MEDRx（4586） TSE Mothers

Cipla, a leading pharmaceuticals company, is the ultimate partner

Yuya Okamura, Analyst

Company profile	
Location	Higashikagawa-shi, Kagawa
Representative	Yonehiro 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 September 12)	
Stock price	¥695
Outstanding shares	8,514,700 shares
Trade unit	100shares
Market cap	¥5.91billion
PER (est.)	-
EPS (est.)	-
PBR (actual)	3.02x

■ 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. In April, a global development and sales licensing contract was executed with Cipla, a major global pharmaceuticals manufacturer. Phase I of the adhesive skin patch with lidocaine, 'MRX-5LBT', ended in May last year, and the current goal is early NDA acquisition. The adhesive skin patch with oxycodone, 'MRX-1OXT', is scheduled to start phase I in 2017. Multiple pipelines are progressing simultaneously.

■160 million yen received as a lump sum payment for the licensing contract

For the current term ending December, 2017, predicted sales are 186 million yen (8.37x the previous period), yielding a passive balance in the ordinary profit and loss of 1,244 million yen (a reduced passive balance), and a passive balance in net earnings of 1,206 million yen (a reduced passive balance). As part of the licensing contract executed with Cipla USA for MRX-4TZT, a lump sum payment of 160 million yen is expected. Initial forecasts for sales were raised by 160 million yen in April to reflect this.

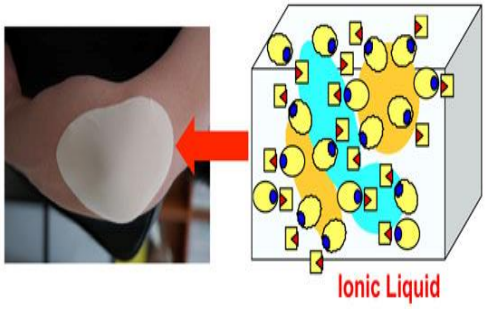
■Good prospects for large-scale 'MRX-4TZT' cooperation

MRX-4TZT started phase I in October last year. In just 6 months, a major deal was signed. This was a licensing contract with Cipla, a major pharmaceuticals manfuacturer based in India. With Cipla providing backing, MRX-4TZT has taken a big step forward toward a New Drug Application (NDA). Added phase I clinical trials have started, and transition to phase III is planned for the next step. Progress in research and development is especially good, and there are no financial concerns whatsoever at present. Moving forward, waiting for progress reports, including for all the multiple pipelines proceeding simultaneously, is the only thing to do. The start of phase I for 'MRX-1OXT' is anticipated within the year, and this will probably have a positive impact on stock prices.

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 Chairman 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 market. Unlike other regular venture companies, MEDRx's aim is not to develop new drugs. MEDRx is a 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) Because unlike orally taken medicines, these drugs do not pass through the liver, this organ does not bear the burden of breaking them down.
(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 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 Chairman 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.

●Reasons the company differs from a normal pharmaceuticals venture

Many pharmaceuticals venture companies develop drugs such as cancer medication, and the process from research to sales is typically a 10-year cycle. The long process starts with non-clinical trials, then clinical trials in 3 phases, then finally reaches applying for approvals and launch of sales. As the development stage progresses, the scope of trials increases, and the cost of running them increases alongside this.

According to some calculations, the percentage of drugs that have completed phase I clinical trials and eventually enter the market is only about 9%, and the percentage that have completed phase II that do is only about 15%. Although there is a large return on investment for drugs that overcome these odds, there is also a major risk that drugs will never enter the market.

The company seems to have been considered identical to these types of pharmaceuticals ventures up until now. However, that is a mistake. The reason is that even if the clinical trials process is the same, in this case, the company is not carrying out detection and creation of new active ingredients.

The company is attempting to convert the existing compounds of tizanidine and lidocaine to an adhesive patch delivery format, and this project model reduces the risks on returns.

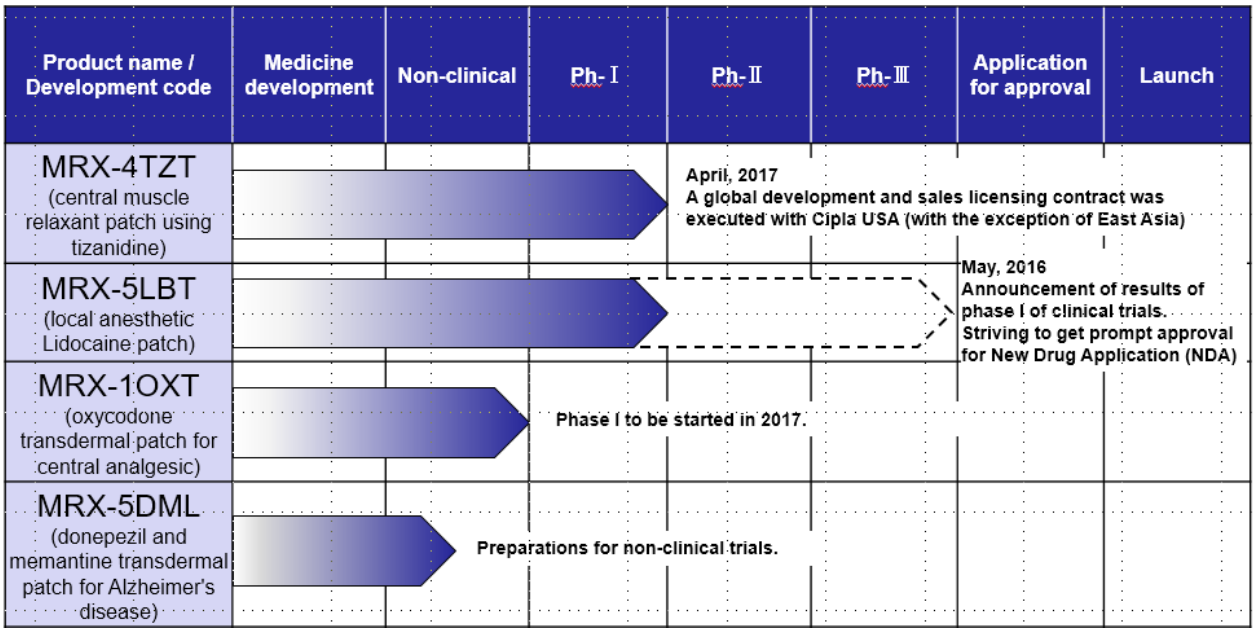
Development pipeline: present conditions and prospects (1)

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. 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 provided for milestones in development and sales progress and graduated royalty income for sales after products enter the market.** The added phase I of clinical trials was announced on September 1st, and the plan for the next step is shifting phase III.

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 110 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. **The goal is to acquire NDA quickly, and as soon as there are any developments on this front, they will be reported to the company's investors.**



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 transdermal 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**). The high growth potential of oxycodone is supported by the massive market for it. 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. **Clinical trials (phase I) are scheduled to start before the end of 2017.**

<NEW> *Proprietary technology developed to counteract important social problems: 'AMRTS (Abuse and Misuse Resistant Transdermal System)'

Opioids such as morphine and oxycodone are highly addictive drugs likely to cause dependency. In spite of this fact, they are easy to acquire in the United States as long as you have a doctor's prescription. This system is problematic, and has caused the number of opioid addicts in the United States to reach over 2 million as of 2014, with reports of over 1,000 overdoses in need of emergency treatment per day. Not only abuse, but also accidental use is a social problem current affecting the United States. There have been cases of infants accidentally applying opioid patches after the patients they were prescribed for and dying from it. Due to these kinds of background factors, the FDA is showing increased caution with measures such as refusing to approve new drugs without a means for preventing accidental use in place.

In order to handle this change in the FDA's policy, the company has been developing technology for preventing incidents caused by the abuse and misuse of opioid patches since last year. The result of these efforts is a proprietary new medicine technology called 'AMRTS' (patent pending). AMRTS provides several high-level functions.
The four functions are as follows
(1) **Low extraction** (because the medicine is extracted slowly, it makes abuse difficult).
(2) **Intense bitterness** (even if a child accidentally puts a patch in their mouth, this bitterness ensures they won't swallow it).
(3) **Re-absorption prevention** (once the patches have been peeled off, almost none of the drug can be absorbed).
(4) **Re-application prevention** (once the patches have been peeled off, they are no longer very sticky and fall off easily).
A pre-IND meeting (a meeting held prior to the start of clinical trials) was held in April to present this new technology to the FDA. The AMRTS technology was understood, and the agency also provided helpful advice related to development objectives and steps.

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.)	186	737%	-1,244	-	-1,206	-	-

- For the interim period ending December 2017, net sales were 18 million yen (up 80% from the previous term), with a passive balance in the ordinary profit and loss of 519 million yen (decreased passive balance), and a passive balance of net earnings of 477 million yen (decreased passive balance). All net sales are of Iodine Coating Ointment and similar products. Compared to the previous term, clinical trial implementation costs were decreased (previous term this cost was 600 million yen, while this interim period was only 381 million yen), resulting in decreased passive balances.

- For this term (term ending December 2017), anticipated net sales are 186 million yen (8.37x the previous term), with a passive balance in the ordinary profit and loss of 1,244 million yen (decreased passive balance), and a passive balance of net earnings of 1,206 million yen (decreased passive balance). In April, initial sales predictions were raised by 160 million yen. This is due to the anticipated 160 million yen lump sum payment for the licensing contract executed with Cipla USA related to MRX-4TZT.

  Both MRX-4TZT and MRX-5LBT are currently in clinical development, and MRX-1OXT is also scheduled to start phase I of clinical trials in this term. As this will be a prior investment period for these pipelines, sales and general administrative expenses are anticipated by the company to be 1,443 million yen (with 1,165 million yen of this for research and development expenses) as initially planned.

  In addition, the development of ETOREAT was terminated in the previous term. The joint manufacturing contract with Kaneka was dissolved, and affiliated company stock was sold to Kaneka. Special profits of 64 million yen were acquired due to causes such as profit on sales.

Investment appraisal (1)

- When the February report was released, it included the following statement. "At present, the announcement of a licensing contract for MRX-4TZT would have the strongest possible impact for stock purchasing.” Less than 2 months afterward, the big news was announced. On April 6th, the company announced the signing of a licensing contract for MRX-4TZT with Cipla, a pharmaceuticals company in India. At the end of April 6th, the stock price was 544 yen, and after explosive growth including 3 days where the prices were stopped due to exceeding the maximum allowable single-day gain, shares reached their highest levels since the start of the year, closing at 1,255 yen, a growth of 2.3x in just 8 business days.

  The speed of this announcement took many investors by surprise, and the favorable conditions of the big deal were also a factor. The immediate response on the market is a clear indication that this surprise was a positive one. MRX-4TZT started phase I of clinical trials in October last year. This means that just 6 months afterward, a licensing contract was signed for the drug, and of course the other party in this contract also contributed to the rapid increases in stock prices.

  Cipla is an established pharmaceuticals company in India, and has developed into a global company manufacturing over 1,000 products for a variety of treatment fields. The total value of its public stock is approximately 450,000 million Indian rupees (in Japanese yen, approximately 760,000 million yen). Cipla provides anti-retrovirus combination drugs to HIV-positive patients in Africa for the incredibly low price of less than 1 dollar per day, and is known as a company that has saved the lives of large numbers of patients.

  When the company was looking for a pharmaceuticals company to partner with for licensing, Cipla contacted the company first, an incredible development.
  Cipla was in a transitional period in its business strategy, and was planning to shift from focusing its activities in India and Europe to a stronger emphasis on the United States market. In addition, Cipla was advocating for specialty pharma using its international competitiveness as a strength. These conditions fit perfectly with the superior technology of MEDRx and the company's desire to enter the American market.

  With the support of Cipla, MRX-4TZT took a huge step forward toward the completion of a new drug application (NDA).

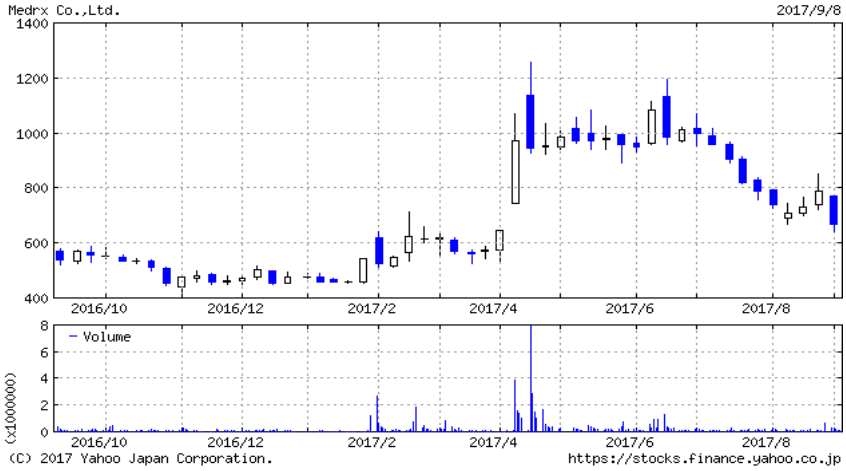
Investment appraisal (2)

- Although the prospective milestone income of more than 1,000 million yen from the ETOREAT linked company were a major loss, this big deal could provide even greater earnings of up to 3,000 million US dollars. MRX-4TZT has started phase I of additional clinical trials, and there are plans to shift to phase III as the process continues. The progress in research and development is especially good news, and there is no cause for concern on the financial side at this time (although the difficult pace of 3 clinical trials in one year will result in a matter of 1,100 million yen in research and development costs, 2,179 million yen in funds remain as of June 2017). Moving forward, waiting for progress reports, including for all the multiple pipelines proceeding simultaneously, is the only thing to do. Although the timing of the start of phase I clinical trial for MRX-1OXT may seem a bit fast, a positive impact on stock prices is anticipated.

- The rising and falling of the company's stock price (and this is common to most all Mothers Index companies) is mainly due to the structural liquidity of short-term individual investors. The balance of the Mothers Index as a whole affects all constituent companies, and this is unavoidable. As a result, the tone of the Mothers Index worsens, and purchasing stock in the company when value is decreased due to these factors is a lucrative method of entry.

  In terms of the supply and demand unique to the company, the surge in valuation following the announcement of cooperation with Cipla is one example. The sales volume for the individual price range of 1,050 to 1,100 yen from the start of the year yields the production volume (approximately 13,400,000 shares). Considering that the moving average yield for the 25th is just under 130,000 shares, it is undeniable that the pressure to return to a share pricing level above 1,050 yen is quite strong. The prospects for the near future predict stock shares at pricing levels at an upper limit between 830 yen and 860 yen blending at the 13-week and 26-week marks.
  Since the company has linked with Cipla, the perspective of the market has definitely changed, and the development of opioid adhesive medications for the American market is being anticipated as a possible game changer, due to the company's proprietary AMRTS technology, born in the midst of adversity. These and other factors this year are definitely worthy of special mention.

(Okamura)



Stock Price (historical)	
Year high	¥1,255
Year low	¥453
Highest since the IPO	¥7,500
Lowest since the IPO	¥341

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