MEDRx（4586） TSE Mothers

A year to reap the fruits of a well-balanced business portfolio MEDRx has established so far

Yuya Okamura, Analyst

Company profile	
Location	Higashikagawa-shi, Kagawa
Representative	Yonehiro Matsumura
Established	January 2002
Capital	¥5,997 million
Listing	February 2013
URL	http://www.medrx.co.jp/index.html
Sector	Medicine

Stock price data (closing price on March 8)	
Stock price	499
Outstanding shares	10,394,100shares
Trade unit	100shares
Market cap	¥5.1billion
PER (est.)	-
EPS (est.)	-
PBR (actual)	2.49x

■ 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. 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 2018. 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 several promising pipelines originating in MEDRx.

■"Cooperative pipelines" MEDRx managed to establish capitalizing on its widely recognized high technical capabilities

In August 2018, MEDRx concluded a technology license agreement for 'ILTS' and 'NCTS' with 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 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.

■Outstanding balance of margin trading has diminished by half, and if MEDRx is to come up with some positive news, the impact on the stock price will be substantial

The initial forecast made in the beginning of the term projected net sales of one billion yen. The major premise for this forecast is a milestone income MEDRx expects to receive from CPN-101, one that initially was expected to be posted in the previous term. The scaling-up of manufacture that MEDRx could not finish as planned in the previous term has been already completed. The P1b trials are expected to be launched somewhere in the second quarter, and the result will be known sometime in the third quarter. First and foremost, MEDRx would want to get the milestone income of 690 million yen. At the same time, announcements on implementation of trials in other pipelines are also much anticipated.

Due to a deteriorating trend in the emerging stocks market in the end of last year, the high level of outstanding balance of margin trading, which had served as a lever propping up the stock price, rapidly fell. The proportion of outstanding balance of margin trading among the total number of issued shares has dropped to a little less than 10%, which is why in case MEDRx comes up with some positive news, the impact on the stock price will be quite significant.

Point summary (1)

●What kind of company is MEDRx?

MEDRx is a venture company established in January, 2002 in Higashi-Kagawa-shi, Kagawa. 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 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 are the attractions of the U.S., the intended market?

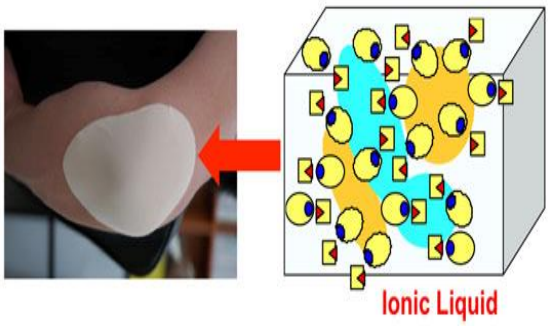
The U.S. people are said to be a 'population that is prone to pain'. The mainstay of the market of medicine for sharp pain in the U.S. is medicine for internal use, and the Americans use very strong analgesic drugs – morphine and other opioids.

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).

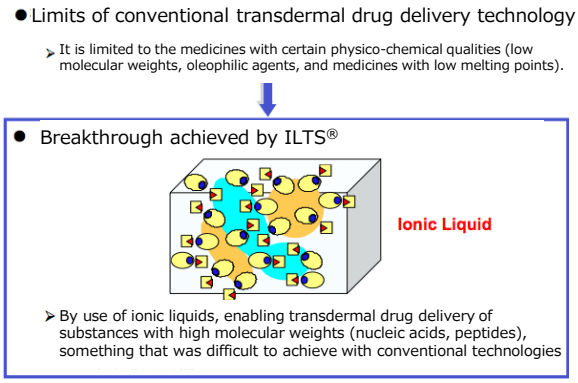
There is thus already a well-established track for selling adhesive skin patches in the U.S., and the market is starting to expand with new medicine also being developed for depression, ADHD, Parkinson, Alzheimer, and other diseases.

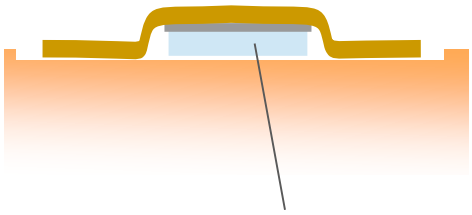
Point summary (2)



● **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 2018, 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.

In August 2018, 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 pipelines originating in MEDRx 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.

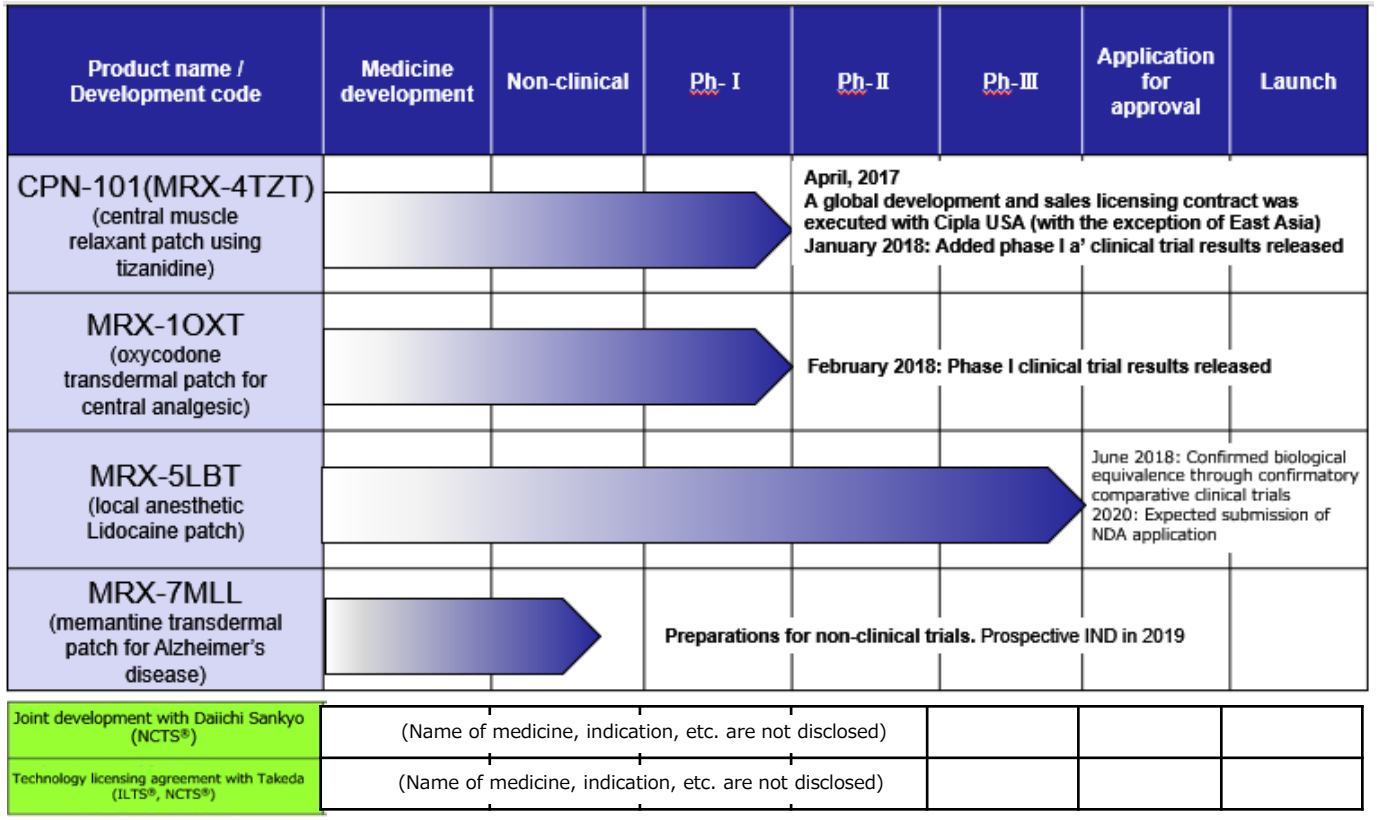
Development pipeline: present conditions and prospects (1)

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 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. After that, MEDRx planned to implement during the 2018 fiscal year added PK (pharmacokinetics) trials (hereinafter "P1b") and PD (pharmacodynamics) trials (hereinafter "P2"). In this 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'. However, the scaling-up could not be completed during the 2018 fiscal year, and the development was carried over to the current term ending December 2019. The scaling-up itself has been already completed, the trials are to be started, according to MEDRx, "somewhere in the second quarter," while the results are to become clear "somewhere in the third quarter."



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 October 2017, 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 2018, 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. As of present time, the company is also advancing with improvements of the drug, tackling a number of aspects such as adhesiveness, and is to launch the P1b trials before the year is out.

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 2018, 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. MEDRx has also conducted a face-to-face meeting with the FDA in November 2018, is to conduct clinical trials centering on trials to ascertain long-term safety in 2019-2020, 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 high 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 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. In the meeting with the FDA held in December 2018, it was confirmed that (1) for the implementation of phase I of clinical trials, the non-clinical trials that are being implemented now will suffice, and (2) if the company can show that the drug is equivalent to the already existing oral agent, phase II and phase III trials will not be required.

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	8	-96%	-1285	-	-1267	-	-
December 2019 (est.)	1009	11922%	-656	-	-643	-	-

●In the previous term (term ended December 2018) the company posted net sales of 8 million yen, a passive balance in the ordinary income of 1,285 million yen, and a passive balance in net income of 1,207 million yen. Net sales only reflect the figures from the Iodine Coating Ointment, a product already launched in the market, which were posted in the first half (net sales in the latter half of the year are zero). The company failed to post the amount of 690 million yen during the previous term. This was a miscalculation, and the current account deficit increased further than was estimated. This amount of 690 million yen is a milestone income for MRX-4TZT (hereinafter "CPN-101") that the company expected to receive from Cipla and post during the latter half of the fiscal year. After a success with P1a', MEDRx was going to advance into P1b and P2, but could not conduct even the trials. Still, as favorable results were achieved with the P1a' trials in January of last year, the possibility for the P1b trials (which are to be conducted with the same content) to go wrong is low. Although in the P1a' trials, the company used a drug manufactured on a laboratory scale, in the P1b trials there will be a need to use a drug manufactured on a commercial production scale. The process of scaling up the manufacturing is what took time, and in the end the company was not able to launch trials during the previous term.

●The initial projection for the current term (term ending December 2019) made in the beginning of the term is net sales of 1,009 million yen, a positive balance in the ordinary income of 656 million yen, and a positive balance in net income of 643 million yen. For the P1b and P2 trials for the CPN-101, which MEDRx could not implement in the previous term, the scaling-up has already been completed, and the company is due to start the trials before the fiscal year is out. And the primary cause for the significant increase of income is the milestone income (of 690 million yen) the company expects to post in the current fiscal year (one that initially was expected to be posted in the previous term). The company expects to receive a milestone income of approximately 300 million yen from Daiichi Sankyo and Takeda as well. It seems that MEDRx does not include in the calculations income with high uncertainty (up-front-payment income related to other pipelines originating in the company, etc.)

The research and development expenses are expected at 1,371 million yen (compared with 980 million yen of the previous term) due to the expected increase in the expenses required for implementation of the clinical trials. If fund procurement announced in February proceeds smoothly, it seems that the funds will be appropriated for the expenses, etc. required for the clinical trials to confirm the safety of the MRX-5LBT, which is the leading pipeline of the company (this amount is not included in the earnings forecast).

As of the December 31, 2018, cash and deposits were 1,796 million yen, a substantial increase from 1,126 million yen at the end of the previous year. The company shall have no problems with financing.

Investment appraisal

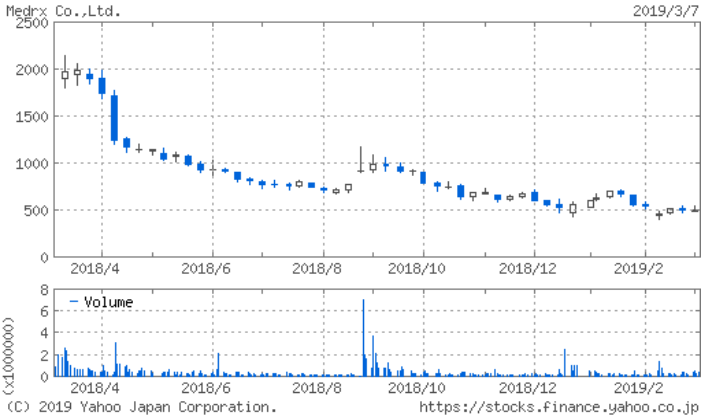
●It is nonsense to demand changes of business results on a short-term basis from a bio-venture operating on a prior investment model. On the other hand, looking from the point of view of investors, there is a strong tendency to look for short-term developments. In many cases, investors tend to overreact on the negative side when they encounter short-term information on operating performance. This is exactly what happened on February 8, when the financial results for the previous term ended December 2018 were announced. MEDRx failed to post the milestone income for CPN-101, resulting in the company's results ending up significantly lower than the initial projection. Probably, in many cases investors acted on a short-term perspective - simply looked at the figures and sold off the shares on hand, without trying to dig deeper.

But the reason for the downturn of the previous term is very clear. The company has already completed the scaling-up of the manufacture that could not be finished in time during the previous term, thus overcoming the challenge already. The hurdle the company needs to overcome is not high, as all it has to do is get a result of the same level it has already achieved with the repeated dose trials done in P1a'. For that reason, first and foremost, MEDRx should get the job done with the milestone income of 690 million yen from Cipla. All the company has to do is show a sure achievement, and the market will instantly change its perception of the company's value and interest in its shares should increase again.

MEDRx also expects to receive milestone income, etc. from Daiichi Sankyo and Takeda Pharmaceutical Company, listing in the initial projection for the current term a net sales figure of one billion yen. This is the first time for the company since the term ended December 2014 to project net sales of a billion yen. At that time, the company did not manage to take its leading pipeline, ETOREAT, to the stage of submission of an application for a new drug and failed to achieve the projections. Five years have passed since. During this period, the company has been reborn with a new business portfolio comprising both pipelines originating in the company and cooperative pipelines, where the company provides its fundamental technologies to major pharmaceutical companies; MEDRx is developing in both directions simultaneously. The most important turning point will be when we see whether this new and more ample business model will bring the company net sales of a billion yen, thus turning the scales around.

●During the current term, we can expect quite a number of announcements from the MEDRx management resulting in favorable effects on the stock price. Firstly, announcements related to the CPN-101, which is one of the main premises, on which the forecast of net sales of one billion yen is based. Preparations are already finished, and the company is likely to announce the start of the P1b trials in the second quarter. The result quite possibly will be clear in the third quarter. Moreover, with the MRX-5LBT pipeline, which is the one closest to commercial production, the company is due to implement trials confirming long-term safety, etc. during the current term. Announcements regarding the two remaining pipelines are also quite possible - regarding the implementation of the repeated PK trials (P1b) for the MRX-1OXTA and P1a for MRX-7MLL.

●As fluctuations of shares of new bio-ventures are usually quite large, there are many individual investors, who buy such shares for the purpose of short-term trading using margin trading. The same is true for MEDRx, which at the time of our previous report (August 31, 2018) had a very high proportion of outstanding balance of margin trading at 21% among the total number of issued shares, or 2,140,000 shares (peaking at 2,820,000 shares on May 25, 2018). However, the individual unrealized profit/loss ratio deteriorated rapidly during a phase of a sudden decline of valuation of Mothers stocks that happened in the end of last year. There was a rush of individual investors selling off with complete disregard for prices, and outstanding balance of margin trading for MEDRx also showed a substantial decrease. The outstanding balance of margin trading as of March 1 is 1,030,000 shares, and, as the adjustments between supply and demand have advanced at a rapid rate, we can surely say that the pressure to sell on a temporary recovery has subsided. And, if we see some positive news of the kind I mentioned above, the effect driving the stock price up will be quite significant. (Okamura)



Stock Price (historical)	
Year high	¥2,139
Year low	¥407
Highest since the IPO	¥7,500
Lowest since the IPO	¥341

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