MEDRx (4586) TSE Mothers

Eagerly awaiting mass production of a patch system for vaccination

Yuya Okamura, Analyst

Company profile	
Location	Higashikagawa-shi, Kagawa
Representative	Yonehiro Matsumura
Established	January 2002
Capital	¥6,934 million
Listing	February 2013
URL	http://www.medrx.co.jp/index.html
Sector	Medicine

Stock price data (closing price on August 31)	
Stock price	317
Outstanding shares	16,540,100shares
Trade unit	100shares
Market cap	¥5.24billion
PER (est.)	-
EPS (est.)	-
PBR (actual)	3.24x

■ A bio venture striving to enter the American market with adhesive skin patches – a product that has never seen in the U.S.

MEDRx is a venture company that was established in Higashi-Kagawa-shi, Kagawa in January, 2002. Capitalizing on 'ILTS', MEDRx's proprietary technologies using ionic liquids, the company is engaged in development of adhesive skin patches. The company has successfully passed the P1b trials and preparations are underway to implement the phase II trials in 2020. MRX-5LBT, which is expected to be used as a therapeutic drug for post herpetic neuralgia, is the closest pipeline to sales. MEDRx concluded a joint development agreement with D.Western Therapeutics Institute in April 2020 (will receive a maximum of 200 million yen from DWTI in the form of milestones according to the progress of commercialization). On August 27, the company announced the submission of NDA to the U.S. FDA.

■Full-scale start of microneedles attracting great attention during COVID-19 pandemic

Microneedles are a painless transdermal administration system for vaccines and drugs. In addition to being painless, they have advantages such as improved immune effectiveness during vaccination. Consequently, microneedles are attracting attention as a promising medical device in the future. In April, MEDRx started operation of a microneedle factory for investigational drugs. There are still no industry players who reached the mass production stage. MEDRx has a unique applicator that securely and easily inserts microneedles into the skin. There are expectations for future development, including business alliances, etc.

■Awaiting the adjustment of outstanding balances during heavy April business

The projection for the current term is net sales of 334 million yen, a negative balance in the ordinary income of 1,088 million yen, and a negative balance in net income of 1,091 million yen. As the estimate for net sales was calculated mainly based on the allocated recorded portion (approx. 210 million yen) of development milestone income from CPN-101 and the milestone income (100 million yen) from DWTI, with whom the company signed the MRX-5LBT joint development agreement in April, we can say with a high degree of certainty that the company will achieve the goal. In April, the stock price soared in response to microneedles. Due to a rapid increase in outstanding balances of margin trading during this period, the price is being held back by selling on rally. Nevertheless, the pipeline is steadily progressing through initiatives such as submitting a new-drug application for MRX 5LBT, which was the largest catalyst. If the supply and demand adjustments come full phase, review is expected.

Point summary（1）

●What kind of company is MEDRx?

MEDRx is a venture company established in January, 2002 in Higashi-Kagawa-shi, Kagawa. In February, 2013, the company was listed in the Tokyo Stock Exchange Mothers. Capitalizing on 'ILTS', MEDRx's proprietary technologies using ionic liquids, the company developed adhesive skin patches and is currently trying to create the topical/transdermal tape product for the U.S., country boasting an enormous market. Unlike other regular venture companies, MEDRx's aim is not to develop new APIs. MEDRx is a company, which is engaged in development of a new platform for APIs already used in a range of medicines for internal use or injection drugs, with the idea to use these APIs in adhesive skin patches or ointments. For that reason, although the company is expecting same high returns as a venture developing new APIs, the risks are on a much smaller level, so the business model of MEDRx is quite special.

●What are the special advantages of adhesive skin patches in the first place?

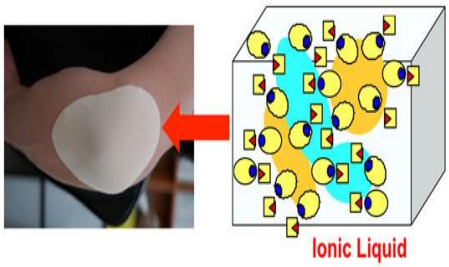
The best known kind of adhesive skin patch in Japan is surely the anti-inflammatory analgesic plaster. There are many kinds of drugs including oral medicine, injection drugs, ointments, etc., but the adhesive skin patches including anti-inflammatory analgesic plasters have four major advantages.

(1) The first is that the pharmacologically effective agent is released gradually. Because the medicine comes out slowly, it is easier to keep blood concentration constant and continuously maintain benefits of the drug.

(2) Because these drugs do not pass through the liver like orally taken medicines, the liver does not bear the burden of breaking them down. Side effects are rare.

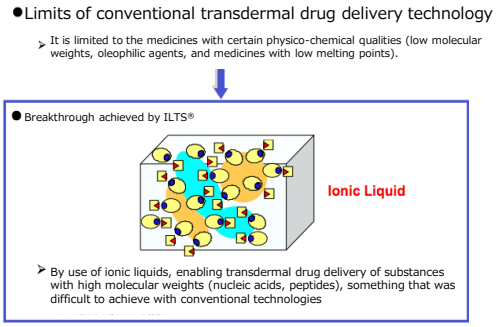
(3) Risk of forgetting to take medication can be eliminated. In case of overdosage, one can simply remove the patch. One can even apply the patches to the backs and other parts of the body of infants and young children where they won't be seen.

(4) There is no pain like with injected pharmaceuticals.



●What sort of technology is 'ILTS', the proprietary technology of MEDRx?

The skin serves as the first barrier protecting the human organism from invasion of foreign substances. For this reason, many of the drugs could not be efficiently delivered into the body using the conventional transdermal drug delivery technology. MEDRx pioneers the use of ionic liquids to create adhesive skin patches for drugs that could not previously be administered through such patches.



The key features of ionic liquid are its low melting point (100 degrees and below), that it remains liquid at room temperature, and that its (equilibrium) vapor pressure is virtually zero. Furthermore it is incombustible, and boasts excellent solubility. MEDRx is the first company in the world that took a technology, which was commercially exploited by other industries in such areas as lithium-ion and solar cells, and managed to use it for medication. The company has acquired medical patents for every pipeline, protecting high barriers to entry.

Point summary（2）

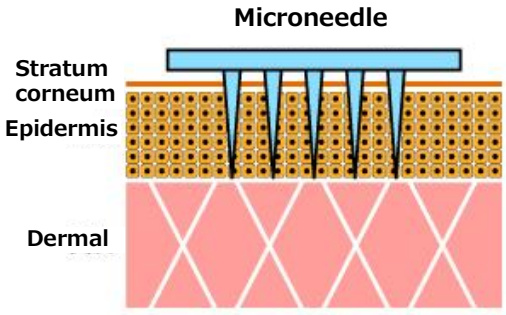


Image 1

Image 2

Image 3

● What is a microneedle?

A collection of tiny needles made of biodegradable resin is called a microneedle (MN). As shown in the figure on the left, the MN is inserted into the skin, but it has the advantage of being painless because it consists of tiny needles. MN is a painless transdermal administration system that locally punctures the stratum corneum and administers vaccines and drugs to the dermal layer.

Currently, the development of a vaccine for COVID-19 is an urgent issues throughout the world. When administrating this vaccine, MN is expected to enhance the effect of immunity compared to conventional injection. Additionally, it has the merit of being expected to provide a faster effect than oral drugs. Consequently, MN is attracting attention as a promising administration device in the future.

● Innovative vaccination device with high potential!

MN, which is subject to high expectations as a new medical device, has a potential market size of up to 1 trillion yen. In Japan, corporations such as Fujifilm and Nipro are also attempting to enter the MN market; however, no industry players have reached the stage of mass production as medical devices.

In April 2020, MEDRx began operation of an investigational drug factory for MN, a device with high potential. The company's unique applicator (the Japan Patent Office made a decision for a patent grant in August 2020) is an extremely innovative device that reliably and easily inserts MN into the skin.

The applicator is the size of a business card or smaller (back of device shown in Image 1; front shown in Image 2) and it is lightweight. Multiple applicators can be placed in an envelope for mailing. This would enable vaccines to be distributed to all households, even in the event of an infectious disease pandemic.

Moreover, the applicator has an advantage over conventional injections because self-administration can be easily performed by anyone upon delivery. The MN patch is attached simply by placing the applicator holding the MN on your arm and pressing it vertically (Image 3).

This innovative medical device is expected to achieve outstanding performance after being commercialized and put into mass production. This performance will be achieved in terms of protecting the medical system in the event of a pandemic and contributing to emerging countries where the medical environment is not well established.

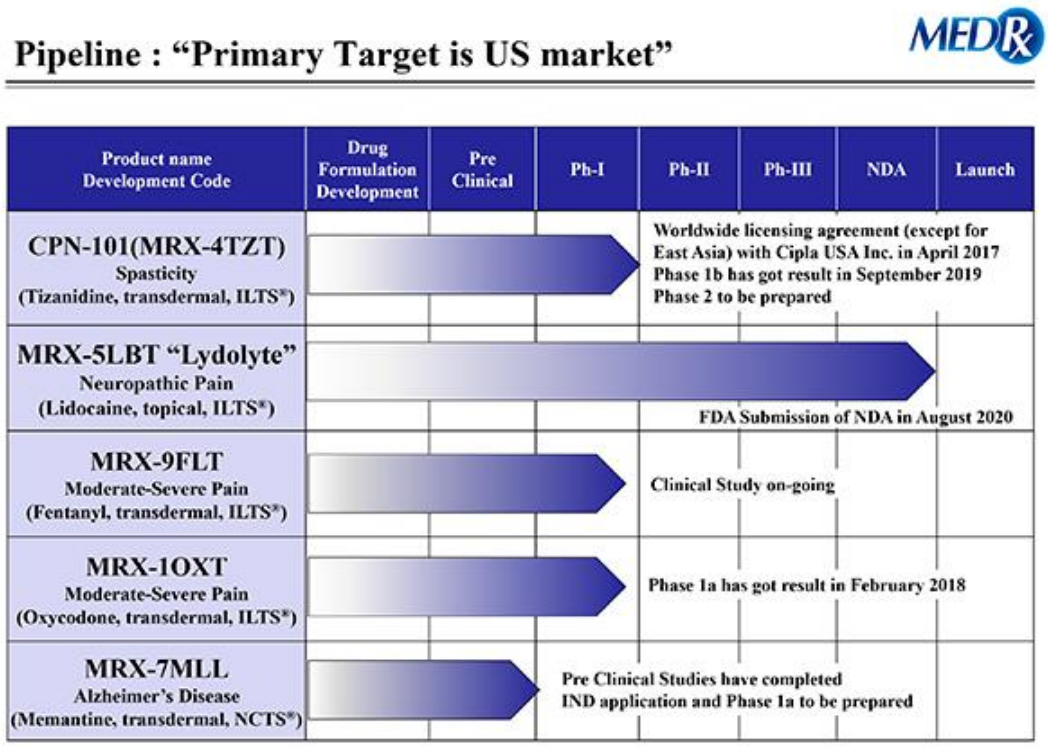
Development pipeline: present conditions and prospects (1)

① 「CPN-101」 (「MRX-4TZT」)

An adhesive skin patch containing tizanidine, a centrally acting muscle relaxant that is used in Japan to treat a number of symptoms including stiffness of the shoulders. The size of the US market for neuromuscular junction blocking drugs is huge: approximately 88 billion yen as of the 2016 fiscal year. Oral tizanidine medication requires 3 doses per day, and there are also side effects such as liver dysfunction and drowsiness. If made into an adhesive skin patch, one needs to apply the patch only once during the day and the medicine will be effective throughout the day slowly entering the body and keeping the blood concentration on the same effective level.

Phase I of clinical trials for MRX-4TZT was completed in February 2017, and the results were favorable. The same level of blood concentration as with medicine for internal use containing tizanidine currently on the market was confirmed, and there was almost a complete absence of side effects such as drowsiness. Also, this April, the company signed a global (with the exception of East Asia) development and sales licensing contract with Cipla USA, the American 100% subsidiary of Cipla, a major pharmaceuticals company in India. In addition to the lump sum payment for executing this contract, this large-scale contract features favorable conditions such as a maximum of 30 million USD (about 3.3 billon yen) provided for milestones in development and sales progress and graduated royalty income for sales after products enter the market.

The added phase I clinical trials (P1a'), which were started in September 2017, yielded, in January 2018, favorable results (in terms of effectiveness and drowsiness score), meeting the standards, which had been determined in cooperation with Cipla beforehand.
The next challenge is the process (P1b), MEDRx had to manufacture an investigational new drug in the form scaled up to the commercial production level, and conduct, using the investigational new drug, the same repeated dose trials as were done during P1a'. MEDRx started P1b trials in May 2019. In September 2019 the company was judged to have achieved good results that satisfied the criteria determined beforehand. By successfully passing the trials, the company got entitled to receive a development milestone income from Cipla. The development milestone income is 6 million U.S. dollars. However, in order not to fall under the stock delisting criteria of the Mothers section (yearly net sales of 100 million yen or more for companies in and after the 6th year since listing), MEDRx made arrangements with Cipla to receive it in installments (for the term ended December 2019, MEDRx received only 1 million U.S. dollars). The following phase II trials are due to be implemented by the end of 2020, with Cipla taking the lead.



Development pipeline: present conditions and prospects (2)

②「MRX-5LBT」"Lydolyte"

An adhesive skin patch with lidocain, a local analgesic. The product is developed to be used as a therapeutic drug for neural pain. The lidocain patch market in the U.S. is estimated to be about 50 billion yen (2018 estimate). In June 2018, biological equivalence of MRX-5LBT with Lidoderm was demonstrated in a pivotal comparative clinical trials. This trial compared MRX-5LBT with Lidoderm, a drug that had scored a major hit in the target U.S. market (bringing in annual sales of over 100 billion yen at the peak). MEDRx's product showed the ability to achieve the same efficacy with just a little amount of lidocaine. Subsequently, the company implemented all clinical trials necessary to submit a new-drug application (hereinafter: NDA) as required by the U.S. FDA. In April 2020, MEDRx entered into a joint development agreement with D.Western Therapeutics Institute (hereinafter: DWTI) (the company will receive up to 200 million yen from DWTI in the form of milestones depending on the progress of commercialization). On August 27, MEDRx announced submission of the NDA to the U.S. FDA in accordance with the original plan.

③「MRX-9FLT」

MRX-9FLT is an adhesive skin patch containing fentanyl, a designated medical opioid. The U.S. market of fentanyl patches is about 34 billion yen (estimated in 2018). Fentanyl patches have been used in the U.S. since their arrival in March 2002 to relieve severe acute pain, chronic pain, and cancer pain. Although the company is not a pioneer in this area, fatal accidents of infants and children caused by misuses of the existing patches have been reported. This new pipeline was established by MEDRx to ensure that such accidents do not happen again. If the company succeeds in adding value by using its proprietary technology to prevent such misuse-induced accidents, such innovation may help MEDRx to increase its market share. At a meeting with the company in May 2019, the FDA identified this feature as an important and valuable goal. Precedence suggests that the probability of approval is high. The lowered costs in association with less testing should restrain the cost of development. On July 28, 2020, the company announced that clinical trials in the U.S. have started. Although the start was slightly delayed due to COVID-19, the clinical trials are proceeding smoothly in accordance with the original plan.

④「MRX-7MLL」

An adhesive skin patch with memantine, an agent used to treat Alzheimer's disease. The company has been developing '5DML', a patch containing donepezil and memantine. However, in the U.S., which is the market the drug is intended for, memantine is prescribed not as a mixed oral agent, but as a single-agent drug. To move more in line with this market environment, MEDRx also changed its policy. As the formulation development of memantine single-agent patches was completed in July 2018, the company started non-clinical trials. Although the mainstream of medicine for Alzheimer is oral medicine, considering the fact that with oral medicine there are always risks of the patient forgetting to take medication, over-medication, etc., there are some truly substantial merits for both patients and their families if the drug can be manufactured in the form of adhesive skin patches. Non-clinical trials for the drug are complete, and it has already been confirmed that phase II and phase III trials will be unnecessary if the company can show that the drug has the bioequivalency as existing oral preparations. MEDRx plans to conduct the P1a trials by the end of 2020. The company seems to have already started to select a consigned manufacturer in expectation of commercial production.

Results of Operations

Performance (million yen, %)

Fiscal year end	Net sales	YoY	Ordinary income	YoY	Net income	YoY	EPS(¥)
December 2015	37	43%	-990	-	-878	-	-
December 2016	22	-40%	-1301	-	-1259	-	-
December 2017	198	787%	-988	-	-884	-	-
December 2018	8	-96%	-1285	-	-1267	-	-
December 2019	169	1923%	-1633	-	-1616	-	-
December 2020 (est.)	334	98%	-1088	-	-1091	-	-

● During the first half of the term ending December 2020, the company posted net sales of 15 million yen, a passive balance in the ordinary income of 713 million yen, and a passive balance in net income of 713 million yen. Net sales consisted solely of 15 million yen from Iodocoat Ointment currently on the market. Compared to the same period of the previous term, losses decreased due to high research and development expenses in the same period of the previous term caused by earlier implementation of clinical trials for MRX-5LBT, and due partly to delays in clinical development caused by the impact of COVID-19 in the first half of this term. Sales and general administrative expenses for the first half of the term were 717 million yen, down from 902 million yen in the same period of the previous term.

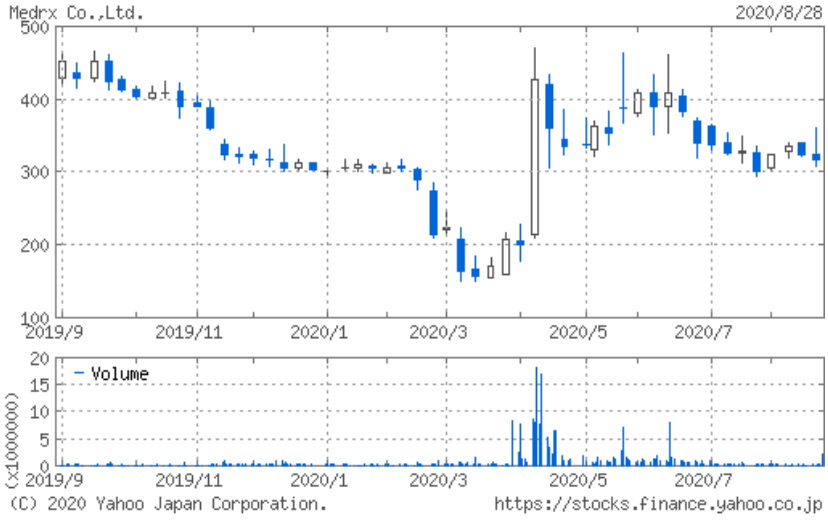
● The projection for the term ending December 2020 is net sales of 334 million yen, a passive balance in the ordinary income of 1,088 million yen, and a passive balance in net income of 1,091 million yen. As the estimate for net sales was calculated mainly based on allocated recorded portion (approx. 210 million yen) of development milestone income from CPN-101 and the milestone income (100 million yen) from DWTI, with whom the company signed the MRX-5LBT joint development agreement in April, we can say with a high degree of certainty that the company will achieve the goal.

Results of Operations

● The company's stock price was traded at its lowest level since listing, with the stock price falling to 150 yen and market cap decreasing to 2,500 million yen on March 13. This was due to deterioration of the Tokyo Stock Exchange Mothers caused by COVID-19, which occurred at the same time as stopping development for the promising pipeline MRX-1OXT. However, just one month later, on April 17, the stock price temporarily reached 471 yen, the highest price for the year so far. After the Japanese government issued an emergency declaration, there were active sales and purchases of stocks by individual investors who were spending more time at home. Since the declaration of an emergency, the stock trades of individual investors who have spent a lot of time at home have become active. In particular, sales and purchases of stocks listed on Mothers stocks increased sharply and the liquidity improved, resulting in a significant increase in the Mothers Index. With the timing of favorable conditions in emerging markets, MEDRx showed outstanding price movement as a lightweight bio stock.

● On April 15, the daily trading volume reached a yearly record high of 18.24 million shares. The number of 18.24 million shares is calculated as the number of issued shares (16.54 million shares) that were traded at least once. It was the first time that this high level of daily trading had been reached since February 15, 2013, immediately after the IPO. Most recently, the daily trading volume exceeded 11.25 million shares on October 27, 2017. This surge in trading volume seems to have been caused when some industry newspapers identified MEDRx as a stock related to measures against COVID-19. The reporting was focused on microneedles, which were introduced as an injection patch that is applied to the skin. At this point in time, prices had soared for bio stocks related to vaccine development, and it seems that the reports on MEDRx resonated with individual investors. Immediately afterwards, on April 17, the company issued a press release announcing the start of operations at a microneedle therapeutic drug factory. On this same day, the stock reached its yearly high of 471 yen.

● Unpredictable factors have increased recognition for MEDRx among individual investors. However, there has been an increase in the number of investors who use margin trading to buy on a short-term basis, and the outstanding balance of margin trading remains at a high level. Although the outstanding balance of margin trading fell to 1.19 million shares in the second week of March, when the stock price reached an all-time low, it exceeded 3 million shares in the third week of April, when the stock price was high. As of the third week of August, it remained at a high level of 2.78 million shares, with the outstanding balance of margin trading reaching approximately 17% of the number of issued shares. It is assumed that the outstanding balance of margin trading was done in the stock price range of 350 yen to 460 yen in stock prices, of which the supply and demand adjustment for this amount will suppress the price increase. Normally, the company's largest catalyst for this term should have been the new-drug application for MRX 5LBT. The company steadily advanced the important pipeline and announced submission of NDA to the U.S. FDA on August 27. Although this was good news for existing shareholders, the stock price slumped after temporarily rising to 360 yen on August 28. This trend can be interpreted as the result of suppression due to selling on rally for outstanding balances of short-term margin trading created by other factors. After adjustment for outstanding balances of margin trading, MEDRx will be seen as a bio stock that steadily advances its pipeline. (Okamura)



Stock Price (historical)	
Year high	¥471
Year low	¥150
Highest since the IPO	¥7,500
Lowest since the IPO	¥150

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