D.WESTERN THERAPEUTICS INSTITUTE

Q2 FY12/21

Financial Results Briefing Materials

August 10, 2021

D. Western Therapeutics Institute, Inc.

Stock Code: 4576

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DWTI

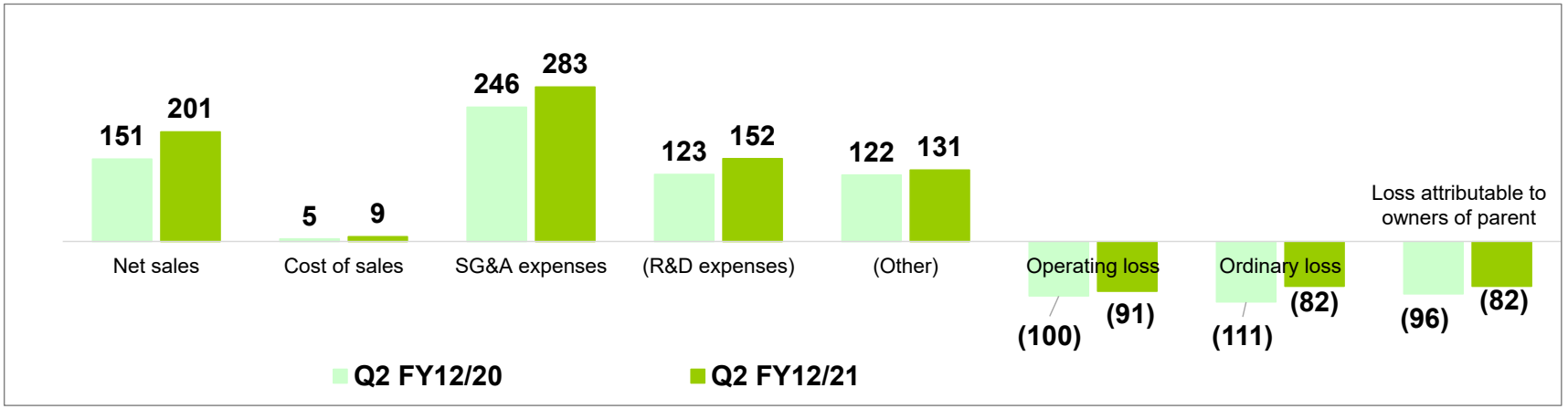
1. Q2 FY12/21 Financial Results

January 1–June 30, 2021

DWTI

Consolidated Statement of Income (YoY comparison)

(JPYmn)



Net sales

- Growth of GLANATEC®
- Full-year contribution from DW-1002 in US (launched in April 2020)
- Rise in joint research funding received from Glaukos beginning in October 2020

R&D expenses

- Higher research expenses due to rise in outsourcing expenses for in-house drug discovery activities, as well as increases in expenses for existing drugs and collaborative projects

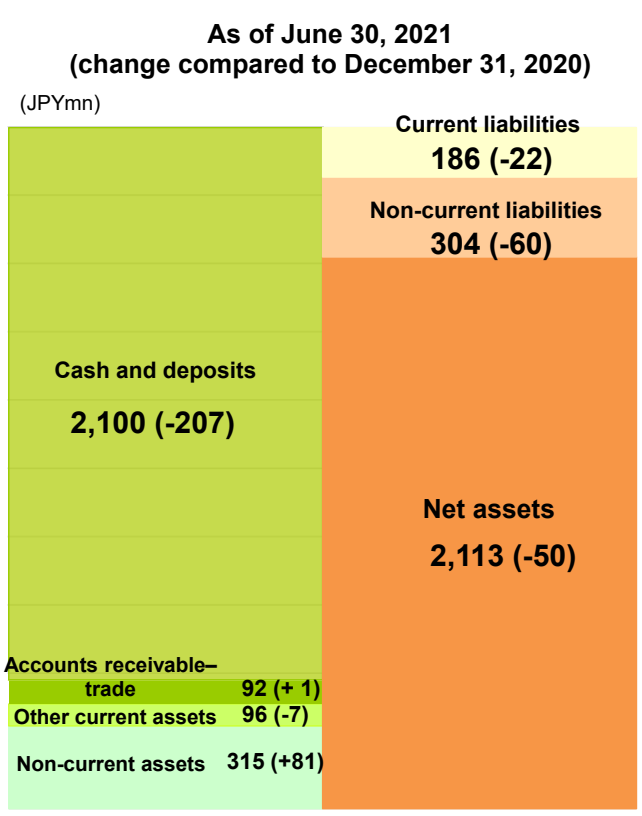
Consolidated Statement of Income (vs. full-year forecast)

(JPYmn)

	FY12/20		FY12/21				
	1H results	FY results	1H results	YoY change	FY forecast (out Feb. 12)	Progress	Primary factors
Net sales	**151**	**355**	**201**	**50**	**340**	**59.3%**	• **Favorable progress thanks to growth in royalty revenue**
SG&A expenses	246	604	283	36			
R&D expenses	123	350	152	28	610	24.9%	• **Use of research funds partially pushed back** • **Projected increase in H-1337 development expenses in 2H; planned payment of expenses for DW-5LBT**
Other SG&A expenses	122	253	131	8			
Operating loss	**(100)**	**(265)**	**(91)**	**9**	**(580)**	**—**	
Ordinary loss	**(111)**	**(289)**	**(82)**	**29**	**(580)**	**—**	
Loss attributable to owners of parent	**(96)**	**(276)**	**(82)**	**14**	**(530)**	**—**	

DWTI

Consolidated Statement of Income



Cash and deposits

- JPY100mn investment in UBiENCE and JPY60mn repayment of long-term borrowings
- Cash and deposits declined primarily due to higher R&D expenses, but remained at a favorable level

Accounts receivable–trade

- About the same as on December 31, 2020

Non-current assets

- Increase in investment securities due to investment in UBiENCE
- Amortization of contract-related intangible assets related to DW-1002 (Europe)

Current liabilities

- Decrease in accounts payable–other due to the payment of joint research and other expenses; decrease in income taxes payable

Non-current liabilities

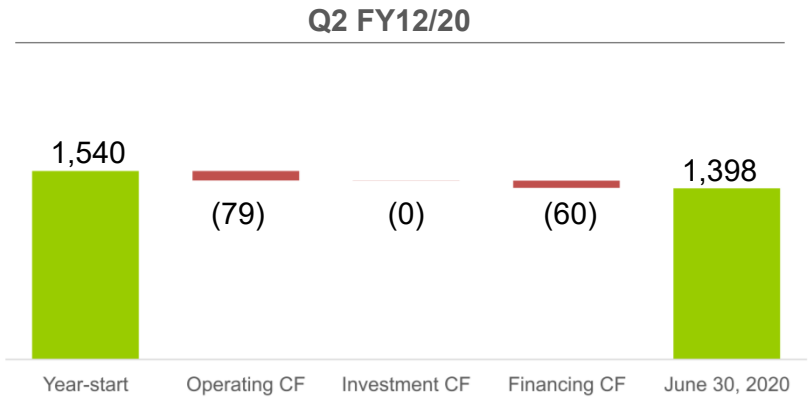
- Decrease in long-term borrowings

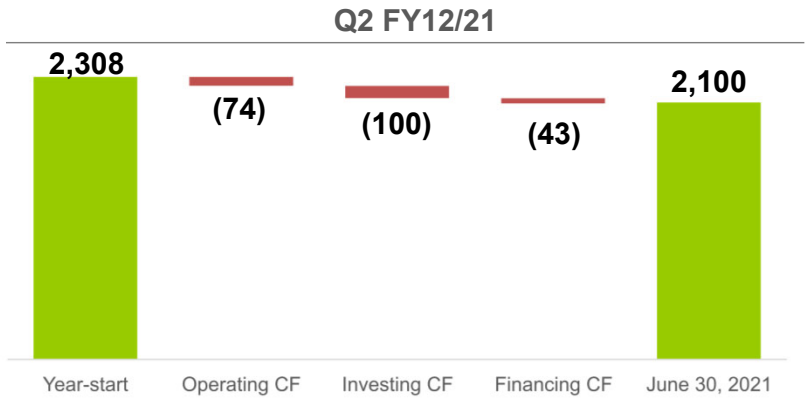
Net assets

- Net loss of JPY82mn
- Increases in share capital and capital surplus due to the exercise of share acquisition rights

Cash Flow Statement

(JPYmn)





Cash flow from operating activities

- JPY82mn outflow due to the recording of loss before income taxes

Cash flow from investing activities

- JPY100mn outflow from investment in UBiENCE (acquisition of investment securities)

Cash flow from financing activities

- JPY60mn outflow from the repayment of long-term borrowings and JPY16mn inflow from the exercise of share acquisition rights

On-hand liquidity on June 30, 2021 consisted only of JPY2.1bn in cash and deposits (no securities)

Capital procurement associated with Series 10 stock acquisition rights (as of July 31, 2021)

- ✓ Rights exercised: 2,993,200 shares (57.6%)
- ✓ Total funds procured: JPY1,050mn

2. Progress of Business in FY12/21

Topics in FY12/21

Development pipeline

Jan.: Obtained approval for DW-1002 in Canada (indication: ILM peeling)
⇒ Launch planned for autumn 2021 by licensee (DORC)

Apr.: Announced development plan for H-1337
⇒ US Phase IIb study to be conducted through internal development

Jul.: Received complete response letter (CRL) from FDA for DW-5LBT (indication: neuropathic pain after shingles)
⇒ Currently in consultations with FDA along with joint developer MEDRx

Research projects

Apr.: AI-based drug discovery project
DWTI began joint AI-based drug development with SyntheticGestalt to create new kinase inhibitors for the treatment of inflammatory and CNS diseases

Jul.: Development project for proteolysis targeting chimeras (PROTACs)
DWTI acquired compounds with kinase-degrading effects; we therefore extended joint research agreement with UBiENCE and formed capital alliance

Development Pipeline

Original products

Products		Clinical indication	Region	Non-clinical	P-I	P-II	P-III	Application	Approval	Launch	Licensee
Ripasudil hydrochloride hydrate	GLANATEC®	Glaucoma and ocular hypertension	Japan								Kowa
			Asia						*Approval already granted in some regions		
	K-321	Fuchs endothelial corneal dystrophy	US								
K-232 (Ripasudil hydrochloride hydrate/ Brimonidine tartrate)		Glaucoma and ocular hypertension	Japan								
H-1337		Glaucoma and ocular hypertension	US								Developed internally

In-licensed products

Products	Clinical indication	Region	Non-clinical	P-I	P-II	P-III	Application	Approval	Launch	Licensee
DW-1001	Ophthalmic treatment agent	Japan								ROHTO Pharmaceutical
DW-1002	ILM peeling	Europe, US								DORC
	ILM peeling	Canada								DORC
	ILM staining, cataract surgery	Japan								Wakamoto Pharmaceutical
DW-5LBT	Neuropathic pain after shingles	US								Jointly developed with MEDRx
Treatment for retinopathy of prematurity	Retinopathy of prematurity	Japan								Developed by subsidiary JIT

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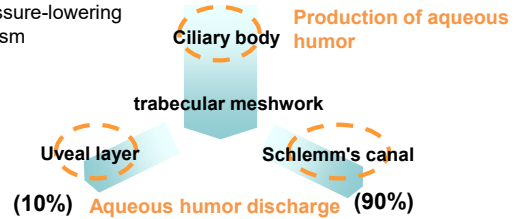
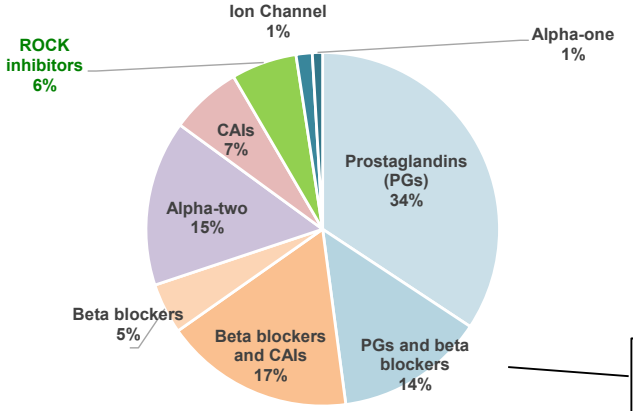
Glaucoma

- **Glaucoma is the most common disease causing visual impairment in Japan**
- **Glaucoma damages optic nerves through increased intraocular (IOC) pressure and causes narrowing in fields of vision**
- **Estimates indicate that one in twenty adults aged 40 or above will develop the disease**
- **The total number of glaucoma patients throughout the world is estimated at 76 million (according to the World Health Organization's 2019 World report on vision)**

IOC pressure-lowering mechanism



Shares of Japanese Market (approx. JPY95bn in FY2018)



Share of combination drugs expanding

*Calculated by DWTI based on the 5th NDB Open Data released by Japan's Ministry of Health, Labour and Welfare

Scale of global market

- **Global market: Approx. JPY600bn worldwide (2018)**
  (US market: Approx. JPY300bn)
  - ✓ **Number of patients expected to continue increasing**
  - ✓ **Wider treatment options are now available, including surgical procedures (devices) and multidrug therapies**

*According to the company's research

Glaucoma Treatment GLANATEC® Ophthalmic Solution 0.4%

(Generic Name: Ripasudil hydrochloride hydrate)

Single drug

- ✓ **Sales are steadily increasing**
- ✓ Japan: Sales projected to peak at JPY7.6bn (Kowa Co., Ltd. sales)
  (Ten years following launch; 250,000 patients)

  ⇒Enhance sales activities to achieve the projected peak sales
- ✓ Overseas: Approved in four Asian nations; application under review in Vietnam

Combination drug

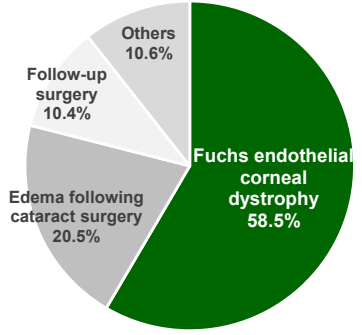
- ✓ **Phase III study underway for combination drug with brimonidine tartrate (development code: K-232)**

  Outline of Phase III study (from JAPIC)
  - Long-term study: Confirm safety and efficacy following administration period of 52 weeks
  - Comparative study: Compare results with control groups who received only ripasudil eye drops or brimonidine eye drops

Expansion of indications

- ✓ **Phase II study underway in US for Fuchs endothelial corneal dystrophy (Development code: K-321)**
- ✓ Exploratory clinical pharmacological study complete for diabetic retinopathy

Diseases treated with Descemet stripping Endothelial keratoplasty procedure



*Source: 2016 EYE BANKING STATISTICAL REPORT

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Glaucoma Treatment H-1337

Internally developed products

Characteristics of H-1337

- **Formulated as a kinase inhibitor following GLANATEC®**
- **Confirmed safety and efficacy in Phase I/IIa studies (clinical POC obtained)**

Characteristics
✓ Strong and long-lasting IOC pressure-lowering effect
✓ Facilitates drainage of aqueous humor through the trabecular meshwork and Schlemm's canal
✓ Multikinase inhibitor effective on various types of protein kinases, including leucine-rich repeat kinase (LRRK)

Development Plan (announced April 28)

Region	P-I/IIa	P-IIb		P-III
US		**2022**	**2023**	

- ✓ **Phase III study expected to begin in FY2024 or later (internal development and out-licensing to pharmaceutical companies are both considered)**
- ✓ **Secured necessary funding through the exercise of Series 10 stock acquisition rights**

Summary of Phase I/IIa study results

Efficacy

	Median diurnal IOP change (8 hours) on Day 28
0.6% dosage group (n=21)	-5.1mmHg
Placebo group (n=22)	-0.4mmHg
Difference	-4.7mmHg

- ✓ IOC-lowering effect demonstrated in all three groups (0.06%, 0.2%, and 0.6%) compared to placebo group

Safety

Rate of occurrence	5% or above*1	0.1~5%
Eyes	Discomfort	Conjunctival hyperemia

*1: Common to all three groups

- ✓ Mild erythema on the applied area
- ✓ Well tolerated

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H-1337 Prospects as Glaucoma Treatment: First Choice as Second-Line Drug

Standard treatments for glaucoma
✓ The sole reliable evidence-based method of treatment for glaucoma (including normal-tension glaucoma) is the reduction of intraocular (IOC) pressure
✓ Prostaglandin analogues (PGs) demonstrate the strongest IOC pressure-lowering effect among first-line drugs; generic drugs are available and are most frequently used
✓ However, PGs also have little to no effect on many patients, and more than half of drug-treated patients use multiple medications

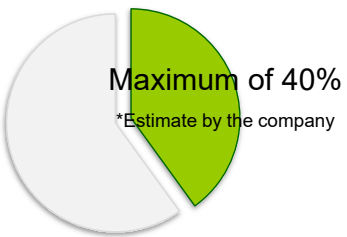
Issues with standard glaucoma treatments

1. First-line drugs have little to no effect on a surprisingly large number of patients, and single-drug treatment has shown limited efficacy
2. Multiple-drug treatments are standard (three to four or more drugs used in some cases); however, side effects are more common when using multiple drugs

⇒ Needs and promising markets for new drugs that are 1) sufficiently effective, 2) highly safe to administer (either alone or with other drugs), and 3) have a site of action that differ from that of PGs

Target market estimates

1. Patients who do not respond to first-line drugs
2. Patients who receive multiple drugs



US market
Approx. JPY300bn

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Neuropathic Pain Treatment DW-5LBT (Jointly Developed with MEDRx)

- August 2020: Applied for approval in US as treatment for neuropathic pain after shingles (brand name: Lydolyte)
  - ⇒Received complete response letter (CRL) from FDA on July 5, 2021; DWTI is currently conducting appropriate response to specified issues
  - Approval expected in the latter half of 2021 (no changes made to development plan)
- ○ Exploring possible sales alliances within US

Development Plan

Region	Application	Approval	Launch
US	2020	**2021**	**2022**

US market

- The market scale for transdermal lidocaine patches was estimated at about JPY27bn in 2020.

*Based on data released by MEDRx

Characteristics

- Confirmatory comparative (bioequivalence) clinical trial using Licoderm® as an advance indicator generated successful results
- Low dermal irritation
- Excellent adhesive strength
- Capable of maintaining adhesive strength during exercise

Primary details of agreement with MEDRx

- Milestone payment of up to JPY200mn according the progress of commercialization in US
- After launch, DWTI expects to receive royalties commensurate with sales

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Other Drugs in Development Pipeline

Ophthalmic treatment agent DW-1001 (Indication: undisclosed; region: Japan)

- Licensee Rohto Pharmaceutical is currently conducting non-clinical trials

Development Plan

Characteristics of DW-1001

- Low R&D risks due to repurposing of existing drug as new ophthalmologic treatment

Ophthalmic surgical adjuvant DW-1002 (Indication: ILM peeling, etc.; region: worldwide)

- Steady sales in Europe and US
- Received approval in Canada in January 2021 (brand name: TissueBlue™); launch planned for autumn 2021
  ⇒Royalty revenue expected to increase in the future

Development Plan (Japan)

Indication	Licensee	~P-III	Application	Approval	Launch
ILM staining	Wakamoto Pharmaceutical		2022	2023	
Cataract surgery			2022	2023	

Surgeries in Japan

- Vitreous surgery: about 100,000 per year
- Cataract surgery: about 1.2 million per year; estimated market scale for DW-1002 is about 10% of these operations

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Internal Drug Discovery and R&D

DWTI conducts R&D with a primary focus on **ophthalmologic fields**

✓ Enhance ophthalmologic disease project

➢ Project targeting the creation of new devices

DWTI is conducting joint research with Glaukos Corporation (US) to create new intraocular drug products
Compound evaluation is proceeding smoothly, and clinical trials are expected to begin within the next two years

➢ Development project for proteolysis targeting chimeras (PROTACs)

DWTI is conducting joint research with UBiENCE to create proteolysis targeting chimeras (PROTACs; see p.18)

➢ Discovery, research, and in-licensing of drug candidate compounds for posterior eye segment disease

✓ Research into non-ophthalmologic diseases

➢ Research aimed at adding indications other than glaucoma

➢ Research based on the characteristics of internally developed compounds

➢ AI-based drug discovery project

Along with SyntheticGestalt, we are conducting AI-based joint research to create new kinase inhibitors (see p.19)

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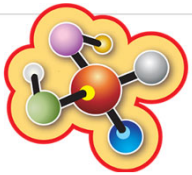
Joint Research into PROTACs

Several compounds confirmed as generating kinase-degrading effects through joint research launched in 2019

June 17, 2021: Extended joint research agreement with UBiENCE and formed capital alliance
DWTI aims to accelerate this joint research and develop superior new drugs

Our initiatives and goals

- Develop new drugs using our core technologies
- Generate therapeutic benefits not obtainable from kinase inhibitors



Create new PROTACs

Compared with kinase inhibitors…

- ✓ Strong medicinal effects
- ✓ Long-lasting effects
- ✓ High degrees of safety

Joint research partner UBiENCE Inc.

- ➢ Startup established in 2018 that conducts R&D of PROTACs using its core SNIPER technology

UBIENCE

What are proteolysis targeting chimeras (PROTACs)?

- ✓ Therapeutic technology attracting attention as a novel treatment method
- ✓ Drugs that break down disease-causing abnormal proteins, using mechanisms found within living organisms
- ✓ Major pharmaceutical companies in Japan and overseas are currently working on development of PROTACs

DWTI

Joint AI-Based Drug Discovery

April 2021: Launched joint drug discovery efforts to create new kinase inhibitors

Joint research partner SyntheticGestalt Ltd.

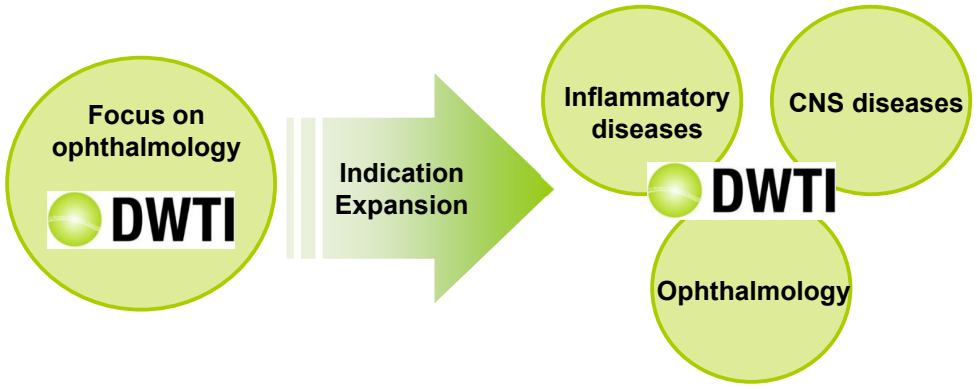
- Established in 2018, SyntheticGestalt conducts AI-based internal and joint drug discovery and performs contract research
- Possesses technology to identify candidate compounds with superior drug properties out of as many as four billion compounds
- Leading company in the practical application of AI technology with track record of collaboration with multiple pharmaceutical and life science companies

What is AI-Based Drug Discovery?

- ✓ An umbrella term for technologies that utilize AI (mainly machine learning) to practice and support drug discovery research
- ✓ AI-based drug discovery is attracting attention in recent years because it can dramatically save cost and time compared to conventional technologies

Goals of joint drug discovery

- ✓ Create new kinase inhibitors for treatment of inflammatory and CNS diseases
- ✓ Expand our target disease areas and enhance core technologies through the application of AI



DWTI is reviewing conditions for conducting AI-based predictions

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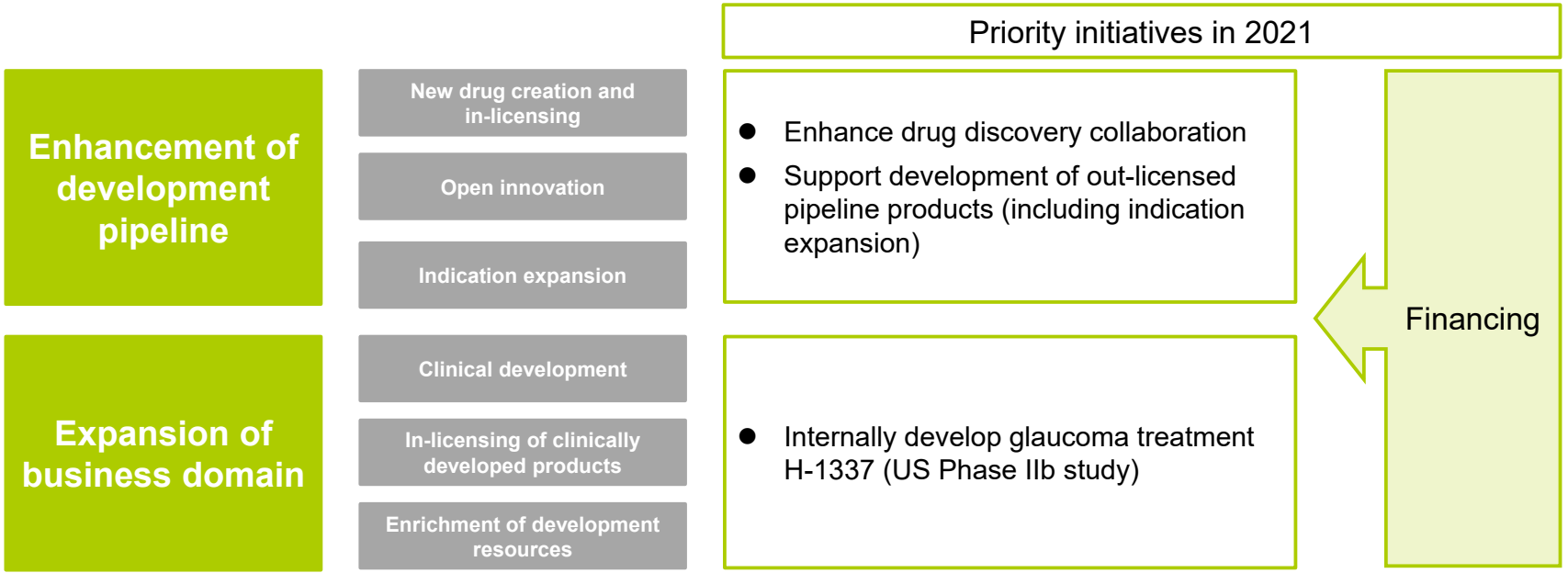
3. Growth Strategies

DWTI

In Pursuit of Our Philosophy, “Innovative New Drugs to the World from Japan”

With a focus on ophthalmology, DWTI targets further growth and higher corporate value through two priority measures

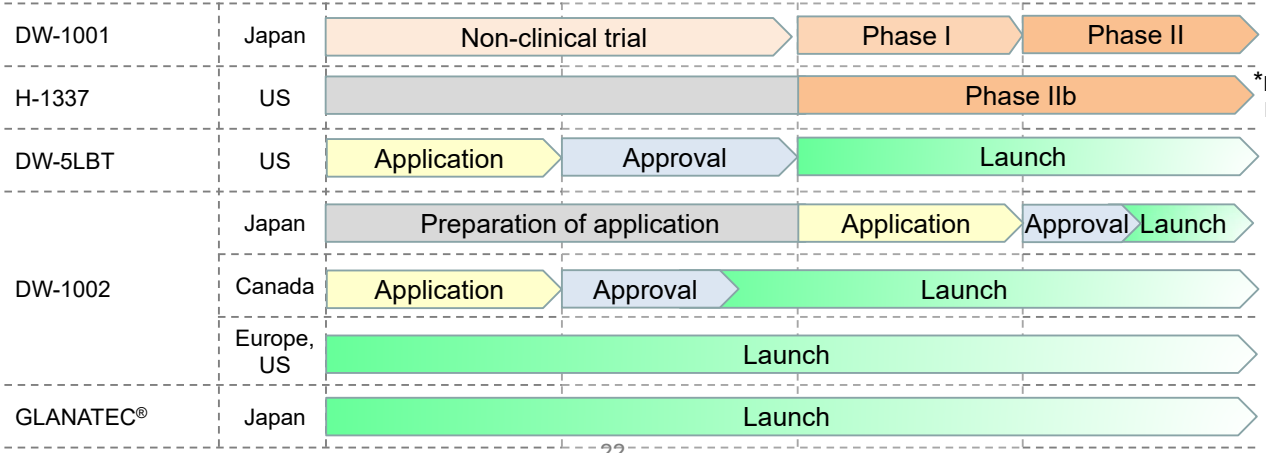


Medium-Term Targets (Consolidated) (announced on February 12, 2021)

(JPYmn)

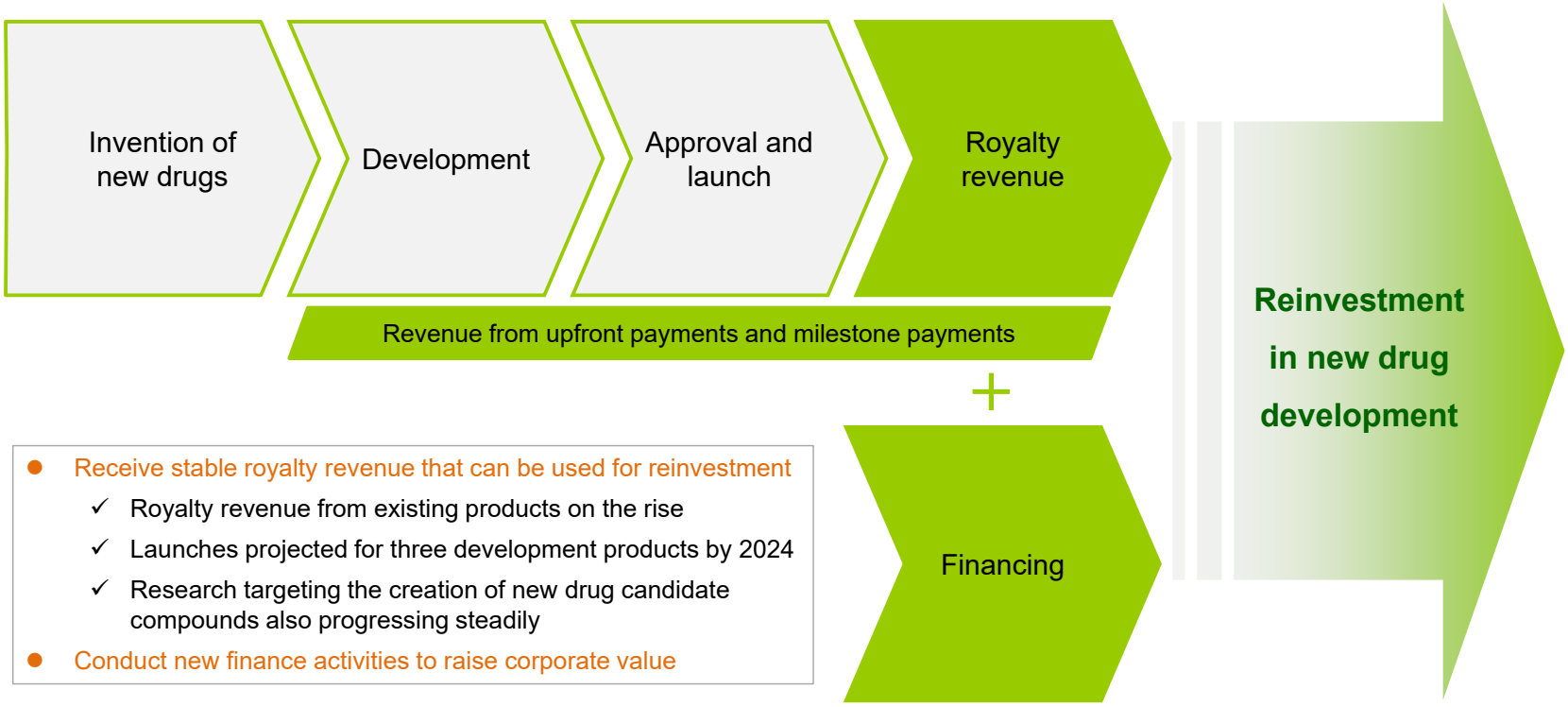
	FY12/20 results	FY12/21 forecast	FY12/22 targets	FY12/23 targets
Net sales	355	340	390–690	480–820
Operating profit	(265)	(580)	(370)–(70)	(660)–(320)
Ordinary profit	(289)	(580)	(380)–(80)	(660)–(320)
Profit attributable to owners of parent	(276)	(530)	(320)–(30)	(630)–(290)
R&D expenses	350	610	450	810

Development Pipeline Plan



*Development plan for H-1337 out on April 28

Our Ongoing Growth Cycle



- Receive stable royalty revenue that can be used for reinvestment
  - ✓ Royalty revenue from existing products on the rise
  - ✓ Launches projected for three development products by 2024
  - ✓ Research targeting the creation of new drug candidate compounds also progressing steadily
- Conduct new finance activities to raise corporate value

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(Reference) Business Overview

DWTI

DWTI Group Overview

Name	D. Western Therapeutics Institute, Inc. (DWTI)
Business	New drug discovery, research, and development
Established	February 1999
Head office	Naka-ku, Nagoya-shi, Aichi, Japan
Capital	JPY573mn

Consolidated Subsidiary

Name	Japan Innovative Therapeutics, Inc. (JIT)
Business	Pharmaceutical R&D and consulting
Established	December 2014
Head office	Naka-ku, Nagoya-shi, Aichi, Japan
Capital	JPY254mn

Japan Innovative Therapeutics

As of June 30, 2021

New drug discovery (research and invention)

New drug development

Demonstrate group synergy

DWTI

History

2014: A strategic turning point—DWTI shifted away from specializing in basic research to focus on internal development and license acquisition

1999 Founded

2002 Out-licensed antiplatelet drug K-134 and glaucoma treatment K-115 to Kowa Co., Ltd.

2006 Established R&D institute at Mie University

2009 Listed on Tokyo Stock Exchange JASDAQ (Growth)

JPX 東証JASDAQ上場

2014 Added JIT as consolidated subsidiary

Japan Innovative Therapeutics

In-licensed ophthalmic agent DW-1001 from UK company

Launch of K-115 (GLANATEC®)

2015 Acquired business for ophthalmic surgical adjuvant DW-1002

2017 Conducted US clinical trial for glaucoma treatment H-1337 (our first internally developed product)

2018 Began joint development of neuropathic pain treatment DW-5LBT

2020

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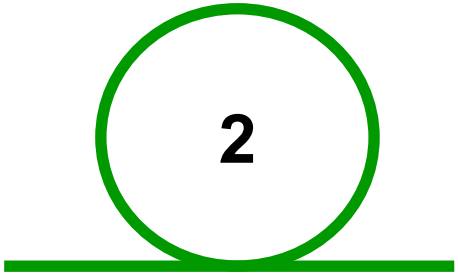
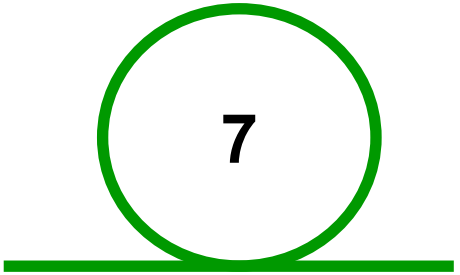
Business Highlights



- Two products available on the market
- Four products in late stages of development (Phase III study or later)

- About 1,500 kinase inhibitors included in DWTI's compound library
- A pioneer in the field of kinase inhibitors



- Out-licensed seven products
- Internally developing three additional products (including joint development)

Our Businesses

Drug Discovery	Internal drug discovery	●Create promising kinase inhibitors from our original compound library with efficiency ●Create new drug seeds by collaborating with other companies
Drug Development	Clinical development	●Internal clinical development (including the evaluation of safety and efficacy in humans)
	Business development	●Out-licensing activities for original products and in-licensed products ●Consider in-licensing of products in late development stages and repurposed drugs

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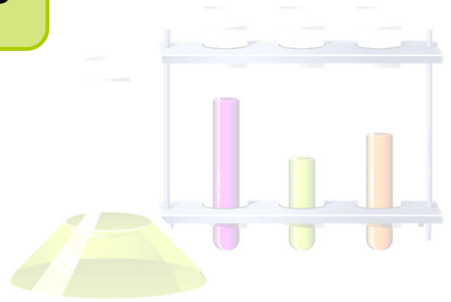
Features of Our Core Technologies

1. Core technologies to continuously create new drugs



- ✓ A team of professionals who create drug seeds
- ✓ Drug discovery engine
- ✓ Launched drugs of our own invention

2. Focus on kinase inhibitors (ophthalmologic indications)

- ✓ Utilize our original compound library
- ✓ Create new products with dramatically improved therapeutic effects by making small changes to compounds in our library

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Core Technologies to Create New Drugs

- **DWTI's drug discovery engine is an original core technology that enables us to continuously create new drugs**
- **A kinase is an enzyme that phosphorylates proteins; excessive phosphorylation is a factor that contributes to the onset of various diseases (kinases regulate protein activity)**

Drug discovery engine

1. **Compound library**
   - ✓ **Superior new drug seeds**
   - ✓ **Includes three launched drugs**
2. **Drug design**
   - ✓ Ability to create new drugs from compounds in our library (experience, data)
3. **Drug-Western Method**
   - ✓ Tool for exploring mechanisms of action of new drugs
   - ✓ Enhance value by estimating mechanisms (estimate safety and elements of therapeutic effects)

Potential uses of kinase inhibitors

1. **Various indications**
   - ➢ Kinases play a critical role in a variety of diseases
   - ➢ Kinase inhibitors are primarily used in anti-cancer agents; development of kinase inhibitors to treat immune, neurodegenerative, and inflammatory diseases is also under consideration
2. **Large market scale**
   - ➢ Total annual sales of kinase inhibitors exceed JPY2tn
3. **DWTI is a pioneer in the field of kinase inhibitors**
   - ➢ Launched in 1995, fasudil is the world's first kinase inhibitor (and is included in our compound library)

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Innovative New Drugs to the World from Japan

D. Western Therapeutics Institute

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- These materials have been created with the goal of facilitating understanding regarding the company and were not produced for the purpose of soliciting investment in the company.

- Earnings forecasts and projections regarding future events included within these materials are based on determinations made by the company using information that was available at the time at which these materials were produced and are therefore subject to impact from potential risks and uncertainties. Consequently, actual results may differ significantly from these forecasts and projections due to a variety of factors, including changes in business environment.

- Information related to other companies included in these materials has been taken from publicly available information and other sources. The company has not verified the accuracy or suitability of this information and therefore provides no corresponding guarantees.

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