MEDRx (4586) TSE Mothers

Portfolio emphasizing certainty in trying times

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Company profile	
Location	Higashikagawa-shi, Kagawa
Representative	Yonehiro Matsumura
Established	January 2002
Capital	¥6,704 million
Listing	February 2013
URL	http://www.medrx.co.jp/index.html
Sector	Medicine

Stock price data (closing price on March 11)	
Stock price	184
Outstanding shares	14,214,100shares
Trade unit	100shares
Market cap	¥2.61billion
PER (est.)	-
EPS (est.)	-
PBR (actual)	1.39x

■ 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 intends to implement the phase II trials in 2020. "MRX-5LBT," a product developed to be used for alleviating post herpetic neuralgia, is the pipeline that is the closest to sales. MEDRx has already completed all of the clinical trials required by the FDA and plans to submit a new-drug application as early as 2020. The company decided to suspend the development of MRX-1OXT, an adhesive skin patch containing oxycodone, in view of the deterioration of the environment in the U.S.

■ CPN-101 development milestone income appropriated in the fiscal year

The initial forecast made in the beginning of the current term (ending December, 2020) projected net sales of 234 million yen, ordinary loss of 1,188 million yen, and net loss of 1,191 million yen. As the estimate for net sales was calculated mainly based on the development milestone income from CPN-101, which is to be distributed over several years, we can say with a high degree of certainty that the company will achieve its goal. For the time being, the yen/dollar exchange rate is volatile. When the yen is stronger than expected, sales decrease in yen terms. However, the research and development expenses accompanying the clinical trials in the U.S. are greater than sales. For that reason, as the loss declines in yen terms, the advantages of the strong yen rates outweigh the demerits. As of December 31, 2019, cash and deposit were 1,410 million yen.

■ Approval for MRX-5LBT as a new drug expected

In addition to the suspension of the development of MRX-1OXT, the company was also significantly affected by an excessive global risk avoidance mood triggered by the current spread of the COVID-19. The company's shares plunged 39% from the beginning of year, renewing the record low level since listing. We should note though that the Tokyo Stock Exchange Mothers Index fell by 29% in the same period, and a number of major bioventures listed on the TSE Mothers experienced a drop in the price of their shares that was even worse than that of the MEDRx. Of course, it would be great if the situation went back to normal, but predicting what market conditions will be in the near future is not a simple task. From a long-term perspective, the company's scenario remains unchanged: It will stay listed until 2021, when MEDRx will be able to appropriate sales of MRX-5LBT, which has already passed all necessary clinical trials. The company will reward its shareholders later on. This year, the new-drug application for the MRX-5LBT is the greatest catalyst for MEDRx. It is not the only one – there are actually quite a few, including the start of clinical trials for the MRX-9FLT in the U.S. and the start of the P1a trials for the MRX-7MLL.

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?

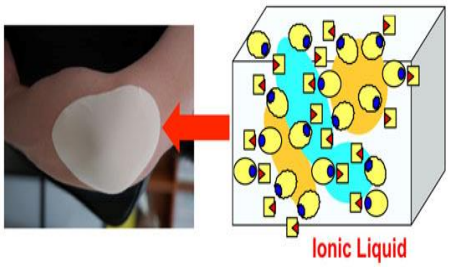
The best known kind of adhesive skin patch in Japan is surely the anti-inflammatory analgesic plaster. There are many kinds of drugs including oral medicine, injection drugs, ointments, etc., but the adhesive skin patches including anti-inflammatory analgesic plasters have four major advantages.

(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.

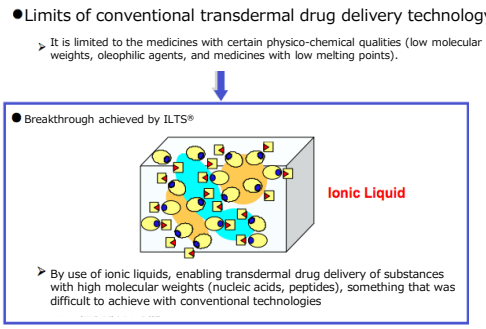
(3) Risk of forgetting to take medication can be eliminated. In case of overdosage, one can simply remove the patch. One can even apply the patches to the backs and other parts of the body of infants and young children where they won't be seen.

(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.

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. Originally the development milestone income the company was entitled to was 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.

Pipeline : "Primary Target is US market"

MEDRx

Product name Development Code	Drug Formulation Development	Pre Clinical	Ph-I	Ph-II	Ph-III	NDA	Launch
CPN-101(MRX-4TZT) Spasticity (Tizanidine, transdermal, ILTS®)				Worldwide licensing agreement (except for East Asia) with Cipla USA Inc. in April 2017 Phase 1b has got result in September 2019 Phase 2 to be prepared			
MRX-5LBT Neuropathic Pain (Lidocaine, topical, ILTS®)			Confirmation of Bioequivalence in comparative pivotal clinical study in June 2018			NDA to be submitted to FDA in 2020 Start of Development in Europe	
MRX-9FLT Moderate-Severe Pain (Fentanyl, transdermal, ILTS®)		Drug Formulation Development has completed Start of Development in USA					
MRX-1OXT Moderate-Severe Pain (Oxycodone, transdermal, ILTS®)				Phase 1a has got result in February 2018 Phase 1b to be prepared			
MRX-7MLL Alzheimer's Disease (Memantine, transdermal, NCTS®)			Pre Clinical Studies have completed IND application and Phase 1a to be prepared				

Development pipeline: present conditions and prospects (2)

②「MRX-5LBT」

An adhesive skin patch with lidocain, a local analgesic. The product is developed to be used for alleviating post herpetic neuralgia. In June 2018, biological equivalence of MRX-5LBT with Lidoderm was demonstrated in confirmatory comparative clinical trials. These trails 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). However, the trials went even further, showing the ability of MEDRx's product to achieve the same efficacy with just a little amount of lidocain. Subsequently, the company implemented clinical trials necessary to submit a new-drug application (hereinafter: NDA) as required by the U.S. FDA. Firstly, in July, 2019, MEDRx passed the "Adhesive Power Evaluation Test" achieving a score for adhesive power (numerical value indicating the extent the patches can tightly stick to the skin) satisfying the requirements. Next, in January 2020, the company conducted "tests of effects from exercise" that displayed sufficient adhesive power when a subject is in perspiration-inducing motion. In February 2020, MEDRx also successfully passed the "Photoallergy Test" related to photosensitivity, thus completing all the clinical tests required by the FDA. The company is ready to submit an NDA in the middle of 2020 to enter the U.S. market of lidocain patches, which boasted a scale of approx. 50 billion yen in 2018.

③「MRX-9FLT」

MRX-9FLT is an adhesive skin patch containing fentanyl, a designated medical opioid. The U.S. market of fentanyl patches was 34 billion yen in 2018. Although the market is not large, 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, it is affected by the social problems associated with the patches. For example, fatal accidents of infants and children caused by misuse of the 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. These lowered testing costs should restrain the cost of development. The company plans to launch the clinical development in the U.S. by the end of 2020.

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. With commercial production right around the corner, the company seems to have already started to select a consigned manufacturer.

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	2023%	-1633	-	-1616	-	-
December 2020 (est.)	234	38%	-1188	-	-1191	-	-

● In the previous term (term ended December 2019) the company posted net sales of 169 million yen, a passive balance in the ordinary income of 1,633 million yen, and a passive balance in net income of 1,616 million yen. Net sales consisted primarily of the 1 million U.S. dollars of the development milestone income from CPN-101 appropriated in the second half of the previous term (along with income from Iodocoat Ointment currently on the market and medical patches supplied as samples). Development costs rose, due to overlap with the clinical trials required by the FDA for MRX-5LBT, widening the account deficit. Funds for expenses incurred in these clinical trials were secured through fundraising by means of a capital increase in May 2019.

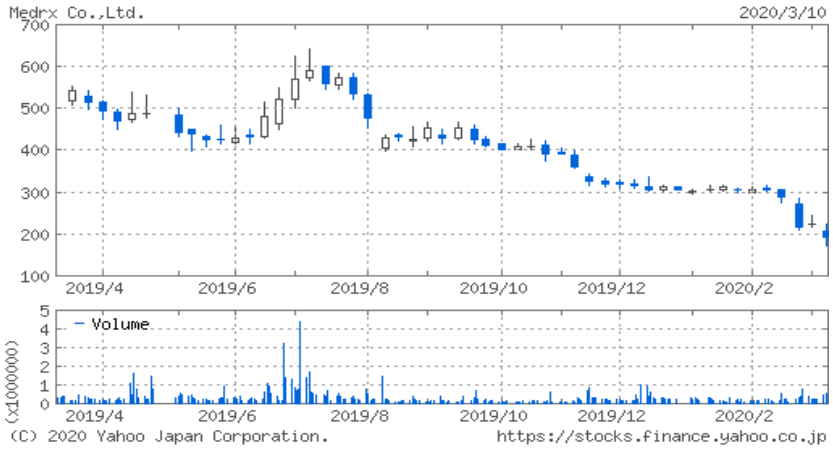
● The initial projection for the current term (term ending December 2020) made in the beginning of the term is net sales of 234 million yen, a positive balance in the ordinary income of 1,188 million yen, and a positive balance in net income of 1,191 million yen. As the estimate for net sales was calculated mainly based on the development milestone income from CPN-101 (with Iodocoat Ointment bringing in 14 million yen), which is to be distributed over several years, we can say with a high degree of certainty that the company will achieve the goal. The yen/dollar exchange rate has become volatile. When the yen is stronger than expected, sales decrease in yen terms. However, the research and development expenses accompanying the clinical trials in the U.S. are greater than sales. For this reason, a strong yen also has the advantage of making the account deficit in yen terms smaller. Furthermore, as of December 31, 2019, cash and deposit was 1,410 million yen, marking a decrease as compared with the previous year, but the company has the funds required to cover the net loss expected for this term.

Results of Operations

●The company's stock price was traded at its lowest level since listing, with market cap decreasing to 2,610 million yen on March 11. Operationally, one of the negative factors that triggered the plunge was the suspension of the development of MRX-1OXT which was a promising pipeline. MRX-1OXT was for an adhesive skin patch containing oxycodone, an opioid, and with it MEDRx intended to enter into the sustained-release opioids market in the U.S. boasting a market size of about 450 billion yen (as of 2016). This was the largest market targeted by the company so far. On the other hand, it is also widely known that opioid abuse is a severe social problem in the U.S. Unfavorable winds started to blow in September 2019, when Purdue Pharma, one of the most prominent companies in the U.S. opioid analgesics market filed for bankruptcy (due to the immense amount the company had to pay according to the settlement package of a lawsuit). This development greatly increased pharmaceutical companies' reluctance to develop new medicines, and prompted the U.S. FDA to take a more negative view of the field as well. Although it was a meaningful endeavor to develop an adhesive skin patch using the company's unique proprietary technology to confront a serious social problem, MEDRx decided to suspend development, given the prohibitive market environment. This is an unfortunate negative factor, but a factor, for which the company cannot be held responsible.

● Another unfortunate factor is the exceedingly poor environment surrounding the Mothers market, where the company is listed. Probably, as a negative factor, it is overwhelmingly more important than the suspension of the MRX-1OXT pipeline. In Japan, concerns regarding the expansion of the COVID-19 infections surfaced from the end of January, and by late February the mood spread to the Western markets as well. When an excessive risk avoidance mood triggers a substantial drop in stock prices, the Japanese Mothers stocks decline rapidly due to their high outstanding balance of margin trading, as each wave of selling triggers the next. At some net-based securities companies, the credit valuation profit/loss margin of Mothers stocks was −39% as of March 9, 2020. This dismal state of affairs is the worst in eight years, since March 2011. Although the company's shares fell 39% from the beginning of the year, TSE Mothers Index fell quite sharply as well by 29%. If we look at the shares of bioventures listed on the Mothers market, in the same period, Sosei fell 39%, SanBio 45%, and GNI 56%. Thus it would be unreasonable to interpret the fact that the company's shares hit a record low since the listing based on the reasons peculiar to the company itself.

● Although market cap fell to 2.6 billion yen, this figure is nowhere near the criterion for delisting (1,000 million yen). MEDRx's CPN-101 successfully passed P1b trials in the previous term. As the company decided at the outset to distribute its milestone income (of 6 million U.S. dollars) over several years, it is assured that, for several years at least, the company will not fall under the stock delisting criteria (an annual sales of 100 million yen or more) set for companies in and after the 6th year since listing. The company's scenario remains unchanged: MEDRx will stay listed until and beyond 2021, when it can appropriate sales of its MRX-5LBT lidocain tape patches, which have already passed all necessary clinical trials. The company will reward its shareholders at that time. For this year, an NDA for MRX-5LBT will surely be the main catalyst. MEDRx has numerous other potential catalysts as well. MRX-9FLT development is beginning in the U.S., and P1a trials for MRX-7MLL have begun as well. Although neither of the two can rival the market size of the discontinued MRX-1OXT, the probability of the company getting the drugs approved is quite high, while the costs required for development are small. If the company succeeds in demonstrating that these pipelines are making good progress, the rebound in its stock price should be its most striking ever, given the company's recent reduction in market cap. The outstanding balance of margin trading, which was 2,029,000 shares in the second week of January 2020, has also decreased by the first week of March to 1,431,000 shares. Trading volume on this stock is currently thin. (Okamura)



Stock Price (historical)	
Year high	¥710
Year low	¥172
Highest since the IPO	¥7,500
Lowest since the IPO	¥172

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