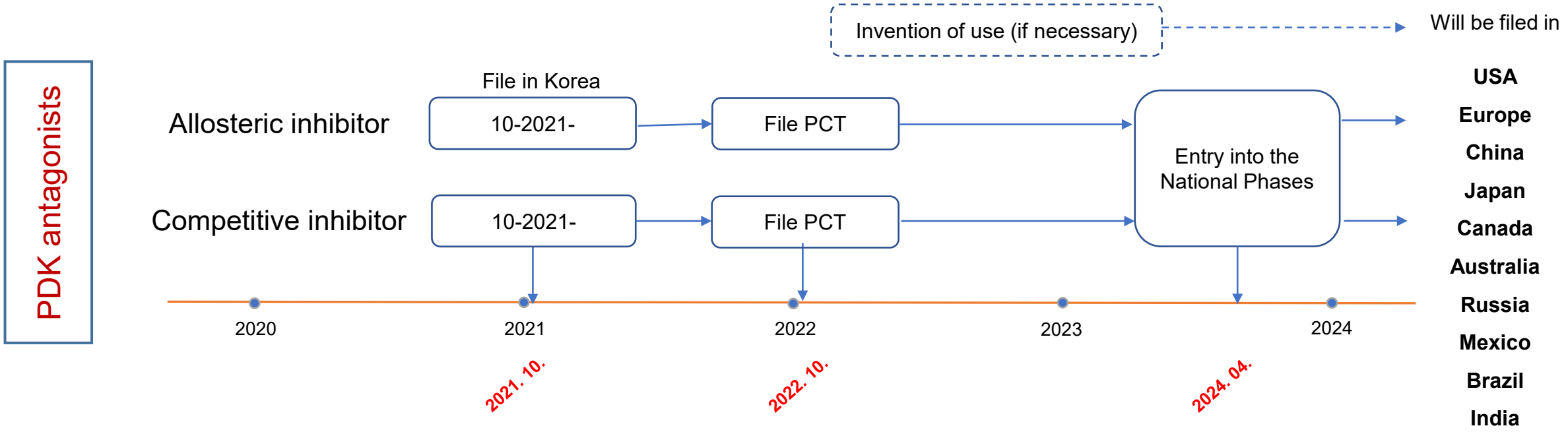
Intellectual property management plan

- Patents for the composition of matters of both allosteric inhibitors and competitive inhibitors of PDK are being filed and will enter national phases by 2024.



Summary of the IBD pipeline

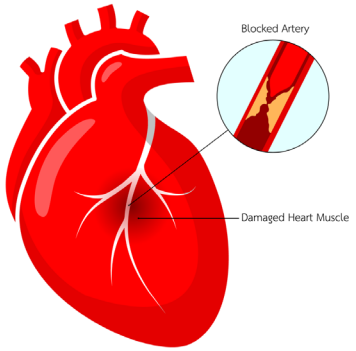
- According to our findings, PDK4 can modulate the activity of intestinal immune cells by suppressing mitochondrial functions, indicating that PDK4 is tightly connected with IBD progression.
- Based on this finding, we synthesized both competitive and allosteric inhibitors of PDK4 to provide novel drug candidates for IBD.
- The in vivo efficacy and chemical stability of GM-X3, a potent inhibitor of PDK4, were tested, and a pre-clinical trial of GM-X3 will be initiated after finishing the current non-GLP toxicology study.
- Disease indications for PDK inhibitors will be expanded into other inflammatory diseases, such as acute pancreatitis.

2-3. Heart Disease

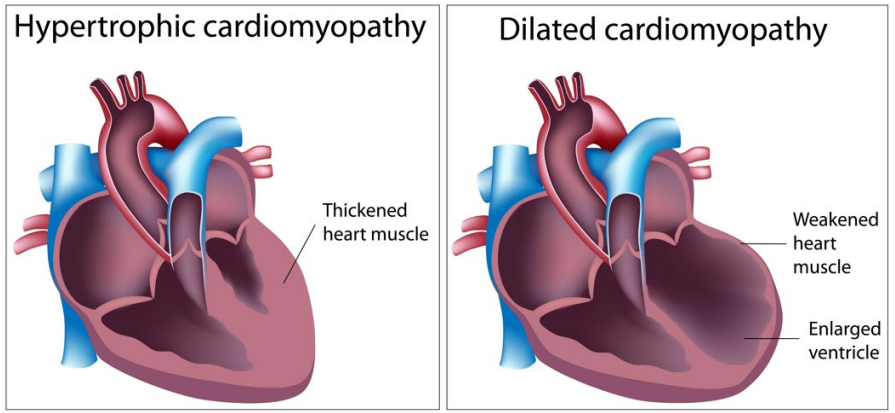
JD BIOSCIENCE

- Heart disease, a leading cause of death globally, can be categorized into ischemic heart disease, cardiomyopathy, and myocarditis.
- Ischemic heart disease is involved in the reduction of blood flow due to the accumulation of fatty deposits in the coronary arteries. Cardiomyopathy, including hypertrophic or dilated cardiomyopathy, is a disease of the heart muscle that can occur due to various risk factors. Finally, myocarditis is characterized by the inflammation of the heart muscle, which often occurs due to a viral infection. All of these can ultimately lead to fatal heart failure.

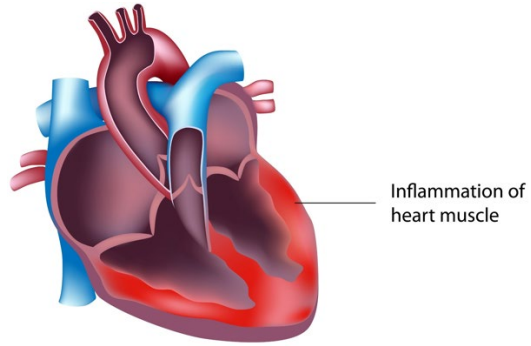
Ischemic heart disease



Cardiomyopathy



Myocarditis



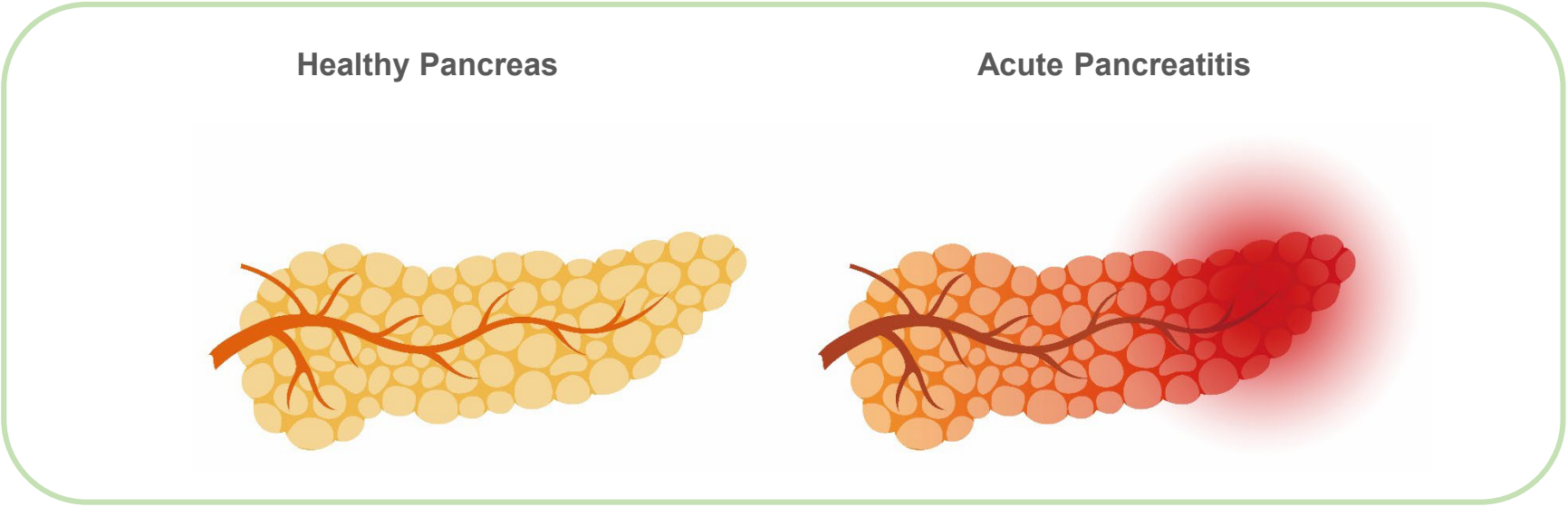
- Different types of medication are available to treat heart disease, for example, cholesterol-lowering medications, beta-blockers, nitroglycerin, and calcium channel blockers. However, none of these can rescue the function of cardiomyocytes once heart failure is in progression.
- JDB is developing a novel drug candidate for heart disease that can rescue heart function at a cellular level, and can eventually help improving heart function

2-4. Acute Pancreatitis

JD BIOSCIENCE

Risk factor and causes of IBD

- Acute pancreatitis (AP) is characterized by the sudden inflammation of the pancreas and occurs when digestive enzymes within the pancreas are abnormally activated. The main risk factors of AP are gallstones, which make up 40% of cases, and alcohol misuse, which makes up 30% of cases. Recent findings also indicate that type 2 diabetes or smoking can increase the risk of non-gallstone-related AP.
- AP was the second-highest cause of total hospital stay and the fifth leading cause of in-hospital death in the USA in 2015. However, to date, no specific causal treatment for AP is available. Instead, supportive care, such as pain control, is the only available treatment.



- JDB is developing a novel drug candidate for acute pancreatitis that can effectively reduce inflammation of the pancreas by modulating mitochondrial functions in pancreatic cells.

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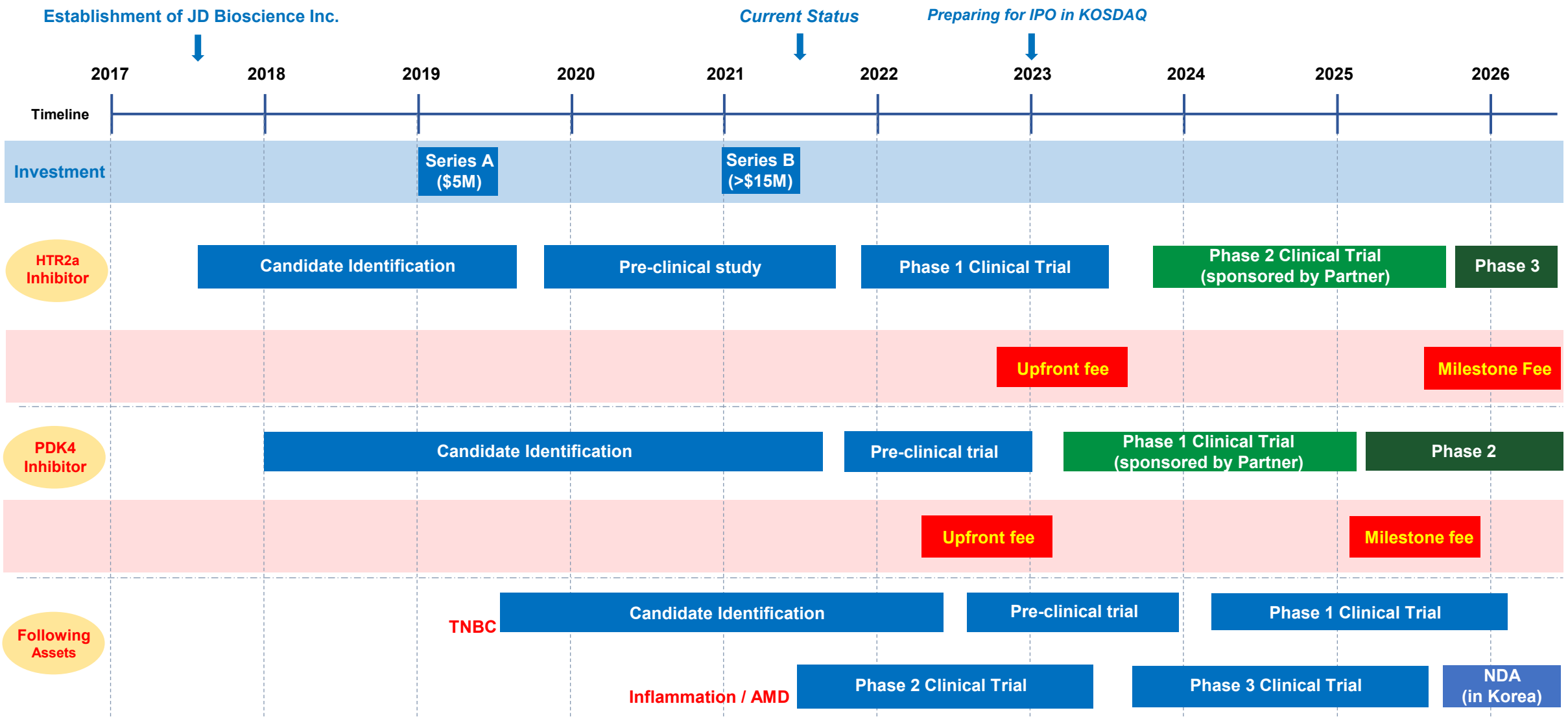
3. Business Plan

- Financial plan
- Plan for tech. commercialization
- Partnerships for collaborative research

Plan for technology commercialization

JD BIOSCIENCE

Making technology licensing deals with big pharmaceutical companies



Partnerships for collaborative research

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Creating stable sales revenue by expanding collaborative research with pharmaceutical companies

(We provide medicinal chemistry services to our partners.)

Industry Partners

2019 (3)

- ENHANCEDBIO INC
- SoVarGen Somatic Variations Genomics
- RaND Bioscience

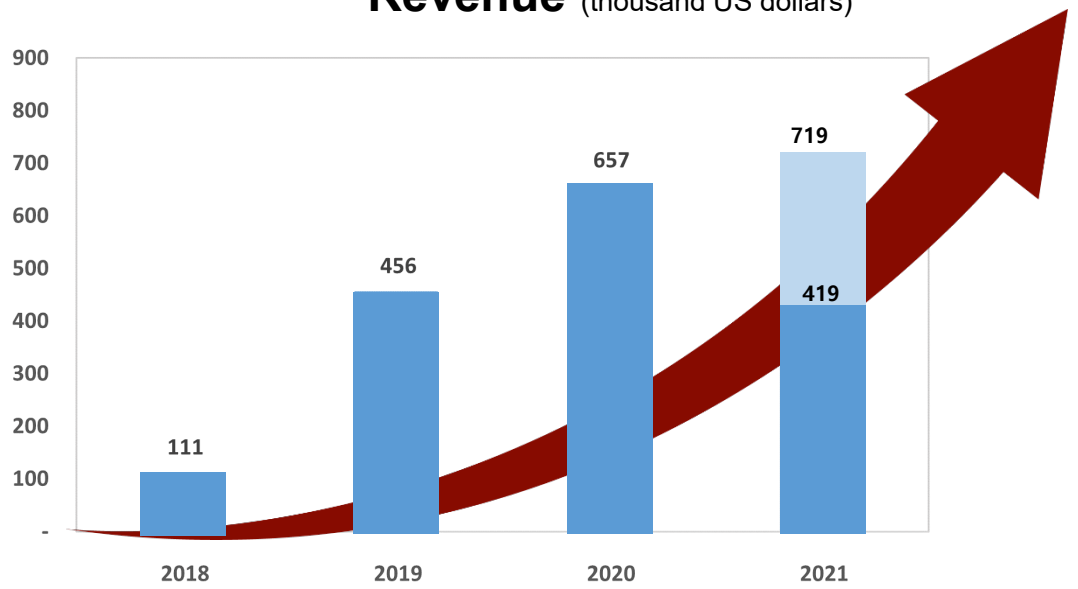
2020 (4)

- 연세대학교 의과대학 YONSEI UNIVERSITY COLLEGE OF MEDICINE
- AVENTI BIOTECHNOLOGY
- (주)라이조테크
- INNOVO THERAPEUTICS
- 가천의대길병원 Gachon University Gil Hospital

2021 (7)

- KBlueBio
- CELLTRION
- 주식회사 휴엔켐
- cellus Therapeutics and Diagnostics with us
- COWELL BIODIGM
- Pioneering research & Consulting Group PCG Biotech
- GENOME OPINION

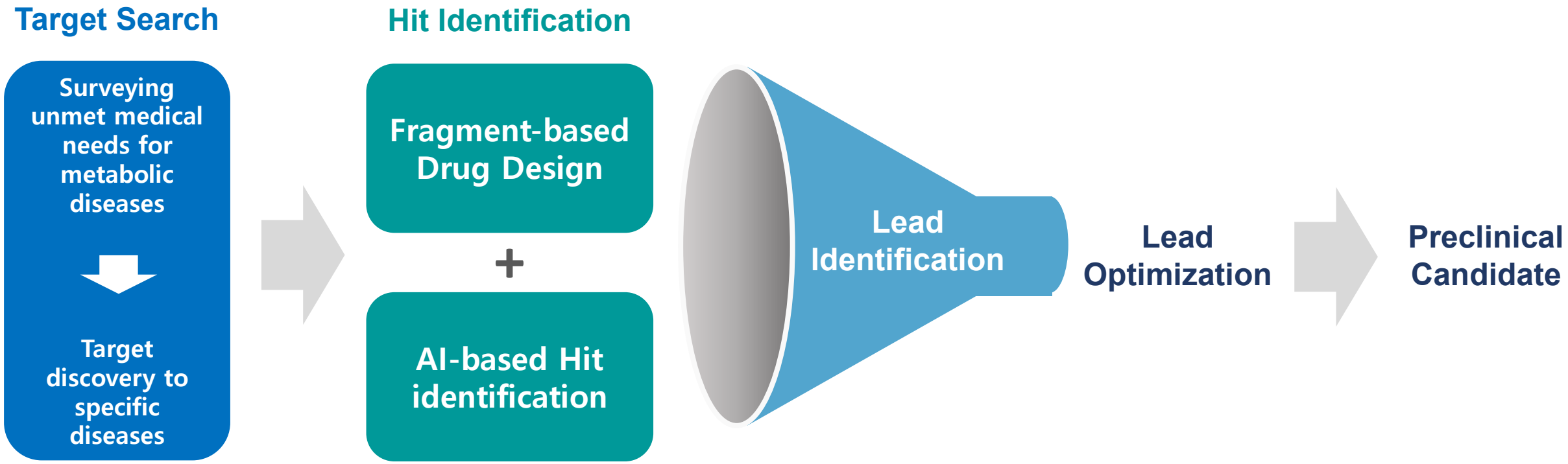
Revenue (thousand US dollars)



Expanding the drug pipeline

JD BIOSCIENCE

We are discovering novel therapeutics for metabolic diseases with unmet medical needs



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

THANK YOU

JD Bioscience

801ho, TJS knowledge industrial center 17-23, Cheomdangwagi-ro, 208 beon-gil, Buk-gu, Gwangju, South Korea

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