



GNI Group Ltd.

Financial Results for Q2 FY2025



# We Bring New Hope to Life.

# Agenda

## 1. Company Overview

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## 2. Financial Highlights

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## 3. Q2 FY2025 Segment

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## 4. Growth Strategy

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## 5. Financial forecast for FY2025

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## 6. Appendix

# 1. Company Overview

# Company Overview

## ■ Head Office

3rd Floor, Nihonbashi Honcho YS Building,  
2-2-2, Nihonbashi-Honcho  
Chuo-ku, Tokyo 103-0023

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## ■ Incorporation

November 2001

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## ■ Paid Capital

13,463 million yen (as of June 30, 2025)

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## ■ Listing

TSE Growth Market  
Listed in August 2007  
Securities code: 2160

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## ■ Main Business

Global pharmaceutical R&D,  
manufacturing and distribution,  
and biomaterials business

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## ■ Director, Representative Executive Officer, President, and CEO

Ying Luo Ph.D.

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## ■ Number of Employees (group-wide)

915 (as of June 30, 2025)

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## ■ Operating Countries

Japan, the People's Republic of China, USA,  
and Australia

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**Director, Representative Executive Officer,  
President, and CEO**

**Ying Luo Ph.D.**

To develop new treatments for unmet medical needs, we are leveraging the unique strengths of the pharmaceutical industries in Japan, the U.S., and the PRC, and pioneering a new, highly profitable business model.

He obtained a Ph.D. in Molecular Biology/Biomedical Sciences from the University of Connecticut Health Center in 1991. He has co-authored over 35 research studies and publications and is an inventor on over 16 patents during his 30+ years of biotech career.

Developed our Group's flagship product, Etuary (Pirfenidone), a treatment for pulmonary fibrosis, which was the first drug to be approved in the PRC as a Class 1.1 new drug. Additionally, F351 (Hydronidone), a potential treatment for liver fibrosis, was designated by the CDE as the first Breakthrough Therapy, underscoring our leadership in the research and development of innovative pharmaceuticals.

He was selected as one of the "Forbes China 100 most influential Chinese 2024".

# Major Pharmaceutical & Drug Discovery (Candidate)

## [Pharmaceutical]

**ETUARY®** (Generic name : Pirfenidone) Chinese : 艾思瑞、English : ETUARY®



- Treatment for idiopathic pulmonary fibrosis (IPF)
- Our Current Main Products

**CONTIVA** (Generic Name: Avatrombopag Maleate Hydrochloride) Chinese Name: 康曲欣®

- Launched in March 2025
- A treatment for liver diseases, showing synergy with F351 (for thrombocytopenia caused by chronic liver disease and chronic idiopathic thrombocytopenia).

**ETOREL** (Generic Name: nintedanib, ethanesulfonate soft capsules) Chinese Name: 伊妥瑞®

- Launched in June 2025
- Indicated for SSc-ILD and PF-ILD

## [Drug Discovery]

**F351** (Generic name : Hydronidone)

- A potential blockbuster drug candidate for liver fibrosis, for which no treatments currently exist  
(**May 23, 2025: Positive topline data from Phase 3 clinical trial announced**)
- Recognized as a '**Breakthrough Therapy**' by the China National Medical Products Administration in 2021
- Indicated for Hepatitis B and MASH<sup>#</sup> in the PRC and potentially MASH in the U.S.



**F528** (based on GNI's own view)

- A next-generation potential blockbuster drug candidate for chronic obstructive pulmonary disease (COPD)
- An estimated 100 million patients in China, yet no curative treatments currently exist

## Targeted Protein Degradation



- **Three Phase 1 clinical trials are currently underway: two in the PRC and one in Australia**
- Aiming to create new drugs by leveraging its proprietary targeted protein degradation platform, uSMITE™
- Gaining recognition from major pharmaceutical companies, including investment and board/advisor appointments from AstraZeneca, and licensing agreement with Astellas Pharma, highlighting the platform's high potential

<sup>#</sup>Metabolic Dysfunction Associated Steatotohepatitis



# Making the leap to a global pharmaceutical company through subsidiary listing strategy

Promoting the establishment to recruit high talents for a global management structure to achieve sustainable growth and maximize shareholder value, while mitigating CEO-centric management risks



**Pharmatech**

Promote the Group's value to western investors



**Biotech**

Accelerating the recruitment of talent and the global expansion of R&D initiatives in drug discovery

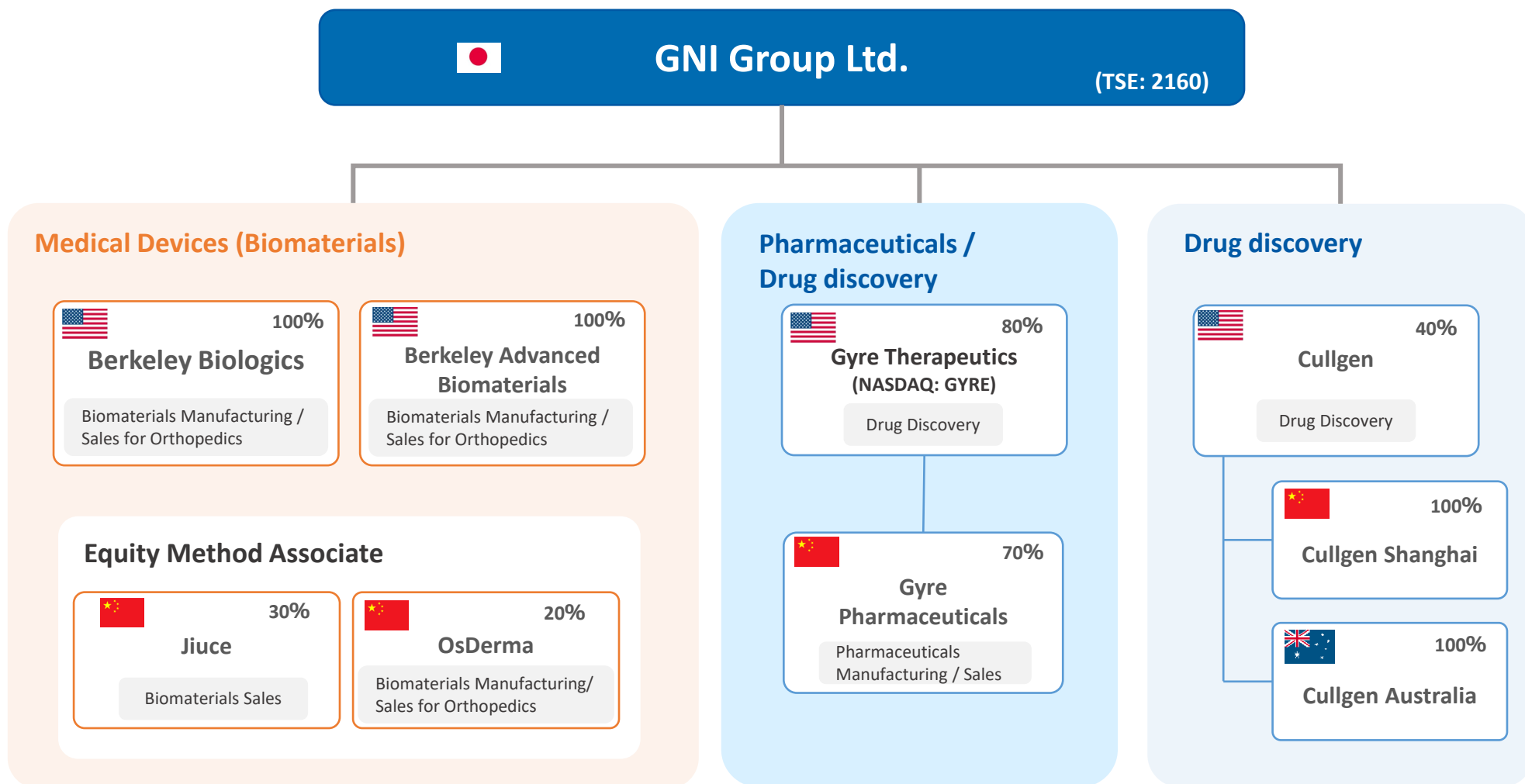


**Medtech**

Accelerating synergies through global expansion, including strategic partnerships



# Main Group Structure



Note: For ease of reference for shareholders, the group structure chart has been simplified. Certain group companies may not be included in the chart; this does not indicate priority for these companies has lowered.

## 2. Financial Highlights

# Consolidated income statement

Millions of yen	Q2 2024	Q2 2025	Inc. / (Dec.)	Factors for increase/decrease
Revenue	11,733	12,252	519	• Increase from the previous year due to record-high sales in the MedTech business
Gross profit	9,568	8,833	(735)	
SG&A	7,117	7,995	878	
R&D	1,419	1,596	177	
Operating profit	1,762	(1,179)	(2,941)	<ul style="list-style-type: none"> <li>• Decrease in the current period due to non-recurrence of reversal of gain from liquidation of doubtful allowance on the loan to GNI USA by approx. JPY 1.6 billion recorded in 2024 from the settlement (repayment) of loans.</li> <li>• Increase in expenses related to Cullgen (due to postponement of the listing)</li> <li>• Includes a loss of JPY 630 million from a forward contract on the Company's own shares recorded in Q1</li> </ul>
Income before income taxes	831	(1,433)	(2,264)	
Net profit	(73)	(2,342)	(2,269)	
Profit attributable to owners of the parent	330	(915)	(1,245)	

## Segment

In the “Others” segment, operating profit is reported due to the recognition of approximately JPY 6 billion in reversal of allowance for doubtful accounts related to the repayment of loans using GYRE shares received from GNI USA in 2024. (Since this is an intercompany transaction, the entire amount is eliminated in the consolidated financial statements, foreign exchange translation adjustments.)

Millions of yen	Pharmatech		Biotech		Medtech		Others	
	Q2 2024	Q2 2025	Q2 2024	Q2 2025	Q2 2024	Q2 2025	Q2 2024	Q2 2025
Revenue	7,844	7,171	754	480	2,509	3,992	633	604
Operating profit	2,399	1,622	(1,487)	(2,274)	707	773	3,060	(1,704)

Note: The performance of Gyre Therapeutics, Inc. is included in "Others."

The difference between the sum of each segment and the consolidated financial statements is due to consolidation adjustments.

# Segment result (cumulative total)

Millions of yen	Pharmatech		Biotech		Medtech		Others	
	Q2 2024	Q2 2025	Q2 2024	Q2 2025	Q2 2024	Q2 2025	Q2 2024	Q2 2025
Revenue	7,844	<b>7,171</b>	754	<b>480</b>	2,509	<b>3,992</b>	633	<b>604</b>
Operating profit	2,399	<b>1,622</b>	(1,487)	<b>(2,274)</b>	707	<b>773</b>	3,060	<b>(1,704)</b>



## Details of the “Other” Segment (for information on the three main business segments, see “3. Q2 FY2025 Segment”)

Segment	Number of companies included in the segment	Company	Explanation
Others	14	<ul style="list-style-type: none"> <li>GNI Group (Japan)</li> <li>Gyre Therapeutics (U.S.)</li> <li>Reef (PRC)</li> <li>Micren (Japan) etc..</li> </ul>	This segment comprises our company and the U.S. listed biopharmaceutical company Gyre Therapeutics, representing a portfolio of businesses engaged in strategic investments that support the foundation for future growth.

### Factors Affecting Operating Profit in Q2 2024

- An operating profit was recorded, primarily due to a reversal of approximately JPY 6.0 billion in allowance for doubtful accounts related to the repayment of a loan using GYRE shares received by GNI Group from GNI USA. (Since this is an intra-group transaction, the full amount is eliminated in the consolidated financial statements, excluding foreign exchange differences.)

### Factors Contributing to Operating Loss in Q2 2025

- Includes upfront investment expenses, such as R&D costs of Gyre Therapeutics (a U.S.-listed subsidiary).
- Operating loss widened due to a JPY 630 million loss recorded in Q1 2025 from a share repurchase transaction conducted by GNI Group.

Note: Any discrepancies between the summed values of each segment and the figures in the consolidated financial statements are due to consolidation adjustments.

# Consolidated Balance Sheet

Millions of yen	Q4 FY2023	Q4 FY2024	Q2 FY2025	Inc. / (Dec.)
<b>Total non-current Assets</b>	<b>33,475</b>	<b>42,720</b>	<b>40,300</b>	<b>(2,420)</b>
Goodwill	14,246	15,994	14,666	(1,328)
Intangible assets	8,852	11,026	11,268	242
<b>Total Current Assets</b>	<b>30,793</b>	<b>29,222</b>	<b>27,422</b>	<b>(1,800)</b>
Trade accounts receivable	3,973	6,236	5,673	(563)
Inventories	2,217	2,529	3,383	854
<b>Total Liabilities</b>	<b>27,764</b>	<b>32,229</b>	<b>29,408</b>	<b>(2,821)</b>
Total non-current Liabilities	19,571	19,764	19,003	(761)
Total current Liabilities	8,193	12,464	10,404	(2,060)
<b>Total Equity</b>	<b>36,504</b>	<b>39,713</b>	<b>38,313</b>	<b>(1,400)</b>
Capital and Other Components of Equity	20,434	19,887	22,322	2,435
Retained earnings	8,790	9,888	8,973	(915)
Other Components of Equity	4,569	6,669	3,973	(2,696)
Equity attributable to owners of the parent company to total assets	33,794	36,446	35,269	(1,177)
Non-controlling Interests	2,710	3,267	3,044	(223)

# Consolidated Balance Sheet/ Goodwill and Intangible Assets

Millions of yen	Major Breakdown	Q4 FY2023	Q4 FY2024	Q2 FY2025	Inc. / (Dec.)	Variance Factors
Goodwill		14,246	15,995	14,666	(1,329)	All changes in goodwill are due to exchange rate fluctuations.
	Gyre Pharmaceuticals	173	188	175	(13)	
	Gyre Therapeutics	7,080	7,616	6,969	(647)	
	Berkeley Advanced Biomaterials	6,701	6,653	6,090	(563)	
	Berkeley Biologics	1,175	1,230	1,126	(104)	
	Micren	271	271	271	0	
	GNI Hong Kong	31	35	32	(3)	
Intangible assets		8,852	11,026	11,268	242	
	Patent rights	0	202	178	(24)	
	Customer base	2,362	2,468	2,189	(279)	BBs' customer base (through partial acquisition of Orthobiologics business in 2023)
	Brand (PPA)	67	69	61	(8)	
	Capitalized development costs	6,383	8,038	7,944	(94)	
	Gyre Therapeutics	4,254	4,745	4,344	(401)	Rights to F351 held by Gyre Therapeutics (does not include actual development costs)
	Gyre Pharmaceuticals	2,128	3,293	3,600	307	R&D expenses for Gyre Pharmaceuticals after phase 3 (to be amortized over 10 years after launch of F351 in the PRC)

# Cash Flow

Millions of yen	Q2 FY2025	Note
<b>Cash Flow from Operating Activities</b>	(931)	<ul style="list-style-type: none"> <li>Although the pre-tax loss of JPY 1.43 billion had a significant impact, the deficit in cash flow narrowed due to factors such as a reduction in corporate tax expenses.</li> </ul>
<b>Cash Flow from Investment Activities</b>	632	<ul style="list-style-type: none"> <li>approx. JPY 740 million was spent to acquire intangible assets (Etoel: Nintedanib).</li> <li>Meanwhile, there was a return of Guarantee deposits by JPY 1.5 billion in connection with settlement of share price forward contract and Cash Flow from Investment Activities was resulted in positive. In total.</li> </ul>
<b>Cash Flow from Financial Activities</b>	1,409	<ul style="list-style-type: none"> <li>approx. JPY 3.29 billion was raised through a public offering conducted by Gyre Therapeutics in May 2025.</li> </ul>
<b>Net effect of exchange rates changes</b>	(700)	
<b>Net (decrease)/increase in cash and cash equivalents</b>	409	
<b>Cash and cash equivalent at beginning of year</b>	10,115	
<b>Cash and cash equivalents at end of year</b>	10,524	



# R&D expense

- The development costs related to Phase III and subsequent clinical trials meet the criteria for capitalization.
- The capitalization of F351's Phase 3 clinical trial conducted in China has been accounted for in accordance with accounting standards and tax regulations.
- Capitalized development costs decreased significantly year-on-year due to foreign exchange impacts and the reduction in F351 development expenses (top-line data from the Phase III trial was released on May 23, 2025).

Millions of yen	FY2022 Actual	FY2023 Actual	FY2024 Actual	Q2 2024	Q2 2025	Inc. / (Dec.)
<b>Consolidated R&amp;D expenses</b>	2,545	2,557	2,811	1,419	1,596	+12.5%
<b>Capitalized development costs</b>	606	940	1,165	568	(94)	—
<b>Total</b>	3,151	3,497	3,976	1,987	1,502	(24.4%)

# Forex sensitivity

## Exchange rate

	FY2023 Actual	FY2024 Actual	FY 2025	
			Forecast	Q2 Actual
USD/JPY	140.67	151.69	145.00	148.40
CNY/JPY	19.82	21.04	20.50	20.44

## Forex sensitivity

Foreign exchange fluctuations affect yen-converted figures, with only a limited impact on profit margins.

	Revenue	Operating profit
USD/JPY $\pm 1$ JPY	$\pm 60$ million yen	$\pm 149$ million yen
CNY/JPY $\pm 0.2$ CNY	$\pm 197$ million yen	$\pm 45$ million yen

## 4. Q1 FY2025 Segment

## Financial Results

Millions of yen	FY2021 Actual	FY2022 Actual	FY2023 Actual	FY2024 Actual	FY2024 (Quarterly)		FY2025 (Quarterly)		Q2 (Cumulative)			FY2025 Forecast
					Q1	Q2	Q1	Q2	2024	2025	Inc. / (Dec.)	
Revenue	9,868	13,346	15,742	15,847	3,982	3,862	3,315	3,856	7,844	7,171	(8.6%)	20,202
Operating profit	2,501	3,735	4,054	4,003	1,501	898	810	813	2,399	1,622	(32.4%)	4,640

## Financial Summary

Quarterly performance excluding foreign exchange effects shows revenue growth driven by the launch of new products.

Compared with the previous quarter (Q1), revenue increased by approx. JPY 500 million QoQ. Meanwhile, operating profit remained flat due to higher upfront investments in marketing and other activities associated with the launch of new products.

	Product (Generic Name)	Indication
Pulmonary disease	ETUARY® (Pirfenidone)	• Idiopathic Pulmonary Fibrosis (IPF)
	Launched in 2014. Current main products	
	Etozel (Nintedanib)	• Systemic sclerosis-associated interstitial lung disease • Chronic fibrosing interstitial lung diseases (progressive phenotype)
	Launched in June 2025. Complementary to Pulmonary fibrosis area	
Liver disease	Contiva (Abatrombopag)	• Thrombocytopenia due to chronic liver disease • Chronic idiopathic thrombocytopenia
	Launched in March 2025 Maximize synergies by securing a sales network for the future launch of F351	

Millions of yen	FY2025 Q2 Revenue	YoY Inc. / (Dec.)
JPY basis	3,856	(0.16%)
CNY basis	193	+ 8.6%

- Despite intensified competition, ETUARY achieved its quarterly budget.
- In Q2, the newly launched products Contiva (avatrombopag) and Etozel (nintedanib) recorded sales of JPY 226 million and JPY 242 million, respectively.
- Etozel (nintedanib) was launched in early June 2025 and is expected to contribute to future sales.

# **F351: Bring New Hope to Life, Powering a Brighter Future for CHB Patients.**

## F351: Bring New Hope to Life, Powering a Brighter Future for CHB Patients.



- 1 1992 Initial Nationwide Epidemiological Survey Conducted: HBsAg Positivity Rate — 9.72% (General Population)
- 2 2006 Second Nationwide Epidemiological Survey: HBsAg Positivity Rate — 7.18% (General Population)
- 3 2014 Third Nationwide Epidemiological Survey: HBsAg Positivity Rate — 2.60% (Limited to Under 29 Years Old)
- 4 2017 Hepatitis B Antiviral Drugs Included in the National Essential Medical Insurance Drug List
- 5 2020 Fourth Nationwide Epidemiological Survey: HBsAg Positivity Rate — 5.86% (General Population)
- 6 2021 F31 Designated as a Breakthrough Therapy
- 7 2022 **China Society of Hepatology (CSH) and Chinese Society of Infectious Diseases (CSID) Lowered the Antiviral Therapy Thresholds**
- 8 2023 The paper on F351 was selected as one of China's Top 10 Original Research Studies
- 9 2024 Gyre Pharmaceuticals was awarded the "Outstanding Innovative Enterprise" recognition by the Beijing Municipal Government.
- 10 2025 May Phase 3 Clinical Trial of F351, Designated as a Breakthrough Therapy, Completed
- 11 2025 June **Revision of the Pricing System for Breakthrough Therapies**

## F351: Bring New Hope to Life, Powering a Brighter Future for CHB Patients.

### Changes in Chronic Hepatitis B Prevention and Treatment Guidelines

The PRC has been working at the national level to address hepatitis B and regularly **revises the *Chronic Hepatitis B Prevention and Treatment Guidelines (Standard Treatments for Prevention and Treatment)***. Initially, the focus was placed on prevention through vaccination, but with the significant drop in new infections by 0.3%, the emphasis has shifted to the treatment and management of already infected patients.

**2005** – Initial guideline published: Antiviral therapy established as the basic policy for treatment, with initiation triggered by an ALT level increase.

**2022** – ALT threshold significantly relaxed; approximately 94% of chronic hepatitis B patients now meet the treatment criteria, strengthening early intervention to prevent cirrhosis and hepatocellular carcinoma.

**202X** – New drug approval for the treatment of HBV-induced liver fibrosis, inclusion in NRDL or commercial insurance.

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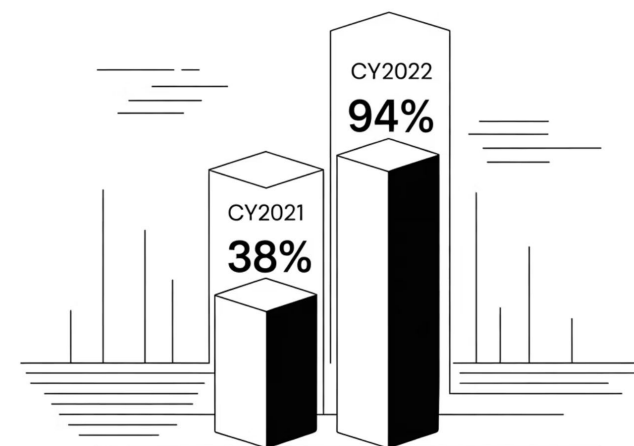
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**2010, 2015, 2019** – Continuous updates to treatment approaches in the revised guidelines.

**2024** – Guideline for prevention of mother-to-child transmission of HBV announced.

**202X** – Aim for early incorporation of HBV-related liver fibrosis treatment drugs into prevention and treatment guidelines.



**Healthcare accessibility**

The 2022 revision was particularly significant, as the ALT criteria were substantially relaxed. This change allowed approximately **94%** of chronic hepatitis B patients to meet treatment eligibility, enabling early therapeutic intervention to prevent cirrhosis and hepatocellular carcinoma. The policy shift also addressed the aging population of unvaccinated chronic patients, marking a pivotal step toward a preventive healthcare approach.

(based on GNI's own view)



## F351: Bring New Hope to Life, Powering a Brighter Future for CHB Patients.

### Revision of Chronic Hepatitis B Guidelines by the Chinese Society of Hepatology

#### Overview of Guideline Revision

The Chinese Society of Hepatology (CSH) and the Chinese Society of Infectious Diseases (CSID) issued the *Guidelines for the Prevention and Treatment of Chronic Hepatitis B*, significantly lowering the HBV DNA level threshold for initiating antiviral therapy to 10–20 IU/mL.

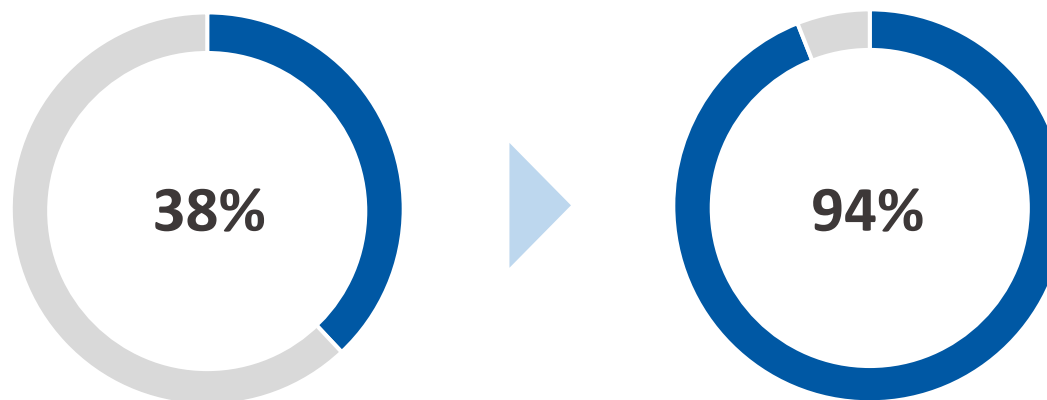
#### Expansion of Eligible Patients

As a result of this revision, the estimated proportion of chronic hepatitis B patients meeting treatment criteria increased to 94%, compared with 38% previously.

#### Impact on F351

Such changes in national strategy have become an important tailwind for innovative treatments like F351. As a therapy specialized for the treatment of CHB liver fibrosis, we expect F351 to bring new hope to an expanded pool of eligible patients.

### Proportion of Chronic Hepatitis B Patients Eligible for Treatment



Previous Guidelines:

Revised Guidelines:



## Favorable New Policies in China and Their Impact on F351

On [June 30, 2025](#), the Chinese government announced a comprehensive reform package to support pharmaceutical innovation. The reform adopts a groundbreaking “[Full-Chain Support](#)” approach, providing seamless assistance from research and development to approval, reimbursement, and clinical application.

One of the most significant advancements of this reform is the unprecedented coordination between the National Medical Products Administration (NMPA), which oversees regulation, and the National Healthcare Security Administration (NHSA), which manages reimbursement.

This collaboration is expected to greatly streamline the process from drug development to patient access.

## Departure from “across-the-board price cuts”:

## The dawn of a new era where pricing strategies can reflect the true value of medicines



### [Background]

The National Healthcare Security Administration (NHSA) has established a new “Commercial Health Insurance Innovative Drug List” (commonly referred to as the Category C List) in addition to the existing National Reimbursement Drug List (NRDL). The aim is to accelerate patient access to innovative medicines while boosting market vitality.

### [Challenges under the previous system]

Until now, even for breakthrough therapies, inclusion in the NRDL was virtually the only pathway to obtain public insurance coverage. As a result, pharmaceutical companies had no choice but to accept the drug price determined by the NRDL, significantly limiting their negotiating power.

### [Changes brought by the new system]

With the introduction of this new framework, pharmaceutical companies can now apply for insurance coverage under both the NRDL and the Category C List at the same time. This means that if the NRDL offers a price that fails to reflect development costs, companies can still negotiate while retaining the alternative of being listed under the Category C List.

### [Significance in conclusion]

In order to avoid losing promising new drugs from the list, the NRDL side is also less likely to unilaterally propose excessively low prices. As a result, this mechanism is considered to effectively enhance the negotiating power of pharmaceutical companies in drug pricing.

(based on GNI’s own view)

## Departure from “across-the-board price cuts”:

### The dawn of a new era where pricing strategies can reflect the true value of medicines

	National Reimbursement Drug List (NRDL)	Commercial Health Insurance Innovative Drug List (Category C)
<b>Funding Source</b>	National and Local Healthcare Insurance Funds (Public Funding)	Commercial Insurance Premiums and Out-of-Pocket Costs (Private Funding)
<b>Primary Goals</b>	Ensuring Broad Access and Affordable Pricing (Basic Coverage)	Providing Access to High-Value Innovations (Supplementary Coverage)
<b>Pricing</b>	Nationwide strict price negotiations (significant price reductions)	Negotiation with Insurers Based on Market Principles (Potential for Higher Drug Prices)
<b>Target Drugs</b>	Cost-effective medicines that meet “basic” needs	High-Value, Highly Innovative Medicines, and Orphan Drugs
<b>Corporate Strategy</b>	Low-margin, high-volume model: drastically lower prices to secure large sales volumes in a massive market	High-Value Model: Maintain premium pricing while focusing on specific patient segments or affluent markets.
<b>Patient Access</b>	Majority of the population can access it affordably.	Accessible only to a subset of patients covered by commercial insurance.
<b>Price</b>	<b>disclosed</b>	<b>Confidential</b>
<b>Overseas Expansion</b>	Due to China’s publicly disclosed low drug prices, there is a risk that countries with higher drug prices may set lower prices in reference. <b>The recent reforms introduce price confidentiality</b> , reducing the risk that China’s NRDL low official prices are referenced overseas and helping to preserve the global value of pharmaceuticals.	Price negotiations aligned with international markets, enabled by <b>confidential</b> drug pricing.

# The Culmination of a Decade of Policy Evolution

The series of reforms announced on June 30, 2025, represents the culmination of a decade of policy evolution since the groundbreaking CFDA reforms in 2015. Behind these policies lies the intent to cultivate globally competitive pharmaceutical companies.

## National Medical Products Administration (NMPA)

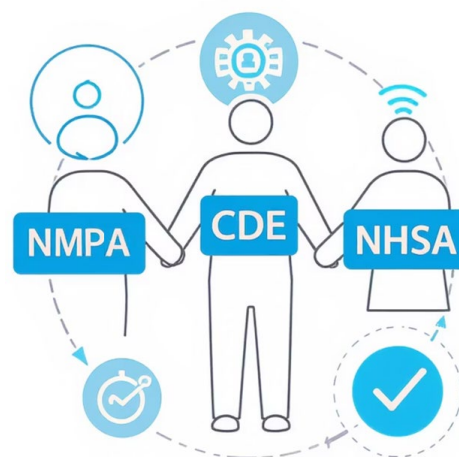
The successor organization to the former China Food and Drug Administration (CFDA), it serves as the top authority responsible for regulating the entire lifecycle of pharmaceuticals and medical devices.

## Center for Drug Evaluation (CDE)

The scientific arm of the NMPA, the Center for Drug Evaluation (CDE) specializes in the scientific review of clinical trial applications (IND) and marketing authorization applications (NDA). It also manages expedited programs, such as the 30-day review process.

## National Healthcare Security Administration (NHSA)

Established in 2018, the NHSA is a powerful agency that manages the national healthcare insurance funds and leads price negotiations and updates for the NRDL. It has also taken on responsibility for establishing the new commercial insurance list.



## Unprecedented Coordination Between the NMPA and NHSA:

Historically, the drug approval process and reimbursement process in China were disconnected. It often took several years for a drug approved by the NMPA to be listed for reimbursement by the NHSA, creating significant uncertainty and lost revenue opportunities for pharmaceutical companies.

**Integrated Agency Action:** While the NHSA establishes a new commercial insurance list for innovative medicines, the NMPA simultaneously accelerates the approval process for these drugs. Measures are jointly announced by the NHSA and the National Health Commission (NHC), and the commercial insurance list progresses in parallel with the NRDL, ensuring close alignment in both timing and policy content.

**Barrier Removal:** This whole-of-government approach eliminates obstacles between regulatory approval, reimbursement decisions, and hospital adoption, potentially impacting the entire value chain of pharmaceutical innovation.

## Hepatitis is the second most common cause of death from infectious disease in the world

### World Hepatitis Summit 9 April 2024

Estimated deaths from viral hepatitis will increase from 1.1 million to 1.3 million by 2022 (2019) 83% of which are hepatitis B

### Second most common cause of death from infectious diseases in the world

Tied with tuberculosis as leading cause of death from infectious diseases 13% of those with chronic hepatitis B infection have been diagnosed (as of the end of 2022)  
About 3% are on CHB therapy

### WHO: Global hepatitis report 2024

- People infected with B virus  
Global: 254 million  
China: 79.7 million
- Western Pacific Area (including China)  
Number of infected: 96.8 million  
Annual deaths: 518,000  
Chronic hepatitis B diagnosis rate: 25.5%  
Treatment rate after diagnosis: 23.2%  
Treatment rate for all hepatitis B infected: 5.9%

Source: [WHO sounds alarm on viral hepatitis infections claiming 3500 lives each day](#)  
[WHO: Global hepatitis report 2024](#)

## An estimated 60-79.7 million people in China are infected with hepatitis B virus

Stage	Description
1. HBV Infection	Infection with the hepatitis B virus. If the acute hepatitis does not resolve and becomes chronic, it is referred to as a persistent infection (HBV carrier). Infants are more prone to becoming carriers when infected.
2. Chronic Hepatitis B (CHB)	A condition in which the virus persists, causing ongoing inflammation in the liver. Liver function fluctuates depending on the virus's activity.
3. Liver Fibrosis	A condition in which the liver tissue becomes hard and <b>fibrotic</b> due to chronic inflammation. There are often no subjective symptoms in the early stages.
4. Liver Cirrhosis	Progression of <b>fibrosis</b> results in the loss of normal liver structure. Liver function declines significantly, and various complications may arise.
5. Hepatocellular Carcinoma (HCC)	It often occurs against a background of cirrhosis, but can also occur in conditions of chronic hepatitis and <b>liver fibrosis</b> . Regular screening is crucial for early detection.
6. Liver Transplant (if necessary)	One of the treatment options when liver function cannot be maintained due to end-stage cirrhosis or liver cancer progression.
(Note)	Not all individuals progress through this sequence. Some may remain in the asymptomatic carrier state for an extended period. Disease progression can be delayed with existing CHB therapies and other treatments.

Note: 60 million from GYRE Therapeutics estimated low range. 75 million from 2024 published national serological survey HBsAG 5.86% (n=91869), 79.7 million from 2024 WHO report on CHB



## F351: Bring New Hope to Life, Powering a Brighter Future for CHB Patients.

Due to changes in underlying assumptions, number of F351 patients has been changed from approximately 3 million into to a range of 3–7.5 million, raising the upper end of the range.

(based on GNI's own view)

### [Previous Estimate] Estimated Number of Patients: **approx. 3 million**

*Based on materials disclosed May 15, 2025*

Patients in the PRC with known HBV infection:	44,085,000	—
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F351, an anti-fibrotic agent, is planned to be used in combination with existing therapies

#### 3. Number of patients under treatment with known infection

Terms	Number of people	proportion
Off-label for CHB therapies	27,222,488	61.8%
Indicated for CHB therapies, not receiving treatment	9,222,582	20.9%
Indicated for CHB therapies, under treatment	7,639,931	17.3%

F351 for patients with F2 or higher

#### 4. Patients on treatment with an Ishak score of 2 or higher

Terms	Number of people	proportion
Ishak Less than 2	4,583,958	60.0%
Ishak 2 or higher*	3,055,972	40.0%

### [Updated Estimate] Estimated Number of Patients: **approx. 3 million – 7.5 million**

Patients in the PRC with known HBV infection:	44,085,000	—
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F351, an anti-fibrotic agent, is planned to be used in combination with existing therapies

#### 3. Number of patients under treatment with known infection

Terms	Number of people	proportion
Off-label for CHB therapies	2,645,100	6.0%
Indicated for CHB therapies, not receiving treatment	22,672,615	51.4%
Indicated for CHB therapies, under treatment	18,767,285	42.6%

F351 for patients with F2 or higher

#### 4. Patients on treatment with an Ishak score of 2 or higher

Terms	Number of people	proportion
Ishak Less than 2	11,260,371	60.0%
Ishak 2 or higher*	7,506,914	40.0%

Note: The estimated patient population was calculated by GNI Group (August 2025). This forecast is subject to change depending on variations in the underlying assumptions used in the estimation.

## F351: Bring New Hope to Life, Powering a Brighter Future for CHB Patients.

### Estimated number of patients for F351: approximately 7.5 million<sup>#</sup> (based on GNI's own view)

#### 1. Number of Hepatitis B Patients

Terms	Number of people	proportion
Population of China	1,411,100,000	-
Total number of HBV-positive persons	82,690,460	5.86%
Number of HBV-positive persons (exempted age deductions)	75,000,000	-9.30%

#### 2. Hepatitis B patients with or without awareness of infection

Terms	Number of people	proportion
No awareness of infection	30,915,000	41.22%
Aware of infection	44,085,000	58.78%

F351, an anti-fibrotic agent, is planned  
to be used in combination with existing  
therapies

#### 3. Number of patients under treatment with known infection

Terms	Number of people	proportion
Off-label for CHB therapies	2,645,100	6.0%
Indicated for CHB therapies, not receiving treatment	22,672,615	51.4%
Indicated for CHB therapies, under treatment	18,767,285	42.6%

F351 for patients with F2 or higher

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Terms	Number of people	proportion
Ishak Less than 2	11,260,371	60.0%
Ishak 2 or higher*	7,506,914	40.0%

#### Survey results: published in 2024

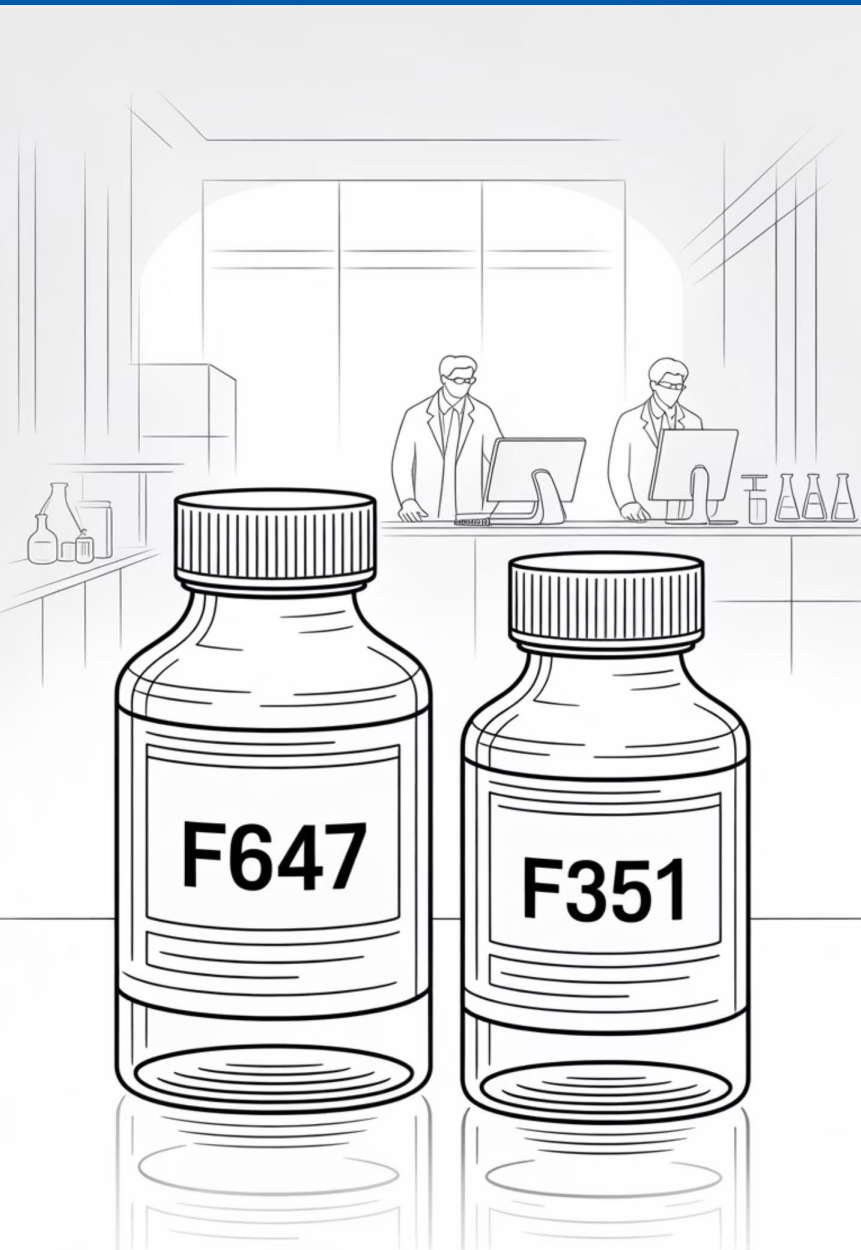
- Positive rate of recognized HBs antigen of infection estimated at **5.86%**
- Only about **58.78%** of participants aged 15 years and older recognized their infection status
- Of those who were aware of their own HBV infection status,
  - 38.25%** are indicated for CHB therapy
  - 17.33%** actually received CHB treatment

#### Tailwind from National Policy : 18 December 2022

The Chinese Society of Hepatology (CSH) and the Chinese Society of Infectious Diseases (CSID) have revised the *Guidelines for the Prevention and Treatment of Chronic Hepatitis B*, significantly lowering the threshold for initiating antiviral therapy to a detectable HBV DNA level (above 10–20 IU/mL). As a result of this revision, an estimated 94% of patients with chronic hepatitis B (previously 38.25%) now meet the treatment eligibility criteria.

Note: The estimated patient population was calculated by GNI Group (August 2025). This forecast is subject to change depending on variations in the underlying assumptions used in the estimation.

<sup>#</sup>Source : [Prevalence of hepatic steatosis, fibrosis and associated factors in chronic hepatitis B](#)  
Journal of Clinical and Translational Hepatology, "Hydronidone treatment for liver fibrosis associated with CHB"



## Shifts in the Era of New Drug Approval Applications

### Background: The Early Stage of China's New Drug Development Market

In the 2000s, “drug development” in China primarily referred to generic medicines, and the development of new drugs was not mainstream. At that time, the approval process for new drugs had not been fully established. There were no significant sources of funding for the pharmaceutical industry in China, such as venture funds, private equity, or banks. In light of this situation, and with the stock exchange’s initiative to attract Asian companies, we chose to list our company in Japan.

# 1. New Drug Application Process

## The Era of F647: An Opaque Process

One reason the process was opaque was the lack of experienced personnel on both the regulatory and company sides. Although the new drug application was submitted in November 2009, the actual review involved three stages: a preliminary review in Shanghai, a formal review in Shanghai, and a formal review in Beijing. Moreover, this was only a theoretical process, with no strict deadlines established.

## Current Status of F351

The review process is now systematized, with clearly defined timelines.

# Approval Process and Timelines for Breakthrough Therapies at China's NMPA

## Key Points: NMPA Review Period – 130 Working Days

China's National Medical Products Administration (NMPA) applies **Priority Review** to drugs designated as **Breakthrough Therapies**. Under this accelerated review, the **New Drug Application (NDA) review period is shortened to 130 working days**.

## Legal Basis

This acceleration measure is based on the following regulations:

**Regulation:** Provisions for Drug Registration

**Relevant Article:** Article 70

**Promulgation Date:** March 30, 2020

**Effective Date:** July 1, 2020

## Overview of the Breakthrough Therapy Designation System

### 1. Purpose:

To accelerate the development and review of drugs that demonstrate **significant clinical advantage over existing therapies** for serious diseases.

### 2. Benefits of Designation:

- **Priority Review:** Eligible drugs are subject to the shortened review period of **130 working days**.
- **Close Collaboration with CDE:** Sponsors can engage in **intensive communication and guidance** from the Center for Drug Evaluation (CDE), facilitating a smoother development process.
- **Conditional Approval Possibility:** Approval may be granted based on **early clinical data**, with the requirement to submit **additional post-marketing data**.

## 2. Insurance System

### **The Era of F647: Underdeveloped Insurance Reimbursement Process**

At the time F647 was approved, the process for obtaining insurance reimbursement for new drugs was not well defined. There was only unverified information suggesting updates would occur every five years, but in practice, this schedule was not followed. As a result, F647 (an IPF treatment) was included in insurance coverage only 7–8 years after its approval.



In 2020, the National Reimbursement Drug List (NRDL) was reformed, and a system for annual updates to the insurance coverage list was implemented. Furthermore, the major reform on June 30, 2025, is expected to further accelerate the determination of reimbursement prices.

### 3. Disease Awareness



#### **The Era of F647: Extremely low awareness**

At the time F647 was approved as a treatment for idiopathic pulmonary fibrosis (IPF), there were only nine physicians nationwide in China capable of accurately diagnosing IPF. In addition, there were no public or private patient organizations related to lung fibrosis.



#### **Current Status of F351: High public awareness as a widespread disease**

On the other hand, hepatitis B, the target indication for F351, is a widespread disease in China, and public awareness of the condition is relatively high. Antiviral treatments for hepatitis B are also well known. In addition, since traditional Chinese medicine is sometimes used to address liver fibrosis, there is a certain level of awareness that hepatitis B can lead to liver fibrosis.

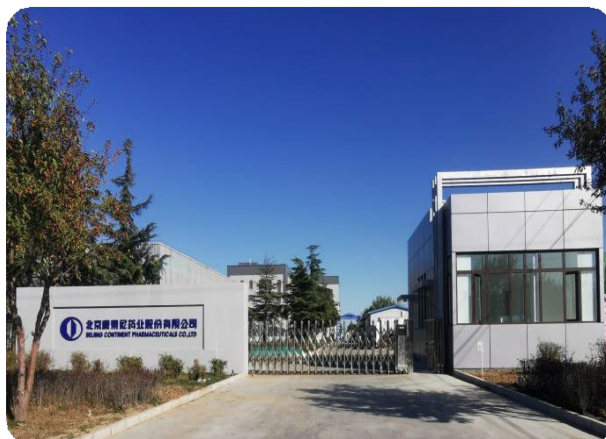
(based on GNI's own view)



**F351: Bring New Hope to Life,  
Powering a Brighter Future for CHB Patients.**



**Active Pharmaceutical Ingredient (API)  
Facility (Cangzhou)**



**Formulation / Finished Dosage Facility (Beijing)**

## 4. GMP-Certified Manufacturing Facilities

### **The Era of F647: Lack of Experience and Opaque Processes**

At that time, there were no GMP-certified facilities in China, and both companies and regulatory authorities had limited experience with GMP certification. As a result, the certification process and required timelines were unclear.

Although the new drug application was submitted in November 2009 and approval was granted in 2011, the manufacturing and marketing license was not issued until 2013.

### **Current Status of F351: Established Manufacturing Infrastructure**

Currently, two facilities are already operational for both capsule formulations and active pharmaceutical ingredient (API) production.

## 5. Sales Infrastructure

### **The Era of F647: Building the Infrastructure from Scratch**

At the time, F647 was recognized as China's "Class 1.1" new drug and formed alliances with nine major trading companies. However, due to the extremely low disease awareness, sales were sluggish, and it became necessary to spend time building an in-house sales force of around 400 medical representatives (MRs).

### **Current Status of F351: Leveraging an established sales network**

This time, we are able to leverage our already established sales network and set up a fully staffed sales infrastructure from the outset. In addition, Contiva, launched in March 2025 as a treatment for liver diseases, is being used to develop sales channels and marketing activities **ahead** of the full-scale market launch of CHB liver fibrosis F351.

## 6. Government-backed support

### **The Era of F647: Approval process without support**

Although F647 was a groundbreaking “Class 1.1” new drug, it took many years from the application to eventual approval.

### **Current Status of F351: Strong support from national policy**

F351 benefits from favorable national policies. In 2022, the treatment criteria for insured hepatitis B patients were significantly relaxed, improving patient access. Combined with the aforementioned healthcare insurance reforms, the environment for development and commercialization is highly supportive.

**POLICY**



# **F528: Bring New Hope to Life, Powering a Brighter Future for COPD Patients.**

## Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide

According to a WHO report

### The “Silent Killer”: Chronic Obstructive Pulmonary Disease (COPD)

According to the World Health Organization (WHO), there were 3.23 million deaths from COPD worldwide in 2019, making it the third leading cause of death globally. The 2019 estimates from the Global Burden of Disease Study indicate that approx. 391.9 million people aged 30–79 worldwide were living with COPD.

Major causes include smoking, air pollution, and exposure to dust and chemicals in the workplace. In particular, indoor air pollution is a significant factor in low - and middle-income countries.

### According to the WHO report, there are approx. 100 million COPD patients in China

According to the WHO, there are approximately 100 million people with chronic obstructive pulmonary disease (COPD) in China, accounting for about one-quarter of the global COPD population. This estimate is based on the large-scale survey “China Pulmonary Health Study”, conducted between 2012 and 2015.

COPD is one of the leading causes of death in China, with high smoking rates and air pollution identified as major risk factors.

## A massive market of 100 million driven by national policy — the next decade of growth starts here

### COPD (Chronic Obstructive Pulmonary Disease)

COPD is a disease in which the lung structure is irreversibly destroyed, leading to progressive shortness of breath.

Its main pathological features are:

1. **Narrowing of the airways due to inflammation and thickening of the bronchi,** and
2. **Destruction of the alveoli, which are responsible for oxygen exchange, resulting in a reduced gas exchange surface area.**

Underlying these changes is persistent inflammation, which further worsens the condition.

### One quarter of the world: the largest market in China (based on GNI's own view)

The number of estimated patients in China is about 100 million.

Due to 1. the aging of patients, which is increasing the prevalence rate, and 2. the Chinese government's infrastructure improvements, the market size for existing standard COPD treatments is projected to expand from an estimated 370 billion yen (2.5 billion USD) in 2021 to about 666 billion yen (4.5 billion USD) by 2030.

### Tailwind: Policy support from the Chinese government

In China, COPD is currently the fifth leading cause of death, representing a serious public health concern.

In response, the Chinese government has designated COPD countermeasures as a national priority under its "Healthy China 2030" plan, launching strong policy support.

Given the extremely low diagnosis rate of just 11%, improving early detection has become an urgent task. As part of its initiatives, the government has equipped over 50% of primary care institutions with diagnostic devices and provided specialized training to approximately 140,000 healthcare professionals between 2020 and 2023. Subsequently, free diagnostic services were also introduced.

These government-led measures are expected to promote early detection of undiagnosed patients and significantly expand the patient population seeking effective treatment.

A massive market of 100 million driven by national policy  
— the next decade of growth starts here

**GNI Group has the potential to bring about a groundbreaking paradigm shift in the global standard of care for COPD**

The current standard treatment for COPD (Chronic Obstructive Pulmonary Disease) focuses primarily on symptomatic therapy using long-acting bronchodilators (LAMA/LABA) and inhaled corticosteroids (ICS).

While these treatments aim mainly to maintain patients' quality of life (QOL), they face a serious limitation in that they do not provide a fundamental cure.

Although biologics have also been approved and adopted into standard care, they cannot repair the underlying lung tissue damage that drives disease progression. Moreover, their effectiveness is largely limited to the 20–40% subset of patients who present with Type 2 inflammation.

**As a result, the majority — 60–80% of patients with non-Type 2 inflammation — still have very few therapeutic options available.**

F528, however, has the potential to address all of these root causes, making it a groundbreaking therapeutic candidate. GNI Group places high expectations on its potential to transform COPD treatment.



A massive market of 100 million driven by national policy  
— the next decade of growth starts here

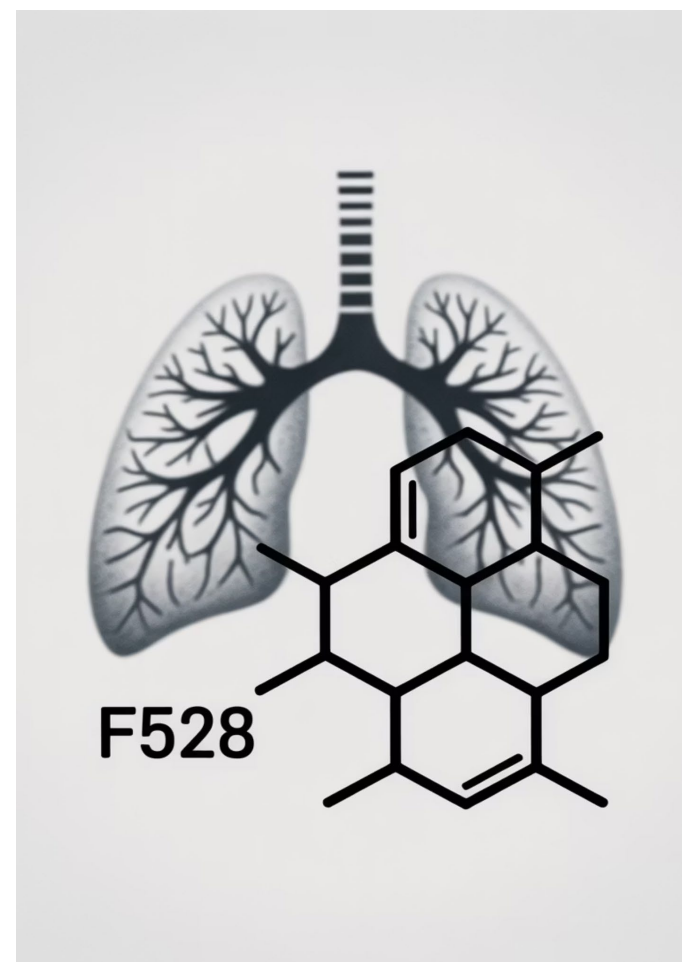
## Features and Mechanism of Action of F528

The majority of COPD patients (60–80%) exhibit non-type 2 inflammation (neutrophilic inflammation), which is resistant to existing steroid therapies and for which effective treatment options remain limited.

F528 is designed to directly target the root cause of this steroid resistance. As a macrolide-based agent without antibacterial activity, it avoids the issue of drug resistance and can be used long-term for chronic disease management.

Its primary pharmacological action is the inhibition of the NF- $\kappa$ B signaling pathway, a transcription factor central to the inflammatory response. NF- $\kappa$ B acts as a “master regulator,” orchestrating multiple inflammatory processes that drive COPD pathogenesis, including cytokine production and expression of cell adhesion molecules.

By suppressing this pathway, F528 has the potential to halt the fundamental inflammatory cascade underlying the disease.



(based on GNI's own view)



A massive market of 100 million driven by national policy  
— the next decade of growth starts here

## Shifting COPD Treatment from Symptom Management to Root-Cause Therapy F528 Targets True Disease-Modifying Effects

(based on GNI's own view)

In studies using COPD model mice treated with F528, the following efficacies were observed:

### Potent suppression of lung inflammation

The number of inflammatory cells and the levels of pro-inflammatory cytokines in bronchoalveolar lavage fluid (BALF) were **significantly** reduced.

### The structural damage of the lungs was inhibited

The increase in mean linear intercept (MLI), an index of alveolar destruction, was **significantly** suppressed, and the expression of tissue-destroying enzymes (MMP-2 and MMP-9) was also reduced.

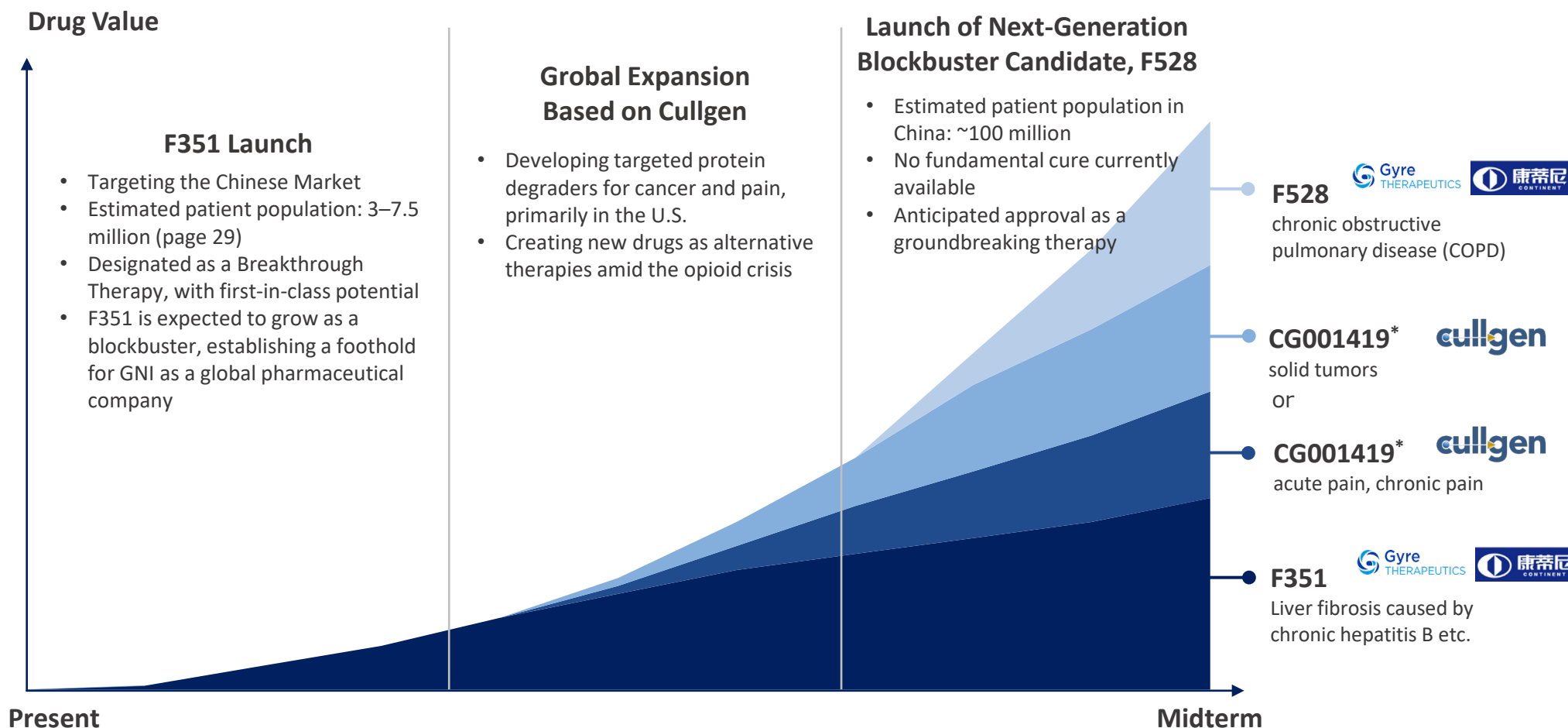
These results strongly suggest that F528 not only suppresses inflammation but also inhibits the progression of emphysema and **protects** lung function. This indicates a significant potential for F528 to act as a disease-modifying drug, capable of intervening in the irreversible structural destruction (remodeling) of the lungs caused by COPD.

Unlike existing therapies, which primarily focus on symptom relief, if F528 can demonstrate in future clinical trials a reduction in the annual decline of FEV1 or suppression of emphysema progression on CT imaging, it would mark a historic milestone in COPD treatment and support its approval as a breakthrough therapy aligned with national health policy.

**A major drug candidate aligned is set to launch in early 2026**

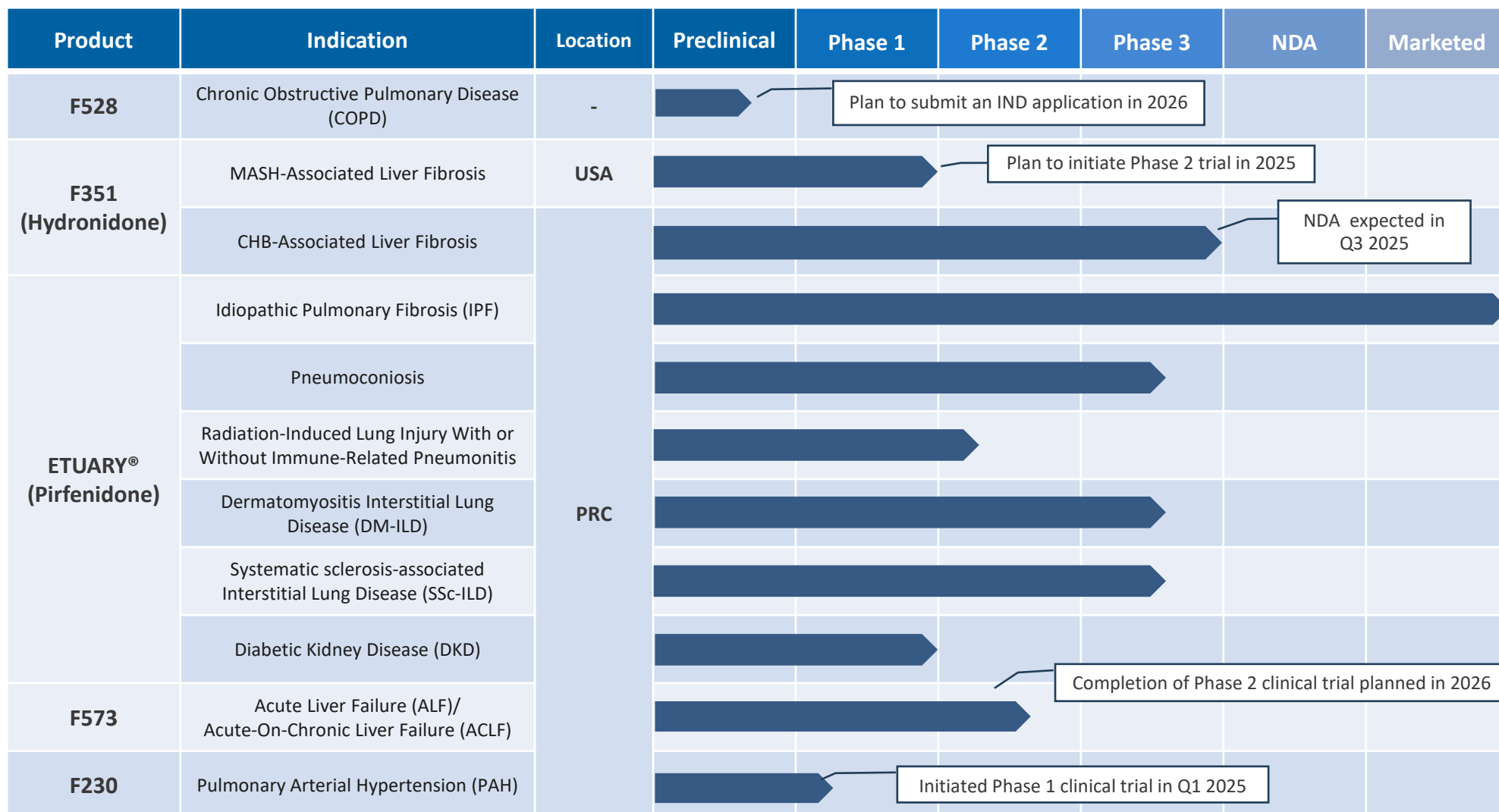
# GNI Group Growth Vision through In-House Development Pipeline

**Sustainable Growth Through the Development of Multiple Blockbuster Candidates** (based on GNI's own view)



\*This illustration conceptually represents the potential drug value of products developed within our group and does not indicate the order or timing of development progress.

# [Pharmatech] Development Pipeline



# [Biotech]

Millions of yen	FY2021 Actual	FY2022 Actual	FY2023 Actual	FY2024 Actual	FY2024 (Quarterly)		FY2025 (Quarterly)		Q2 (Cumulative)			FY2025 Forecast
					Q1	Q2	Q1	Q2	2024	2025	Inc. / (Dec.)	
Revenue	0	0	5,805	1,439	401	353	353	127	754	480	(36.3)%	955
Operating profit	(1,920)	(2,794)	2,374	(3,371)	(744)	(743)	(1,138)	(1,136)	(1,487)	(2,274)	—	3,982

## Outlook for this fiscal year (based on GNI's own view)

- Cullgen's listing is still waiting for approval. Will become equity income method company from consolidated subsidiary
- Although the operating loss is expected to widen due to drug discovery activities, unpaid interest under the preferred share agreement will be converted into profit upon the listing, and operating profit is still expected to remain positive.

Program and Description	Discovery	IND Enabling	Phase 1a	Phase 1b/2	Future Milestone
Degrader   TRK <b>CG001419</b> Acute and Chronic Pain					1. Phase 1a clinical trials are underway in Australia, with Phase 1 results expected to be reported in Q4 2025
Degrader   TRK <b>CG001419</b> Solid Tumors					2. Expanded capacity study for solid tumors to begin in Q3 2025
Degrader   GSPT1 <b>CG009301</b> Leukemia and MYC+ cancers	★ Non-enzyme target				3. Phase 1 trials for advanced hematopoietic malignancies (blood cancer, leukemia, etc.) began in April 2025
DAC   Epigenetic Factor <b>Undisclosed Target</b> Prostate, lung & bladder cancers	Degrader-antibody conjugate (DAC)				
Degrader   Cell cycle protein <b>Undisclosed Target</b> Breast cancer and multiple solid tumors	Utilizing proprietary Cullgen E3 ligands				

Partnered with astellas

# [Biotech] Reverse Merger Transaction

## ■ The process for listing on Nasdaq is awaiting response (based on GNI's own view)

- One of the listing conditions — approval of the proposal at Pulmatrix's shareholders' meeting — was achieved on June 16, 2025, completing the reverse merger transaction.
- The remaining condition, approval of the transaction by the CSRC (China Securities Regulatory Commission), is still under review.
- From the quarter following the listing, the company will reclassify Cullgen from a consolidated subsidiary into an equity-method affiliate.

## ■ Assumed listing gain at the end of the transaction

### 1. Accrued interest (one-time earnings accrued at listing)

Accrued interest expense of 10% per annum under the preferred stock agreement is recorded every period. The due amount will be pardon upon listing. Previously booked interest expenses will be reverted back as operating income under IFRS rules.

- |   |                   |
|---|-------------------|
| • November 13, 2024 (at the time of listing announcement) | JPY 3,995 million |
| • As of the end of June 2025                              | JPY 4,960 million |

### 2. Listing valuation gains

#### (one-time gains accrued at the time of listing)

Gain on valuation of shares arising from conversion of preferred shares to common shares and valuation at market value. Recorded as other income (within operating income) at the time of listing. → Included in "Other segment"

- |   |                    |
|---|--------------------|
| • November 13, 2024 (at the time of listing announcement) | JPY 10,768 million |
| • As of August 13, 2025 (reference value)                 | JPY 19,249 million |

## [Biotech] Cullgen's Challenge

# Cullgen's Challenge: Creating Next-Generation Medicines with uSMITE™ Technology

Cullgen is a clinical-stage biopharmaceutical company specializing in the innovative drug discovery approach known as targeted protein degradation (TPD). At the core of its research and development is the company's proprietary platform technology, uSMITE™ (ubiquitin-mediated, small molecule-induced target elimination).

The uSMITE™ platform is designed to efficiently generate potential first-in-class drug candidates for diseases that have historically been difficult to target through conventional drug discovery.

In general, the probability of a new drug obtaining regulatory approval is extremely low, and the process requires more than ten years and substantial financial investment; as a result, business plans in this field are inherently subject to a high degree of uncertainty.

### Technical Risks

In particular, novel technologies such as targeted protein degradation may face unforeseen challenges, including unexpected side effects or unanticipated regulatory hurdles.

### Financial Risks

Continuous fundraising to support this lengthy and challenging development process carries the risk of equity dilution.

### Competitive Risks

The presence of intense competition, including from major pharmaceutical companies, is also a significant factor that can influence the future value of the project.

# [Biotech] Cullgen's Challenge

## Drugs developed using the uSMITE™ platform act as a bridge

The core of this technology lies in harnessing the cell's natural protein degradation system, the **Ubiquitin-Proteasome System (UPS)**, to work in its favor.

### Target Capture

One end of the molecule binds specifically to the disease-causing target protein.



### Induces the degradation system

The other end binds to an enzyme called E3 ubiquitin ligase, which plays a role in tagging proteins for degradation inside the cell.

Through this "bridging," the target protein is tagged with ubiquitin, a marker for degradation. The proteasome— the cell's "processing factory" that recognizes this tag— then degrades and removes the target protein.

# [Biotech] Cullgen's Challenge

## Innovative Drug Discovery Enabled by uSMITE™

This innovative approach holds the potential to overcome challenges associated with conventional drugs, such as inhibitors.

### Tackling “Undruggable” Targets

Proteins that are not affected by conventional drugs can also be targeted for degradation.

### Overcoming Drug Resistance

Even if mutations occur in proteins that allow them to evade drugs, continued effectiveness is expected because the entire protein is removed.

### High Specificity and Safety

Because it can be designed to precisely degrade only the targeted protein, a clean pharmacological effect with fewer side effects can be expected.

### Superior Drug Characteristics

Using this platform, Cullgen aims to create compounds with high potency and selectivity that are also suitable for oral administration.



## [Biotech] Cullgen's Challenge

### **Cullgen's Novel Drug Candidate Compound (Development Code: CG001419)**

CG001419 is a first-in-class, orally available drug candidate compound created by Cullgen using its proprietary targeted protein degradation platform, uSMITE™.

This compound entered a Phase 1 clinical trial for pain as the indication on January 22, 2025, and a Phase 1/2 clinical trial for cancer as the indication on July 31, 2023. These two clinical trials are being conducted in parallel, aiming for practical application in two different disease areas.

# [Biotech] Cullgen's Challenge

## Pain relief through a novel approach distinct from existing drugs

### There are problems, but no alternative treatments are available

Current pain treatments face issues such as dependency and constipation with opioid analgesics, and gastrointestinal and cardiovascular risks with non-steroidal anti-inflammatory drugs (NSAIDs). CG001419 is being developed to address the high unmet medical need for therapies that are neither opioid-based nor NSAIDs.

#### Mechanism of Action of CG001419

CG001419 **selectively degrades and eliminates** Tropomyosin Receptor Kinase (TRK) proteins (TRKA, TRKB, TRKC), which play a crucial role in pain transmission. The TRK family of receptors is important for nerve growth, survival, and the induction and maintenance of pain hypersensitivity.

#### Differences from Conventional Drugs

Unlike conventional inhibitors, which block protein activity, CG001419 degrades the causative proteins themselves, offering a more comprehensive and sustained blockade of pain signaling.

#### Development Challenges

The success of development depends on overcoming known adverse events associated with targeting TRK—such as weight gain, dizziness, and withdrawal pain after treatment discontinuation—and demonstrating a favorable efficacy and safety profile.

(based on GNI's own view)

## [Biotech] Cullgen's Challenge

# The Vast Pain Market and Expectations for New Treatment Options

### Massive Market Size

The global pain management drug market is a massive industry, valued at over USD 60 to 80 billion as of 2024 according to multiple research firms. The fact that opioids and NSAIDs still dominate the majority of this market highlights low treatment satisfaction and significant unmet medical needs.

### Promising Target Market

Among them, **the neuropathic pain market** is showing particularly strong growth, projected to double from approximately USD 8 billion (about JPY 1.2 trillion) in 2024 to over USD 16 billion (about JPY 2.4 trillion) by 2034. Since TRK proteins are deeply involved in this condition, if CG001419 demonstrates efficacy, it could secure a highly advantageous position in the market.

(based on GNI's own view)

# [Biotech] Cullgen's Challenge

## Clinical Trial Status

July 31, 2023

### Initiation of Clinical Trial in the Oncology Field (China)

An adaptive Phase 1/2 clinical trial targeting patients with advanced or metastatic solid tumors harboring NTRK fusion genes was initiated in China. The early safety and pharmacokinetic (PK) data obtained from this oncology trial are expected to be leveraged in the design and advancement of clinical trials in the pain field.

### Future Outlook

In general, there are cases where results from Phase 1 trials conducted in Australia are used to initiate Phase 2 trials in the United States. Notably, Cullgen is targeting both acute and chronic pain.

1

2

3

January 22, 2025

### Initiation of Clinical Trial for Pain Treatment (Australia)

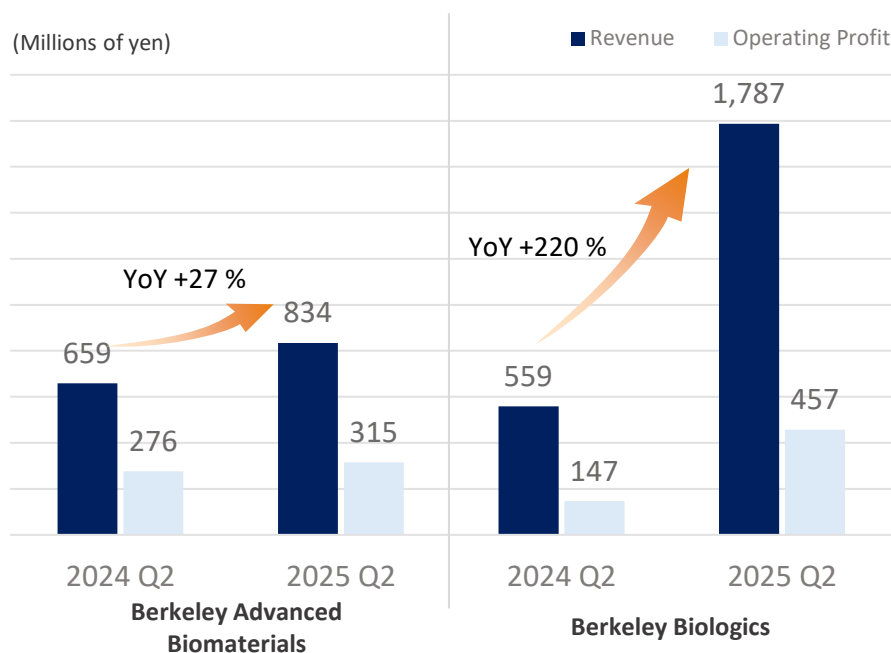
A Phase 1 clinical trial involving healthy adults was initiated in Australia. This randomized, placebo-controlled, double-blind comparative study aims to evaluate safety, tolerability, and pharmacokinetics. If favorable safety is confirmed in this Phase 1 trial, it is expected to progress to a Phase 2 trial targeting patients with specific types of pain.

# Medtech

Millions of yen	FY2021 Actual	FY2022 Actual	FY2023 Actual	FY2024 Actual	FY2024 (Quarterly)		FY2025 (Quarterly)		Q2 (Cumulative)			FY2025 Forecast
					Q1	Q2	Q1	Q2	2024	2025	Inc. / (Dec.)	
Revenue	1,795	2,428	2,841	5,189	1,290	1,220	1,370	2,621	2,509	3,992	+59.1%	6,159
Operating profit	844	1,110	1,133	942	283	424	245	528	707	773	+9.3%	1,269

## Outlook for this fiscal year

Record-high revenue achieved / No change in outlook for record-high revenue in the Medtech business.



- FDA review process is underway for the launch of the new product Accelagen. Approval is expected in the second half of the year, with potential for revenue recognition.
- This will be the first collagen product outside of bone applications, with potential to become a key product.



- Achieved sales twice the budget, benefiting from a large new order.
- Additional orders from new major customers acquired this fiscal year are expected to maintain stable revenue in the second half, similar to the first half.

# [Medtech] Expansion into Osderma and Medical Aesthetics Market



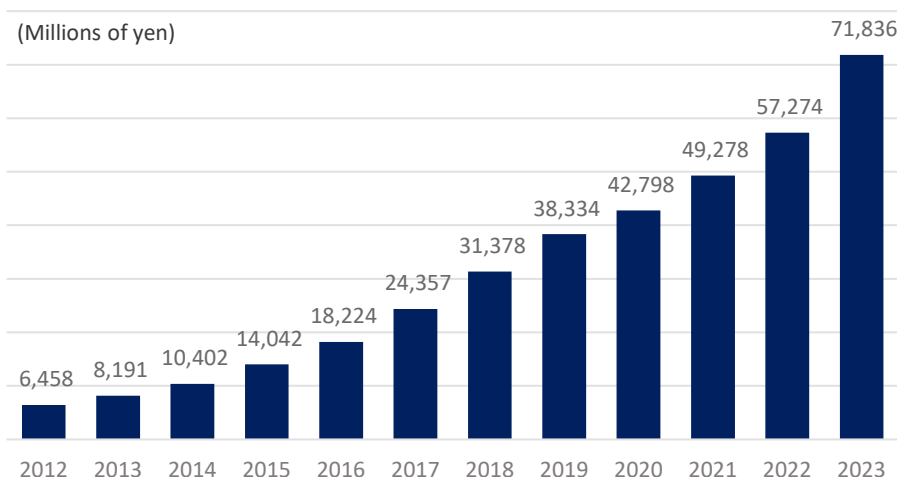
## GNI Group's Business Platform Synergies to be Realized

### Expand market share in the high-end cosmetic medicine market and establish a brand

Osderma's DermiraCa®

- Highly biocompatible and biodegradable product containing hydroxyapatite (HAp), a major component of bones and teeth
- Promotes tissue repair and collagen regeneration, with proven safety and efficacy in clinical trials
- Both immediate and sustained regenerative effects

#### Medical Aesthetics Market Size in the PRC 2012-2023#



### Competitive advantage over peers

Tighter regulations on off-label use in the cosmetic surgery field is a tailwind for the company.

#### 1. Synergies with Medtech Group

- Proof of competitive functional materials
- Integrated production from raw materials to manufacturing, including in-house development of manufacturing facilities, enables high profit margins

#### 2. Synergies with Drug Discovery Group business

- While other companies in the industry have limited experience in clinical trials, we have extensive experience
- Authoritative investigators and hospitals Established network

#### 3. Capital strength of the group

- Other companies need to raise funds for clinical trials

### State of Progress

#### April 18, 2025

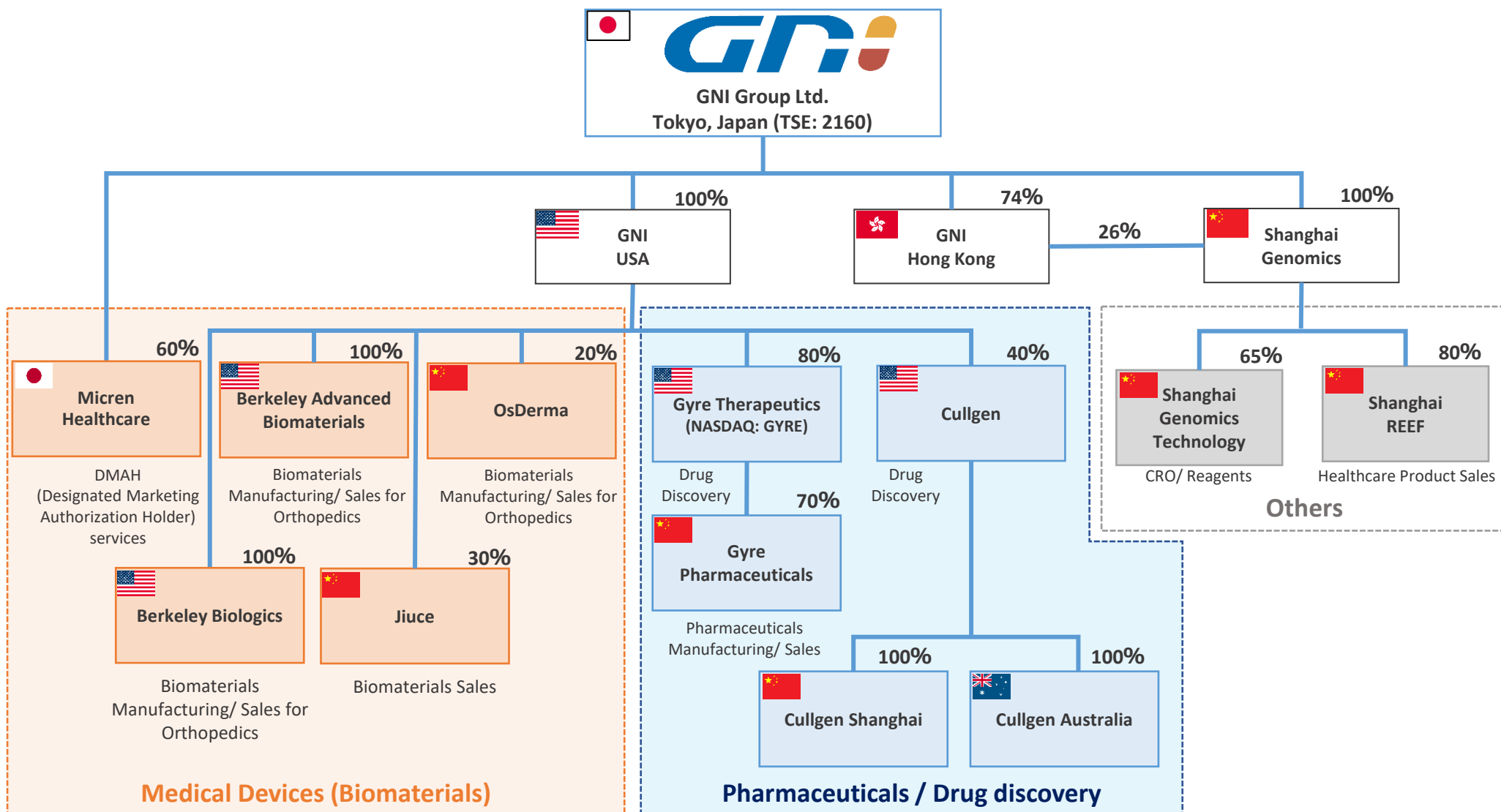
First subject enrollment completed in a multicenter clinical trial led by Professor Luo Shengkang, a renowned domestic plastic surgery expert, in collaboration with six prestigious medical institutions, including Beijing Cooperative Medical Center.

Note: OsDerma Medical, Inc. is accounted for under the equity method, with our company holding a 20% ownership interest.

# Source: iResearch (converted to JPY by GNI Group)

## 4. Growth Strategy

# Group structure





# New Share Issuance Project through International Offering

**In July 2025, GNI Group conducted its largest-ever fundraising since its IPO.**

Amount Raised (JPY)

**12.59<sub>bn</sub>**

Dilution Rate

**9.98%**

Discount Rate

**7.5%**

## Purpose / Use of Funds

- Aiming to become a global pharmaceutical company and enhance recognition among global institutional investors with strong expertise in healthcare
- Sustainable profit growth for GNI and the Group as a whole

Breakdown of Use of Funds	Amount (Ratio)	Deadline
<b>1. Direct Acquisition of Shares in Gyre Pharmaceuticals</b>	<b>JPY 4.86 billion (40%)</b>	<b>End of December 2026</b>
By acquiring shares held by minority (non-controlling) shareholders ahead of the launch of F351, the Company aims to suppress future profit outflows and maximize the corporate value of the Group as a whole.		
<b>2. M&amp;A</b>	<b>JPY 6.07 billion (50%)</b>	<b>End of December 2027</b>
Acquire domestic and international companies engaged in the medical device business to expand the revenue base		
<b>3. Loans and Investments to Group Companies</b>	<b>JPY 1.21 billion (10%)</b>	<b>End of December 2026</b>
Provide investment capital to support further growth of the rapidly expanding medical device business.		

# Background for Choosing an International Offering

## ■ Current Situation of Japan's Biotech / Pharmaceutical Industry and the Advantages of Overseas Markets

As indicated in reports such as the Ministry of Economy, Trade and Industry's "[Innovation Report 2.0](#)," Japan's biotech and pharmaceutical companies face the following challenges in fundraising.

The Company chose an international offering to overcome these challenges and obtain an appropriate corporate valuation.

### Issue in the Domestic Market

Japan's biotech and pharmaceutical market still has few success stories, resulting in a limited number of specialized biotech indexes and investors. Consequently, it is often difficult to secure large-scale financing.

As a result, financing methods such as new warrants (with downward revision clauses for exercise prices, e.g., MS warrants) — which can easily result in unfavorable conditions for issuers and existing shareholders — have become mainstream.

### Advantages of Overseas Markets

In contrast, overseas markets have a deep pool of specialized institutional investors who understand the risks and growth potential of biotech and pharmaceutical businesses.

Aiming to become a global pharmaceutical company, and based on the above context, the Company appointed Jefferies LLC, which has world-class experience in biotech and healthcare fundraising, together with SMBC Nikko Securities, which has a top-class track record in Japan in the same field, as joint bookrunners for this offering.

## Use of Funds: 1. Direct Acquisition of Shares in Gyre Pharmaceuticals

■ Additional acquisition of a minority interest in the core subsidiary responsible for the manufacturing and marketing of new drugs

**F351, regarded by our company as a major new drug candidate for the treatment of hepatitis B–related liver fibrosis, is expected to have a substantial impact on the GNI Group’s earnings upon receiving marketing authorization.**



We plan to submit a New Drug Application (NDA) for F351, our drug candidate for the treatment of liver fibrosis, within this year. GP operates a high value-added business model, handling the entire process from active pharmaceutical ingredient and tablet manufacturing to sales and marketing. A current challenge is that approximately 30% of GP’s shares are held by external shareholders, meaning that a proportional share of future profits will flow outside the GNI Group. To address this, we are in negotiations to potentially acquire additional shares of GP before its corporate value increases following the launch of F351.

### Forward-Looking Statements Disclaimer

Statements in this material referring to a “major new drug” or indicating that “the Group’s revenues will be significantly impacted” are based on the Company’s forecasts and expectations at the time of preparation. Such statements do not constitute a guarantee, promise, or assurance that the product will become a blockbuster (sales of USD 1 billion, approximately JPY 150 billion). Actual results may differ from the Company’s expectations due to numerous uncertain factors, including future marketing and educational activities, awareness among physicians and patients, insurance coverage or pricing, and the presence or effectiveness of anticipated government support measures in China.

# Use of Funds: 1. Direct Acquisition of Shares in Gyre Pharmaceuticals

**Additional acquisition of a minority interest in the core subsidiary responsible for the manufacturing and marketing of new drugs**

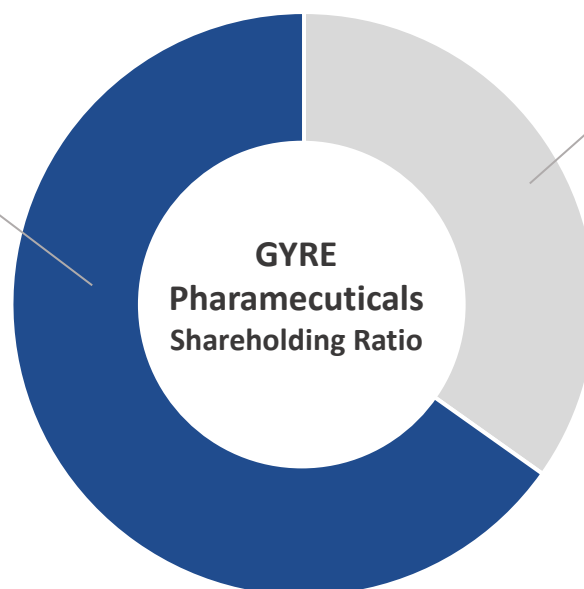
## Shareholding Structure of GP (at the time of this fundraising announcement)



**65.18%**

Owned by Gyre Therapeutics ("GT"), one of consolidated subsidiaries.

- 65.18% of GP's corporate value is represented by GT, which is listed on NASDAQ. This listing serves as one of the reference points for acquiring minority shares in GP.



Minority Shareholders (Non-controlling Interests)

**34.82%**

Owned by shareholders outside the GNI Group.

- After the launch of F351, 34.82% of GP's profits would be attributable to these minority shareholders (profit outflow outside the Group).
- To suppress future profit outflows and maximize the corporate value of the Group, **JPY 4.86 billion from the funds raised will be allocated to acquiring part of GP's shares.**

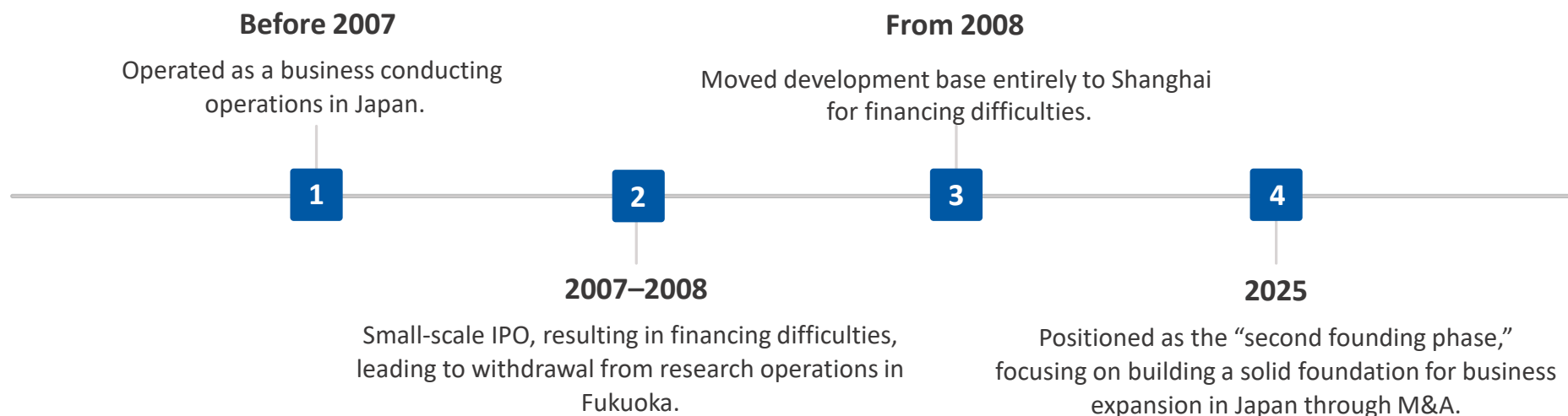
### August 2025 (after the fundraising announcement):

Prior to the fundraising, GT used its own funds to acquire additional shares in GP, **increasing its stake in GP from 65.18% to 69.72% (+4.54%).**

## Use of Funds: 2. M&A

### The “Essential Piece” in the GNI Group’s Business Model

Positioning 2025 as the “Second Founding Period” following the public offering fundraising in 2007, the Company will embark on establishing a solid foundation for business expansion in Japan through M&A.



### Future M&A Policy

The targets for M&A are primarily selected based on the following three criteria

Businesses that generate cash flow and can serve as a foundation for our operations in Japan.

Businesses that can generate synergies with our U.S. or China-based subsidiaries responsible for medical device operations.

A company expected to be delisted for failing to reach the new benchmark of a market capitalization of ¥10 billion within five years of listing, but with potential for synergies.

GNI Group was listed on August 31, 2007. Five years later, its market capitalization was ¥9.97 billion yen.

## New Share Issuance Project through International Offering

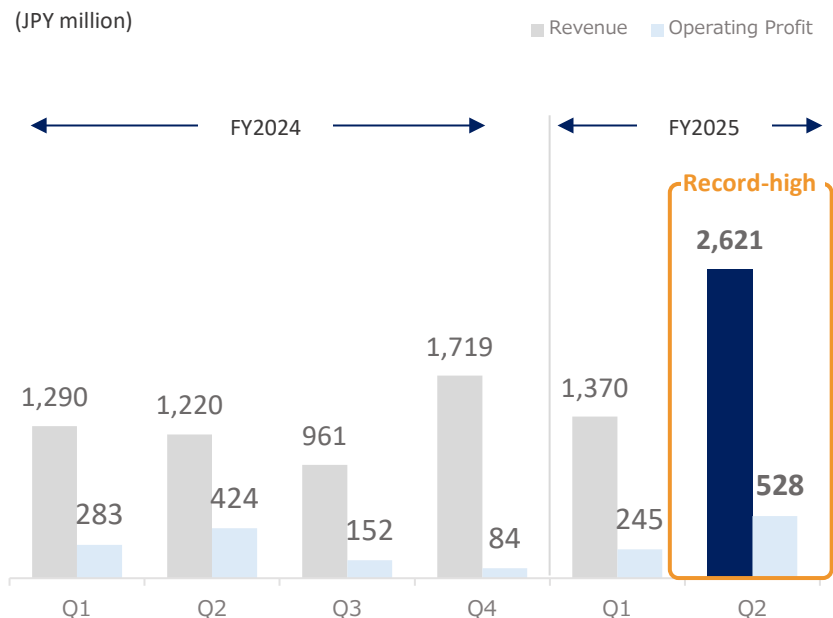
# Use of Funds: 3. Loans and Investments for the Rapidly Growing Medtech Businesses

To seize growth opportunities, provide working capital through financing.

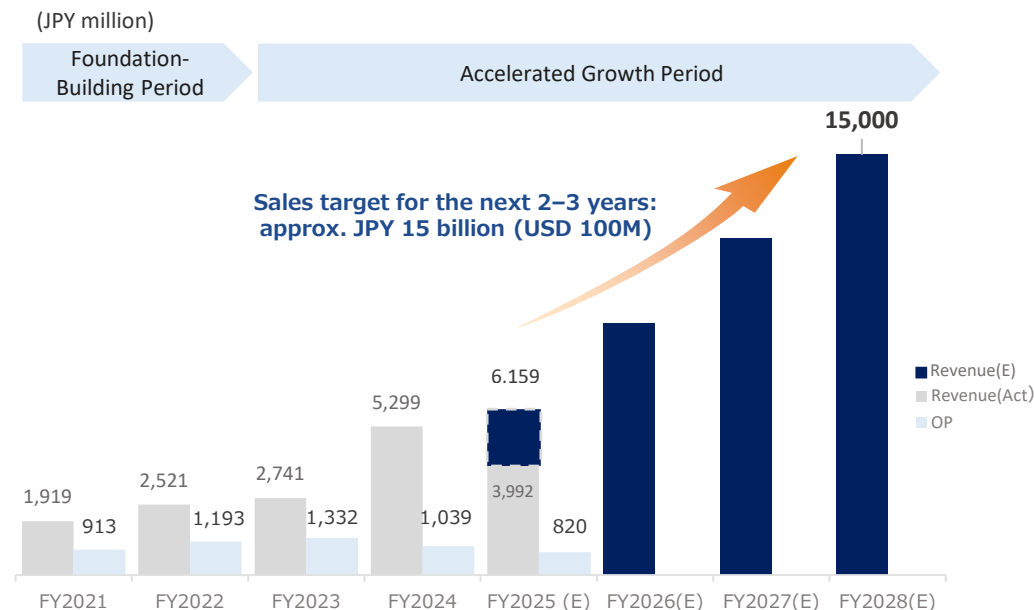
Revenue and profit reached record highs on both a monthly and quarterly basis, driven by newly acquired customers.

Due to new clients and orders exceeding in-house manufacturing capacity, outsourcing had to be used, putting pressure on profit margins.

## Quarterly Revenue (BAB + BB)



## Revenue Trend (BAB + BB)



	2021	2022	2023	2024	2025 Q2
Operating Profit Margins	47.5%	45.7%	39.9%	18.2%	19.4%

## New Share Issuance Project through International Offering

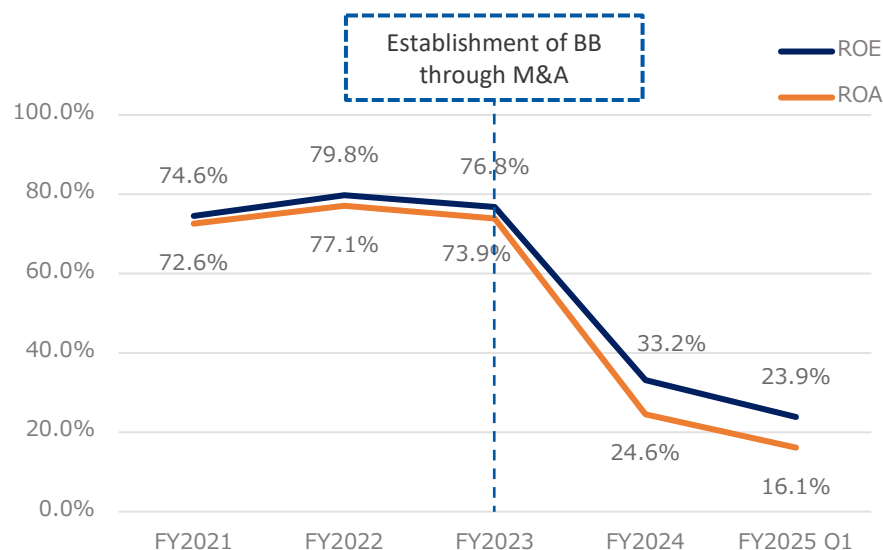
# Use of Funds: 3. Loans and Investments for the Rapidly Growing Medtech Businesses

To seize growth opportunities, provide working capital through financing

Driven by newly acquired customers, both sales and profit reached record highs on a monthly as well as quarterly basis.

Due to receiving orders exceeding our anticipated manufacturing capacity, we have been compelled to use outsourced processing, which has put pressure on our profit margins.

## ROA/ROE



## Balance Sheet (JPY million)

	FY2021	FY2022	FY2023	FY2024	FY2025 Q2
Cash	158	335	172	212	313
<b>Accounts Receivable</b>	<b>210</b>	<b>403</b>	<b>364</b>	<b>1,323</b>	<b>1,737</b>
<b>Inventory</b>	<b>355</b>	<b>425</b>	<b>599</b>	<b>1,269</b>	<b>1,810</b>
Tangible Fixed Assets	552	630	648	1,235	1,149
Intangible Fixed Assets	0	0	0	2,179	1,964
<b>Total Assets</b>	<b>1,287</b>	<b>1,807</b>	<b>1,796</b>	<b>6,287</b>	<b>7,035</b>
Accounts Payable	2	36	26	724	1,156
Borrowings	0	0	0	0	0
<b>Total Liabilities</b>	<b>29</b>	<b>74</b>	<b>62</b>	<b>1,616</b>	<b>1,987</b>
Shareholders' Equity	1,258	1,733	1,734	4,671	5,047
Cash	1,287	1,807	1,796	6,287	7,035

## 5. Financial Forecasts for FY2025



# Financial Forecasts for FY2025

## Consolidated Results

No change in the forecast

Millions of yen	FY2024 Actual	FY2025 Forecast
Revenue	23,611	28,733
Gross profit	18,037	22,954
Operating profit	1,402	23,217
Income before income taxes	238	22,541
Net profit	(9)	15,868
Profit attributable to owners of the parent	1,098	12,058

## Segment

No change in the forecast

Millions of yen	Pharmatech	Biotech	Medtech	Others
Revenue	20,202	955	6,159	1,525
Operating profit	4,640	3,982	1,269	16,314

Note: The results of Gyre Therapeutics, Inc. are included in Others.

The discrepancy between the sum of each segment and the company's forecast for FY 2025 is attributable to consolidation adjustments.

## 6. Appendix

# F351 Phase 3 Clinical Trial – Top-Line Results Overview (Announced May 23, 2025)

## 1. The primary endpoint Met with Hight Statistical Significance

- $\geq 1$ -stage fibrosis improvement at Week 52:  
Hydronidon: 52.85% vs. Placebo: 29.84% ( $P = 0.0002$ )

## 2. Key Secondary Endpoint Achieved

- $\geq 1$ -stage improvement in inflammation without fibrosis progression at Week 52:  
Hydronidon: 49.57% vs. Placebo: 34.82% ( $P = 0.0246$ )

## 3. Favorable Safty Profile

- Serious adverse events: 4.88% (6/123, Hydronidon) vs. 6.45% (8/124, Placebo)
- **No discontinuations due to adverse events**

## 4. Clinical and Regulatory Pathways

- **Designated as a Breakthrough Therapy (China NMPA<sup>1</sup>, 2021), with potential for First-in-Class approval.**
- The NDA (New Drug Application) is planned for Q3 2025, aiming for accelerated approval.

1. NMPA = National Medical Products Administration of China

# Overview of F351 Phase 3 Clinical Trial

Efficacy and safety of F351 compared with placebo in patients with liver fibrosis caused by CHB

## Eligibility Criteria for Study Subjects (N=248)

- Individuals infected with HBV (chronic hepatitis B)
- Fibrosis score (Ishak) of 3 or higher
- Aged 18 to 65
- Continuous administration for 52 weeks (study period)
- No use of antiviral drugs or antifibrotic agents (including traditional Chinese medicine) within the past 3 months

123

### ① Hydronidone:

270mg/day + Antiviral drug 0.5mg/day

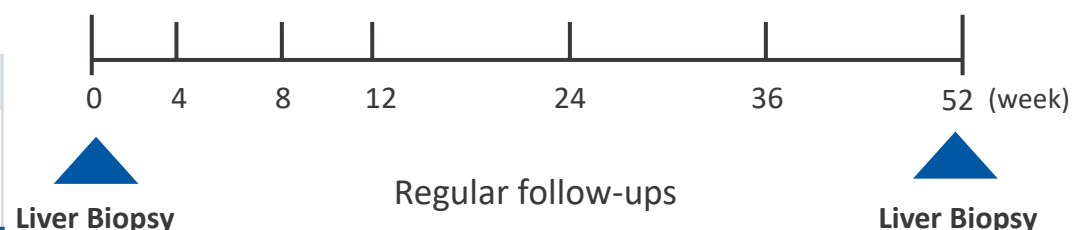
124

### ② Placebo:

Matching placebo capsules + Antiviral drug 0.5mg/day

## Classification of Ishak Score

Score	State of Fibrosis	Description
0–2	No to mild fibrosis	Fibrosis is not evident to mild; although fibrosis may be present in some areas, the overall liver architecture is preserved.
3	Moderate fibrosis	Fibrosis has spread, and alterations in liver structure have begun to appear.
4	Severe fibrosis / Early cirrhosis	Distortion of liver architecture becomes apparent, representing a precursor stage to regenerative nodule formation.
5	Near-cirrhotic condition	Fibrosis progresses to a nodular form; clear signs suggestive of cirrhosis appear.
6	Cirrhosis / End-stage fibrosis	Fibrosis has advanced to a definitive stage; liver function is significantly impaired.



### Primary Endpoint:

Efficacy of fibrosis reversal, defined as a decrease in the Ishak stage score of liver fibrosis  $\geq 1$  after 52 weeks of treatment compared to baseline.

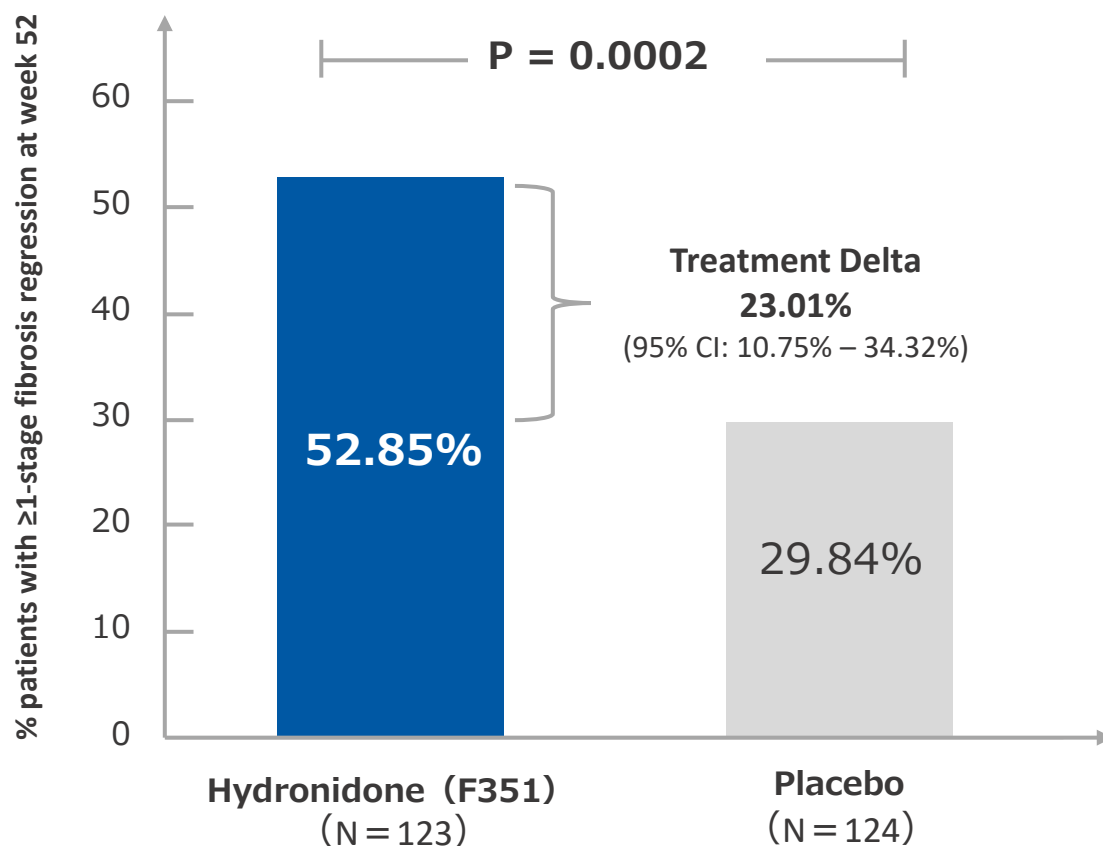
### Key Secondary Endpoint:

A decrease in liver inflammation grade by  $\geq 1$  after 52 weeks of treatment relative to baseline, without progression of fibrosis (Scheuer score).

# Primary Endpoint Met with Statistically Significant Fibrosis Regression

Compared to the placebo group, a statistically significant improvement of at least one stage in fibrosis was achieved at Week 52 of treatment.

≥1-stage Fibrosis Regression at Week 52  
(ITT analysis)



- **+23.0% treatment delta** vs. placebo
- Highly statistically significant (**p=0.0002**)
- Consistent with fibrosis regression rates observed in Phase 2

**P-value:** An important statistical indicator used to determine the significance of differences.  
A p-value of less than 0.05 is typically considered statistically significant.

## Safety Profile

- No treatment discontinuation, interruption, or dose reduction due to serious adverse events occurred during this study
- All serious adverse events were assessed as unrelated to Hydronidone (F351)

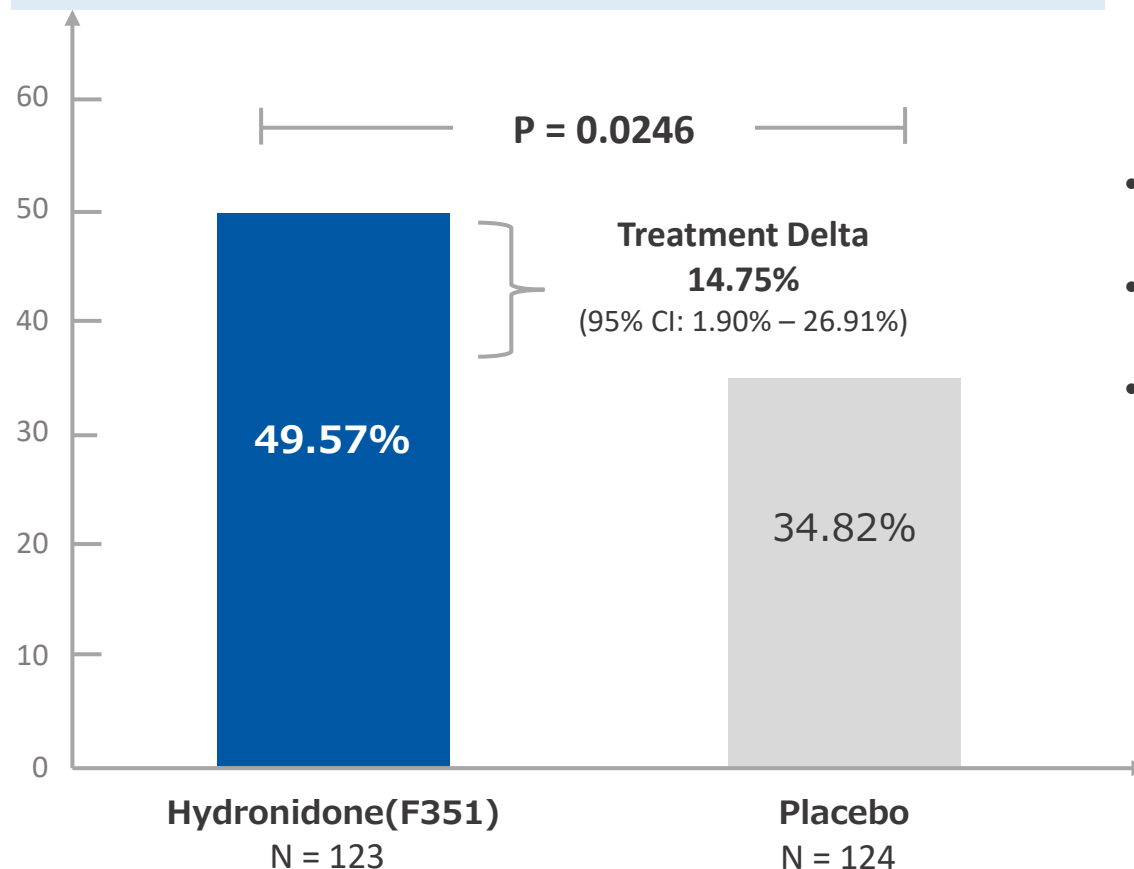
Safety Event	Hydronidone (N=123)	Placebo (N=124)
Any TEAE	98 (79.67%)	103 (83.06%)
Grade 1 AEs	27.64%	33.06%
Grade 2 AEs	43.90%	43.55%
Grade ≥3 AEs	8.13%	6.45%
Drug-related AEs (ADRs)	32.52%	33.87%
Grade ≥3 ADRs	1.63%	1.61%
<b>Discontinuation due to AE</b>	<b>0</b>	<b>0</b>
<b>Temporary interruption due to AE</b>	<b>0</b>	<b>0.81%</b>
<b>Dose reduction due to AE</b>	<b>0</b>	<b>0</b>
<b>Any SAE</b>	<b>6 (4.88%)</b>	<b>8 (6.45%)</b>
<b>Due to Investigational Drug:</b>		
<i>Possibly unrelated</i>	<b>2</b>	<b>3</b>
<i>Unrelated</i>	<b>4</b>	<b>5</b>
Death	0	0

#Adverse Event: An undesirable occurrence following drug administration. All such events must be reported regardless of whether a causal relationship with the drug is established.

## Key Secondary Endpoint Met: Significant Reduction in Liver Inflammation

Achieved statistically significant improvement in liver inflammation By combining anti-fibrotic and anti-inflammatory effects, a more comprehensive treatment approach is made possible

≥1-Grade inflammation improvement  
without progression of fibrosis at Week 52  
(ITT analysis)



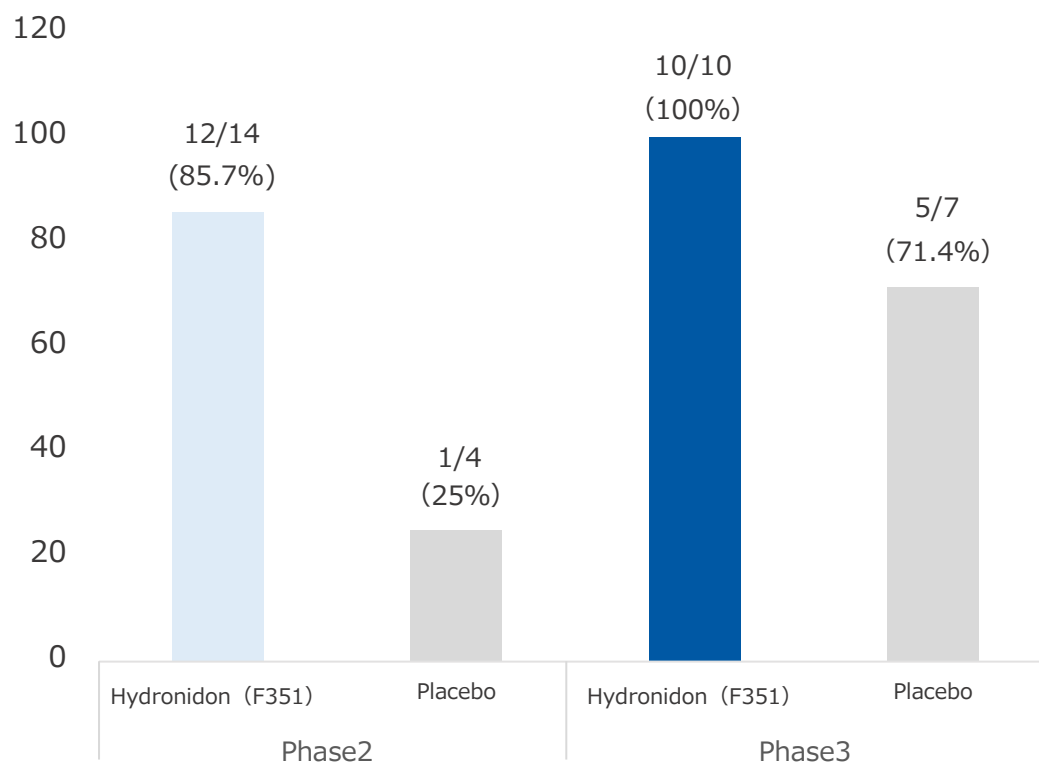
- Statistically significant (p=0.0246)
- +14.75% treatment delta vs placebo
- Reinforces **anti-inflammatory** activity

Note : Other secondary endpoints are omitted from this description (all endpoints were met).

# Meaningful Fibrosis Regression Observed in Ishak 6 (F4) Patients in Two Independent Trials

Although statistical significance was not confirmed due to the small sample size, **F351 may also be effective against cirrhosis caused by CHB.**

**Fibrosis Regression in Cirrhosis Patients (Ishak 6)**



## Phase 2:

- **36% (5/14)** of cirrhotic patients (Ishak 6) achieved **≥2-stage regression** and were considered **no longer cirrhotic** at Week 52.
- **12/14 (86%)** showed **≥1-stage improvement**, indicating broad antifibrotic activity.
- In the placebo arm, only **1 patient improved**, which happened to be a **≥2-stage regression**.

## Phase 3:

- **100% (10/10)** of cirrhotic patients (Ishak 6) in the treatment group had **≥1-stage regression** at Week 52.
- **Mean improvement** was **-1.5** vs. **-1.0** in placebo.
- Placebo response: **5/7 patients (71.4%)** showed **≥1-stage regression**, but **mean score change** remained lower than Hydronidone.



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