# MEDRx ( 4586 )

TSE Mothers

## Proprietary technology serving as a hub for development of adhesive skin patches

Yuya Okamura, Analyst

| Company profile | |
|---|---|
| Location | Higashikagawa-shi, Kagawa |
| Representative | Yonehiro Matsumura |
| Established | January 2002 |
| Capital | ¥5,992 million |
| Listing | February 2013 |
| URL | http://www.medrx.co.jp/index.html |
| Sector | Medicine |

| Stock price data (closing price on August 30) | |
|---|---|
| Stock price | 1,012 |
| Outstanding shares | 10,205,100shares |
| Trade unit | 100shares |
| Market cap | ¥10.3billion |
| PER (est.) | - |
| EPS (est.) | - |
| PBR (actual) | 3.74x |

### ■ 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. In April 2017, a global development and sales licensing contract was executed with Cipla, a major pharmaceuticals company in India, for 'MRX-4TZT,' an adhesive skin patch which contains tizanidine, a centrally acting muscle relaxant. In phase I of clinical trials for the 'MRX-10XT' adhesive skin patch, which contains oxycodone, this product also achieved favorable results in February of this year. There was a high probability of achieving the appropriate blood concentration of the drug and no side effects worthy of special mention were observed. There are a number of promising pipelines, and each of them is progressing smoothly.

### ■ MEDRx grants license for its proprietary technologies to Takeda Pharmaceutical Company

MEDRx announced conclusion of a technology license agreement for 'ILTS' and 'NCTS' with Takeda Pharmaceutical Company (Takeda). Takeda will use the technology for pipeline compounds in a focused therapeutic area it is currently developing to enable transdermal drug delivery. According to the agreement, MEDRx will be eligible to receive milestone income based on the progress of the development at Takeda, as well as royalties based on the sales of the products after they are released. This is an important step for the company, as its original technologies, which so far have been used in the company's own proprietary pipelines, will now be supporting clinical development of drugs at a major pharmaceutical company, thus their range of application is expanding. This development will substantially contribute to the status of MEDRx as it clearly shows how advanced its technologies are, and the fact that its partners are such big names in the pharmaceutical world as Daiichi Sankyo and Takeda is also highly significant.

### ■ Earning high marks from the market by platform provision

On a medium-to-long term, licensing of technologies to Takeda is likely to change the way MEDRx is perceived. Provision of basic technologies to other entities allows MEDRx to have pharmaceutical companies bear some part of the substantial costs to be incurred in clinical trials, at the same time allowing the company to post some profit at the start of a new phase. The same business model of making profits through platform provision is used by PeptiDream and the Sosei Group. Both of the companies have received high recognition from investors in Japan and in other countries. The successive alliances with big names in the business are already establishing MEDRx as a reputable company, creating a virtuous circle that may well lead to the next big deal. I am sure that the company will not disappoint our expectations and will follow this announcement with more good news such as licensing agreement with a pharmaceutical company other than Takeda, as well as new developments in its own pipelines.

# 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 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. In February, 2013, the company was listed in the Tokyo Stock Exchange Mothers.

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

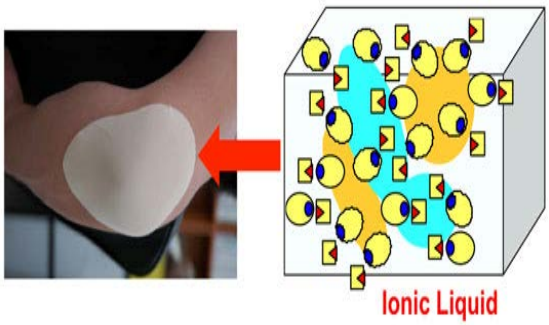
The U.S. people are said to be a 'population that is prone to pain'. The mainstay of the market of medicine for sharp pain in the U.S. is medicine for internal use, and the Americans use very strong analgesic drugs – morphine and other opioids.

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).

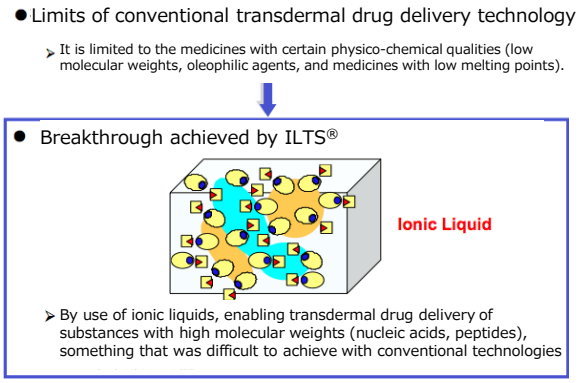
There is thus already a well-established track for selling adhesive skin patches in the U.S., and the market is starting to expand with new medicine also being developed for depression, ADHD, Parkinson, Alzheimer, and other diseases.

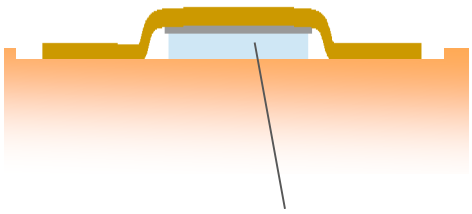
# Point summary (2)




**● 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 acquired medical patents for every pipeline, protecting high barriers to entry.



Layer impregnated with nano-sized colloid solution

**● MEDRx grants license for its proprietary technologies to Takeda Pharmaceutical Company**

In February of this year, MEDRx concluded an agreement with Daiichi Sankyo for joint development of a product using 'NCTS', its transdermal drug delivery technology. Following the example set by Daiichi Sankyo, Takeda Pharmaceutical Company (hereinafter: Takeda), one of the top-level pharmaceutical manufacturers in Japan, also requested license to use the transdermal delivery technology of MEDRx.

On August 24, MEDRx announced that the company concluded a technology licensing agreement for 'ILTS' and 'NCTS' with Takeda. According to the announcement, Takeda will use the technology of MEDRx for pipeline compounds in a focused therapeutic area it is currently developing to enable transdermal drug delivery.

According to the agreement, MEDRx, which supplied the license for the technology, will be eligible to receive from Takeda milestone income based on the progress of the development and commercialization of the product(s). Moreover, the agreement also stipulates royalties to be received based on the sales of the applicable product(s) when they are launched.

This technologies, which so far have been used in the company's own proprietary pipelines, will now be supporting clinical development of drugs at a major pharmaceutical company, thus their range of application is expanding. The fact that its partners are such big names in the pharmaceutical world as Daiichi Sankyo and Takeda is also highly significant. And the reason for it is an important step for the company, as its original is that this development will substantially contribute to the status of MEDRx showing that the technology of this company originating from Shikoku is of a world-class level.

# Development pipeline: present conditions and prospects (1)

**① 'MRX-4TZT' (CPN-101)**

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 development code is the one requested by Cipla, 'CPN-101.' From Cipla's perspective, their desire to market it as an authentic new medicine is evident from the development code. The added phase I clinical trials started last September, and in January of this year, favorable results meeting the standards determined in cooperation with Cipla were achieved. Cipla is planning to transition to phase III as the next step after the added trials are completed. This is currently at the stage where Cipla is waiting for the applicable authorities, the FDA, to make their decision.

| Product name / Development code | Medicine development | Non-clinical | Ph- I | Ph-II | Ph-III | Application for approval | Launch |
|---|---|---|---|---|---|---|---|
| CPN-101(MRX-4TZT) (central muscle relaxant patch using tizanidine) | | | | April, 2017 A global development and sales licensing contract was executed with Cipla USA (with the exception of East Asia) January 2018: Added phase I a' clinical trial results released | | | |
| MRX-1OXT (oxycodone transdermal patch for central analgesic) | | | | February 2018: Phase I clinical trial results released | | | |
| MRX-5LBT (local anesthetic Lidocaine patch) | | | | | | June 2018: Confirmed biological equivalence through confirmatory comparative clinical trials 2020: Expected submission of NDA application | |
| MRX-7MLL (memantine transdermal patch for Alzheimer's disease) | | | Preparations for non-clinical trials. Prospective IND in 2019 | | | | |
| Joint development with Daiichi Sankyo (NCTS®) | (Name of medicine, indication, etc. are not disclosed) | | | | | | |
| Technology licensing agreement with Takeda (ILTS®, NCTS®) | (Name of medicine, indication, etc. are not disclosed) | | | | | | |

# Development pipeline: present conditions and prospects (2)

**② '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. There are some calculations which estimate the total scope of the opioid analgesic market in the United States at 447 billion yen. Oxycodone is a massive market which comprises approximately 40% of this, and it is the pipeline the company most focused on.

In the U.S., opioid abuse is an important social problem, and last year in October, US President Donald Trump has even declared opioid crisis a national Public Health Emergency. To combat this frequent abuse and misuse, MEDRx developed its proprietary new medicine technology called 'AMRTS' (patent pending). The technology offers a number of superior functions, including low extraction and prevention of re-application. Furthermore, regarding the clinical trials started at the beginning of last year (phase I), in February of this year, the results were favorable and indicated both that 'there is a high probability of achieving sufficient blood concentration of the drug' and that there were no side effects worthy of special mention observed. Presently, as the company moves forward with development, they will be simultaneously searching for partners to collaborate with. The company is checking various possibilities in search of ideal partners to collaborate with.

**③ '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.

In June of this year, MEDRx announced the results of confirmatory comparative clinical trials conducted to verify the efficacy of 'MRX-5LBT' as compared with 'Lidoderm', which scored a major hit in the U.S., the country the company wishes to sell the drug in (bringing in the peak period annual sales of 110 billion yen). The trials showed biological equivalence of 'MRX-5LBT' with 'Lidoderm', which was used as benchmark. Having thus achieved good results, the company's next step will be to advance with clinical trials on healthy subjects, and the prospects look now very bright for the possibility of submission of an application for a new drug in 2020. Although the market for this pipeline is not enormous, it is still very attractive from the point of view of time required before the drug is approved and the reliability of the prospect.

**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 (in 2017, the U.S. market of Alzheimer-related medicine was approximately 150 billion yen, and memantine oral agents accounted for approximately half of the total at 75 billion yen). To move more in line with this market environment, MEDRx also changed its policy. As the development of memantine single-agent patches was completed in July of this year, 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.

# Results of Operations

## Performance（million yen, %）

| Fiscal year end | Net sales | YoY | Ordinary income | YoY | Net income | YoY | EPS(¥) |
|---|---|---|---|---|---|---|---|
| December 2013 | 68 | -21% | -616 | - | -621 | - | - |
| December 2014 | 26 | -61% | -1,012 | - | -1,016 | - | - |
| December 2015 | 37 | 43% | -990 | - | -878 | - | - |
| December 2016 | 22 | -40% | -1301 | - | -1259 | - | - |
| December 2017 | 198 | 787% | -988 | - | -884 | - | - |
| December 2018 (est.) | 698 | 252% | -734 | - | -719 | - | - |

● For this interim fiscal period (January to June 2018) the company posted net sales of 8 million yen, a passive balance in the ordinary profit and loss of 588 million yen, and a passive balance in net earnings of 572 million yen. Although MEDRx estimated nest sales for the period at zero, the delivery time of the Iodine Coating Ointment, a product already launched in the market, went ahead of schedule, which is why the company managed to post some sales. And although the estimate for ordinary profit and loss was a passive balance of approximately 800 million yen, clinical trials for the pipelines currently in development ended up behind the initial schedule. As the expenses required for implementation of the clinical trials proved to be lower that expected, the current account deficit ended up being lower than the estimate.

The earnings forecast for the full fiscal year has been revised to reflect this factor. After the revision, the earnings forecast for the current term ending December 2018 is net sales of 698 million yen (an increase of 252% over the previous period), with a passive balance in the ordinary profit and loss of 734 million yen (as against the previous estimate of a passive balance of 1,115 million yen), and a passive balance in net earnings of 719 million yen (as against the previous estimate of a passive balance of 1,100 million yen). The net sales of 690 million yen, which are expected to be posted during the latter half of the fiscal year, are mainly comprised of the milestone income for MRX-4TZT to be received from Cipla. Other pipelines (MRX-1OXT, etc.) remain uncertain, so contract lump sum payments, etc. for them are not included in the predictions.

The prerequisite research and development expenses for the same reason are lowered from the initial 1,562 million yen to 1,136 million yen. Nevertheless, compared with the previous term (888 million yen), the expenses are still quite high, which is a sure sign of a smooth progress made with the pipelines. Furthermore, because clinical trials implementation expenses were lower than the predictions and since the company managed to procure funds through a private placement, as of the end of June 2018, cash on hand and in banks increased to 2,529 million yen (increase by 791 million yen compared with the corresponding period of last year). For the time being, the company shall have no problems with financing either.

## Investment appraisal

●The most recent news is that MEDRx granted license for its proprietary technologies to Takeda, and that is great news no matter how you look at it. The company's stock price quickly rose right after the announcement made in the early morning of August 27, and that is only to be expected. As compared to the closing price of 765 yen recorded on August 24, the highest price by now was reached on August 29 at 1,167 yen (thus making the largest increase at 52%). Nevertheless, it is much lower than what the closing price after the announcement of the previous report was made on February 14 (1,441 yen). But the question remains - in this news of a kind that can be discounted with a mere initial reaction of the stock prices?

●'ILTS' and 'NCTS', superior proprietary technologies MEDRx was carefully protecting with high entry barriers. It seems that the significance of the fact that the company decided not to monopolize on them and supplied them to other pharmaceutical companies as a platform cannot be overstressed. And the reason for it is that the moment they made the decision was a moment they shifted to an entirely new business model.

●So far, when determining the merits of the company, we were only focusing on the progress they were making with clinical trials for their proprietary development pipelines. And in that sense, the same is true for the most listed bioventures. But with this time's provision of their fundamental technologies, MEDRx now finds itself in a new position - that of a supporting party for clinical trials of their partners to the agreement. And to add to that, MEDRx is entitled to some milestone income and royalty depending on how the clinical trials of the pharmaceutical companies it entered into an agreement with progress.

The merit of this business model is that some portion of the large costs required to complete the clinical trials are to be covered by other pharmaceutical companies, and another is that MEDRx can get profits at the start of a new phase. There is a limit to the number of pipelines one bioventure can pursue on its own. And although the very fact that such companies have to depend on the success of a limited number of pipelines is the reason they are in the high-risk category, if they provide a platform, they can participate in development of various new medicines involving several pharmaceutical companies. And if the suppliers of platforms can rip the fruits of those processes, they can substantially reduce business risks.

●The business model of earning profits through such platform provision is highly regarded by the stock market. Two companies are representative examples of this point. One is PeptiDream, a company growing through provision of license for its proprietary drug development platform 'PDPS' (First Section of the Tokyo Stock Exchange; aggregate market value as of August 30: 532.3 billion yen). And another is the Sosei Group, which received an enormous sum as milestone income by provision of its 'StaR' platform (Mothers of the Tokyo Stock Exchange; aggregate market value as of the same date: 126.4 billion yen).

The successive alliances with big names in the business are already establishing MEDRx as a reputable company, creating a virtuous circle that may well lead to the next big deal. There is also a fledgling possibility that the change of business model will change the way the company is perceived by investors. Many market participants (particularly institutional investors) will notice the change that happened to the company and start saying that 'the current aggregate market value of a mere 10 billion yen might be an underestimation of the company's value' the second MEDRx actually receives a milestone income from a company it entered into an agreement with. I am sure that the company will not disappoint our expectations and will follow this announcement with more good news such as licensing agreement with a pharmaceutical company other than Takeda, as well as new developments in its own pipelines. (Okamura)


| Stock Price (historical) | |
|---|---|
| Year high | ¥2,139 |
| Year low | ¥678 |
| Highest since the IPO | ¥7,500 |
| Lowest since the IPO | ¥341 |

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