

# 4576 D. Western Therapeutics Institute

Sponsored Research  
March 14, 2022



## Development pipeline is steadily expanding

Key initiatives in FY12/22 include starting Phase IIb trials in the US for H-1337, and filing an application for DW-1002 in China

### SUMMARY

- Over time with progress in execution of the development pipeline, and as part of growth strategy to diversify revenue streams, the basic business model of drug discovery and early out-licensing has evolved to include 1) from 2015, in-licensing of later stage development products, 2) from 2018, collaborative drug creation applying DWTI's technical expertise to assist in joint R&D of products of other firms, and 3) from 2018, extending development of original in-house products beyond early out-licensing as far as proof of concept (PoC) through Phase IIb.
- Major milestones coming in the next 2-3 years include: 1) high expectations for Phase IIb US trials for H-1337 as "first choice as a second-line Glaucoma drug" for patients who do not respond to PGs, 2) high expectations for 2023 application and 2024 approval for DW-1002 in Japan, as well as 2023 approval and 2024 launch in China, 3) high expectations for 2023 approval and subsequent launch of DW-5LBT in the US, and 4) high expectations for the joint R&D agreement with US Glaukos Corporation, with clinical trials anticipated to begin at an early date.
- In addition to these major milestones, there is also expected to be a fairly steady and regular flow of announcements regarding enhancing the number of drugs in the development pipeline. As can be seen in the graph below, DWTI is aiming to increase the number of drugs in the development pipeline from 7 to 10 by the end of 2024. The lower exhibit on the following page outlines key concrete initiatives toward achieving that target.
- US development of H-1337 to Phase IIb trials is DWTI's first foray into late-stage clinical development. H-1337 is a multi-kinase inhibitor that inhibits various protein kinases, chiefly leucine-rich repeat kinase 2 (LRRK2), for the treatment of glaucoma and ocular hypertension. Its strong effectiveness in lowering intraocular pressure is attributed to its new mechanism of action. It has strong prospects as "first choice as a second-line Glaucoma drug" for patients who do not respond to prostaglandins (PGs), and those who suffer side effects from multiple drug regimens. DWTI estimates potential up to 40% of the US market, or ¥136bn.

## 4Q Follow-up



D. WESTERN THERAPEUTICS INSTITUTE

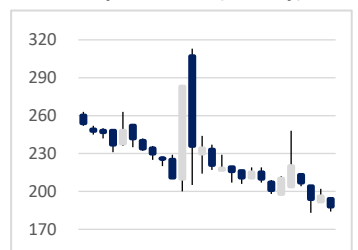
### Focus Points:

Drug discovery bio-venture with strengths in the kinase inhibitor mechanism and treatments for ophthalmic diseases such as glaucoma and ocular hypertension.

### Key Indicators

Share price (3/11)	188
YH (21/2/5)	350
YL (22/2/24)	183
10YH (13/5/8)	3,755
10YL (13/1/4)	130
Shrs out. (mn shrs)	29.358
Mkt cap (¥ bn)	5.519
Shr equity ratio	81.4%
22.12 P/S (CE)	14.9x
22.12 P/E (CE)	—
21.12 P/B (act)	2.75x
21.12 ROE (act)	—
22.12 DY (CE)	—

### 6M price chart (weekly)



Source: SPEEDA

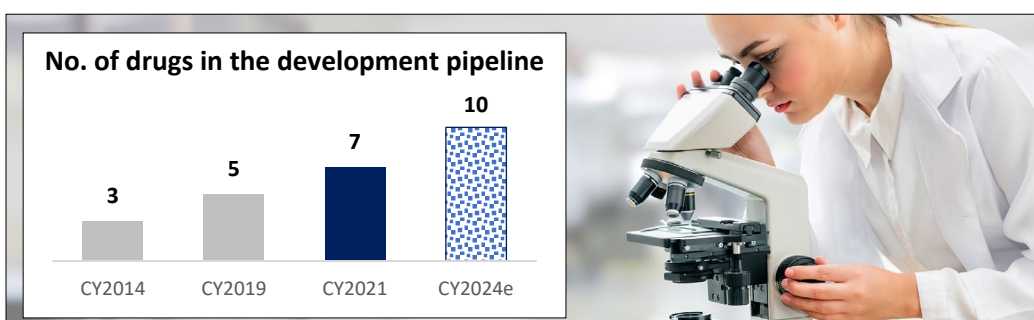
### Chris Schreiber CFA

Company Specialist

[research@sessapartners.co.jp](mailto:research@sessapartners.co.jp)



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Source: compiled by Sessa Partners from company IR materials.



**PIPELINE DRUGS**  
FY12/24 CE: 7 → 10

**Aiming to boost the number of drugs in the development pipeline to 10**

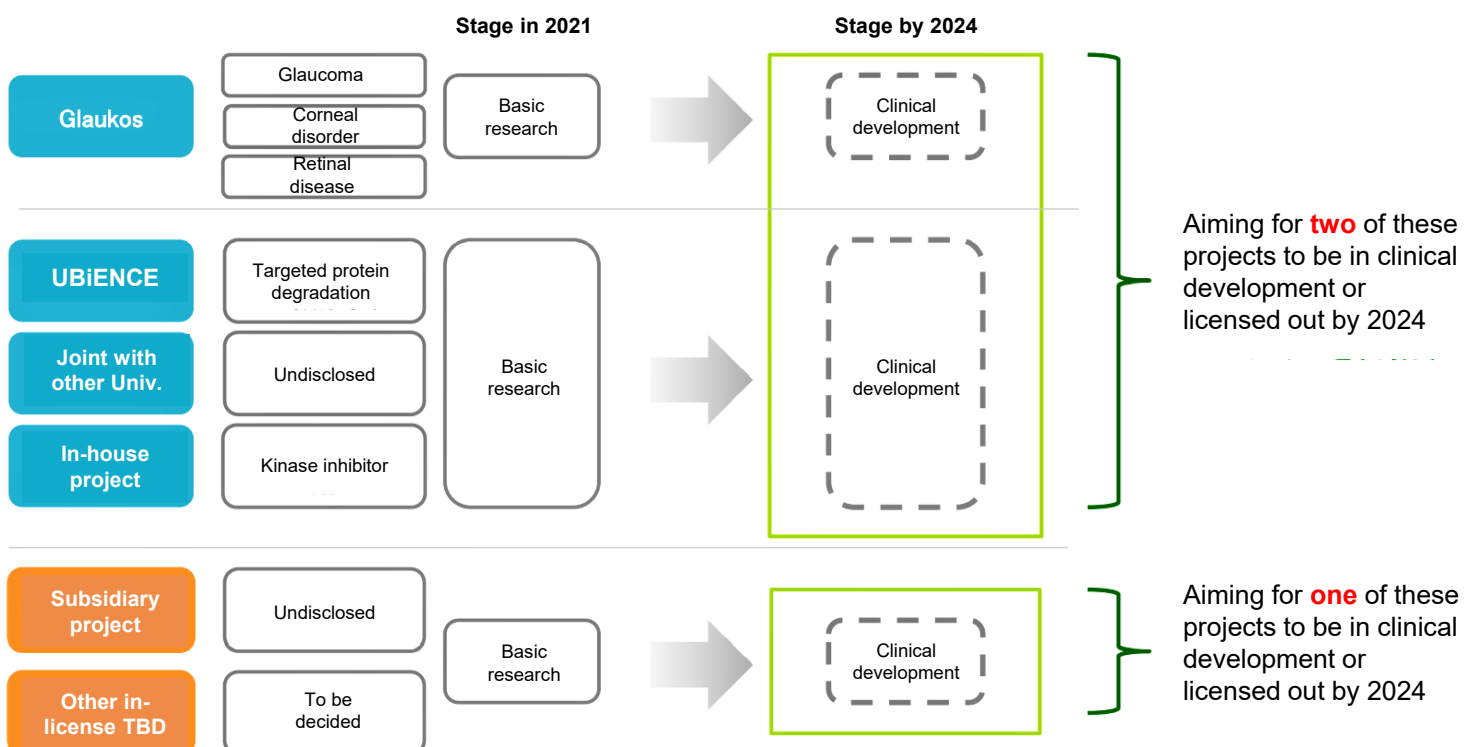
The two exhibits below show the current development pipeline of 7 drugs, and key initiatives to increase the number to 10 over the next three years by the end of FY12/24. In addition, with a focus on ophthalmology, DWTI targets further growth and raising corporate value through two priority measures: ① enhancement of the development pipeline, through new drug creation and in-licensing as well as indication expansion, and ② expansion of the business domain, through clinical development.

**Status of Drugs in the Development Pipeline: 7 as of FY12/21-end**

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, Asia*	[Yellow bar]							Kowa
	K-321	Fuchs endothelial corneal dystrophy	US	[Green bar]							
K-232 (Ripasudil hydrochloride hydrate/ Brimonidine tartrate)		Glaucoma and ocular hypertension	Japan	[Green bar]							
DW-1002		ILM peeling	Europe, US, Canada	[Yellow bar]							DORC
		ILM staining	Japan	[Green bar]							Wakamoto Pharmaceutical
		Cataract surgery	Japan	[Green bar]							
DW-1001		Ophthalmic treatment agent	Japan	[Green bar]							ROHTO Pharmaceutical
H-1337		Glaucoma and ocular hypertension	US	[Green bar]							Developed internally
DW-5LBT		Neuropathic pain after shingles	US	[Green bar]							Jointly developed with MEDRx
Treatment for retinopathy of prematurity		Retinopathy of prematurity	Japan	[Green bar]							Developed by subsidiary JIT

\*Launched in Thailand. Included "Application" and "Approval" in other Asian regions.

**Initiatives to Increase Drugs in the Development Pipeline by 3 to 10 as of FY12/24-end**



D. Western Therapeutics Institute Consolidated Financial Highlights

Selected Items from Consolidated Statements of Income

[J-GAAP] JPY mn, %	FY12/15 act	FY12/16 act	FY12/17 act	FY12/18 act	FY12/19 act	FY12/20 act	FY12/21 act	FY12/22 init CE	FY12/21 MTP	FY12/22 MTP	FY12/23 MTP
Net sales	62	168	254	293	581	356	414	370	340	390 ~ 690	480 ~ 820
YoY	—	171.8	51.2	15.3	98.2	(38.7)	16.5	(10.7)			
<i>by region</i>											
• Japan	62	168	190	158	417	184	175				
• Europe	—	—	64	97	88	107	170				
• US	—	—	—	38	75	59	70				
• Other (SE Asia)	—	—	—	—	—	5	—				
<i>by major client (10%+ of net sales)</i>											
• Kowa Company, Ltd.	62	97	120	139	158	166	172				
• WAKAMOTO PHARMACEUTICAL	0	50	50	—	209	—	—				
• Dutch Ophthalmic Research Center	—	—	64	97	88	107	170				
• Glaukos Corporation	—	—	—	38	63	59	70				
Major clients total	62	147	234	274	518	332	412				
Others	0	21	20	19	62	24	2				
Cost of sales	0	6	7	14	26	17	20				
Gross profit	62	162	247	279	555	339	394				
SG&A expenses	352	482	880	1,066	437	604	566				
• R&D expense	144	227	603	795	249	351	316	790	610	450	810
<i>as % of net sales</i>	232.6%	135.1%	237.5%	271.5%	43.0%	98.6%	76.3%	213.5%			
• Other	209	255	277	270	188	254	250				
Depreciation	3	18	45	52	44	44	45				
Goodwill amortization	13	—	—	—	—	—	—				
EBITDA	(274)	(302)	(589)	(735)	162	(222)	(126)				
Operating profit (loss)	(291)	(320)	(634)	(786)	117	(266)	(172)	(690)	(580)	(370) ~ (70)	(660) ~ (320)
Ordinary profit (loss)	(295)	(304)	(669)	(797)	110	(290)	(160)	(700)	(580)	(380) ~ (80)	(660) ~ (320)
Impairment losses	0	0	1,040	7	0	0	0	0			
Profit (loss) ATOP	(296)	(254)	(1,563)	(749)	133	(276)	(149)	(670)	(530)	(320) ~ (30)	(630) ~ (290)

Selected Items from Consolidated Balance Sheets and Consolidated Statements of Cash Flows

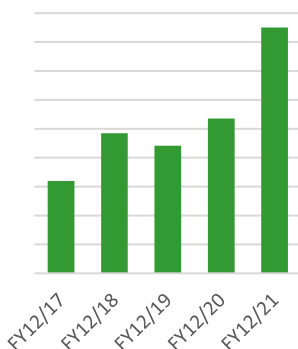
• Cash and deposits	1,747	2,292	2,133	1,584	1,541	2,308	1,934				
• Accounts receivable - trade	23	41	61	71	104	92	102				
Total current assets	2,025	2,776	2,516	1,764	1,716	2,503	2,162				
Contract-related intangible assets	—	—	329	288	247	206	165				
Total non-current assets	115	136	362	309	266	234	301				
Total assets	2,140	2,913	2,877	2,074	1,981	2,738	2,463				
Current portion of LT borrowings	—	—	—	120	120	120	130				
Total current liabilities	27	36	156	268	189	210	193				
LT borrowings	—	—	600	480	360	340	210				
Total non-current liabilities	—	—	625	505	384	364	234				
Total liabilities	27	36	782	774	573	574	428				
• Share capital	2,400	2,945	3,365	35	35	557	573				
• Capital surplus	2,390	2,935	3,355	2,133	2,133	2,656	2,631				
• Retained earnings	(2,904)	(3,157)	(4,721)	(908)	(775)	(1,051)	(1,200)				
Total shareholders' equity	1,886	2,723	1,999	1,260	1,393	2,161	2,004				
Share acquisition rights	30	16	2	—	—	3	3				
Non-controlling interests	196	139	95	40	15	—	28				
Total net assets	2,113	2,877	2,096	1,300	1,408	2,164	2,035				
<i>Shareholders' equity ratio</i>	88.1%	93.5%	69.5%	60.8%	70.3%	78.9%	81.4%				
Total liabilities and net assets	2,140	2,913	2,877	2,074	1,981	2,738	2,463				
CF from operating activities	(323)	(334)	(797)	(540)	176	(216)	(176)				
CF from investing activities	835	(231)	(763)	(8)	(100)	(13)	(111)				
CF from financing activities	98	1,067	1,407	—	(120)	1,004	(104)				
Cash and CE at beginning of period	1,167	1,767	2,292	2,133	1,584	1,541	2,308				
Cash and CE at end of period	1,767	2,292	2,133	1,584	1,541	2,308	1,934				
Book value per share (BPS)	83.49	109.96	76.14	47.95	53.02	73.88	68.27				

Source: compiled by Sessa Partners from company TANSHIN financial statements and company IR materials.

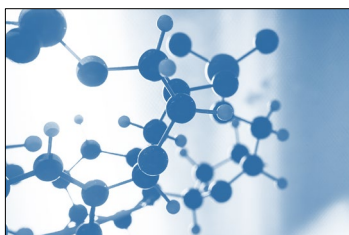
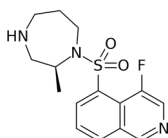


**4Q Review**  
**FY12/2021 results and**  
**FY12/2022 outlook**

**DW-1002 royalty income trend**



**Ripasudil**  
 hydrochloride  
 hydrate molecule  
 skeletal formula



**Summary of FY12/2021 results**

The company reported full-term 4Q FY12/21 results at 15:00 on February 10, and it held a results briefing from 13:30 on February 18. A summary of results is shown in the table on P3. Relative to initial guidance for a -4.4% decline in net sales to ¥340mn, actual results came in at ¥414mn, +16.5%. This strong performance was attributed to the sharp increase in royalty income from GLANATEC® ophthalmic solution 0.4% and DW-1002. Royalty income for DW-1002 increased nearly +60% YoY from increased US sales, the full-term US contribution, as well as launch in Canada in the 4Q (see left-hand graph).

Relative to initial guidance for an operating loss of (¥580mn), actual results came in at an operating loss of (¥171 mn). In addition to net sales beating initial guidance by ¥74mn, actual R&D expense of ¥316mn came in ¥294mn below initial budget for ¥610mn, due to additional studies required for DW-5LBT resulting in the expected milestone payment to MEDRx being pushed back, and timing of expenses related to the start of Phase IIb trials in the US for H-1337 also pushed back into 2022.

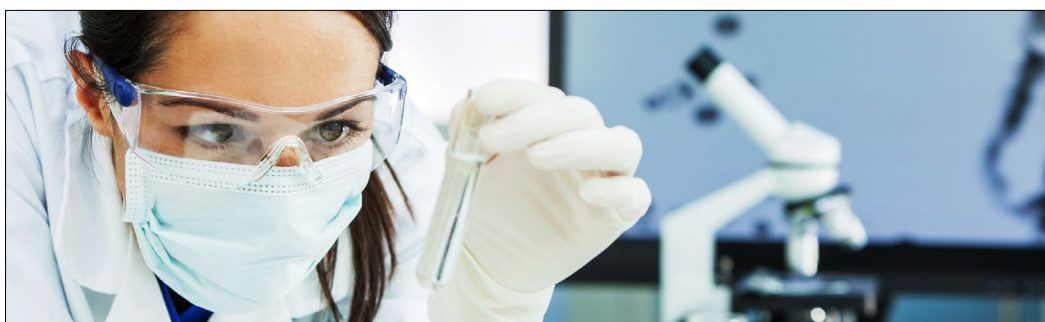
Net cash used in investing activities included roughly ¥100mn associated with the capital tie-up with UBIENCE (see P10), and net cash used in financing activities included ¥120mn for repayment of long-term borrowings, versus proceeds of ¥16mn from the exercise of share acquisition rights. Cash and cash equivalents at the beginning of the period of ¥2.3bn declined to ¥1.9bn at the end of the period. According to the company, funds procurement associated with Series 10 stock acquisition rights (as of December 31, 2021) is:

- Rights exercised: 2,993,200 shares (57.6%)
- Total funds procured: ¥1,050mn

**Outlook for FY12/2022 and beyond**

Initial guidance for FY12/22 is net sales ¥370mn (-10.2% YoY), and an operating loss of (¥540mn). According to the company, assumptions for net sales include: ① growth in royalty income from launched products (GLANATEC®, DW-1002), ② a milestone payment associated with the start of Phase I trials for DW-1001, and ③ no research payments from joint research partners (joint research ongoing; DWTI’s part completed for now). Regarding initial guidance for the operating loss, the initial budget for R&D expense is ¥790mn, up ¥473mn from the previous year, mainly due to start of Phase IIb trials in the US for H-1337, the crown jewel in the current development pipeline. This is the first of DWTI’s internally developed drugs to reach late-stage development.

The two exhibits on the following page highlight the progress achievement plan for the development pipeline and estimated timing of the revenue contribution from the development pipeline.



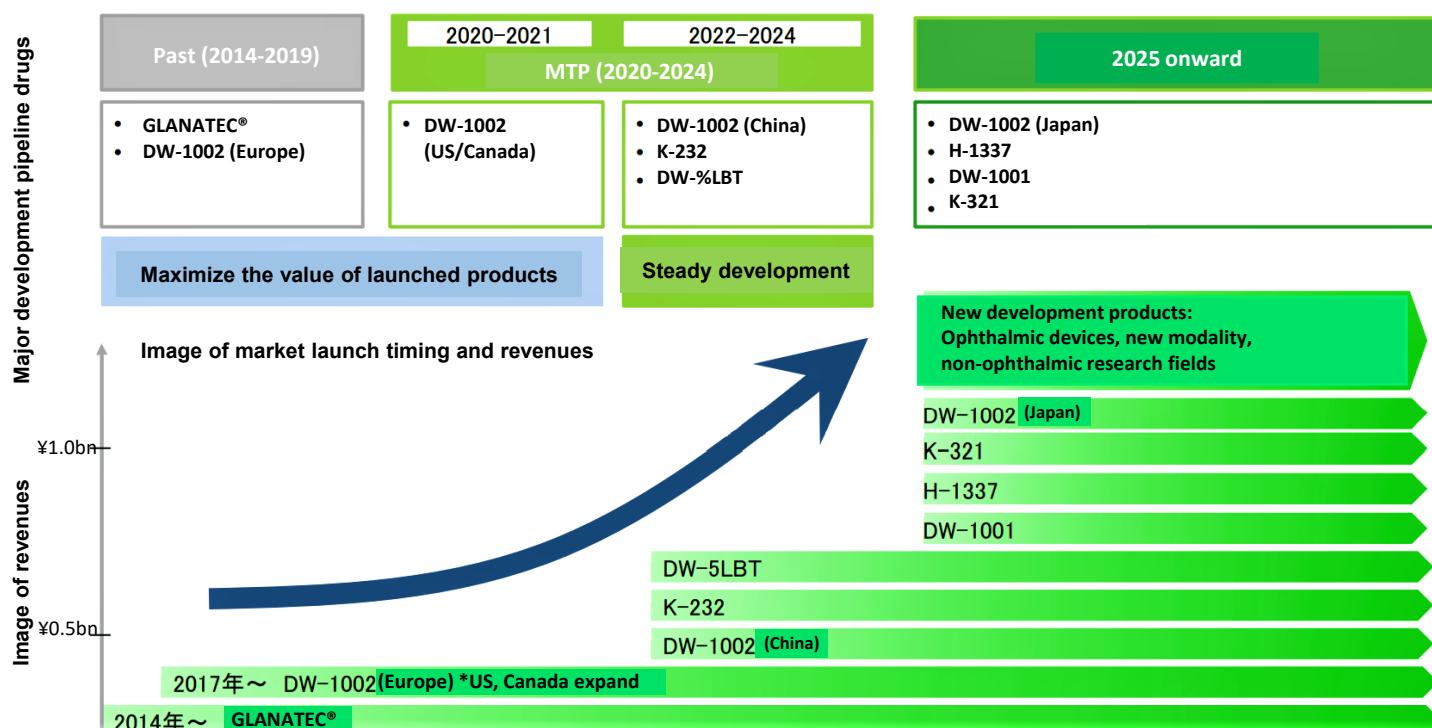
Progress Achievement Plan for the Development Pipeline

Products and Clinical indication		Region	2021	2022	2023	2024
H-1337	Glaucoma and ocular hypertension	US	Preparing for P2b	P2b		P3 *2024 or later
DW-5LBT	Neuropathic pain after shingles	US	Received CRL	Additional study	Approval/Launch *Approval expected in 2023	
K-232	Glaucoma and ocular hypertension (combination eye drop)	Japan	Application	Approval	Launch	
K-321	Fuchs endothelial corneal dystrophy	US		P2	*Phase II study underway in US. Future plan undecided.	
DW-1001	Ophthalmic treatment agent	Japan	Non-clinical	P1	P2	
DW-1002	ILM peeling	China Added		Application	Approval	Launch
	ILM staining Cataract surgery	Japan			Application	Approval

\*Development plans for out-licensed products are based on development plans of the licensees and the company's expectations. Hence, actual development progress may differ from the plan.

Source: FY12/21 IR results briefing materials released on February 10, 2022.

Estimated Timing of the Revenue Contribution from the Development Pipeline



Source: "Matters concerning the Business Plan and Growth Potential," released on February 10, 2022.

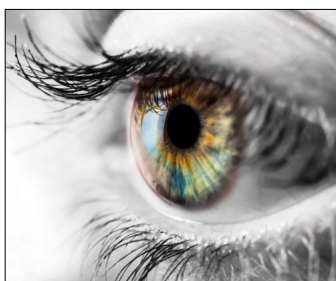




**PIPELINE**

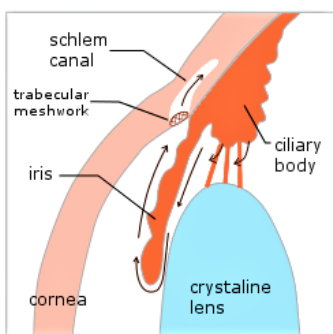
**Original and Licensed-in**

GLANATEC® ophthalmic solution 0.4% (K-115) sold by Kowa in Japan



**GLANATEC® point of action**

High pressure due to blocked fluid drainage damages the optic nerve. GLANATEC® ophthalmic solution 0.4% promotes outflow of aqueous humor through Schlemm's canal, relieving ocular hypertension.



**① Glaucoma and ocular hypertension [GLANATEC® ophthalmic solution 0.4%]**

This drug is an eye drop preparation with a novel mechanism of action, the first of its kind in the world, for treating glaucoma. The drug lowers intraocular pressure by inhibiting rho-kinase, a type of protein kinase, and promoting the outflow of aqueous humor from the main collector channel via the trabecular meshwork/Schlemm's canal.

In 2002, DWTI out-licensed the rights to the drug to Kowa Co., Ltd., which then moved ahead with development and launched the drug in Japan under the brand name Ripasudil hydrochloride hydrate in December 2014. \*Because all rights in Japan and worldwide relating to Ripasudil hydrochloride hydrate have been out-licensed to Kowa, the following two drugs are also being developed by Kowa. The company announced on February 25, 2022 that GLANATEC® has been launched by Kowa in Singapore.

**② Fuchs endothelial corneal dystrophy [K-321]**

Since Ripasudil hydrochloride hydrate is a rho-kinase inhibitor, it has been suggested that the compound may also act on other kinases in the eye, leading to investigations of its applicability to other ophthalmic diseases. As part of these efforts, development of the compound as a treatment for Fuchs endothelial corneal dystrophy (FECD) is underway. FECD is a disease in which corneal edema and opacity occur as a result of damage to corneal endothelial cells, resulting in diminished acuity of vision.

Although there are few patients suffering from FECD in Japan, it is a common disease in Europe and the U.S. There is currently no effective drug treatment for FECD, which is often treated with corneal transplant surgery. We hope that our compound will become a new drug for treating FECD.

**③ Glaucoma and ocular hypertension [Fixed-dose combination eye drop (Ripasudil hydrochloride hydrate and Brimonidine tartrate) K-232]**

This drug is being developed as the first fixed combination eye drop containing Ripasudil hydrochloride hydrate. Since the standard treatment for glaucoma involves the use of multiple drugs, we are seeking to improve the quality of life for glaucoma patients by providing a combination drug. **November 25, 2021: Application filed for Japan domestic manufacturing and marketing approval. Approval expected in 2022, launch expected in 2023 (\*DWTI estimates).**

**Development Stages of Ripasudil hydrochloride hydrate**

	Non-clinical	Phase I	Phase II	Phase III	Application	Approval	Launch
<b>1</b>					● in Vietnam	● in Korea, Singapore, Malaysia and Thailand	● in Japan
<b>2</b>			● in U.S.				
<b>3</b>					● in Japan		

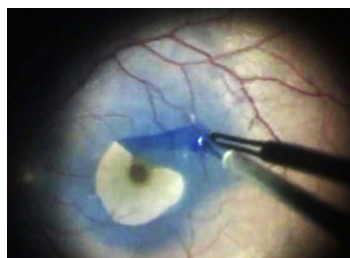
Source: DWTI website.



**PIPELINE**

**Original and Licensed-in**

ILM BLUE® (DW-1002) sold by DORC in Europe



Source: Journal of Ophthalmology

**[DW-1002]**

Brilliant Blue G-250 (BBG250) is an ophthalmic surgical adjuvant whose active ingredient is a dye with high staining ability. The dye temporarily and safely stains the capsule protecting the inner limiting membrane or crystalline lens in the back of the eye, making it easier to perform vitreous or cataract surgery.

BBG250 was discovered by a research group at Kyushu University, and it has since been commercialized. DWTI acquired the business from Healios K.K. in 2017, and we have since been developing the dye under exclusive license from Kyushu University.

We have granted an exclusive sublicense for DW-1002 for all regions worldwide outside Japan to Dutch Ophthalmic Research Center (International) B.V. (DORC), which has been manufacturing and selling the product in Europe and other countries since September 2010. Approved in the US in 2019, and launched in April 2020. Approved in Canada in 2021, and launched in October 2021.

Wakamoto Pharmaceutical Co., Ltd. has been granted an exclusive sublicense for Japan, and is moving forward with development aiming to obtain approval. **Wakamoto is expected to file applications for ② and ③ in 2023, and receive approvals in 2024.**

Clinical indications:

- ① ILM peeling (Europe, US and Canada)
- ② ILM staining (Japan)
- ③ Cataract surgery (Japan)

Development stages:

- ① Launched (Europe, U.S. and Canada)
- ② Phase III clinical trials (Japan) completed
- ③ Phase III clinical trials (Japan) completed

**\*Newly added: DORC is filing an NDA in China in 2022 for indication ILM peeling, targeting approval in 2023 and sales launch in 2024.**

**Development Stages of DW-1002**

	Non-clinical	Phase I	Phase II	Phase III	Application	Approval	Launch
①							● in Europe, U.S. and Canada
②				● in Japan			
③				● in Japan			

Source: DWTI website.



**PIPELINE**

**Original and Licensed-in**

**[H-1337]  
US development schedule**

- Phase IIb – 2022 to 2023
- Phase III – 2024 or later
- Secured necessary funding through the exercise of Series 10 stock acquisition rights

**[H-1337]**

We are developing a multi-kinase inhibitor that inhibits various protein kinases, chiefly leucine-rich repeat kinase 2 (LRRK2), for the treatment of glaucoma and ocular hypertension. Animal studies and other tests have confirmed that this pipeline drug has the effect of lowering intraocular pressure. We believe its strong effectiveness in lowering intraocular pressure is attributed to its new mechanism of action.

In 2018, we carried out in-house Phase I/IIa clinical trials in the US, and safety and efficacy were confirmed (clinical PoC was obtained). **For DWTI, which has typically focused on basic research, this was the first foray into clinical development.** DWTI is currently preparing for late-stage Phase II clinical trials to commence in 2022. In addition, in efforts to expand indications for the drug, we confirmed its effects on pulmonary hypertension in animal studies, etc.

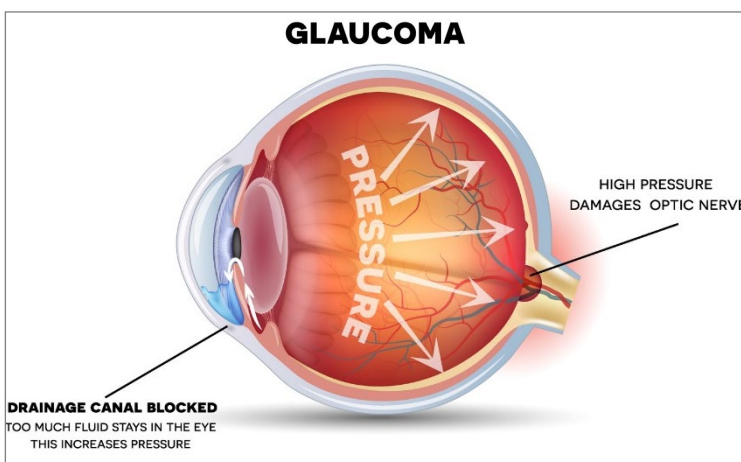
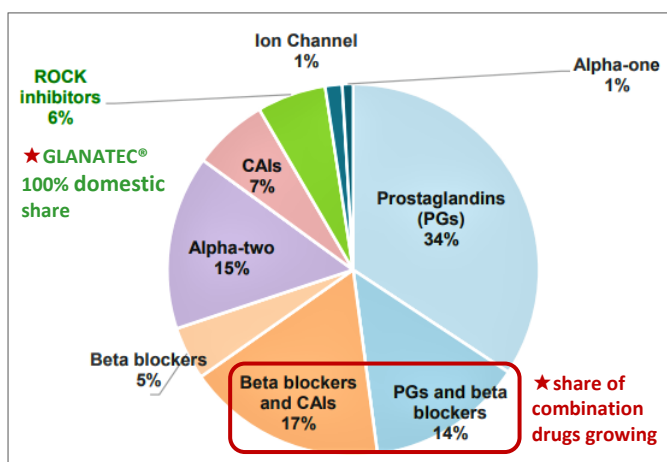
**Strong prospects as “first choice as a second-line Glaucoma drug”**

Similar to Ripasudil, H-1337 facilitates drainage of aqueous humor through the trabecular meshwork and Schlemm’s canal, and it has demonstrated a “strong and long-lasting IOP pressure-lowering effect.” The sole reliable evidence-based method of treatment for glaucoma (including normal-tension glaucoma) is the reduction of intraocular (IOP) pressure.

Prostaglandin analogues (PGs) demonstrate the strongest IOP pressure-lowering effect among first-line drugs; generic drugs are available and are most frequently used (see pie chart below). However, PGs also have little to no effect on many patients, and more than half of drug-treated patients use multiple medications. First-line drugs have little to no effect on a surprisingly large number of patients, and single-drug treatment has shown limited efficacy. Multiple-drug treatments are standard (3–4 drugs used in some cases); however, side effects are more common when using multiple drugs.

**DWTI estimates the target market for 1) patients who do not respond to first-line drugs and 2) patients who receive multiple drugs and suffer side effects is up to a maximum 40% of the estimated US market ¥340bn (i.e. ¥136bn\*).**

**Glaucoma treatment market in Japan:  
¥95bn in FY2018**



Source: calculated by DWTI based on the 5th NDB Open Data released by Japan’s Ministry of Health, Labour and Welfare.  
Note: CAI = topical carbonic anhydrase inhibitors, which reduce eye pressure by decreasing the production of intraocular fluid

Source: image licensed from Adobe Stock.  
\*Note: according to the company’s research based on IQVIA MIDAS Dec-2020 MAT.





**PIPELINE**

**Original and Licensed-in**

**Characteristics**

- Confirmatory comparative (bioequivalence) clinical trial comparing DW-5LBT with innovator product Lidoderm® generated favorable results.
- Low dermal irritation
- Capable of maintaining adhesive strength during exercise



Source: MEDRx website.

**[DW-5LBT] neuropathic pain treatment (Jointly developed with MEDRx)**

DW-5LBT (MRX-5LBT) is a new type of lidocaine patch for the treatment of post-herpetic neuralgia (neuropathic pain after shingles) that uses the ILTS® (Ionic Liquid Transdermal System), an exclusive MEDRx technology incorporating the company’s ionic liquid expertise. MRX-5LBT is being developed with the goal of its “Lidolyte” targeting the market for innovator product Lidoderm®, a lidocaine patch.

In April 2020, DWTI concluded a collaborative development agreement with MEDRx, and August filed the NDA application in the US. DWTI received a complete response letter (CRL) from the FDA on July 5, 2021, and the company is currently responding appropriately to specified issues. Following consultation with the FDA, DWTI plans to apply for approval again after conducting additional studies. The company expects to obtain approval in 2023.

Based on data from MEDRx, the US market for transdermal lidocaine patches was estimated at about ¥27bn in 2020. The primary details of the development agreement with MEDRx are ① milestone payment of up to ¥200mn according to progress of commercialization in the US (expected payment delayed from 2021), and ② after launch, DWTI will receive royalties commensurate with sales.

**Development Stage of DW-5LBT**



Source: DWTI website.

**(4586 Mothers) MEDRx ILTS® and transdermal drug delivery**

Transdermal drug delivery technology has been applied to developing local analgesics, anti-Alzheimer's drugs and antidepressants, since transdermal preparations have advantages of being able to improve patients’ QOL. Developing and providing transdermal preparations represent the fulfillment of unmet medical needs.

However, skin works as the barrier for human bodies to repel foreign substances. So, it is rather difficult for drugs to penetrate the skin barrier unless the drug has some penetration capability, which is influenced by the melting point, molecular weight, solubility, lipophilicity, etc. Under the circumstances, we have applied our proprietary ILTS® technology to various drugs, including even compounds with low solubility and/or weak absorbability, such as biopharmaceuticals, etc.

Transdermal drug delivery has various advantages:

1. Overcome first pass effect.
2. Easily achieve stable blood level and high bioavailability.
3. Free of pain and fear due to needleless injection.



## PIPELINE

### Joint R&D projects

#### Joint research and development projects

As part of its medium-term growth strategy, DWTI has begun work on collaborative R&D projects, some focused on its expertise in ophthalmic diseases, and others aimed at new investigative areas. Attractive features of these joint development projects include ① earning supplemental income in the form of R&D fees received for its core expertise in R&D as pipeline product developments move ahead, but take time in the clinical trials phase, and ② some include provisions for milestone payments and royalty income (margin of sales after launch).

#### US Glaukos Corporation: Joint R&D to create new intraocular drug delivery devices

Founded in 1998, Glaukos Corporation is an ophthalmic medical technology and pharmaceutical company focused on novel therapies in drug delivery for the treatment of glaucoma, corneal disorders, and retinal diseases. Glaukos was the first company to bring to market Micro-Invasive Glaucoma Surgery (MIGS), the micro-invasive procedure which revolutionized the treatment and management of glaucoma. In 2012, the company launched its first MIGS device—the iStent®—in the United States, followed by its next-generation iStent inject® device in 2018 and the iStent inject® W in 2020. In November 2019, Glaukos acquired Avedro, maker of the first and only FDA-approved cross-linking technology for progressive keratoconus (eye disease that affects the structure of the cornea, resulting in loss of vision).

In September 2020, Glaukos amended the joint research contract and license agreements it had concluded with DWTI in 2018, expanding the area of indications from glaucoma to include corneal disorders and retinal diseases, and the agreements incorporated milestone payments upon certain events during product development and royalties after product launch. The target of the 2018 joint research was related to iDose, a device which could provide a long-term sustained release of DWTI's rho-kinase inhibitor for the treatment of glaucoma. Glaukos highly evaluated the potential of DWTI's drugs, and its ability to design drugs suitable for delivery through its devices. **Compound evaluation is proceeding smoothly, and expectations are for clinical trials to begin at an early date.**

#### UBIENCE: Joint R&D to create targeted protein degradation through SNIPER

Several compounds were confirmed as generating kinase-degrading effects through joint research launched in 2019. On June 17, 2021, the joint research agreement with UBIENCE was extended and a capital alliance was formed. DWTI aims to accelerate this joint research and to develop superior new drugs. Goals include developing new drugs with DWTI's core technologies that generate therapeutic benefits not obtainable from kinase inhibitors. SNIPER, the core technology of targeted protein degradation (TPD), simultaneously allows for double function of anti-tumor action and abnormal protein degradation, so it's like doing multidrug combination therapy with one medicine.

#### SyntheticGestalt: Joint R&D for AI-based drug discovery

Established in 2018, SyntheticGestalt conducts AI-based internal and joint drug discovery and performs contract research. It possesses technology to predict and identify candidate compounds with superior drug properties out of as many as four billion compounds. It is leading company in the practical application of AI technology with proven track record of collaboration with multiple pharmaceutical and life science companies. DWTI's goals include expanding target indications from ophthalmology to create new kinase inhibitors for treatment of inflammatory and CNS diseases



**CHART ROOM**  
Share Price, Valuations



**Performance and Valuations:**  
SESSA Smart Charts

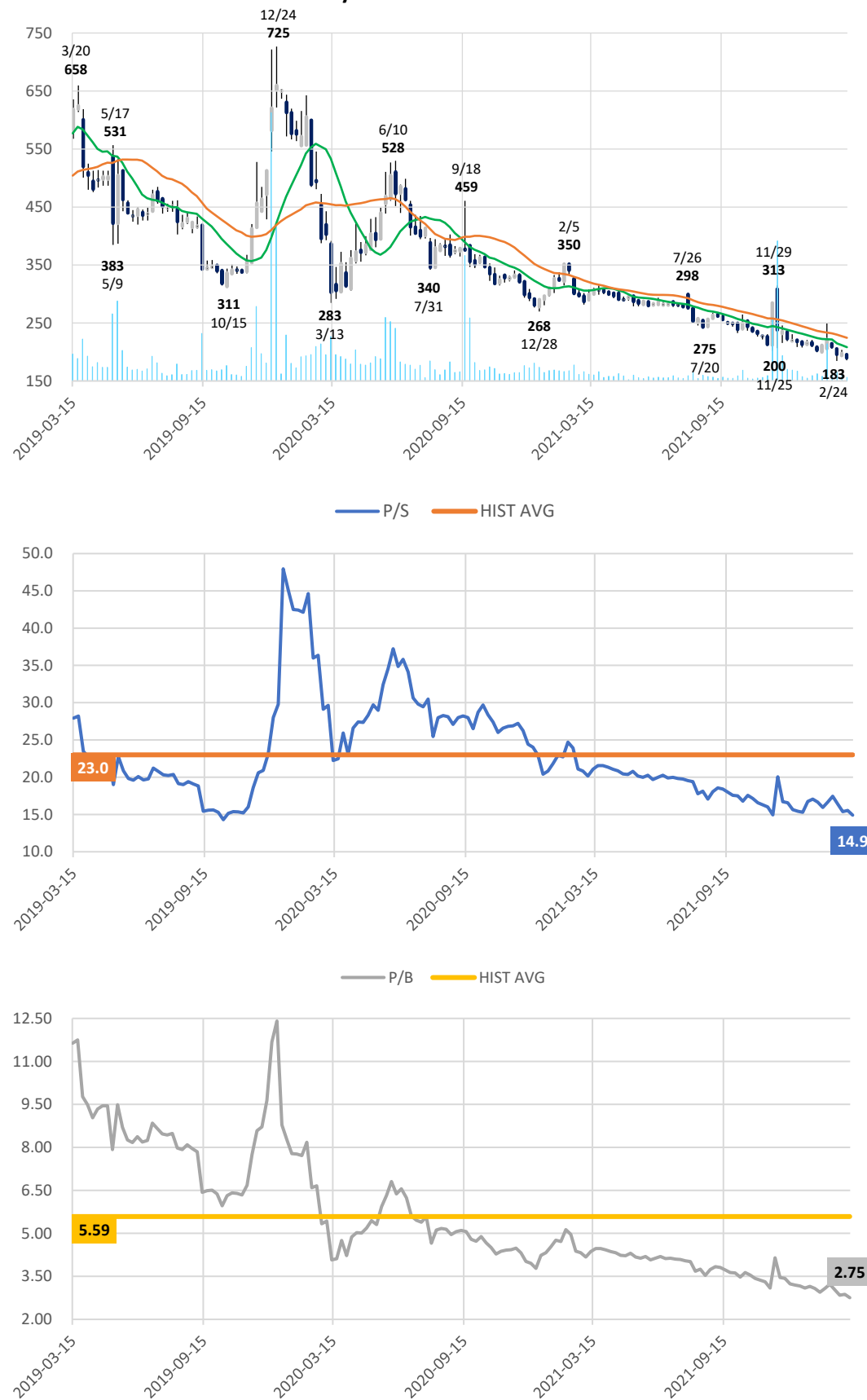
- ✓ On price-to-sales ratio, DWTI compares favorably with US peer Aerie Pharmaceuticals which is based in a much larger home market. Both companies are still in the early development phase.
- ✓ On price-to-book ratio, both companies fluctuate based on current cash position. DWTI appears undervalued on both metrics.

**5-Year historical valuations**

FY (times)	Price-to-sales		Price-to-book	
	DWTI	AERI	DWTI	AERI
18.12	51.5	67.9	12.0	7.2
19.12	29.4	16.0	12.2	6.7
20.12	23.8	7.6	3.9	26.4
21.12	15.3	2.3	3.2	—
current	14.9	3.2	2.8	—

Source: SPEEDA.

**Sessa Smart Charts: 3-Year Weekly Share Price and Valuations Trend**



Source: compiled by Sessa Partners from SPEEDA historical earnings and price data. Valuations calculated based on CE.

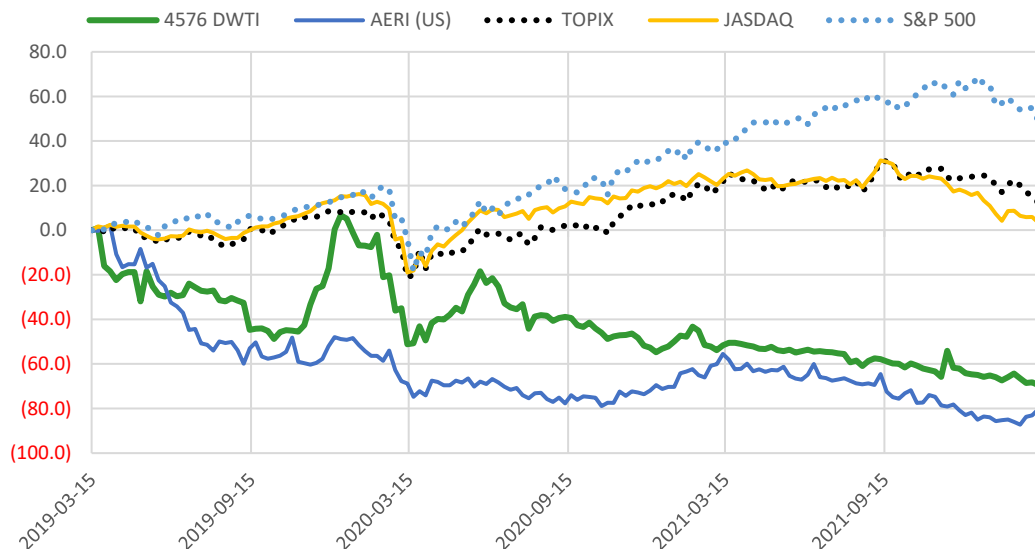


Analyst's view

✓ Over the last three years, both DWTI and US peer AERI have significantly under-performed their respective markets. Ultimately bio-ventures are relatively high-risk business due to 1) high R&D costs, 2) low probability of success and 3) steady red ink in the early growth stage with limited revenue.

✓ DWTI's PSR is trading on a 35% discount to historical average, and PBR on a 50% discount to historical average. Risk appears weighted on the upside given current valuations and potential for positive news flow.

3-Year Weekly Relative Performance (local currency basis)

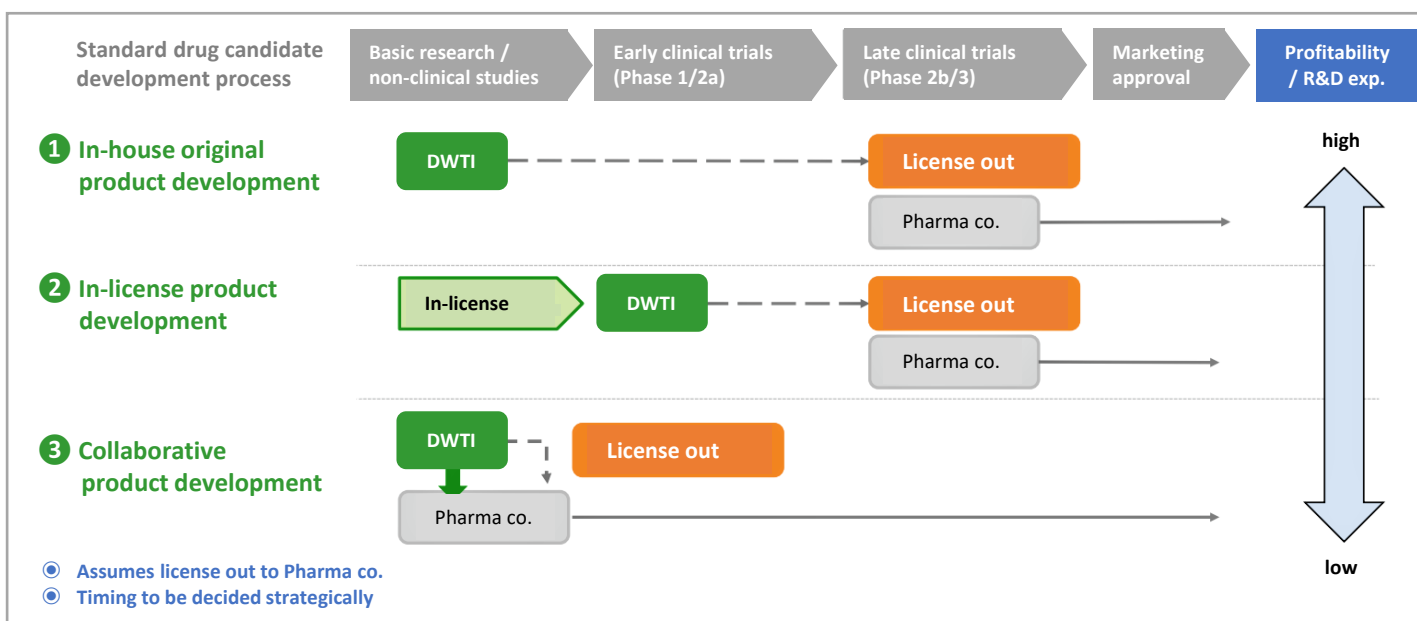


Source: compiled by Sessa Partners from SPEEDA price data. Note: not adjusted for foreign exchange rates.

Growth strategy has expanded business models along with enhancing the pipeline

Over time with progress in execution of the development pipeline, and as part of growth strategy to diversify revenue streams, the basic drug discovery business model has evolved to include ① from 2015, in-licensing of later stage development or repositioning products, commencing in-house clinical development, ② from 2018 collaborative drug creation applying DWTI's technical expertise to assist in the development of products of other firms, and ③ from 2018 extending development of original in-house products beyond early out-licensing as far as proof of concept (PoC) through phase IIb. The revenue stream for collaborative research projects includes receipt of payment of R&D fees from the partner.

★ DWTI's initial drug discovery basic business model has evolved into three business models



Source: company IR materials.



DWTI Group Head Office and R&D Labs

**Japan Innovative Therapeutics**

**Rohto Research Village Kyoto**

**DWTI**  
D. WESTERN THERAPEUTICS INSTITUTE

**Nagoya Head Office**

**Mie University Faculty of Medicine R&D Lab**

Source: compiled by Sessa Partners from company IR materials.

**President and CEO**  
Yuichi Hidaka



**DWTI Corporate Profile**

	Details
<b>Company Name</b>	D. Western Therapeutics Institute, Inc.
<b>Business Field</b>	Discovery and development of new drugs
<b>Established</b>	February 26, 1999
<b>Share Capital</b>	573 million yen (as of December 31, 2021)
<b>Head Office</b>	1-18-11, Nishiki, Naka-ku, Nagoya-shi, Aichi 460-0003, Japan
<b>Main Switchboard</b>	052-218-8785
<b>R&amp;D Laboratory</b>	Institute of Human Research Promotion and Drug Development, Mie University Faculty of Medicine, Room 432, University Research Hall, Mie University, 2-174, Edobashi, Tsu shi, Mie, Japan 514-8507
<b>Employees</b>	DWTI: 16, JIT: 3 (as of December 31, 2021), total 32 including executive officers
<b>Group Subsidiary</b>	Japan Innovative Therapeutics, Inc. (consolidated subsidiary)

Source: company website.



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**Sessa Partners Inc.**

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5-3-18 Hiroo, Shibuya-ku, Tokyo  
info@sessapartners.co.jp