MEDRx (4586) TSE Mothers

Indomitable spirit lighting the torch of next pipelines

Yuya Okamura, Analyst

Company profile	
Location	Higashikagawa-shi, Kagawa
Representative	Masayoshi Matsumura
Established	January 2002
Capital	¥5,101 million
Listing	February 2013
URL	http://www.medrx.co.jp/index.html
Sector	Medicine

Stock price data (closing price on February 16)	
Stock price	¥526
Outstanding shares	8,514,700 shares
Trade unit	100shares
Market cap	¥4.47billion
PER (est.)	-
EPS (est.)	-
PBR (actual)	1.84x

■ A 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. MEDRx has completed phase I for 'MRX-4TZT', an adhesive skin patch containing tizanidine, a centrally acting muscle relaxant in February of this year, and the result was favorable as the trials showed that the product is just as effective as medicine for internal use currently sold at the market. With 'MRX-5LBT', an adhesive skin patch with lidocain, a local analgesic, the company has completed phase I in May of last year confirming the superiority of its 'ILTS' technology. The 'MRX-1OXT', an adhesive skin patch containing oxycodone, is scheduled to enter phase I already in 2017. The company is thus simultaneously getting along with a number of promising pipelines.

■Conducting clinical development of 'MRX-4TZT' and 'MRX-5LBT'

For the current term ending December, 2017, the company expects volume of sales of 26 million yen, a passive balance in the ordinary profit and loss of 1,404 million yen, and a passive balance of net earnings of 1,366 million yen. In addition to going ahead with the clinical development of 'MRX-4TZT'and 'MRX-5LBT', which showed good results in phase I, the company also plans to launch clinical trials (phase I) of 'MRX-1OXT'. As this will be a prior investment period for these pipelines, the company expects sales and general administrative expenses at 1,443 million yen (of which research and development expenses are 1,165 million yen).

■Putting hopes in 'MRX-4TZT', a product that does entail any serious problems with financing

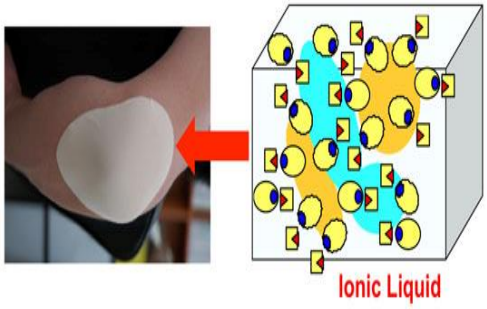
The company made efforts to procure necessary funds, and the efforts resulted in a cash equivalent of a little more than 2,600 million yen as of the end of December, 2016. Research and development expenses in the previous term, during which clinical trials have been done on a tight schedule, were 1,074 million yen. Even if the company conducts capital investment at the same pace, it will still have enough funds to last it for two terms. And although MEDRx had no choice but to give up on ETOREAT, 'MRX-5LBT' scored some good results in phase I last year, while 'MRX-4TZT' performed just as well in February of this year.

The company has an important advantage in the case of 'MRX-4TZT', because as it is possible to directly discern the efficacy of the medicine from blood concentration, the effectiveness can be confirmed at quite an early stage. Phase I has already been completed and presently the company is conducting negotiations for licensing agreements with a number of pharmaceutical companies both in Japan and overseas. For the time being, the good news we are to expect most of all are the news about 'MRX-4TZT'.

Point summary (1)

●What kind of company is MEDRx?

MEDRx is a venture company established in January, 2002 in Higashi-Kagawa-shi, Kagawa. Masayoshi Matsumura, the founder and the current President of the company, served as vice president at the Teikoku Seiyaku Co., Ltd. until 2000. Capitalizing on 'ILTS', MEDRx's proprietary technologies using ionic liquids, the company developed a number of adhesive skin patches and is currently trying to create the topical / transdermal tape product for the U.S., country boasting an enormous pain-relief market. Unlike other regular venture companies, MEDRx's aim is not to develop new drugs. MEDRx is a venture company, which is engaged in development of a new platform for active substances already used in a range of medicines for internal use or injection drugs, with the idea to use these substances in adhesive skin patches or ointments. For that reason, although the company is expecting same high returns as a venture developing new drugs, the risks are on a much smaller level, so the business model of MEDRx is quite special. In February, 2013, the company was listed in the Tokyo Stock Exchange Mothers, the first bioventure from Shikoku to achieve such a feat.



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

With the conventional percutaneous absorption technology, there are many drugs which do not easily penetrate through the skin. MEDRx is striving to utilize its technology using ionic liquid to pave the way for adhesive skin patches with drugs, which so far were not available for this kind of application. 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 also acquired medical patent for every pipeline.

●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.

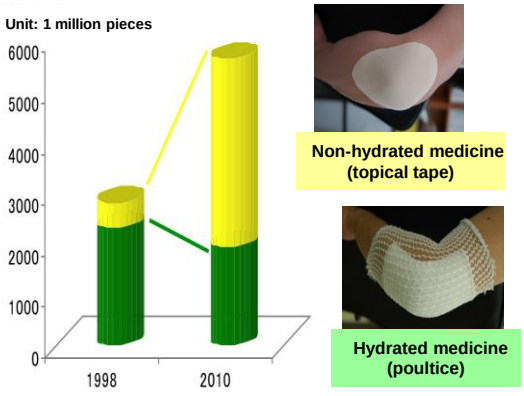
(1) The first is that the pharmacologically effective agent is released gradually. Because the medicine comes out slowly, it is easier to keep blood concentration constant and continuously maintain benefits of the drug.

(2) The second is that as the medicine does not have to pass through the liver unlike orally taken medicine, it does not remain there. Side effects are thus less likely to emerge.

(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.

Point summary (2)



●What are successful examples of adhesive skin patches?

Ethical pharmaceutical made by Hisamitsu Pharmaceutical called Mohrus Tape (efficacy: osteoarthritis, etc.) The annual sales of the entire range of the Mohrus Tape products are running at just over 60.0 billion yen making this a major, revenue-generative product. Formerly, the only kind of anti-inflammatory analgesic patches available was the hydrated type - plasters containing water (PAP products). As the cooling effect of the PAP products was caused by evaporation of moisture content, they gave the user a pleasant, cooling feeling when applied to the skin. Hisamitsu Pharmaceutical, on the other hand, succeeded in developing their Mohrus Tape – a topical tape that did not contain any water. Their products do not come off easily so they can also be used in sports just as they are. Also, they do not dry out like the hydrated type plasters, which need to be changed several times a day as the water evaporates, and thus save the user time and effort. Hydrated type patches have already lost in market share to the non-hydrated ones in the Japanese market (if we take a look at Hisamitsu alone, the annual sales of the entire range of the Mohrus PAP products are about 6 billion yen adding up to a mere 1/10 of the tape product group).

●What are the attractions of the U.S., the intended market?

The U.S. people are said to be a ‘population that is prone to pain’. The mainstay of the market of medicine for sharp pain in the U.S. is medicine for internal use, and the Americans use very strong analgesic drugs – morphine and other opioids. The drug that holds the top share in this opioids market is oxycodone, a centrally acting analgesic drug. And MRX-1OXT is the pipeline, with which the company is trying to create a transdermal therapeutic drug blending its ILTS technology with oxycodone. In the U.S., the adhesive skin patch market has been already expanding since 2008 with products for mild to moderate pain. The pioneer of this trend was ‘Lidoderm’ by Teikoku Seiyaku, for which the President of MEDRx, Matsumura had served as vice president. ‘Lidoderm’ was quite successful after its release in 2000 and ‘Flector’, which was released after that, was also quite successful. The two together scored sales in the 100 billion yen per year range (both are hydrated type). There is thus already a well-established track for selling adhesive skin patches in the U.S., and the market is starting to expand with new medicine also being developed for depression, ADHD, Parkinson, Alzheimer, and other diseases.

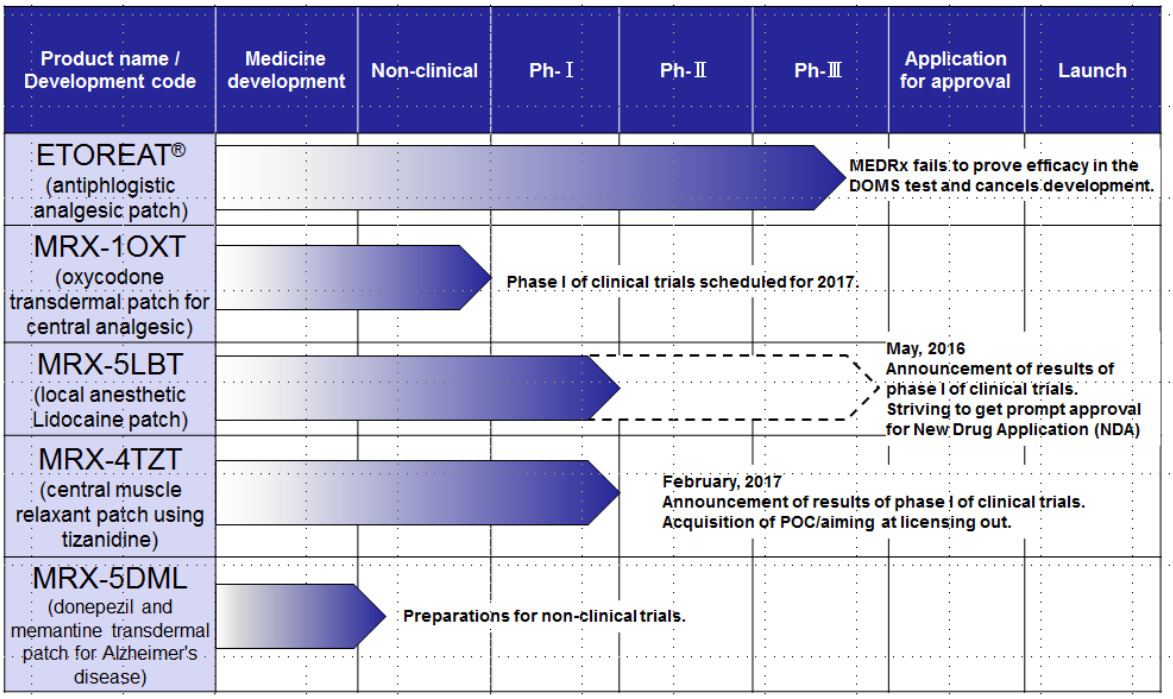
Development pipeline: present conditions and prospects (1)

① '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 market of neuromuscular junction blocking drugs in the case of the U.S. is very large with trial calculations putting it at approximately 120 billion yen. One drawback of tizanidine when used as medicine for internal use is that one needs to take it three times a day; another is its side effects, such as liver damage and sleepiness. 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. Clinical trial of phase I was started in the U.S. in October, 2016. **Phase I was completed in February, 2017 and the result was good proving that use of the product results in the blood concentration equivalent to that of medicine for internal use containing tizanidine currently sold at the market.** Almost no side effects such as sleepiness were found and the company intends to acquire Proof of Concept (POC; validation of developmental concept for new medicine) and strive to conclude licensing agreements at an early stage. The company stated that it is conducting negotiations for that purpose with a number of pharmaceutical companies both in Japan and overseas.

② 'MRX-5LBT'

An adhesive skin patch with lidocain, a local analgesic. The product is developed to be used for alleviating acute nerve pain associated with shingles. An investigational new drug application was submitted to U.S. FDA in February, 2016. Phase I was completed in May confirming the superiority of 'ILTS' technology. The fact that all went smoothly was made possible as there is a precedent, an adhesive skin patch 'Lidoderm', which scored a major hit in the U.S. (bringing in the peak period annual sales of 120 billion yen). Also, clinical trials of phase I implied some very good results. One is that the speed of percutaneous absorption of lidocain was faster than that of Lidoderm, and another is that with the area attached to the skin of only half (considerably smaller than that of Lidoderm), the amount of lidocain penetrating the skin per unit area of subcutaneous tissue is about 2.6 times more than that of Lidoderm. **MEDRx is making efforts to acquire new drug approval as early as possible and when there is any progress on this front, the company intends to make an announcement to the investors promptly.**



Development pipeline: present conditions and prospects (2)

③ 'MRX-1OXT'
An adhesive skin patch containing oxycodone, one of strong analgesics (opioids). This is a pipeline, with which MEDRx is currently trying to use its technologies that use ionic liquid to create a topical tape-type medicine containing oxycodone, which does not easily penetrate skin. With the pain-relief market in the U.S. alone worth some ￥1 trillion and opioids holding a share of about half of the total, it is reasonable to believe that oxycodone holds about 40% of the opioid share (**oxycodone accounts for around 200 billion yen of the market**). Non-clinical trials have been launched from November, 2015, and in December, MEDRx outsourced the task of manufacturing the investigational new drug to Tapemark, a manufacturer in Minnesota, U.S. (Since oxycodone is classified as a "narcotic for medical use", manufacturing it in Japan and then exporting it is not allowed.) Tapemark has an ample track record in development and manufacture of percutaneous absorption patches spanning over 60 years. The company made an announcement that the clinical trials (phase I) are going to be launched in 2017. Although there are many serious obstacles to overcome including regulations, the potential of oxycodone with its enormous market size looks very attractive indeed.

④ 'MRX-5DML'
An adhesive skin patch with two therapeutic agents for Alzheimer. A medicine with the two ingredients for internal use is already on the market. If it can be made in the form of an adhesive skin patch, it is possible to deal with risks of patients forgetting to take the medicine or forgetting they took it and taking it again exceeding the dosage. MEDRx is zealously preparing to launch phase I start.

⑤ 'ETOREAT' → decision to cancel further development was made in November, 2016
'ETOREAT' (an anti-inflammatory analgesic patch) has been regarded as the company's most important pipeline. Although in phase II and phase III, placebo (drugs not containing any active/effective elements) comparison tests have established a statistically significant differential in efficacy in comparison to the placebos, the drug ran into difficulties in the second stage of the clinical trials commenced in December 2013. FDA (Food ad Drug Administration), the U.S. regulatory agency, demanded an additional clinical trial because depending on methods of the analysis, a statistically significant differential was, in fact, established. FDA gave the company a new test model comprised of tests for DOMS (delayed onset muscle soreness), and the trials were commenced in March, 2016. However, the result that was announced in August of the same year stated that no statistically significant differential in comparison to the placebos was found. The company still kept the spirits high and tried five tests in phase III but, in the end, had no choice but to give up. Based on the substance of discussion with the FDA, a meeting of the Board of Directors held on the 22nd of November of the same year opted for cancellation of further development.

Results of Operations

Performance（million yen, %）

Fiscal year end	Net sales	YoY	Ordinary income	YoY	Net income	YoY	EPS(¥)
December 2012	87	-88%	-578	-	-571	-	-
December 2013	68	-21%	-616	-	-621	-	-
December 2014	26	-61%	-1,012	-	-1,016	-	-
December 2015	37	43%	-990	-	-878	-	-
December 2016	22	-40%	-1,301	-	-1,259	-	-
December 2017 (est.)	26	20%	-1,404	-	-1,366	-	-

● In the previous term ended December, 2016, MEDRx posted net sales of 22 million yen (a 40.6% decrease compared with the previous term), ordinary loss of 1,301 million yen (an increase of deficit), and a passive balance of net earnings of 1,259 million yen. Based on the results of the DOMS test for 'ETOREAT', MEDRx made a decision to cancel further development of the product. Partly due to the fact that the development costs for the latter half of the year decreased, the deficit was less than the initial estimations. The pipelines other than ETOREAT that MEDRx has been working on at the same time are making satisfactory progress, and research and development expenses at 1,074 million yen increased as compared with the previous term (716 million yen). The increase in the expenses needed for clinical and non-clinical trials are a sure proof that the company is making progress with other pipelines.

● For this term (term ending December, 2017), MEDRx expects net sales of 26 million yen (a 20.7% increase compared with the previous term), ordinary loss of 1,404 million yen (an increase of deficit), and a passive balance of net earnings of 1,366 million yen (an increase of deficit). In addition to getting along with the clinical trials for 'MRX-4TZT' and 'MRX-5LBT', which showed good results in phase I, MEDRx plans to also launch the phase I trials for 'MRX-1OXT' during this term. As this will be a prior investment period for these pipelines, the company expects sales and general administrative expenses at 1,443 million yen (of which research and development expenses of 1,165 million yen). Sales in this term are only expected from the 'Iodine Coating Ointment' that the company currently sells.

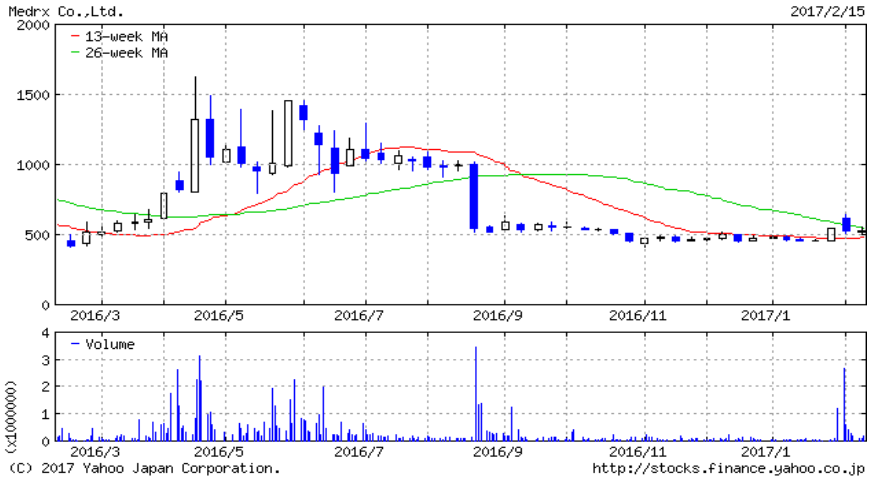
Investment appraisal

● MEDRx was very close to getting its hands on a piece of the American Dream, but with abandonment of development of ETOREAT, the company will have to wait for that much longer. But this does not at all mean that the company is back where it started. Even when the ETOREAT project was going smoothly, the company was strongly working to ensure that it has a number of strong cards to play. The strategy proved to be successful, as the company achieved good results in phase I trials – last year with 'MRX-5LBT' and in February of this year with 'MRX-4TZT', both very good news confirming that the company is making good progress thanks to the effectiveness of its portfolio. MEDRx has an important advantage in the case of 'MRX-4TZT', because it is possible to directly discern the efficacy of the medicine from blood concentration. Unlike ETOREAT, a painkiller, whose effect is hard to express numerically, the efficacy of this product can be confirmed at quite an early stage. Phase I has already been completed and presently the company is in the process of negotiations for licensing agreements with a number of pharmaceutical companies both in Japan and overseas. And the moment MEDRx concludes a licensing agreement with one company, other pharmaceutical companies are certainly going to see MEDRx in different light. For the time being, **we can safely say that the second MEDRx announces a licensing agreement for 'MRX-4TZT', the demand for the company's shares will skyrocket.**

● The company expected that submission of an application for approval of ETOREAT would result in a milestone income of over a billion yen from a partner posted. As for this term, MEDRx is operating on the assumption that no milestone income or up-front payments are going to be received, the company's forecast is a net loss of 1,366 million yen – just as it was in the previous term. From the point of view of investors, the funding shall be the largest reason for steering clear of the company, but MEDRx has amassed a cash equivalent of 2,639 million yen as of the end of December, 2016. The company conducted fund procurement through issue of new shares, as a result of which it increased the cash equivalent by 2,060 million yen as compared with the end of December, 2015. During the previous term, MEDRx was working on a tight schedule with clinical trials for three pipelines, which is why annual research and development expenses were quite high at 1,074 million yen. **But even if the company continues at this maximum pace, it will have enough funds for the present term and the next one. Now what feels to be the greatest yield though is that the fighting spirit of the company's managing team has not diminished one bit.**

● The shock of ETOREAT was strongly reflected in the share price. As soon as the failure in the DOMS test was reported on August 22 of last year, the share price plummeted. If we look at the stock price average during 120 business days before and after this turning point of August 22, this is absolutely clear. The average closing price for 120 business days before August 22, when everyone was full of expectations regarding the results of the additional test for ETOREAT, was 948 yen. But if we look at the average closing price for the period from August 22 to February 16, 2017, a date not so long ago, the stocks were traded for the average of 508 yen, which is a drop of no less than 46%. This number together with the 7.5% drop in the Tokyo Stock Exchange Mothers Index in the same period clearly shows that ETOREAT failure was the primary cause behind it. And it is highly probable that **after the loss of ETOREAT, in the struggle in the lower price range the market eventually came to the conclusion that the appropriate stock price is about 500 yen. The 13-week MA is at 482 yen, and the 26-week MA is at 505 yen, so probably the cleverest stance is to wait for a drop, purchase the stocks and wait for some favorable news regarding 'MRX-4TZT'.**

(Okamura)



Stock Price (historical)	
Year high	¥1,629
Year low	¥341
Highest since the IPO	¥7,500
Lowest since the IPO	¥341

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