MEDRx Co., Ltd.

（4586 Mothers） Issue Date: March 4, 2019

Significant Developments Expected in the Second Half of 2019

Proprietary technology in a niche market

MEDRx Co., Ltd. develops transdermal absorption formulations based on the active ingredients of existing oral and injection drugs. Its business model is based on the collection of milestone payments from pharmaceutical companies to whom it has licensed out its products and, after product launch, the collection of royalty payments.

Unlike most drug development businesses, the company's focus on the active ingredients of existing drugs gives its products a higher probability of success, and its position in a niche market limits competition. In addition, its proprietary ILTS® and NCTS® technologies give it a distinctive competitive edge.

Progress in product development and the current financing

The company has four promising products under development, the most advanced of which is the lidocaine tape formulation. However, since this product can to be used over a prolonged period for the treatment of chronic conditions the FDA requires more extensive testing than was initially envisaged. This is likely to drive up R&D costs. In the case of another product, the tizanidine tape formulation, which has already been licensed out, the need to carry out further tests on repeat doses means that the receipt of milestone payments has slipped from 2018 to, it is estimated, late 2019. Further, for 2019 the company is estimating SG&A costs (including R&D but not the costs for additional lidocaine tape trials) at JPY1.65 billion, about the same level as the end-2018 JPY1.79 level. In order to progress the steady development of all four products the company recently gave careful thought to raising funds of about JPY1.27 billion at an early date.

Positive developments expected in the second half of 2019

We model the company's pipeline value at around JPY45.5 billion (it should be noted that this estimate is based on various preconditions). The current market value stands at around JPY4.9 billion so that, even after adjusting for the JPY1.27 billion capital raising exercise, there is still a sizeable gap. We surmise that this is because of the previously noted delays in development and the finance problems which necessitated the temporary suspension of the microneedle business. However, in the second half of the year we can look forward to a series of positive events, including the receipt of milestone payments from Cipla, the finalisation of repeat dose tests on oxycodone tape and its successful licensing-out, and the release of information on joint development projects with major pharmaceutical companies. These events are likely to constitute a catalyst in the market's evaluation of the company.

<Note：This report is the English version of the original report which is made in Japanese on 4th March 2019. For the precise description, please refer the original report.>

Basic Report

Fair Research Inc.

Tsuyoshi Suzuki

Company Information	
Location	Kagawa Prefecture
President	Yonehiro Matsumura
Established	Jan. 2002
Capital	JPY5,997 mil
Listed	Feb.2013
URL	www.medrx.co.jp
Industry	Pharmaceuticals
No. of employees	28 (consol. basis)
Key Indicators (as of Mar. 1 2019)	
Share Price	499
Year High	2,060
Year Low	425
Shares Outstanding	10,214,100
Trading Unit	100 shares
Market Cap	5,097 mil.
Dividend (est)	0
EPS (est)	-63.03 JPY
Forecast PER	Na
BPS (actual)	203.19 JPY
PBR (actual)	2.46X

Note: calculated on the basis of total shares outstanding, excluding treasury shares

Results	Revenue JPY mil	YoY %	OP Income JPYmil	YoY %	RP Income JPY mil	YoY %	Net Income JPY mil	YoY %	EPS JPY	Share Price High	Share Price Low
Dec-14 Actual	26	-61.7	-1,003	na	-1,012	na	-1,016	na	-152.0	2,518	785
Dec-15 Actual	37	43.1	-999	na	-990	na	-878	na	-131.2	1,446	500
Dec-16 Actual	22	-40.6	-1,342	na	-1,301	na	-1,259	na	-155.5	1,455	341
Dec-17 Actual	198	787.2	-983	na	-988	na	-884	na	-103.2	1,345	453
Dec-18 Actual	8	-95.8	-1,273	na	-1,285	na	-1,267	na	-126.77	2,060	425
Dec-19 forecast	1,009	11,922.3	-650	na	-656	na	-643	na	-63.03		

Company outline – management philosophy

A venture company in the business of developing transdermal absorption formulations

In broad terms the company is involved in developing transdermal absorption formulations using the active ingredients of existing oral and injectable drugs. In terms of business model, it licenses out these formulations to pharmaceutical companies, collecting milestone payments and, after launching in the market, royalties on sales.

Transdermal absorption formulations make up a growing medium to long-term segment of the pharmaceutical market. Among their attributes are maximisation of pharmaceutical effect, reduced side-effects and better quality of life for the patient. These attributes are achieved by the following:

① Providing a consistent and sustained release of active ingredients: enabling the maintenance of a constant volume of the drug in the bloodstream.

② Little or no first-pass effect: while the efficacy of oral drugs can be reduced to 10-20% as they pass through the liver, this is not an issue in the case of transdermal absorption formulations.

③ Better medication compliance: suitable for patients who find it difficult to take oral drugs due to problems swallowing, and also reduces the problem of forgetting to medicate.

④ Unlike drug delivery by injection, transdermal delivery is painless.

⑤ Transdermal delivery lends itself to a wide range of conditions.

The company has proprietary technologies, giving its products a higher probability of success than other new drug discovery businesses

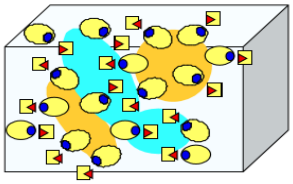
The MEDRx business model is also distinctive in two ways:

(a) It is low risk (i.e. high probability of success) because it does not involve the discovery or development of new active ingredients.

(b) The company has its own transdermal absorption technology using ionic liquids (ILTS®: Ionic Liquid Transdermal System), which distinguishes it from other companies.

Note: Ionic liquids are salts in liquid form at room temperature composed of ions which are resistant to crystalization. They are non-volatile, non-flammable and electric conductive. In recent years these properties have led to applications in lithium battery electrolysis and elsewhere. With ILTS®, MEDRx was the first to develop the technology for the transdermal absorption of ionic liquids, thus facilitating the administration of drugs which are normally difficult to administer transdermally. With existing technology, transdermal absorption was difficult in the case of nucleic acid or macromolecular formulations, but ILTS® has made it much easier.

● ILTS® Breakthrough



➢ The use of ionic liquid facilitates transdermal absorption of drugs previously unsuited to this type of delivery, such as macromolecules like nucleic acid and peptides.

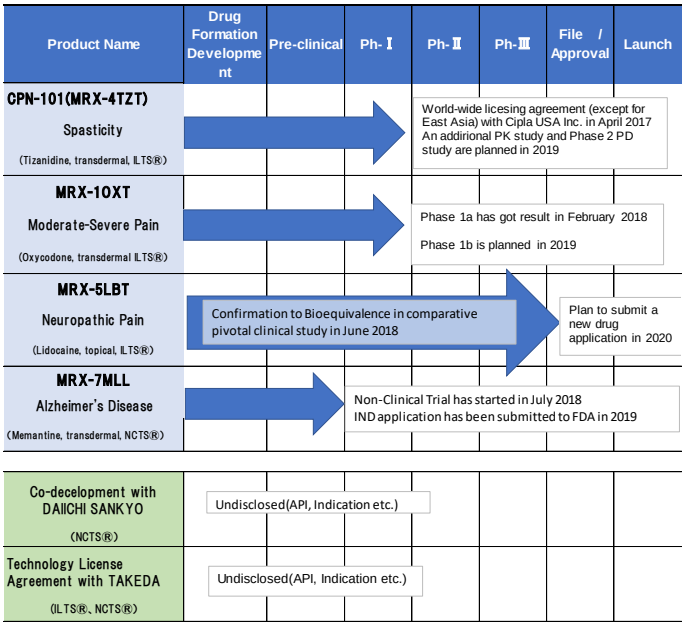
Source: Company briefing materials produced by MEDRx

Another interesting feature of MEDRx's ILTS® is that it has built high barriers to entry. The company has a library of several hundred ionic liquids formed from combinations of compounds with a track record of use on human subjects as pharmaceuticals and additives. It also has extensive know-how on selecting optimum ionic liquids for particular drug properties, and formulation expertise on maintaining and improving the transdermal properties of ionic liquids.

The company's primary target is the US market for transdermal absorption formulations. This preference is based mainly on the potential size of the US market for tape-type formulations.

In addition, by basing its activities in the US on existing formulations, the clinical trials required to win FDA approval are simpler than for new drugs (i.e. although not true in all cases, after Phase 1 Phase 2 can be omitted and the process moves straight to Phase 3). Also, worth bearing in mind is the fact that patch and tape-type drugs tend to command higher prices in the US than in Japan.

Major Current Pipeline



Source: Company briefing materials produced by MEDRx

MEDRx has three products in its main pipeline employing the ILTS® technology. Of these, it is anticipated that the oxycodone tape formulation (MRX-1OXT) could achieve blockbuster sales. It is currently the company's most promising product.

In terms of NCTS® technology making use of nanocolloids there is a memantine tape preparation

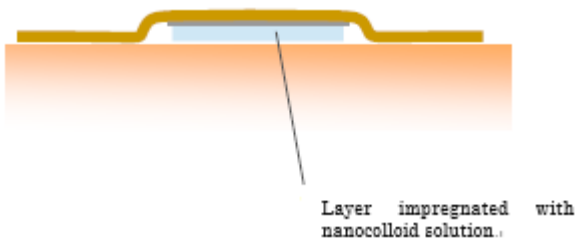
The 3 main products using this ILTS® technology and now under development (at the clinical trial stage) consist of the oxycodone tape formulation (MRX-1OXT), the tizanidine tape formulation (CPN-101, MRX-4TZT), which was successfully out-licensed to Cipla USA, and the lidocaine tape formulation (MRX-5LBT). Of the three, the oxycodone tape formulation is expected to achieve blockbuster sales and is presently the company's most promising pipeline product.

The company also has a transdermal absorption technology using nanocolloids (NCTS®: Nano-Sized Colloid Transdermal System). As mentioned earlier, the ILTS® technology is used in the transdermal absorption of macromolecular agents such as peptides and nucleic acids. The NCTS® technology, however, aims to enhance transdermal absorption of relatively low molecular mass agents by rendering pharmacologically active components into nano-sized colloids. Among products now at the development stage for which information has already been disclosed is MRX-7MLL, a transdermal absorption formulation using memantine (for the treatment of Alzheimer's), which can suppress the skin irritation which memantine usually causes. In addition, there was a report in February 2018 of a

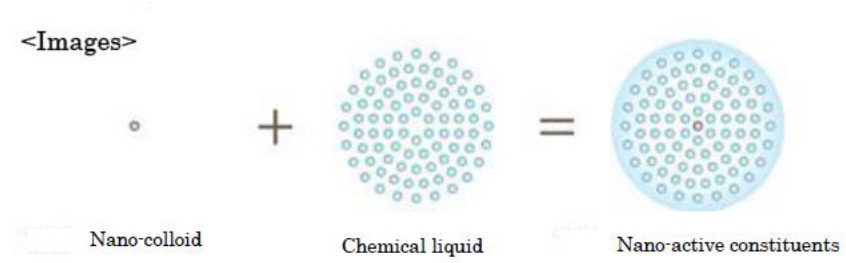
being jointly developed with Daiichi Sankyo which is now at the pre-clinical stage

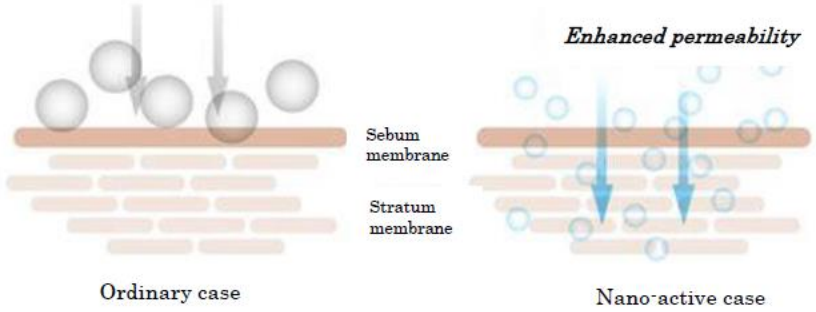
product being jointly developed with Daiichi Sankyo which we surmise uses the NCTS® methodology, although details are scanty because drug name and applicable indications have not been released.

NCTS®: Nano-sized Colloid Transdermal System – Image



"Vaccination patches" using microneedles were being developed and close to practical realization. However, this project, including a test facility plan, is now on hold





Source: Fair Research Inc. using MEDRx company briefing materials

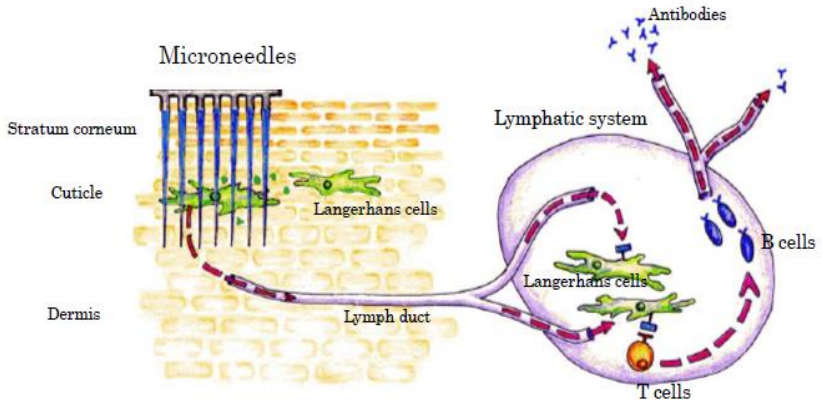
The company has also developed a technology using microneedle arrays as a sort of "vaccination patch". In addition to providing a physical barrier preventing the intrusion of foreign matter into the body, the skin also has the immunological function of expelling foreign matter. Antigen presenting cells, which are present in the epithelium under the stratum corneum as Langerhans cells, and under the dermis as dermal dendritic cells, play an important role in defensive reactions in the body. A powerful immune response can be elicited by efficiently transferring vaccine to these antigen-presenting cells.

However, in practice, when the vaccine is applied it cannot penetrate the skin because of the barrier presented by the stratum corneum. Very fine microneedles, however, puncture the epithelium, allowing the transmission of the vaccine into the skin. Since microneedles are less than 1mm in length they pierce the skin without reaching the nerves, making painless vaccinations possible. This technique is therefore a sort of "vaccination patch".

It has important social implications. Vaccination patches using microneedles avoid the pain of injections (minimally invasive) and their use does not require medical

staff (self-administration). In addition, the application of a solid vaccine antigen to a microneedle represents a promising technique for tackling pandemics in developing countries where room temperature storage is the norm, transportation and preservation is rudimentary, and the medical environment is inadequate.

Image of microneedle array technology



Source: Fair Research Inc. using various materials

On October 4 2018 the company announced a third party allocation of 2.5 million shares (24.8% dilution) to finance a manufacturing project to bring to fruition 15 years R&D work on microneedle technology. However, by November the capital raising had not progressed and the plan was terminated, with the company buying back and cancelling the new share subscription rights.

Evaluating MEDRx's development pipeline

MEDRx's main product line-up currently consists of lidocaine tape (MRX-5LBT), tizanidine tape (MRX-4TZT), oxycodone tape (MRX-1OXT), and memantine tape (MRX-7MLL). The company also has a joint development arrangement with Daiichi Sankyo and a technology licensing agreement with Takeda Pharmaceutical.

1. Lidocaine tape formulation (MRX-5LBT)

Lidocaine tape formulation (MRX-5LBT) is under development as a treatment for neuralgia after herpes zoster. It is MEDRx's most advanced product, and is expected to be the first product launched in the US market

The tape formulation of lidocaine (MRX-5LBT), a local anesthetic, is under development as a treatment for neuralgia after herpes zoster. It is MEDRx's most advanced product and likely to be the company's first product for sale in the US market. That is mostly why the company recently (February 12 2019) announced a plan to raise JPY1.27 billion in the market at an early date, to finance further development of this product (JPY1.1 billion of this is earmarked for MRX-5LBT).

As a brief review of this product's development history, Phase 1 test results in May 2016 suggested that, using the ILTS® methodology, MRX-5LBT could more rapidly and in greater quantity achieve tissue penetration than Lidoderm® (lidocaine patch) (see chart below). At the current time, in the lead-up to an application for approval, the following two avenues suggest themselves:

Plan A: Conduct Phase 3 trials showing superior efficacy to Lidoderm®
Plan B: Show bioequivalence with Lidoderm®

After consultations with the FDA, the company gave comprehensive consideration

to a number of questions: the level of difficulty involved in acquiring approval; the product competitiveness and level of competition assuming development was successful; and the positioning of the product within MEDRx's overall development portfolio. It was decided as a result to select Plan B, since the time required to win approval was shorter and the probability of proceeding that far was greater. The company then announced in June 2018 that test results had shown bioequivalence (BE) with Lidoderm®. The company has indicated that it now plans to carry out clinical trials using the methodology normally associated with the development of transdermal drugs in order to confirm the safety of lidocaine tape on the skin of healthy individuals, and to apply for approval in 2020.

In June 2018 tests successfully demonstrated bioequivalence with Lidoderm®, but the FDA in November 2018 requested more tests than would normally be required to cover therapy for chronic cases

In February 2019 MEDRx issued a 3-point announcement to the effect that: ① In ongoing discussions with the FDA on data required for a new drug approval it was determined in November 2018 that since the drug was for chronic conditions which could require prolonged use, more testing than had originally been anticipated would be necessary; ②The company is aiming to apply for new drug approval in 2020 and the costs of testing needed to that end would exceed the original estimate by an estimated JPY700-800 million; and ③The company would seek funding to the value of around JPY1.27 billion at an early date mainly to finance those costs.

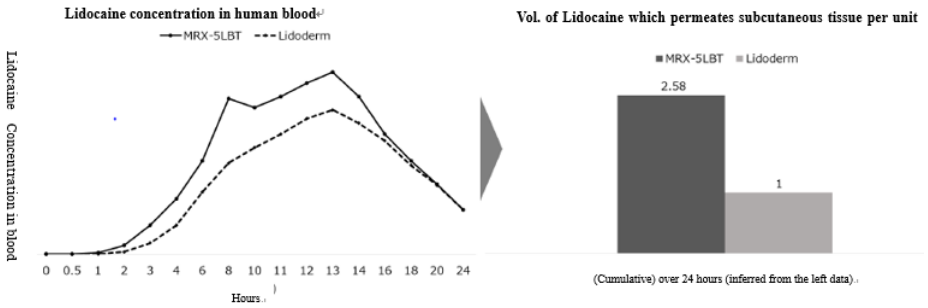
It is expected that a licensee will be found after application is made and approval won.

It will not be necessary to amend the 2020 schedule for new drug application

In volume terms the size of the US market in 2017 was 120 million patches per year. Several Lidoderm® generics already exist with sale prices of around USD2-3 per patch. In value terms the market peaked at around USD1.2 billion but due to falling drug prices it now trends at around one-third of that level. In that context, in October 2018 the US company Scilex Pharmaceuticals Inc. (a subsidiary of Sorrent Therapeutics Inc.) launched a lidocaine tape formulation (ZTlido®) with superior characteristics to Lidoderm®. The price per patch is USD8.95 but it is too early to make an evaluation of the sales trend (Sorrent materials suggest a sales target of at least 3 million patches. MEDRx will be the second entrant to the market and, depending on how sales of ZTlido® go, will probably settle on a similar price per patch.

The size of the targeted market (US) will be 120 million patches. A sales price of USD9 per patch is anticipated

MRX-5LBT and Lidoderm Comparison



Source: MEDRx briefing materials

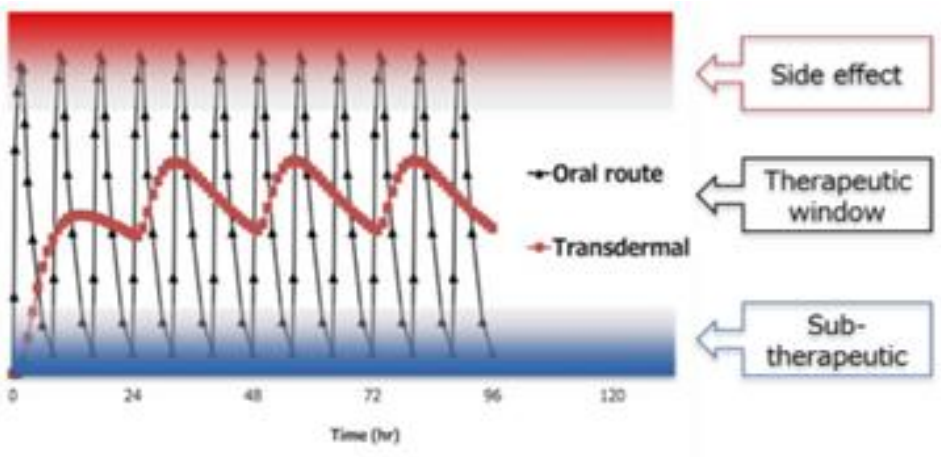
2. Tizanidine tape formulation (MRX-4TZT, CPN-101)

The tizanidine tape formulation is a muscle relaxant working on the central nervous system, one of its uses being as mitigation therapy for shoulder pain. It has no patch competitors.

Tizanidine tape is a formulation of tizanidine, a muscle relaxant acting on the brain/central nervous system and also used to relieve shoulder stiffness and the like, which has been rendered transdermally functional with the use of ILTS®. Unlike lidocaine and ETOREAT® it does not act locally on nerve endings and muscle but enhances pharmaceutical effectiveness through concentration in the bloodstream. The results of US Phase 1a tests (clinical phase 1 preliminary) in February 2017 confirmed the same level of sustainable bloodstream concentration as provided by oral preparations, and reduced drowsiness and other side-effects.

Completed Phase 1a in February 2017, licensed out to Cipla in April 2017

Oral-Transdermal comparison



Source: MEDRx briefing materials

The chart shows that the transdermal method is superior to the oral method in terms of delivering a stable and effective volume of the drug, while making it unlikely that the volume would rise and lead to side-effects

Repeat dose tests (Phase 1a') trials began in September 2017 and the company expected Phase 3 to begin in the second half of 2018. However, development fell behind schedule due to delays in manufacturing scale-up

At the present time the only tizanidine products available are oral preparations. There are no competing patch or tape-type products. The scale of the US market in 2016 was estimated at USD800 million, around one-third of which could, it is thought, be replaced by tape formulations. In April 2017 the company concluded a global (excluding the US and East Asia) development and marketing agreement with Cipla USA, a wholly-owned subsidiary of the Indian pharmaceuticals major, Cipla Inc. (Subsequently, due to a restructuring of the Group the counterparty to the agreement became Cipla Technologies, LLC, referred to below as Cipla.) Cipla made a one-off contractual payment of USD160 million in 2017 and subsequently MEDRx is to receive milestone payments up to a total of USD30 million depending on progress in development and marketing. After going to market the terms of the agreement appear to specify a schedule of royalty payments based on sales. In January 2018 there was an announcement that further Phase 1a' tests had produced the expected results. At that time, it was anticipated that, after manufacturing scale-up of the investigational drug, it would conduct additional pharmacokinetic repeat-dose tests (Phase 1b) and pharmacodynamics tests (Phase 2) during 2018.

As a result milestone payments from Cipla have been deferred from 2018 to the second half of 2019

After Phase 1b and allowing for possible dosage increases the company will advance in stages to Phase 2 and Phase 3, filing an application for approval in 2022

Subsequently, however, due to the unexpectedly long time required for scaling-up of test drug production, Phase 1b trials could not begin during 2018. However, now that the scaling-up of output has been successfully completed Phase 1b trials can soon begin with an estimated completion date of around mid-2019. This means that milestone payments from Cipla would slip from 2018 to the second half of 2019 (revised results were announced in November 2018). In addition, as a result of discussions with the FDA, it appears that a New Drug Application will now be filed in 2022 with approval expected after about 1 year. This period allows for any

increase in dosage used, and for an expected six months or so of Phase 2 trials to test pharmacological effectiveness and side-effects, including drowsiness, on a small group of patients. It also allows for Phase 3 trials lasting 18 months to two years.

3. Oxycodone tape (MRX-1OXT)

The oxycodone tape preparation is the biggest product MEDRx has. It is the tape version of oxycodone, which itself is an opioid for pain relief

The oxycodone tape formulation is MEDRx's biggest and most promising product. Oxycodone itself has the biggest share of North America's market for opioid pain relief, and ILTS® technology makes it transdermally absorbable. Like tizanidine, it acts on the brain/central nervous system and its drug efficacy depends on concentration in the blood stream. The company sees oxycodone tape not only eating into the oxycodone market but also being used to replace some other opioid analgesics.

Note: Opioid is the generic name for opium analogs (not opium) with narcotic properties such as morphine, and is widely used not only in the treatment of moderate to severe pain, but also in anesthesia and cough suppression.

In the US, the abuse and misuse of opioid analgesics is becoming a social problem, and MEDRx's own technology to prevent such abuse and misuse gives it a competitive edge

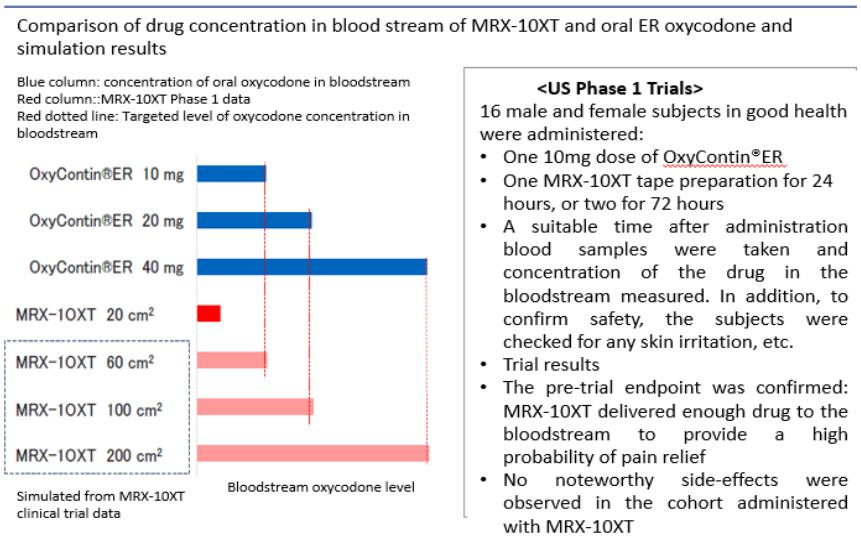
MEDRx holds the patent for its own abuse and misuse prevention technology (AMRTS®: Abuse and Misuse Resist Transdermal System), which we think gives it a leading competitive edge. As background, in the United States a serious social problem has developed out of the use and misuse of the narcotic component of opioid analgesics. Strong opioid analgesics for severe pain and other ailments are generally available on a doctor's prescription, and in 2014 two million Americans abused their medications or became addicted, while there were numerous accidents due to misuse. As a result the FDA has become more attentive to applications for new opioid drugs whose formulations do not lend themselves to abuse.

The oxycodone tape formulation (MRX-1OXT) has already successfully demonstrated a sufficient level of bloodstream concentration but the company is now making improvements to allow a smaller patch to deliver effective bloodstream concentration, and to provide better adhesiveness. These improvements have put back repeat dose trials from the autumn of 2018 to the middle of 2019. After completion of the trials the company is planning to license out in the second half of 2019 and submit a new drug application around 2022

From November 2015 the company initiated non-clinical trials and at the same time subcontracted the production of the investigational drug to the US company, Tapemark. The beginning of Phase 1 trials in the US was announced on October 16, 2017. With the completion in February 2018 of Phase 1clinical trials in the US, it was announced that the formulation was likely to achieve sufficient bloodstream concentration for the treatment of pain. Details are provided in the chart below. There were no side-effects worthy of note and it was established that there was a high possibility of sufficient bloodstream concentration commensurate with patch size to treat pain. However, to achieve the same concentration as a 40mg dose of existing oxycodone administered orally the required patch would be rather large, 200 square cm., while the largest available in the US for Lidoderm® is140 square cm. We assume that the company is now increasing patch absorbability and making improvements to achieve effective blood concentration with a smaller patch, while also increasing adhesiveness. After making those improvements they will probably move on to repeat dose tests. Those tests were slated for completion in the autumn of 2018 but will now only begin some time after mid-2019 for possible completion later in the year. Fair Research Inc. is of the view that the improvements will be completed during 2019, Phase 1 repeat dose supplementary tests will then be carried out and the results discussed with the FDA. In between, Phase 2 trials to demonstrate the effectiveness of the drug's ability to prevent abuse will then be undertaken before proceeding to Phase 3 clinical trials with an expanded number of cases. (We continue to believe Phase 2 and 3 will together take 2 years or so for completion, that application for approval will occur in about 2022 and that approval will be granted in 2023. However, depending on circumstances, the company could seek a faster route by reducing the number of indications (for example, post-operative pain relief) and expanding that number later on.

Like tizanidine tape, the company thinks it is possible to license out at the Phase 1 stage and appears to be planning such a move for the latter part of 2019.

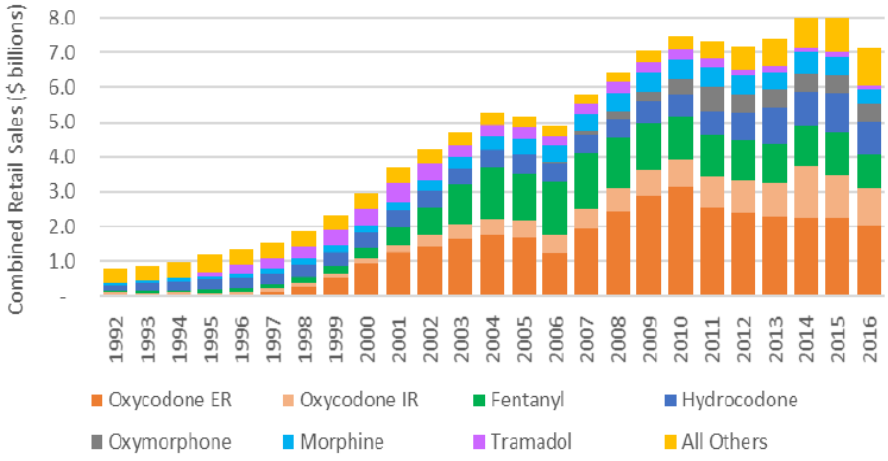
Comparison of blood concentration: MRX-1OXT and oxycodone oral ER



Source: MEDRx company briefing materials
(Extracted with amendments from follow-up report released March13, 2018)

The US market for opioids was valued at around USD3 billion in 2000, but had expanded to approximately USD8 billion by 2015. The main formulations include oxycodone ER (extended release), oxycodone IR (immediate release) fentanyl tape, hydrocodone and morphine.

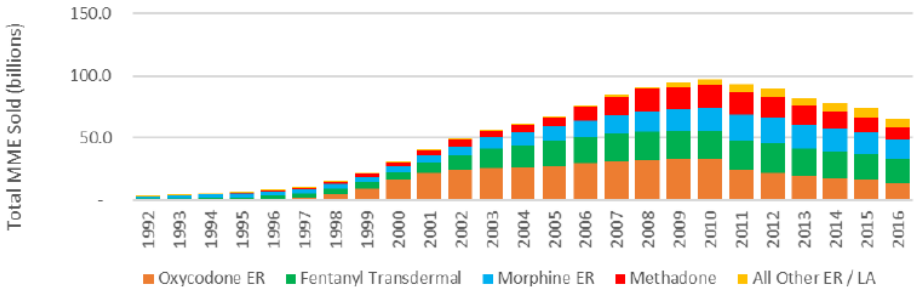
Size of US market for analgesics (USD basis)



Source: FDA

The oxycodone tape being developed by MEDRx targets the extended release market. This market has three formulations with, in volume terms, almost equal market share: oxycodone ER (commercial name OxyContin®), fentanyl tape and morphine. Fentanyl tape sales at one point exceeded USD2 billion, but after the patent lapsed and prices fell sales value shrank to around USD1 billion (with no shrinkage in volume terms). As for oxycodone (OxyContin®) alone, sales stood at USD2.8 billion in 2018, but fell to USD2 billion in 2016, the year in which the patent lapsed, and to USD1.8 billion in 2017. Because of patent lapses and the arrival of generics, sales volume need not change despite sales value changing significantly. For that reason, the question of volume and pricing of new formulations requires careful consideration.

ER opioid market (in volume terms)



Source: FDA
Note: MME units: converted to morphine equivalent, mg.

Here we assume that the oxycodone tape agent is used as a direct replacement for about half the sales of oxycodone ER (commercial name OxyContin®). Further, we assume that it replaces about one-quarter of the sales of other opioids including morphine, compared to which it is less addictive and has an anti-abuse mechanism. If we then assume that the new formulation is priced at about the same level as OxyContin® before patent expiry we arrive at a potential market size totalling approximately USD1.5 billion. This makes it a candidate drug which could have a very big impact (we previously considered it as a replacement also for fentanyl tape but have removed that from our calculation in order to be more conservative).

4. Memantine patches (MRX-7MLL)

The company had been developing a hybrid tape formulation (MRX-5DML) of donepezil and memantine using NCTS®. This was replaced with a memantine-only tape formulation (MRX-7MLL) and non-clinical tests carried out. The company expects Phase 1 to begin in 2019 with a new drug application being submitted in 2021-2022

MEDRx is also developing a tape formulation using memantine (trade name Memary) used in the treatment of Alzheimer's. The company had been developing a patch preparation (MRX-5DML) using NCTS® technology by combining donepezil (trade name Aricept) and memantine. However, in the United States, the sales volume of this combination was lackluster while the proportion of prescriptions for the memantine oral preparation and the donepezil oral preparation was high. The company switched to placing a higher priority on the development of single-agent memantine patches (MRX-7MLL) and single-agent donepezil patches. In the area of donepezil patches a number of companies (Corium Inc., Nitto Denko, Hisamitsu Pharmaceutical) are leading, but with memantine, NCTS® yields greater efficacy. For that reason, MEDRx has given memantine preference and started non-clinical trials in July 2018. In December 2018, as a response to a pre IND meeting request, the FDA indicated that the results of the non-clinical study would be a sufficient basis to start Phase 1, and if bioequivalence with memantine oral preparation could be demonstrated, Phases 2 and 3 would not be required, This indicated to the company that a relatively early NDA was possible. The earliest this could happen is between the end of 2021 and early 2022, since in 2019 there would be an application for permission to conduct trials, followed by the two-stage pharmacokinetic tests and bioequivalence tests, and the simultaneous need to secure the integrity of the commercial production line for NCTS® technology.

Reference:

US market for Alzheimer's drugs: approximately USD150 billion

Of which, memantine oral formulation: approximately USD75 billion

Donepezil-memantine combined formulation: approximately USD14 billion

Source: MEDRx Timely Disclosure filings July 18, 2018

5. Tie-ups with major pharmaceuticals companies

There has been an acceleration in partnerships with major pharmaceuticals companies. In February 2018, MEDRx concluded a joint development agreement with Daiichi Sankyo, and in an agreement concluded in August of the same year granted Takeda Pharmaceutical the use of MEDRx's key technology on transdermal absorption with respect to several drugs under development

On February 28 2018, it was announced that a joint development agreement with a major Japanese pharmaceuticals company, Daiichi Sankyo, had been signed covering MEDRx's NCTS® transdermal absorption technology using nano-sized colloids. Under this agreement MEDRx is to receive milestone payments commensurate with progress in development and sales. After launch the plan is for MEDRx to be the sole supplier of the product to Daiichi Sankyo. Much depends on the details of the agreement, but it seems possible that it will create a pipeline that will impact the company's enterprise value. However, we do not analyse it in this report since there has been no disclosure about the development candidate (drug name, target disease), no concrete financial terms and no comment on the future schedule.

Further, on August 27, 2018 MEDRx concluded a technology licensing agreement with Takeda Pharmaceutical involving the use of ILTS® and NCTS® in certain priority disease areas for that company. MEDRx will only provide the technology and will bear none of the development costs. It will receive milestone income in line with progress in development and commercialisation, and will receive milestone income after launch in line with sales. Needless to say, as with the joint development agreement with Daiichi Sankyo, the name of the drug or drugs in question and the indications targeted were not disclosed so it is difficult to evaluate impact (Fair Research Inc. expects that disclosure will become more detailed as development advances).

MEDRx has several pre-clinical development products. The development of microneedles has been temporarily suspended

We should emphasise an additional significance in that the technology agreement with Takeda does not involve medicinal ingredients that have previously been approved but those which are still under development and which embrace multiple substances. The fact that MEDRx's key technologies, ILTS® and NCTS®, have been supplied to multiple mega-pharma pipelines speaks not only for the quality of MEDRx technology but also suggests the company has the opportunity to turn itself into a platform provider.

In addition to the above, the company has a number of pre-clinical products and a microneedle project under development. Some are at the initial stage of development and the microneedle project is temporarily suspended.

2018 Results and 2019 Outlook

In 2018 there was a lag in milestone income from Cipla, which is now due in 2019. Led to lower revenues and bigger deficit

In 2018 earnings were dented by the delay, until late 2019, in receipt of milestone payments expected from Cipla for the development of the tizanidine tape formulation, leaving only JPY8 million in revenues from sales of iodine coating ointment. In the development pipeline, there were changes in the conduct of pre-clinical and clinical testing and, mainly for this reason, costs generated were less than initially estimated, but the delay in receipt of revenues drove net profits down to a negative JPY1.267 billion.

In its annual plan the company is expecting milestone income from Cipla in the second half of 2019. While the licensing-out of oxycodone should occur later in the year the company has left it out of its

In 2019 sales are expected to come in at around JPY1 billion. Of this, iodine coating ointment should account for JPY24 million and the delayed milestone payment from Cipla for around JPY700 million. It will also include development cooperation revenues from major pharmaceuticals companies. The licensing-out of the oxycodone tape formulation is expected to occur after Phase 1 (planned for the second half of 2019 or 2020) but the lack of certainty means it has not been included in the company's annual plan. Meanwhile, oxycodone tape formulation Phase 1, the start of memantine NCTS® Phase 1a, and pre-clinical studies on unpublicised

plan due to lack of certainty. R&D expenses are expected to rise further

pipeline products are expected to drive R&D expenses up to JPY1.371 billion, higher than the previous year. As a result, a net profit loss of JPY643 million is expected, below the level of the previous year. It should be noted that the R&D costs do not include development costs for the lidocaine tape formulation for which supplementary testing had been requested (the costs total JPY1.1 billion for 2019-2020, of which around JPY400-500 million for 2019 alone).

2018 actual costs and 2019 plan

(JPYmil.)

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019 (Co. forecast)
Sales	291	741	87	68	26	37	22	198	8	1,009
Finished products	84	94	71	33	26	37	22	28	8	24
R&D revenues	206	646	16	36	0	0	0	170	0	985
COGS	58	34	33	8	9	12	8	7	2	5
SG&A expenses	857	1,141	621	664	1,020	1,025	1,357	1,174	1,279	1,654
R&D expenses	695	939	415	397	718	716	1,074	888	980	1,371
Other admin costs	162	202	206	267	302	309	283	286	299	283
Operating income	-623	-434	-567	-604	-1,003	-999	-1,342	-983	-1,273	-650
Recurring profit	-616	-479	-578	-616	-1,012	-990	-1,301	-988	-1,285	-656
Net earnings	-536	-433	-571	-621	-1,016	-878	-1,259	-884	-1,267	-643

Source: MEDRx using results meeting materials and others

Announced fund raising at an early date to propel development.

Cash on the balance sheet at the end of December 2018 stood at JPY1.769 billion. This is nearly on a par with the sum of 2019 R&D costs (JPY1.371 billion) and SG&A costs, which together come to JPY1.654 billion. Bearing in mind the development and other costs associated with the lidocaine tape formulation, it will be necessary to raise funds at an early date in order to achieve steady progress in product development. We assume this was behind the announcement on February 12 of the company's decision to raise a total of JPY1.27 billion. JPY1.1 billion was earmarked for the lidocaine tape formulation, and JPY170 million for the development of the company's new product lines apart from the existing product lines. These amounts will be raised by a third-party allotment of shares to the value of JPY100 million to the company president and to the asset management entity owned by family members, with the balance coming from the issue of new share subscription rights in an allocation to the Evo Fund (approximately JPY1.17 billion). Under the terms for changes in exercise price it is expected that exercise will take place in three months, so that even if milestone income occurs in the second half there will be no fund short in the first half. Further, if the development of the lidocaine tape formulation occurs as planned subsequent to the fund raising then there will be amendments made to R&D spending plans and the earnings outlook.

Trend in the Balance Sheet

(JPYmil.)

	2010/12	2011/12	2012/12	2013/12 IPO	2014/12	2015/12	2016/12 CB issue	2017/12 CB conversion	2018/12 stock option
Liquid assets	730	649	507	4,008	2,857	2,204	2,736	1,836	1,937
Cash	691	614	465	3,937	2,780	2,063	2,640	1,737	1,796
Misc.	39	35	42	71	77	141	96	98	141
Fixed assets	335	304	280	722	831	774	342	296	373
Tangibles	265	240	215	256	346	278	264	220	295
Intangibles	0	0	0	1	3	2	1	0	0
Investments, etc	89	64	65	465	483	494	76	75	77
Total assets	1,085	952	787	4,730	3,685	2,978	3,079	2,133	2,311
Liabilities	80	106	511	227	171	205	573	99	180
Liquid liabs	64	79	450	158	79	110	103	88	170
Fixed liabs	16	27	61	69	92	96	469	10	10
Net assets	1,005	847	275	4,503	3,514	2,772	2,507	2,037	2,130

Source: Fair Research using short-form results reporting

We have re-calculated the value of the company's product pipeline taking into account changes in the development situation

Modelling the pipeline present value

On the basis of the foregoing we have re-worked the present value of each product pipeline using the discounted cash flow method. (Note: this is simply a trial calculation using various demanding assumptions and is therefore only one yardstick approximation.)

Assumptions made for the calculation

The period from product launch until peak sales is approximately 4-5 years, at which point sales fall off at a rate of 5% per year. From 2037 onwards, because of the appearance of generics, this rate of annual attrition rises to a final stage of 10%. We have assumed a rather high discount rate of 12%, given the market's required return on equity of 8% and the fact that the company is regarded as a bio-venture with no major product up and running and a history of negative earnings. We further assume royalty revenues of 10-12% of sales, and probability of success of 60% for Phase 3 lidocaine, and 50% for tizanidine and oxycodone, now subject to a second round of Phase 1 repeat dose trials. For memantine we posit the probability of success at 40% given that it is at Phase 1a. Apart from the tizanidine tape formulation whose milestone value is confirmed, the total value of milestones for each product pipeline is assumed to be around 20% of peak sales for pipelines licensed out at an early stage of development, and around 30% of sales for those licensed out in the latter stages.

On the basis of a number of assumptions we posit the total value of the company's main four product pipelines at approximately JPY45.5 billion

(Results of simulation)

Discounted present value of main pipeline products (before tax)

(100 million Yen)

	Ex-Prob. of success	w/prob. of success
Lidocaine Tape (MRX-5LBT)	86	47
ref: if peak sales is 3 million patches	10	2
Tizanidine Tape (MRX-4TZT)	96	48
Oxycodone Tape (MRX-10XT)	748	372
Memantine Patch (MRX-7MLL)	103	33

Source: Calculated by Fair Research Inc.
Note: It should be noted that the results of the simulation will change depending on the assumptions made, and that the value of the company must take into account not only the value of each product pipeline but also various costs and tax considerations

① We assume that the lidocaine tape formulation peak sales can achieve a 10% market share (12 million patches) and that, with a 60% probability of successful launch in the market, can achieve a value of around JPY2.9 billion. If we assume sales of only 3 million patches (the same as the minimum target for the competing product, ZTlido®) then, using a 60% probability of successful product launch, JPY200 million or so will be enough to cover development costs.

	② We posit the value of the tizanidine tape formulation, assuming peak sales of JPY30 billion and a 50% probability of successful market launch, at around JPY4.8 billion. At a 100% probability of success this rises to JPY9.6 billion. ③ We posit the value of the oxycodone tape formulation, assuming peak sales of JPY165 billion and a 50% probability of success, at JPY37.2 billion, providing further confirmation that this is the company's biggest product. However, the company may seek early approval by limiting the number of conditions and adding them later on, in which case peak sales would lag and the product's value could fall. ④ We posit the value of the memantine tape formulation at JPY22.5 billion, assuming peak sales at one-quarter the level of the memantine oral formulation. After discounting for probability of success we arrive at an estimated pipeline value of JPY3.3 billion. This could rise to a three-digit value if the product replaced half the oral formulation's sales or if the probability of success rose in response to development advances.
We infer that the gap between market value and pipeline value is due to the effect of the development delays of the past year and the problems incurred in funding the microneedle project. However, we expect a lot from a series of positive events due in the second half of 2019.	We can infer the market's current evaluation of MEDRx from the sizeable gap between the company's market value of around JPY4.9 billion and the JPY45.5 billion pre-tax present value of the company's four main pipeline products, even after allowing for the JPY1.27 billion fund raising announced in February. Two factors account for this gap: ① For all pipelines there were delays in development and consequent delays in milestone payments; ② Prior to the announcement of a fund raising for the microneedle project investors had not been made aware of market size and prospects of success, so this turned it into a negative surprise. However, we see the second half of 2019 as providing a good opportunity for the market evaluation to change. One reason for this is the generation of milestone revenues for the tizanidine tape formulation, and another is the promising development of the oxycodone tape formulation and the prospects for a successful licensing-out. In addition, fuller disclosure on the products being developed in collaboration with major pharmaceuticals companies should have an impact on the market's evaluation.

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