D. Western Therapeutics Institute, Inc.

(4576 JASDAQ) Issued: April 22, 2020

A rare growing bio-venture with multiple stable sources of revenue

A drug discovery venture focusing on kinase inhibitors for ophthalmic use

D. Western Therapeutics Institute, Inc. (DWTI) is mainly involved in ophthalmology, a niche area with relatively high barriers to entry. The company has its proprietary unique library of chemical compounds with various kinase inhibiting activities which has been used to create promising new drug candidates. It already licensed out one product, Glanatec® which is now on the market. However, as the out-license of the product was performed at DWTI's R&D fundamental establishment era with the very early basic research activity, the license terms were not necessarily very advantageous. At the present time, however, its target therapeutic indications and geographic territories are steadily expanding. At the same time, DWTI in-licensed products from other companies in order to realize the consistent growth and the expanding range of indications including surgery areas for the in-licensed products is beginning to provide growth for the company's operations. While DWTI has a number of stable and growing sources of income, it is aiming to develop its own new drugs up to the early clinical stage before out-licensing.

Two growth/income enhancing products on the market

Glanatec® is a therapeutic drug for the treatment of glaucoma (out-licensed to Kowa Co., Ltd) and was the first rho kinase (ROCK) inhibitor in the world approved for this indication in 2014. Its sales in the Japanese market have already exceeded JPY5 billion. In February 2019, it was approved in South Korea, starting in August new drug applications were submitted in four Asian countries, and in March 2020 it was approved in Singapore. And then, from August 2019, Phase 2 trials began in the US indicated for Fuchs corneal endothelial degeneration. Further, in February 2020 Kowa began developing K-232, fixed combination formulation for glaucoma of Glanatec® and another exsiting drug with a different action of mechanism. These activities contribute to the product life-cycle management of Glanatec® and would ensure Glanatec® sales growth for the time being.

In addition, the company in-licensed DW-1002, an eye surgery adjunct that provide the company with the time and income necessary before another in-house development like Glanatec® will take over. In addition to the existing sales in Europe, the company submitted an NDA application in Canada in October and, having obtained US approval in December 2019, began sales there in April 2020. As for additional indication, with the completion in August 2018 of investigator-sponsored Phase 3 trial for cataract surgery in Japan, the company out-licensed the cataract surgery rights (for Japan) to Wakamoto Pharmaceuticals Co. Ltd.in February 2019.

Pipeline value JPY17 billion, including H-1337 and Glaukos products

H-1337 is one of the company's original products and its out-licensing activity is on-going. Like Glanatec®, H-1337 is a type of isoquinoline derivative that is a multikinase inhibitor targeting LRRK2. Its development for glaucoma and ocular hypertension began in the US in 2016 with the Phase 1/2a trial starting in March 2018. The trial was completed successfully, ending in September of that year, and now DWTI is conducting out-licensing work with a diligent strategy to complete it in the next 1-2 years. Recently in the glaucoma market, the ocular devices to improve patients' QOL are expected by many ophthalmologists. In this context, in 2018 DWTI began joint research and development with the major global ocular device inventor, Glaukos, of the glaucoma therapeutic devices using DWTI's new ROCK inhibitors. In a calculation based on various assumptions, including expanded sales of existing products and the successful launch of two new products, the pipeline value of DWTI is expected to come in at around JPY20 billion. If we posit the probability of success of two new products at 60%, it is possible to anticipate a pipeline value of some JPY17 billion.

Note: This report is the English-language version of the original Japanese-language report issued on April 22nd, 2020, to which you should refer for precise details

Basic Report

Fair Research

Tsuyoshi Suzuki

Company Outline	
Location	Nagoya
President	Yuichi Hidaka
Established	Feb. 1999
Capital	JPY34 million
Listed	Oct. 2009
URL	www.dwti. co.jp
Industry	Pharmaceuticals
Employees	17 (consol)
Key Indicators as of 2020/4/21	
Share Price	373
Year High	699
Year Low	312
Shrs Outstanding	26,275,200
Trading Unit	100 shares
Market Cap	9,801 mil. JPY
Dividend (est)	0
EPS (est)	-12.94 JPY
Forecast PER	na
BPS (actual)	53.02 JPY
PBR (actual	7.04X

Note: EPS、PER、BPS、PBR calculated on total shares outstanding, excluding treasury shares

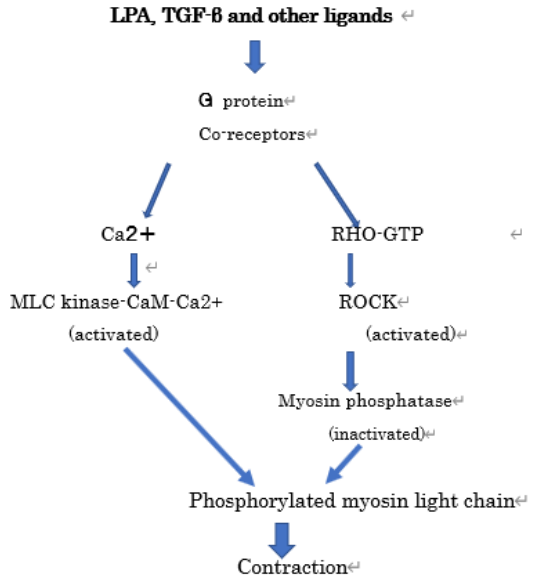
Results	Revenues JPYmil	YoY %	Op. Income JPYmil	YoY %	R.P. JPYmil	YoY %	Net Income JPYmil	YoY %	EPS JPY	Share Price High	Share Price Low
2015/12 Actual	61	-	-290	NM	-295	NM	-296	NM	-12.99	1,069	520
2016/12 Actual	168	171.8	-319	NM	-304	NM	-253	NM	-10.46	862	362
2017/12 Actual	254	51.2	-633	NM	-668	NM	-1,563	NM	-59.89	829	404
2018/12 Actual	292	15.3	-786	NM	-796	NM	-748	NM	-28.51	715	387
2019/12 Actual	580	98.2	117	NM	109	NM	133	NM	5.07	699	312
2020/12 Forecast	310	15.3	-390	NM	-410	NM	-340	NM	-12.94		

Company Outline – Management Philosophy

A research and development-oriented drug discovery company mainly focusing on rho kinase (ROCK) inhibitors	**Business model and history** D. Western Therapeutics Institute, Inc. (DWTI) is a university oriented bio-venture, specialising in the research and development of various kinase inhibitors. It focuses on ophthalmologic diseases, an area with relatively few competitors. A feature of DWTI is that it uses its proprietary unique well-stocked chemical library with variety of compounds having kinase inhibitory activity to invent promising new drug candidate compounds. Kinases are a group of enzymes which, while sharing roles, transmit signals that respond to stimuli from the outside of cells and constantly control complex biological functions through cell differentiation, proliferation, apoptosis, and the like. The 518 kinds of kinases existing in the human body are roughly classified into serine-threonine kinases (STKs) and tyrosine kinases, according to their selective substrate. All kinases are vital for life, controlling complex biological functions and maintaining a delicate balance between them. Any damage to this balance can lead to serious illness. For some time, molecular target drugs such as imatinib and gefitinib have been developed and approved as kinase inhibitors after identifying those kinases that cause particular diseases. Even currently, various companies continue to develop such inhibitors, including Japan's Carna Biosciences, which is developing a bruton's tyrosine kinase inhibitor.
Individual companies are now straining their unique abilities to develop kinase inhibitors approprietely	While the development of chemical compounds to inhibit targeted kinases is regarded as relatively uncomplicated with modern chemical techniques, pharmacokinetic issues, such as absorption and metabolism, and side effects, can present problems. It is thought that the main cause of side effects is derived from the off target effects which work on kinases other than those targeted, and so a major effort is now dedicated into the development of highly selective inhibitors which act only on the target.
Record of the research on intracellular signalling which resulted in new pharmaceutical products on the market	The origin of DWTI's technology comes from the long years of research done by its founder, Hiroyoshi Hidaka (current chairman and chief scientific officer), on intracellular signalling systems using protein kinase inhibitors at Mie University and Nagoya University. Chairman Hidaka has a worldwide reputation in the fundamentals of pharmacology, particularly for his "Cellular level studies on calcium ions", and for his contribution to two novel products developed and brought to market in collaboration with Japanese pharmaceutical companies. One of these is fasudil hydrochloride (Asahi Kasei Pharma: indicated for delayed cerebral vasospasm after subarachnoid hemorrhage), the world's first ROCK inhibitor. Fasudil hydrochloride is a kind of isoquinoline sulfone amide compound, and even now, remains one of the more potent compounds of the specific inhibitor of rho kinase. Similar chemical structures are recognisable in many of the drugs currently being developed by DWTI.
Isoquinoline derivatives constitute the backbone of the company's product pipeline	
ROCK inhibitors contribute to contraction and	Rho kinase, is a type of serine threonine kinase (STK) that acts as a mediator of the MAPK pathway. Previous studies have shown that Rho kinase is deeply involved in such physiological cell functions as contraction, proliferation, migration and gene expression induction. Among them, phosphorylation of various proteins such as myosin, adducin, and the erm family of proteins, is involved in contraction by actin-myosin polymerization, movement of cytoskeleton, remodelling of extracellular matrix, etc. have been linked to drug discoveries. For example, fasudil hydrochloride, mentioned earlier, inhibits ATP from competing with phosphatases such as rho kinase, which prevents phosphorylation of myosin light chains and

movement of cytoskeleton	prevents actin and myosin from polymerizing and contracting, thereby expanding contracted blood vessels.

ROCK and the contraction mechanism



(Source) Fair Research Inc. using various materials

ROCK inhibitors are involved in aqueous outflow in the trabecular meshwork of the eye	When it was verified in the early years of this century that ROCK inhibitors reduce intraocular pressure, there was a big increase in applied research into glaucoma. It was subsequently revealed that contraction due to actin-myosin polymerization, movement of cytoskeleton, remodelling of extracellular matrix, etc. are involved in aqueous outflow in the trabecular meshwork pathway of the eye.
In 2002 DWTI succeeded in out-licensing its ROCK inhibitors to Kowa In 2014 the world's first ROCK inhibitor as a therapy for glaucoma (Glanatec®) received approval	DWTI was established in 1999 with the aim of researching and developing kinase inhibitors. As early as September 2002, the ROCK inhibitor glaucoma treatment agent K-115 and antiplatelet agent K-134 were successfully out-licensed to Kowa Company, Ltd. (at the early basic research stage) becoming the main developer of these two products. In September 2014, K-115 (ripasudil; trade name Glanatec®) was approved, and in December of the same year, was launched as the world's first ROCK inhibitor therapeutic agent for glaucoma. Meanwhile, in October 2009, DWTI was listed on JASDAQ. (The second ROCK inhibitor for glaucoma is netarsudil (trade name Rhopressa®) developed by the US bio-tech company, Aerie Pharmaceuticals Inc. (approved in 2017)). K-134 completed clinical Phase 2a trials in Japan and the US in 2011and in the following year started Phase 2b in Japan, completing them in 2014. In this trial, however, it failed to meet the primary endpoint criteria and at the moment development is suspeneded.
Until an in-house product came on stream to succeed Glanatec®, DWTI is in-licensing ophthalmic products from outside	DWTI continued to promote the development of its own in-house products but, until such a product started producing profits on a stable basis, and to diversify risk, in 2015 it in-licensed an ocular eyedrop painkiller. Also, in 2017, it in-licensed the eye surgery adjunct agent (DW-1002(BBG250)) of Helios Co., Ltd. (the former was licensed out to Rohto Pharmaceutical in 2019, and the Japanese rights to the latter to Wakamoto Pharmaceutical and the US rights to DORC B.V.) It also plans to utilize its knowledge and experience of drug development for stabilizing revenues through in-license of good products even out of ophthalmic

The company also aims to in license candidates outside of ophthalmology which have the potential for early market launch, thereby stabilizing revenues	field which are expected to launch into the market in the short term. In April 2020, the company executed a joint development agreement with the Japanese company, MEDRx Co. Ltd. to develop a unique lidocaine tape preparation in the US (MRX-5LBT; DWTI development code: DW-5LBT; target indication: neuralgia following herpes zoster) for which MEDRx is planning to submit an NDA in the US during 2020. It was expected that DWTI would be in receipt of royalties and related revenues after launch.
Ready to speed up the development of in-house products now that Glanatec® and licensed-in products are contributing to earnings	As noted above, DWTI is promoting the development of several new compounds invented in-house, while Glanatec® already on the market and products acquired externally beginning to earn a certain level of stable profit.
The development of H-1129 has unfortunately been discontinued	H-1129 (WP-130) is a compound with joint inhibiting action of rho kinase inhibitor and HSP90 (a heat shock protein) as a novel mode of action. It was out-licensed to Wakamoto Pharmaceutical and Phase 1 clinical trials were begun in March 2016 for glaucoma given its very potent intraocular pressure-lowering and neuroprotective action. In July 2018, Phase 2b trials were completed, and in January 2019, Phase 3 began. However, development was terminated in September of that year (apparently for reasons of some side effects).
H-1337 produced welcome Phase1a/2a results and the company is now looking to license out	A multi-kinase inhibitor H-1337 (detailed later) showed good US Phase 1/2a results in 2018 and DWTI is in the process of selecting an out-licensing partner (plans to out-license in the next 1-2 years).
Now collaborating with a device maker on development of new products	Further, in 2018 the company started joint research & development of glaucoma therapy device products using novel ROCK inhibitors with Glaukos Corporation, a global ophthalmological devices maker.
Stable earnings sources and an expansion in indications and territories should lead to growth	Additionally, expansion in therapeutic indications and geographic territories of existing DWTI products is driven mainly by mainly licensees. Glanatec® (out-licensed to Kowa, which took over the later development) received authorization to import and sell into South Korea in February 2019, and from August Kowa submitted NDAs to four Asian countries, one of which, Singapore, approved in March 2020. Additionally, in August 2019 a Phase 2 trial began in the US for Fuchs endothelial corneal dystrophy. Further, in February, began the development of a fixed dose combination product (K-232, Japan) containing Glanatec® and a different existing glaucoma drug. DW-1002 is an in-licensed drug originally for use in Europe. Wishing to expand its indications an NDA was submitted in the US in April 2019, followed by an NDA in Canada in October. The approval in the US came in December 2019 and sales in the US began in April 2020. In terms of expanding indications, Phase 3 investigator-sponsored trial in Japan on cataract surgery was completed in August 2018, and in February 2019 the Japanese rights for the indication was out-licensed to Wakamoto Pharmaceutical. Thus, DWTI is engaged in R&D related to ophthalmic indications as its intensive research field. In addition to the above, it is conducting research to expand indications for H-1337 beyond glaucoma including the systemic diseases, and is seeking out new drug candidates for retinal diseases with its research and in-licensing strategy.
Challenging new modalities	Further, the company is looking closely at targeted protein degradation inducers (not typical kinase inhibitors) and has started joint research on this new modality with UBIENCE Co., Ltd. (October 2019).

The history of DWTI

Foundation Period	1999	Feb	D. Western Therapeutics Institute set up as limited company
	2002	Sept	Licensed out to Kowa: K-134（anti-platelet agent), K-115（glaucoma drug)
	2004	Jul	K-134 starts Europe Phase 1
		Nov	Becomes incorporated
	2005	Apr	K-134 Completes Europe Phase 1
	2006	Apr	K-134 Starts Japan Phase 1
		Jul	K-115 Starts Japan Phase 1
	2007	Oct	K-134、K-115 Completes Japan Phase 1
	2008	Jul	K-134 Starts Japan Phase 2
		Dec	K-134 Starts US Phase 2a
	2009	Mar	K-115 Starts Japan Phase 2
		Oct	JASDAQ Listed
	2011	Jan	K-134 Completes US Phase 2a K-115 Completes Japan Phase 2
		Jun	K-134 Completes Japan Phase 2a
		Sept	K-115 Completes Japan Phase 3
	2012	Jan	K-134 Starts Japan Phase 2b
	2013	Mar	Licenses out H-1129 (WP-1303) to Wakamoto Pharm.
		Apr	K-115 Completes Japan Phase 3
		Oct	K-115 Japan NDA (glaucoma, intra-ocular pressure)
		Dec	H-1129 Starts pre-clinical tests
	2014	Sept	K-115 Glanatec® approved
		Dec	K-115 Glanatec® launched K-134 Finishes Japan Phase 2b
Growth Period	2015	Jun	Licenses in drug for ocular pain (first licensing-in)
		Sept	Issues share options allotted to Credit Suisse Securities
		Nov	JIT becomes consolidated subsidiary
	2016	Mar	H-1129（WP-1303) Starts Japan Phase 1 (milestone received)
		Apr	H-1337 (glaucoma treatment) Start of pre-clincal tests by US Alleysta Corp.
	2017	Jan	Pays JPY1.3 billion for transfer from Helios of surgical adjuvants business, including BBG250.
		Feb	Borrows JPY600 millin from Mizuho Bank. Repayment 2019-2023 H-1129 (WP-1303)contract on overseas option license (optiion fee) Milestone: JPY7.3 bil. Completion of exercise of warrants allotted to Credit Suisse Secs - raises JPY1,994 mil.
		Mar	H-1129 (WP-1303) Japan Phase 1 completed
		Aug	H-1129（WP-1303) Starts domestic Phase 2b
		Sept	H-1337 Signs co-op research agreement with Chiba Univ. on pulmonary hypertension
		Oct	DW-1002(BBG250) Starts investigator led Phase 3 on additional indication (cataracts surgery)
	2018	Mar	H-1137 Starts US Phase1/2a
		Jul	H-1129 Domestic Phase 2b finishes; non-exercise of overseas option rights notified
		Aug	Agreement with US Glaukos on joint research and licensing DW-1002(BBG250) Additional indication (cataracts surgery) investigator-led Phase 3 finished
		Sept	H-1137 US Phase 1/2 successfully completed
	2019	Jan	H-1129 Starts Japan Phase 3
		Feb	DW-1002(BBG250：cataracts surgery llicensed out to Wakamoto Pharm Glanatec® Receives permit to import pharamceuticals into S. Korea
		Apr	DW-1002(BBG250）US NDA
		Aug	Glanatec: Start of US Phase 2 targeting Fuchs corneal endothelium degeneration NDA's submitted in S'pore, Malaysia, Thailand
		Sept	H-1129: Decision to terminate development
		Oct	DW-1002(BBG250）NDA submitted in Canada Joint research agreement with UBIENCE on targeted protein degradation inducer
		Dec	Licensed out products from 2015 to Rohto Pharm. DW-1002(BBG250）: Receives US approval
	2020	Feb	Starts development of Granatec® alpha2 blocker compound (K-232) in Japan
		Mar	Glanatec® receives approval in Singapore
		Apr	DW-1002(BBG250）launched in US as "TissueBlue" Joint dev.contract with MEDRx for Lidocaine Tape (DW-5LBT)

(Source) Fair Research Inc. using the company's securities filings and other materials

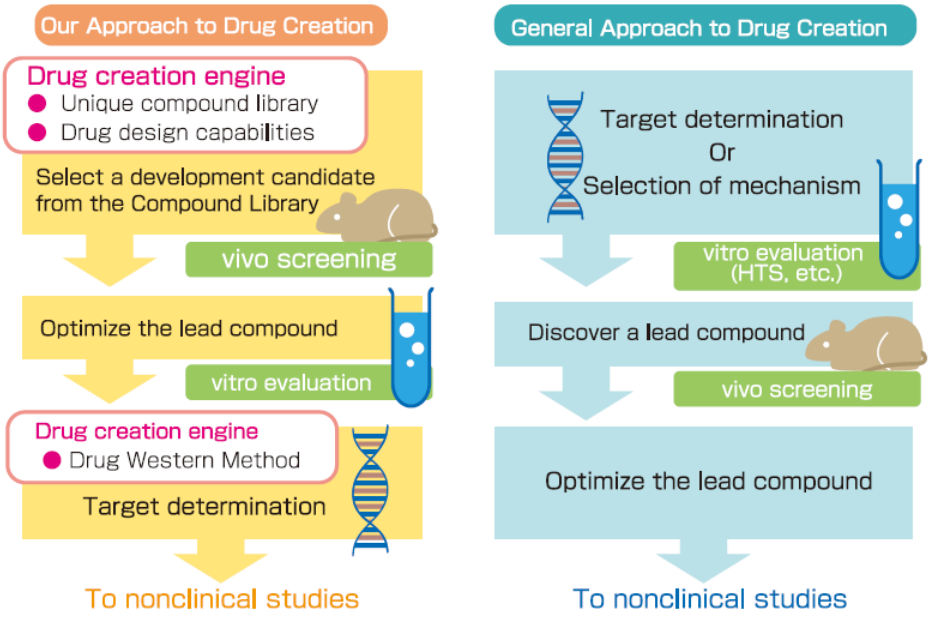
The Drug Western Method

DWTI drug discovery characterised by its Drug Western Methodology

DWTI is expanding into drug discovery using its proprietary "Drug Western Method."

DWTI's "Drug Western Method" of drug development involves a different approach to that currently in use more generally in pharmaceutical industry. In the conventional approach to drug discovery and development, the mechanism of the target disease is subjected to a screening and, from a very extensive compound library, a lead compound for development is selected. In DWTI's case, the leading compound is selected from its unique compound library which is one of the company's drug discovery engines. That is then subjected to a second engine, the Drug Western Method, which elucidates the compound's mode of action, and a decision made as to target. By conducting *in vivo* screening at an early stage, DWTI's approach provides a more efficient way of identifying the lead compound than that employed by other drug discovery companies.

DWTI's approach to drug discovery - image



(Source) DWTI's website

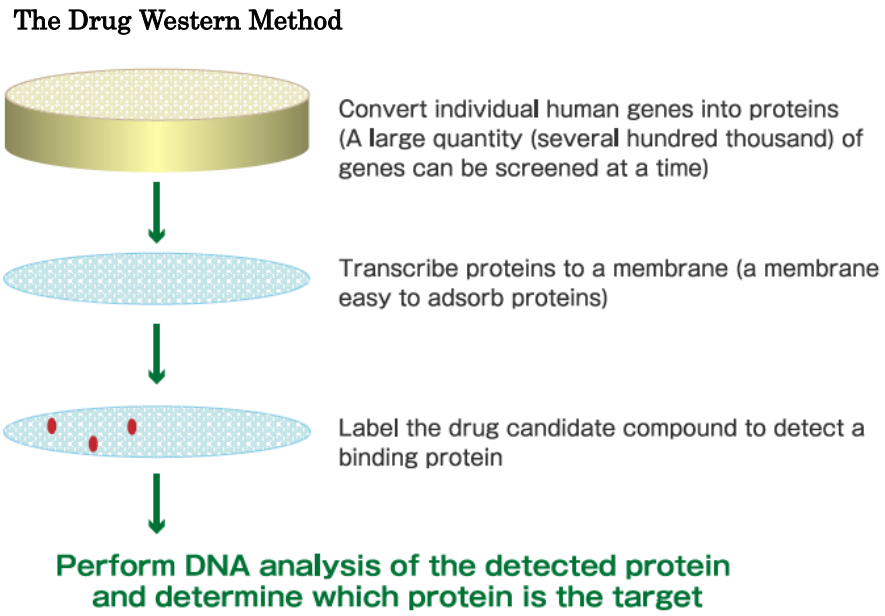
The mode of action and the mechanism of side effects can be elucidated by identifying proteins that bind to drugs

The Drug Western Method provides a way of establishing which types of protein the administered drug is binding to within the body. It is possible to test the viability of a new drug candidate by isolating the gene of a protein that binds to the candidate under certain conditions and identifying the protein so bound by analysing the gene sequence and examining the function of that protein. In addition, in the early stages of a drug development, the identification of the molecular target of the candidate leads to the enhanced efficacy and safety of the drug through elucidation of the mode of action and the mechanism of side effects. Furthermore, analysis of the possibility of combined use with other drugs is facilitated, which leads to expanded opportunities for use and reduced risk.

Drug development can be undertaken efficiently

The use of this Drug Western Method facilitates the identification of the target protein of a new drug candidate, which is difficult when using other conventional methods, in addition to which it is possible to identify multiple target proteins in one

screening. Compared with conventional methods, the Drug Western Method consumes only small amounts of biological material and chemical compounds, and the screening procedure is simple and completed in a short time.



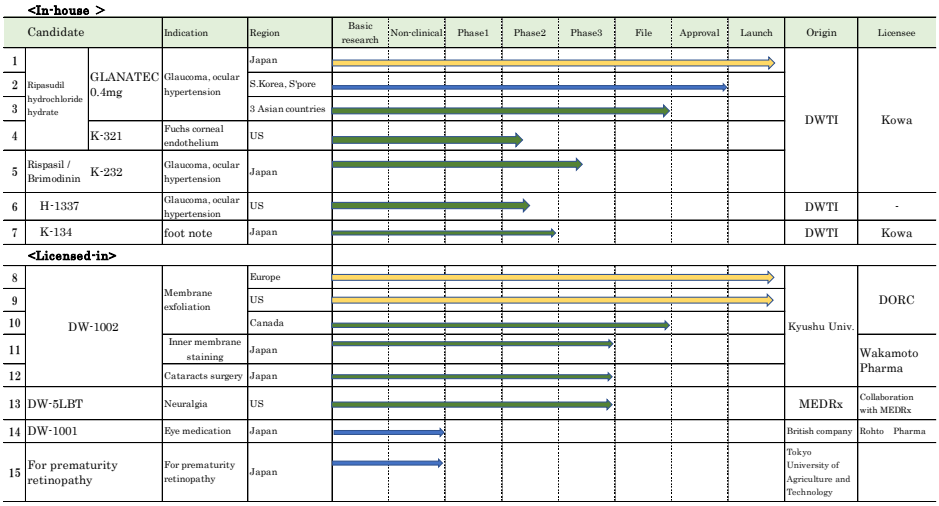
(Source) DWTI website

Outline of the DWTI product pipeline

Has out-licensed Glanatec® and plans to out-license H-1137

The DWTI pipeline is shown in the chart below. Ripasudil (Glanatec®, K-321, K-232) and H-1337 are main products out of in-house research, ripasudil have beenout-licensed to Kowa Pharmaceutical, which expanding both therapeutic indications and geographical territories are diligently pursuing mainly by Kowa.

DWTI – Status of development



(note) Japan Phase 2 trials for atherosclerosis was completed. KOWA is now considering indications

(source)DWTI

(1) Ripasudil (Glanatec® and K-321)

① Drug for glaucoma/ocular hypertension (Glanatec®)

Glanatec® was the first ROCK inhibitor to be approved for the treatment of glaucoma

Ripasudil is a ROCK (rho kinase) inhibitor with an isoquinoline derivative skeleton. ROCK inhibitors' ability to reduce ocular pressure was first reported in 2001, after which, in 2002, DWTI licensed it out at the very early research stage to Kowa, which subsequently it was developed mainly by Kowa and in 2014 Kowa launched it under the name of Glanatec® in Japan first in the world.

(In 2018, netarsudil (product name: Rhopressa®), which has a ROCK inhibitory action, was launched in the US as a therapeutic agent for glaucoma. However, netarsudil shows its effect of suppressing aqueous humor through not only ROCK inhibitory but also norepinephrine transporter inhibitory effect).

Glaucoma is a condition in which the field of vision is gradually reduced. It is generally unconscious in the early stage of disease but by the time the symptoms become apparent it is already in an advanced stage. In Japan, it occurs in one-in-20 people over the age of 40 and is the leading cause of blindness.

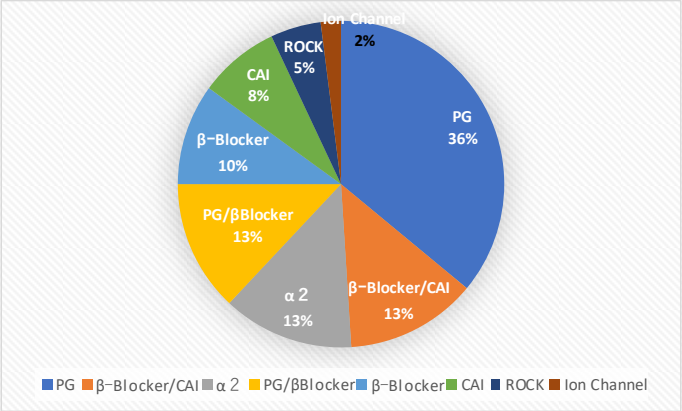
The first choice for glaucoma treatment is the use of an eye drops formulation to reduce

The mechanism of glaucoma onset is: "a rise in intraocular pressure compresses the nerve fibers that are bundled and collected in the optic nerve head to cause partial loss of retinal nerve cells, resulting in visual field loss.".

intraocular pressure	Hence, the first choice of treatment is the administration (by eye drops) of an intraocular pressure lowering drugs.
Eye drops can suppress the production of aqueous humor or promoting the drainage of aqueous humor	Intraocular pressure changes with the amount of aqueous humor filling the space between the lens and cornea (the chamber of the eye). The aqueous humor has two functions: aqueous humor secreted from the ciliary body flows from the posterior chamber to the anterior chamber, transports nutrients, draining waste products from the Schlemm's canal, and regulates intraocular pressure. Normally, secretion and excretion are regulated so that the amount of aqueous humor is constant, and the eyeball is moderately pressured from the inside to maintain a spherical shape. However, if for some reason the secretion and excretion are out of balance and the amount of aqueous humor becomes too large, the intraocular pressure will increase. Glaucoma is classified into several types according to the reason for this imbalance (primary angle-closure glaucoma, primary open-angle glaucoma, normal-tension glaucoma), but the first choice of treatment in all cases is to reduce intraocular pressure with the administration of an eye drop formulation. Medical eye drops come in three types: those that suppress the production of aqueous humor, those that promote the drainage of aqueous humor, and those that have both dual actions. **Medicines suppressing the production of aqueous humor** • Sympathomimetic drugs: Those that stimulate the sympathetic nervous system and thereby suppress aqueous humor production • Carbonic anhydrase inhibitor: suppresses metabolism in the ciliary body and suppresses aqueous humor production • β-blocker: binds to autonomic β-receptors and suppresses sympathetic nerve activity
The most commonly used are PG drugs (such as Xalatan®) which have a strong effect on elevated intraocular pressure	**Drugs that promote the drainage of aqueous humour** • Prostaglandin formulation: promotes the drainage of aqueous humor • Parasympathomimetics: act on parasympathetic nerves and promote aqueous humor drainage **Drugs that suppress aqueous humor production + enhance drainage** • α2 receptor stimulant: binds to α2 receptor of autonomic nerve and suppresses sympathetic nerve According to the glaucoma clinical practice guideline, prostaglandin (PG) drugs and β-blockers are the first-choice for open-angle glaucoma, and second choice drugs include enzyme inhibitors (CAI), α2 receptor stimulants, ROCK inhibitors, etc.

Market share for various glaucoma drugs (Japan)

(Market size; JPY 101.2 billion in FY2017)



(Source) DWTI results meeting materials, February 2020

The most commonly used drugs are prostaglandin (PG) formulations which have a strong potency to reduce intraocular pressure. A well-known example is latanoprost (product name: Xalatan®.) Recently, a prostanoid EP2 receptor agonist (trade name: Eybelis®) that has an intraocular pressure lowering effect comparable to latonoprost has been given regulatory approval and put on the market.

Another central player among glaucoma drugs are beta blockers. Timolol was the first beta blocker to be launched. Because of its drug properties it is widely used in combination with glaucoma eye drops or in compound formulations.

Another drug of first choice are beta blockers (timorol and others)

Among the second-choice drugs, a notable one is the α2 receptor stimulant. This has the effect of both suppressing the production of aqueous humor and promoting the discharge of aqueous humor via the uveoscleral outflow route. A well-known drug of this type is brimonidine, which was approved in the US in 1996. It was approved in Japan in 2012 under the trade name Aiphagan® and, also in Japan in 2019, there was the release of a combination drug consisting of brimonidine and timolol.

The main second choice drugs are alpha-2 blockers (such as brimonidine)

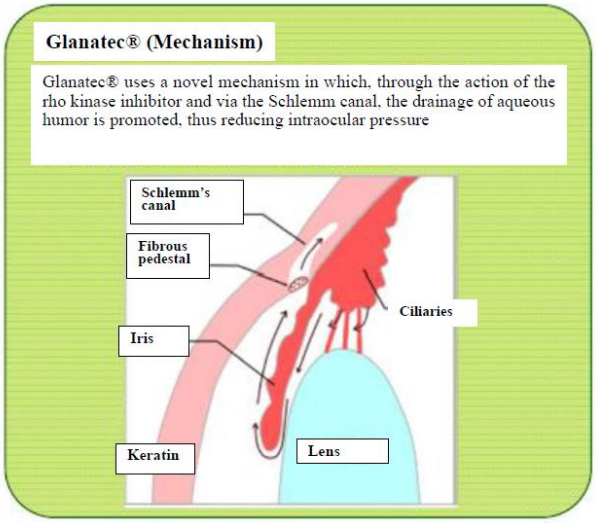
The carbonic anhydrase inhibitor (CAI) was originally used as an oral drug for the purpose of lowering intraocular pressure, but because of side effects, notably liver dysfunction, eye drops were developed. Well-known examples include dorzolamide (trade name Trusopt®) and brinzolamide (trade name Azopt ®). Recently, a combination drug containing dordramide and timolol (trade name Cosopt®) has been launched.

The ROCK inhibitor is a relative newcomer. While not as effective at lowering intraocular pressure as PG drugs, it has been suggested that extended administration

As mentioned earlier the ROCK inhibitor is a relatively new drug. ROCK is also present in trabecular cells of the eye and Schlemm's canal endothelium. Activation of the ROCK signal promotes actin polymerization and cell adhesion, causing tissue contraction and leading to reduced aqueous outflow. ROCK inhibitors have a mechanism to suppress this signal and process intraocular pressure. They are not as effective as PG drugs in reducing pressure but it is believed they become more effective with long-term administration. A side effect is the high frequency of conjunctival hyperemia after administration. This seems to be due to the vasodilatory effect of the ROCK inhibitor by relaxing vascular smooth muscle, but in most cases it is transient and the hyperemia disappears 1 or 2 hours after administration.

improves its effectiveness

How Glanatec® works

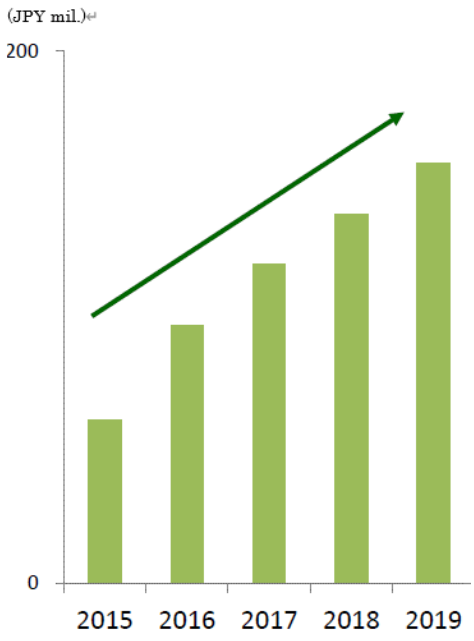


(Source) DWTI company briefing, March 2017

Glanatec® Japan domestic sales exceed JPY5 billion. Peak sales target JPY7.6 billion

Glanatec® was launched in December, 2014 and sales proceeded to grow smoothly. This led to a concomitant growth in royalties income to DWTI (around 7-8% annually). Annual domestic sales of Glanatec® sales stand at around JPY5 billion (FY2017) and the target for 2024 (10 years after launch) stands at JPY7.6 billion (250,000 patients).

Trend in royalties to DWTI



(Source) DWTI results meeting materials, February 2020

Growth is also picking up overseas. The drug import license was obtained in South Korea in February 2019, and since August 2019 a series of four NDA procedures has been completed for Singapore, Malaysia, Vietnam and Thailand. Singapore authorities gave an approval in March 2020.

Growth also picking up in Asia (excl. China) Now targeting corneal endothelium degeneration as an additional indicatiom	② Fuchs corneal endothelium degeneration: K-321 Fuchs corneal endothelium degeneration has few patients in Japan but is a common condition in Western countries, especially the US. It is a disease in which corneal edema, opacity and decreased visual acuity result from damage to the corneal endothelium. It is estimated that a maximum of 4% of Americans over 40 years suffer from this condition (around 6 million patients). At present no effective drug has been developed and more than 90% of patients receive surgical intervention (cornea transplanation). The development of an effective drug would therefore be a major step forward. In August 2019 the company's licensing partner, Kowa, started development and entered Phase 2 in the US. ③ Combination with α2 blocker: K-232 In February 2020, the company's licensee, Kowa, announced it was going to commence domestic Phase 3 clinical trials of an eye drops formulation combining Glanatec® and brimonidine (an α2receptor stimulant) for use on glaucoma/ocular hypertension. The objective of the trials is to confirm the safety and efficacy of long-term use comparing the effectiveness each of the two drugs independently.
Development of a combination with alpha 2 blocker to broaden the market and enhance life-cycle management	In the US, Aerie Pharmaceuticals Inc. developed Rocklatan®, a fixed dose combination drug of Aerie's own Rhopressa® and latanoprost (a PG formulation). Clinical trials showed this combination to be more effective at lowering ocular hypertension than latanoprost alone. In March 2019 it was approved by the FDA, marking another successful inroad overseas. (Latanoprost generic products have arleady been available but there is no brimonidine generic on the market. It would be possible that brimonidine generic products would be launched around on the time of K-232 launch.)

H-1337 new Glaucoma treatment agent

H-1337 is also a type of isoquinoline derivative, and aims at lowering intraocular pressure by inhibitingmultiple kinases including LRRK2 and ROCK

H-1337, a isoquinoline derivative indentified out of DWTI's own proprietary compound library, is a multikinase inhibitor mainly inhibiting LRRK2. Development for glaucoma/ocular hypertension began in the US in 2016 (the works of clinical trial was subcontracted to Allysta Pharmaceuticals, Inc.). Phase1/2a clincial trial began in March 2018 and was completed with a favourable results in September of the same year.

The mechanism of action of H-1337 has been explained in two pathways, LRRK2 (leucine-rich repeat kinase 2) inhibition as the main pathway and ROCK inhibition as the secondary pathway. LRRK2 is a type of serine / threonine kinase that acts to control the polymerization of intracellular microtubules. It is thought that when LRRK2 is mutated, nerve cells degenerate through depolymerization of microtubules, causing Parkinson's disease. The mechanism associated with glaucoma is that when LRRK2 is inhibited, the microtubules that make up the cytoskeleton of trabecular meshwork cells in the eye depolymerize and change the structure of the cytoskeleton. Discharge is promoted and intraocular pressure is lowered.

Phase 1/2a, now complete, produced positive results

The results of Ph1/2a completed in September 2018 showed that intraocular pressure was reduced versus placebo for all three cohorts (0.06%, 0.2%,0.6%) and was well tolerated.

Results of clinical trials- US Phase1/2a

Efficacy

	Intra-day change after 28days . (8 hours)IOP median change
0.6% dosage group (N=21)	-5.1mmHg
Placebo group (N=22)	-0.4mmHg
Difference	-4.7mmHg

All 3 readings (0.06%, 0.2%,0.6%) vs. placebo, effect on ocular pressure

Safety

Rate of occurrence	5% plus（#）	0.1～under 5%
Eye	Discomfort	Conjunctival hyperemia

(#) Common to all 3 groups

＊Mild erythema on the applied area

○Well tolerated

(Source) DWTI results meeting materials, February 2020

Now working to achieve a out-licensingwithin the next 1-2 years

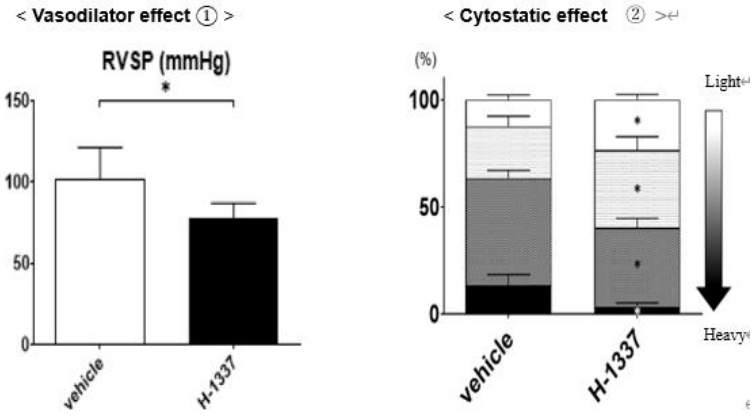
At the present DWTI is actively pursuing in out-licensingt opportunities to other pharmaceutical companies including its subcontractor, Allysta Pharmaceuticals. The company plans to complete out-license within the next 1-2 years and then initiate Ph2b trial. After that, with the results of 2-yaer Ph3 trial (to be conducted around 2023-2024), an NDA in the US will be submitted in around 2025.

Expansion of Indications for H-1337

The company is now promoting research targeting pulmonary arterial hypertension

H-1337 has an effect for expanding contracted blood vessels through ROCK inhibitory action and is also thought to possess an effect for suppressing cell proliferation in the pulmonary artery through LRRK2 inhibitory action. Expanding indications for pulmonary arterial hypertension is also being considered, and an intensive joint research (basic research stage) with Chiba University is on-going.

H-1337 Pulmonary arterial hypertension rat model



(Source) DWTI results meeting materials, February 2020

(2) Ophthalmic surgery adjunct DW-1002（BBG250）

After the launch of Glanatec® the company also adopted a strategy of in-licensing, because it would take time to bring in-house products to profitability

DW-1002 is a product of a ophthalmic surgery adjuct mainly composed of a highly dyeable pigment called BBG250 (BrilliantBlue G-250) owned by Helios Co., Ltd. The business of this product was purchased by the company from Helios for JPY 1.3 billion. (BBG250 was invebted by a research group of Kyushu University)

One of those was the ophthalmic surgery adjuct DW-1002

ILM-Blue®

(BBG250)

BBG250 is an eye surgery adjunct that contains a highly dyeable pigment as the main component. Enables visualisation of the inner limiting membrane (around 0.003mm in thickness). Sold in Europe as "ILM-Blue®" or "MembraneBlue-Dual®"

DORC sells "ILM-Blue®" in Europe

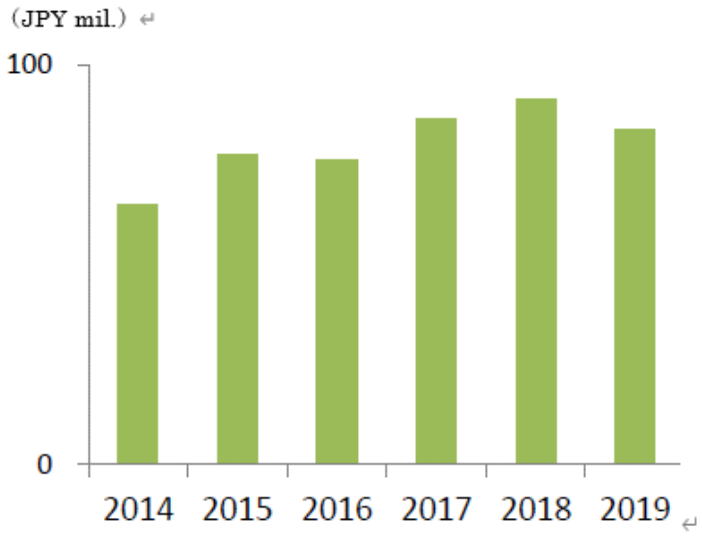
(Source) DWTI results meeting materials, February 2020

Since it was launched in Europe it has already been used in more than 100,000 operations a year

This product utilizes the high stainability of BBG250 to safely stain the inner limiting membrane in the eye, making it easier to remove the membrane in an ophthalmic surgery. The sublicenses for the world other than Japan are granted to the European Dutch Ophthalmic Research Center International B.V. (DORC), and has been manufactured and sold in Europe since September 2010. The product names are ILM-Blue® and MembraneBlue-Dual®, and these are used for approximately 100,000 vitreous surgeries annually. Development in North America was also carried out by DORC. In March 2019 DORC submitted an NDA to the US FDA and it was approved in December 2019. The number of vitreous surgeries in the United States is estimated as approximately 200,000 per year.

In 2019 approved for use in the US where there are 200,000 surgeries per year

DW-1002: Trend in royalties income from the European market (DORC)



(Source) DWTI results meeting materials

The Japan expectation is 100,000 surgeries per year. Application expected this year

Also plans to apply this year for cataracts surgery

In Japan, vitreous surgery application is being developed under a license by Wakamoto Pharmaceutical Co., Ltd., which plans to submit an application in 2020 and expects approval in 2021. The number of surgical operations is thought to be about 100,000 annually.

Out-licensed Japan rights to Wakamoto Pharmaceuticals in 2019

In addition, from October 2017 until August 2018, an investigator-sponsored Phase 3 clinical trial for catract surgery was conducted at Kyushu University Hospital. In February 2019, the company concluded an exclusive sublicensing agreement with Wakamoto targeting anterior lens capsule-staining during cataracts surgery in Japan. The plan is to submit an application in 2020 and to launch in the market in 2021. There are some 1,200,000 cataracts operations per year in Japan, with DW-1002 assumed to be involved in around 10%.

(3) Others

DW-1001 was in-licensed by the conpany in 2015 and out-licensed to Rohto Pharmaceutical in 2019

① Ocular eyedrop painkiller （DW-1001）

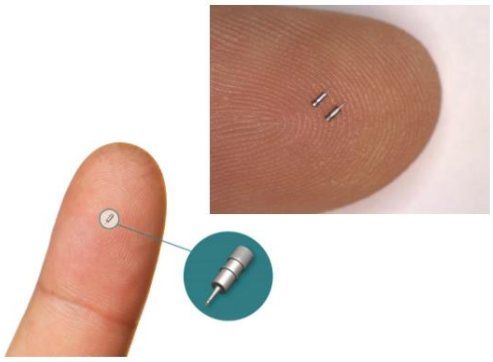
DW-1001 can be used to relieve the pain following ophthalmic surgery etc. It was in-licensed from a UK company in June 2015, and was the first in-licensed product of DWTI. There is a need for non-NSAID drugs because NSAID's suppress 12-HHT production and delay repair of corneal epithelial damage. DW-1001 is an existing drug, so development risk is relatively low. In December 2019 DWTI out-licensed the Japan rights to Rohto Pharmaceutical. It received a contract fee and is expected to receive milestone payments and royalty payments from Rohto. However, the arrangement will generate some royalty payments to the UK company. Plans for further development have not been fixed.

Interest is growing in the device segment of the global glaucoma market

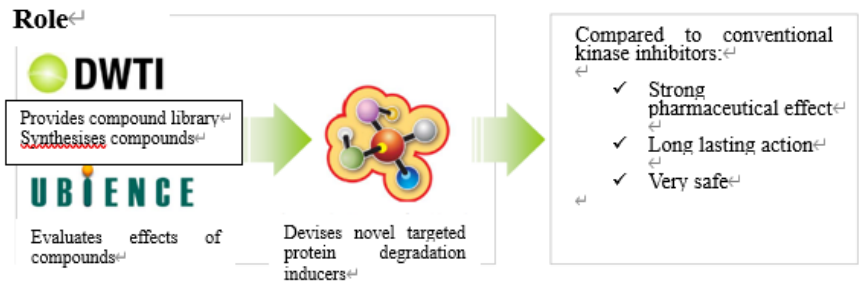
② Joint research with Glaukos Corporation

The development of slow drug release and humor

In August 2018, DWTI concluded a joint research agreement targeting new intraocular glaucoma treatment products with a world-leading ophthalmic device company, Glaukos Corp. Under this contract, in addition to recieving research funds,

drainage devices is useful because it is not always easy for the patients to administer eye drops continuously at precise timing DWTI is now undertaking joint research with the global ocular device maker, Glaukos, to develop slow release devices Plans to provide novel ROCK inhibitors	DWTI is to grant Glaukos all global development, manufacturing and sales rights to development products if approved by the FDA, in exchange for up-front funds, milestone payments and royalties. It is estimated that the global market for glaucoma treatment has a value of around JPY400 billion, while the ocular device market is growing rapidly and already has a value of around JPY30 billion. Glaucoma treatment involves reducing intraocular pressure and delaying progress of the disease by the long-term and timely adminsitration of eye drops. However, forgetting such adminiatration is a common and problematic occurrence. Glaukos is develeoping an extended release device (iDose®) which, once fitted, and for one year or more, releases small amounts of the drug to provide sustained delivery. It is also developing micro-devices to drain aqueous humor (e.g. MicroShunt®, a tube for that purpose). In the joint research DWTI provides Glaukos Corp. with novel ROCK inhibitors appropriately designed to be used to develop novel slow release devices. Glaukos has confirmed the intraocular pressure lowering effect of the compounds in animal and is making progress on prototype inplants. There are also plans to proceed with verification of the profile of the compounds whethere they are suitable for the iDose® system. DWTI expects clinical studies of the new device will start within 2-3 years. **The Glaukos' iDose® system**  (Source) Glaukos website **③ Joint research with UBIENCE Co., Ltd.** In October 2019, DWTI entered into a joint research agreement with UBIENCE for the purpose of identifying targeted protein degradation inducers. It is known that when proteins that are no longer needed in the cell are decomposed, ubiquitin is bound to the proteins (ubiquitination), which leads to the decomposition. DWTI aims to develop compounds decomposing the proteins that cause diseases. The compounds will contain a linked structure of a small molecule that binds to ubiquitin ligase and a ligand that binds to the targeted protein. Under the joint research agreement DWTI provides suitable compounds from its proprietary library of kinase inhibitors, which is the fundamental technology of DWTI, or to synthesize novel compounds, and convert them into targeted protein degradation inducers with UBIENCE, and evaluate the degradation properties. While kinase inhibitors inhibit the action of disease-causing kinases, target protein degradation inducers degrade the disease-causing kinases themselves, producing a number of beneficial effects as described in the figure below:
The company has initiated research aimig to the new modality of targeted protein degradation inducers	

Development of targeted protein degradation inducers



(Source) DWTI results meeting materials, February 2020

④ Others

As the intensive R&D field, DWTI is now tackling drug development in the ophthalmic field also for posterior segment diseases and retinopathy in premature infants

In addition to the field introduced above, DWTI is searching for, and conducting research in, new drug candidate compounds for the back of the eye diseases such as the retinal ones. At the research level, the company has discovered compounds whose effects was confirmed and which are now being continuously researched. However, there are a number of hurdles still need to be overcome, such as the delivering problem into the back of the eye.

In addition, a drug to treat retinopathy of prematurity is under development mainly by a subsidiary, JIT (Japan Innovative Therapeutics, Inc.), and is currently at the non-clinical trial stage.

Outside the field of ophthalmology, as noted earlier, the company is pursuing research into the effect of H-1337 on pulmonary arterial hypertension, and in April 2020 it concluded a joint development agreement with MEDRx Co., Ltd. on a Lidocaine tape formulation for post-herpetic neuralgia/shingles.

(Note) Shingles is a painful disease caused by the reactivation of the varicella-zoster virus latent in the dorsal root ganglia during childhood. In most patients the shingles disappear with the treatment of herpes, but about 10% suffer from post-herpetic neuralgia, with the pain remaining for many years after treatment. The main therapies used to be nerve block and drug therapy with poor effectiveness, but in March 1993, the transdermal patch Lidoderm® was approved in the United States. Lidoderm® acquired the status of first-line treatment for post-herpetic neuralgia treatment, and once its annual sales was about USD1.2 billion. Currently, several generic of Lidoderm® have been launched, and the market size of lidocaine patches in the United States becomes smaller about JPY50.5 billion (2018).) In October 2018, Silex Pharmaceuticals Inc. (parent company Sorrent Therapeutics Inc.) launched a lidocaine tape (ZTlido®) with superior properties to Lidoderm®. Sold for USD8.95 each, 2019 sales grew to around JPY2.2 - 2.3 billion. MEDRx is also developing a tape preparation that utilizes its superior transdermal absorption technology and has already completed all of the FDA's required clinical trials. It plans to submit an NDA by 2020, expecting approval in 2021. After launch, it will be sold at almost same price as ZTlido®. JPY9 billion of peak sales are expected, assuming a 10% share of the market (114 million patches a year in the US).

DWTI will pay a maximum of JPY200 million in milestones as achievements of the US commercialization, but after launch will receive royalties according to the sales.

Earnings/balance sheet structure and medium-term management plan

In 2019, the company turned in its first profit since listing, and cleared the benchmark for delisting

In 2019 the company recorded its first profitable year since listing (in terms of operating profit, recurring profit and net profit). Since it had recorded losses every year until 2018 a loss in 2019 would have put it on the borderline for delisting. In the event, the profit made in 2019 led to the lifting of the delisting grace period on March 26th 2020. Its profitability in 2019 was due to a steady increase in royalties and milestone income. On the other hand, by halting its own contribution to H-1337 development at Phase1/2, and leaving further development to its licensee, it significantly reduced R&D expenditures.

The Tokyo Stock Exchange is currently reviewing market classifications, and has announced that it will also revise the delisting criteria for the DWTI-listed market. As a result, it seems unlikely that DWTI will again fall foul of the standards governing the delisting grace period due to losses.

The company's main revenue sources are royalties from Kowa and DORC, joint research fees from Glaukos, and milestone payments from Wakamoto

DWTI's revenues are composed mainly of Glanatec® royalties from Kowa, milestone income from Wakamoto, DW-1002 royalties from DORC and joint research fees from Glaukos. We assume that in 2019 there was also a one-off contract fee for the out-license of DW-1001 to Rohto. In addition, it is assumed that the income from Wakamoto Pharmaceutical in 2019 was boosted to about JPY200 million due to the receipt of milestone income on achieving Phase 3 of H-1129 (which was discontinued) and the lump-sum contract payment for the licensing out of DW-1002 for cataracts.

Trend in P&L

(JPY mil)

	2015	2016	2017	2018	2019
Sales	61	168	254	292	580
Kowa	61	97	119	138	158
Wakamoto	0	50	50	0	209
DORC			63	96	88
Glaukos				38	62
Cost of sales	0	5	7	13	25
SG&A	352	482	880	1,065	437
R&D	143	226	603	795	249
Others	209	256	277	270	188
O.P.	-290	-319	-633	-786	117
Non-O.P.	4	25	1	0	0
Non-Op. costs	9	10	36	11	8
R.P.	-295	-304	-668	-796	109
Extra. profit	0	0	103	1	0
Extra. losses	0	0	1,040 DW-1002 write-down	6	0
Net profit	-296	-253	-1,563	-748	133

(Source) Fair Research Inc. using company filings

Considering DWTI's medium-term sales outlook:

The following factors should be borne in mind when considering the company's medium-term sales.

Income from Glanatec® royalties should grow alongside an expansion in

① Royalty payments from Kowa are growing as Glanatec® sales grow. Glanatec® sales in Japan (single agent form) could peak at around JPY7.5 billion in around 2023, 10 years after launch, by which time the royalty income generated from domestic sales will have grown alongside. The launch of Glanatec® in S.E. Asia in 2020 will also contribute to growth in revenues from royalties. With the

indications and geographic territories and the development of combination product

development of a fixed dose combination product, we are assuming there are no milestone payments, but it will be launched under the product life-cycle strategy of Kowa around the time that single-agent sales peak (after the period of the medium-term management plan).

Income from Wakamoto Pharmaceutical will now supplement DW-1002 royalties

② It is likely that from now on, income from Wakamoto Pharmaceutical will consist mainly of DW-1002 royalties. In 2020 Wakamoto plans to submit an NDA as an adjunct used for the vitreous surgery related to inner limiting membrane detachment and cataracts. The NDA approval and product launch should be in 2021, after which we assume royalties income will gradually increase

DORC royalties will rise in tandem with US market growth

③ Looking at income from DORC, sales of BBG in Europe should remain stable at about the current level but could roughly triple with receipt of US regulatory approval in 2020.

Income from Glaukos joint research fees will continue, and could rise with the start of clinical tests

④ We surmise that R&D revenues from Glaukos will remain at around the 2019 level until the start of clinical trials (two or three years from now). We can anticipate a rise in milestone income triggered by important events, such as the start of clinical trials.

H-1337 out-licensing contract fee in the offing

⑤ An up-front payment revenue accompanying out-license can be expected in the next 1-2 years.

⑥ DW-5LBT milestone payments should be around JPY100 million in both 2020 and 2021, however after the period of the medium-term management plan the company will be in receipt of royalty income.

The company seems to have taken into accounts the above considerations in its medium-term sales figures.

R & D expenses were swolen during the in-house development of H-1337, but from now on will be affected by basic research expenses + goodwill amortization for DW-1002

Expenditures are mostly accounted for by SG&A (R&D plus miscellaneous). R&D expenditures expanded in 2017 and 2018 due to the company's propulsion of its own H-1337 development in the US. In addition, it is inferred that from 2017 R&D expenditures include DW-1002 goodwill amortization expenses (balance sheet intangible assets). Excluding these we infer basic research costs at around JPY200 million annually.

The medium-term management plan posits R&D at JPY300 to JPY560 million. JPY200 million to JPY300 million yen is expected to be spent each year in the development and basic research of each pipeline, with DW-5LBT milestone payments costing JPY100 million in each of 2020 and 2021. Additionally, it is expected that the R&D amount will change depending on the amount of goodwill amortization for DW-1002.

Medium-term management plan: sales and P&L

(JPYmil.)

	Sales	R&D	O.P.	R.P.	Net
2019 (Actual)	580	249	117	109	133
2020 (Forecast)	310	420	△390	△410	△340
2021 (Target)	420～580	560	△460～△310	△480～△320	△420～△270
2022 (Target)	450～750	300	△170～100	△170～100	△120～110

(Source) DWTI medium-term management plan for period ending December 2020 to period ending December 2022

Net cash JPY1.02 billion (at end of 2019)

Cash and deposits on the balance sheet at the end of December 2019 stood at JPY1.5 billion. Repayments of bank loans started in 2019 (repayments of JPY120 million per year). Since the company's JPY480 million of loan balance at the end of December, its net cash position was JPY1.02 billion. This was bigger than the cumulative loss during the period covered by the medium-term management plan (△JPY880 million - △JPY500 million).

While greater than the cumulative losses expected over the next three years, the company has entered a new borrowing contract for a maximum of JPY200 million. This removes the possibility of a fund shortage.

Further, DWTI has entered into a term-loan agreement (with a commitment period) with Mizuho Bank in order to secure a fast, flexible and stable reserve to meet milestone requirements related to the joint development project with MEDRx (maximum loan amount: JPY200 million; commitment period: from April 30, 2020 to April 30, 2022; repayment: every three months from September 30, 2022, to September 30, 2027). There is very little concern, therefore, that funds will be depleted in the medium term.

Balance sheet trends

(JPYmil)

	2015	2016	2017	2018	2019
Liquid asets	2,024	2,776	2,515	1,764	1,715
Cash, etc.	1,747	2,291	2,132	1,584	1,540
Securities	182	353	0	0	0
Fixed assets	115	136	361	309	265
Tangible fixed	4	25	15	4	3
Intangibles	1	1	330	291	249
Investments, etc.	109	109	16	12	12
Total assets	2,140	2,912	2,887	2,073	1,981
Liquid liabs	27	35	156	268	189
S-T loans	0	0	0	120	120
Fixed liabs	0	0	625	505	384
L-T loans	0	0	600	480	360
Net assets	2,112	2,877	2,095	1,300	1,408
Shareholders equity	1,886	2,722	1,999	1,259	1,393
(Reference)					
Rev. from options issued and exercised	87	1,071	824	0	0

(Source) Fair Research Inc. using securities report and other filings

<Reference> Pipeline value simulation

(a) Assumptions made for simulation

We posit a number of variables for pipeline valuation

Development schedule

The two most important events for Glanatec® are the development schedule for the K-232 compound and the development schedule for K-321 targeting Fuchs corneal endothelium degeneration. Although the current monotherapy formulation sales peak will be approaching, the market penetration of the product containing the compound will sustain sales (Japan and Asia). Also sales will be helped by the strong medical need is for Fuchs corneal endothelium degeneration. Fair Research Inc. has made a number of challenging assumptions, described in the chart below.

Our valuation limited to Glanatec®, DW-1002, H-1337 and the Glaukos products

We assume H-1337 will be licensed out in 2021, that it will enter Phase 3 in 2023 and will be approved and launched in 2026

Next, H-1337, which is one of DWTI's more promising in-house products. We assume it will be licensed out in 2021, will start Phase 2b in the same year before moving on to Phase 3 in 2023. We anticipate an NDA in 2025 and approval/market launch in 2026.

We assume DW-1002 will be approved and launched in the US and Japan in 2021 and cataracts surgery applications will be approved in 2021

Among licensed-in products, DW-1002 can produce constant royalties. For internal limiting membrane exfoliation it should be launched in the US in 2020 and in Japan in 2021. We assume indications will be expanded to cataracts surgery in Japan in 2021.

We assume Glaukos products will enter the clinical phase in 2023 and that an NDA will be submitted in around 2028

In addition to the above, we can be very confident of the income expected from Glaukos research fees. We assume their products should enter into the clinical phase in 2023 and anticipate higher than normal cooperation fee revenue in that year (which makes the upper level in the medium term corporate management plan achievable).We assume Pivotal trials will start in around 2025, and that the scheduled date for submission of an NDA is around 2028.

		2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
Glanatec®	Glanatec®(Japan)				Sales in Japan reach JPY7.5 bil					Incl. compounds JPY20 bil					
	Glaucoma (overseas)	S.E. Asia countries permits, launches					Asia ex-China sales JPY1.5 bil.					Asia ex-China sales incl. compounds JPY6 billion			
	Fuchs corneal endothelium degeneration (K-321)	Fuchs corneal endodothelium degeneration Ph.2	Ph3			NDA (US)	Approval and launch					Peak Sales			
	K-232 compound developments	Dev. starts		NDA(Japan)	Approval & launch (Japan)	NDA (Asia)	Approval & launch (Asia)								
H-1337	Glaucoma (overseas) (2nd line)		Licensing out Start of Ph2b		Ph3		NDA	Approval/launch						Peak Sales	
	Additional indications (pulmonary hypertension)	Pre-clinical stage													
DW-1002	Internal limiting membane exfoliation (overseas)	N. Am. Launch					Peak sales (200,000 cases)								
	Internal limiting membane exfoliation (Japan)	NDA	Approval & launch					Peak Sales (100,000 cases)							
	Extended to cataracts (Japan)	NDA	Approval & launch					Peak Sales (120,000 cases)							
Glaukos	Products for glaucoma (ROCK inhibitors)			Start of clinicals?			Pivotal trials?			NDA?	Approval? Launch?				
DW-1001	Ophthal. treatment	Dev. undecided=>													

In addition, K-134 and drugs to treat retinopthy of immaturity. K-134 now finishing domestic Ph2 but Kowa now deciding on next move.
For retinopathy of immaturity now at pre-clinical stage.

(Note) The above schedule has been prepared by Fair Research Inc. solely for the purpose of simulating pipeline value and is not based on an announcement by DWTI. The actual schedule can be affected by delays, interruptions and suspensions.

We assume DW-5LBT, DWTI beggan development collaboration with MEDRx in April 2020, will be the subject of an NDA in the same year, will be approved in 2021 and launched in 2022. At the time of regulatory approval we surmise the company was looking for a US licensee with a marketing network.

Assumptions as to sales

① Glanatec®

We are positing the domestic peak in the current monotherapy formulation sales at JPY7.5 billion in 2023, ten years after launch. Combination formulation will be launched in Japan in 2023, and by 2028 the total value of monotherapy and combination formulations sales could reach JPY20 billion in value and 13% in domestic market same level of current alpha blockers (brimonidine) share.

In the overseas market (Asia ex-China) the number of patients will exceed Japan, but drug prices are lower, meaning that overall the market will be same level with Japan.

Domestic sales of Glanatec® to reach JPY7.5 billion in 2023, expanding to JPY20 billion with the launch of combination product

Asian market set for growth, but in value terms about level with Japan

On Fuchs corneal endothelium degradation in the US, we surmise that since the maximum number of patients stands at around 6 million and given market penetration of 30%, peak market size would be around JPY54 billion. Since DWTI out-licensed this compound at the basic research stage, its royalty rate might be in the low single digit range.

We posit a peak value of JPY54 billion for Fuchs corneal endothelium degradation. However, the royalty rate may be low

② H-1337

We surmise that, like other ROCK inhibitors, H-1337 would be used more as a second line choice than as a first line choice. We therefore set a peak-sales market share at 2-5%. For comparison, Rhopressa® in the US has a 2% share on a prescribed basis (Aerie Pharmaceuticals). Accordingly, considering its expected drug price we posit a level of around 4% in value.

On the assumption that the European and US market for glaucoma drugs is valued at JPY3 billion we arrive at a hypothetical figure in the JPY6.6-16.5 billion range. Since out-licensing is after Phase 2a we have set the royalties rate at 12.5%.

Since H-1337 is a ROCK inhibitor, it would rank as second line. We assume a market share of 2-5%

Since its out-license comes after Phase 2a we assume a royalties rate of 12.5%

③ DW-1002

We assume that in Europe there are currently 100,000 cases of inner limiting membrane detachment, in the US 200,000 cases, and in Japan 100,000 cases. We apply the current European price of 55 euros each to the other countries. Expected uses in cataract surgery in Japan are about 10% (120,000) of the total (1,200,000) such surgeries. The royalties rate in the U.S. is the same as that in Europe at present because it is being developed by DORC until regulatory approval, but we have set the royalties rate in Japan at a higher level than in the European/US markets because it was licensed out after Phase 3 development.

④ Revenues from Glaukos Corp.

We have set the Glaukos collaborative development fee revenue paid to DWTI at under JPY100 million per year. However, this will rise as the product moves on to the clinical stage, through pivotal trial and on to approval. It is difficult to picture the size of the market after launch but since it is a ROCK inhibitor drug, we assume it will ultimately capture a 5% share of the US market.

We anticipate DW-1002 US royalties income to be double that from Europe.

Japanese cases, including cataracts, are 2.2 times the level of Europe. The royalty rate is high

⑤ DW-5LBT

Assuming this product captures 10% of the market, we posit peak sales at around JPY9 billion. However, no details are available on how DWTI and MEDRx will apportion between them the contract payment and royalties when it is out-licensed in the US to a company with a sales network. We have therefore excluded those considerations from our calculations.

We assume that annual joint research fee revenue from Glaukos amount to around JPY100 million but will rise with milestones

Other assumptions

Post-launch assumptions the

Since the company already has a drugs market presence, we set the discount rate

same as for H-1337

used in our DCF calculation at 10%. We assume peak sales should be reached in the fifth year after launch and that level should be maintained for three years, after which our assumption is that sales will decline by an annual 5% until 2033 when that decline will accelerate to 10% per year. Our calculations were made with success probabilities of 60% and 100% for H-1337 and Glaukos.

Results

Using the challenging assumptions outlined in the previous pages we arrive at a total pipeline value (before tax) for H-1337 and Glaukos products of JPY14.3-17.1 billion with a success probability of 60% and a US/European share of 2-5%. With a success probability of 100% the value rises to JPY16.1-20.8 billion.

Discount rate set at 10%. We have two succcess probability calculations for H-1337 and Glaukos products: 60% and 100%

(Setting a 0% probability of success for H–1337 and Glaukos products and counting only Glanatec® and DW-1002 yields a value (before tax) of JPY11.5 billion (discount rate 10%))

DWTI pipeline value (before tax)

(JPY100mil)

		H-1337 and Glaukos	
		success prob. 60%	success prob. 100%
discount rate	10%	**143.1～171.0**	**161.9～208.4**
	8%	**166.1～200.3**	**188.1～245.2**

The total pipeline value comes to around JPY17 billion on a success probability of 60%, and around JPY20 billion on a success probability of 100%

Glanatec® and DW-1002 alone come to JPY11.5 billion

Market penetration for H-1337 and Glaukos set at 2-5%

(Source)Calculated by Fair Research Inc.

(Note) The calculations can be importantly affected by changes in the variables used, and do not take into accounts taxation, basic research costs, or DWTI operating costs. For that reason, pipeline value and company value cannot be directly compared.

Note that H-1337 combination formulation possibility and DW-1001 not included

Additionally, it should be noted that our calculation does not take into account combination formulation using H-1337, abandoned pipeline products such as DW-1001or DW-5LBT, It should also be remembered that pipeline value can be revised upward in response to further development.

(Note) We posit an overall value for DW-5LBT of approximately JPY7.4 billion with a probability of success set at 90%. Of this, we assume the portion attributable to DWTI is approximately 20% given the JPY200 million milestone payment

Conclusions

The company has evolved from its early days when it was mainly involved in basic research and in out-licensing at the basic research stage. Now it develops its own invented compounds to the early clincical stage before out-licensing

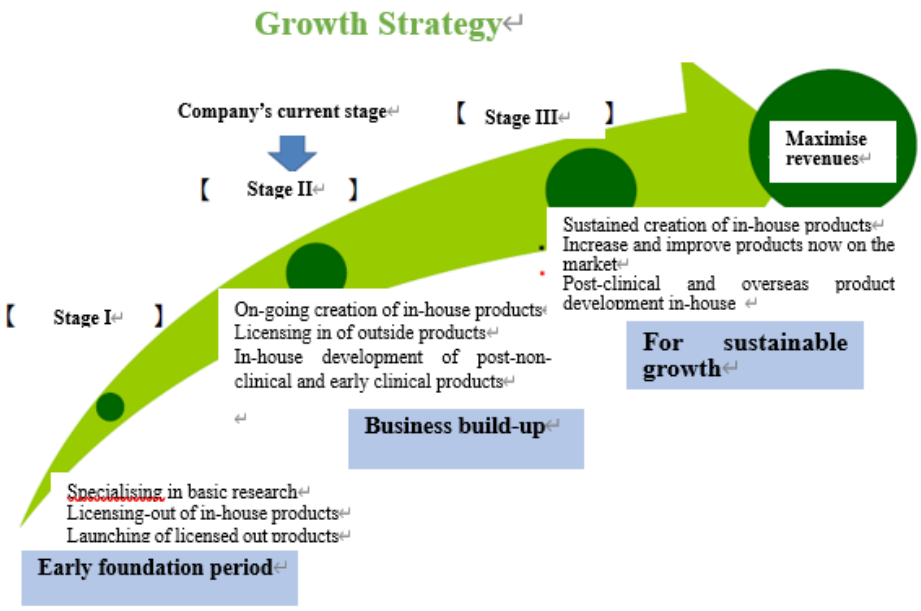
D. Western Therapeutics Institute, Inc. (DWTI) is mainly involved in ophthalmology, a niche area with relatively high barriers to entry. It has its proprietary unique chemical library with various compounds having kinase inhibition profile which lead to promising new drug candidates. It has already one out-licensed on-the-market product, Glanatec®, for which it did the early development. However, the out-license was done in 2002 at the basic research stage when the company specialised in basic research, and therefore the licensing terms were not necessarily very advantageous.

Of course, ultimately DWTI wants to increase the number of in-house candidate products, bring them onto an advanced clinical stage (Japan and overseas) by itself and out-license them on advantageous terms.

The company already has a number of growth products on the market and its business model is not simply dependent on lump-sum payments with out-license of new products

At the present, in order to strengthen its own future in-house products, it is going one step further, promoting its own products to the early clinical stage to secure better out-licensing terms than that were acquired in early days. In addition, it is steadily expanding the range and scope of therapeutic indications and geographic territories for existing products. At the same time, it is expanding the scope and range of therapeutic indications and geographic territories of products in-licensed from other companies/institutions in order to provide a stable source of income until its next in-house product is launched. In other words, the company has several sources of revenue which are providing growth and stability but which the company wants to take products to the early clinical stage of development before out-licensing. For that reason we have estimated current pipeline value quite conservatively at JPY14.3-17.1billion but with plenty of scope for an upward revision.

We posit pipeline value at JPY14.3 – 17.1 billion



(Source) DWTI results meeting materials, February 2020

Note: This report is the English-language version of the original Japanese-language report issued on April 22nd, 2020, to which you should refer for precise details

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